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# Volunteer Information Sheet

## MISSION-MIMS (Molecular Imaging and Spectroscopy with Stable Isotopes in Oncology and Neurology in Molecular Imaging of Multiple Sclerosis)

**C13 substudy**

We would like to invite you to take part in a clinical research study. Before you decide whether or not to take part, it is important for you to know why the research is being undertaken and what it would involve for you. Please take time to read the following information carefully before making your decision and discuss it with others if you wish. Please ask us if there is anything that is unclear or if you would like more information. Take time to decide whether or not you wish to take part.

If you are satisfied with this information and wish to take part in this study, you will be asked to sign a consent form; a member of the research team will also sign it. You are still free to change your mind about taking part even after you have signed the consent form.

This information sheet is in two parts:

- Part 1 tells you why the study is being carried out and what will happen if you take part
- Part 2 gives more detailed information about how the study is carried out

### Part 1

**What is the purpose of this study?**
Multiple sclerosis (MS) is a degenerative condition of the brain, which is caused by changes in the immune system within the brain. Magnetic Resonance Imaging (or MRI) plays an important role in detecting, diagnosing and monitoring the condition. Contrast-enhanced MRI, which involves an injection of a chemical that is visible within the blood vessels using MRI (often called a gadolinium-based contrast agent), is currently the best way to image the condition. To get more information about the changes that occur in multiple sclerosis, we plan to image the brain with two new techniques that also involve MRI. The techniques that we wish to use are known as 'Sodium MRI' and 'Carbon MRI'. These techniques will allow us to assess new biological changes that occur in MS.

Current evidence suggests that there is a build-up of a chemical called 'lactate' in the areas of the brain affected by MS, and that is visible with one of our new imaging techniques which is called Carbon MRI. The other technique allows us to image the salt level in the body which also changes in multiple sclerosis and this technique is called Sodium MRI.

In order to assess these changes, we are looking to image healthy volunteers with brains unaffected by MS, to compare the images with our findings in MS patients.

An MRI scanner is shaped like a long cylindrical machine and uses both a powerful magnet and radio waves, linked to a computer, to create clear and detailed pictures of the tissues inside the body. To produce an image, we place a plastic case (also known as a 'coil') over your head for the exam. The Sodium MRI is very similar to a standard MRI except that it is undertaken with a different coil; it does not involve an additional injection. The Carbon MRI also involves a different coil but in addition, you will receive an injection of a compound called pyruvate (a type of sugar which is found naturally in your body). We can image this compound in your brain which will help us to determine how the brain processes this sugar-like molecule.

If you agree to be involved in this study, you will be scanned using conventional MRI. In addition to the conventional MRI, we will also undertake the new Sodium MRI technique. This is exactly the same as normal MRI imaging, except that it gives information about the salt in the body, not the water. This technique is non-invasive and no injections are needed. You may be asked to do some simple exercises, such as finger tapping, to look at how the brain salt levels change when you move.

The MRI scan will also involve the injection of hyperpolarised carbon - as described above. We would like to test the ability of this new MRI technique to measure the chemicals produced in both the normal brain. You will also be asked to give a small blood sample, which will be used to assess the levels of some simple biochemical molecules in the blood; this will help us to interpret the imaging.

The aim is that this study will allow us to better understand what changes occur in the brain during episodes of multiple sclerosis. Information about tissue lactate levels and surrounding blood vessel structure and function may help predict treatment outcome and enable doctors to decide the best course of treatment for each individual in the future.

The coil for MRI imaging. (It gently slides over your head, and remains in place whilst we scan)

**Who is organising the study?**
The study is being conducted by the Department of Radiology, University of Cambridge and Cambridge University Hospitals NHS Foundation Trust.

**Why have I been invited?**
We are inviting a group of people who have been diagnosed with multiple sclerosis clinically and/or on MRI examination. In order to understand the results, we need to compare them to healthy controls (you).

**Do I have to take part?**
No, it is up to you to decide. We will explain the study and go through this information sheet, which we will then give to you. We will ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason.

**What will happen if I take part?**
If after reading this information sheet you decide to take part, we will discuss the study with you and answer any questions you may have and we will ask some questions about your medical history to ensure it is safe and you are healthy enough to participate. If you are happy and it is safe for you to proceed, you will be asked to give your informed consent to participate. A pregnancy test will be performed for women of childbearing age. The option of performing the scan after six hours of fasting (not eating) may also be discussed. This is **optional** and not an essential study requirement to participate. This will only apply to some volunteers and if this applies to you, the researcher receiving your consent will talk this through with you. A separate appointment will be booked for you at the Department of Magnetic Resonance Imaging and Spectroscopy (MRIS Unit) or the Wolfson Brain Imaging Centre (WBIC) which are both located at Addenbrooke's hospital for the research MRI brain examinations.

On arrival for the MRI scan, an appropriately qualified member of the team will ask you a series of screening questions in preparation for the examination. You will need to remove any metal objects from your body, including watches and jewellery. A thin plastic tube (cannula) will be inserted into a vein in your arm or hand.

You will then be escorted to the MRI scanner where you will be asked to lie face up on a movable bed. The radiographer will then leave the room; if necessary, a member of staff may be able to accompany you in the scan room during the study. You will then be moved inside the MRI scanner as the imaging procedure begins. You be required to lie still for the duration of the study (approximately 60 minutes). The radiographer sits in the control room next to the scanner and observes through the window. You will be able to talk to them, via a two-way intercom, and you will be observed at all times on a monitor.

A full explanation of what to expect with an injection of a substance like liquid sugar (pyruvate) will be given to you. This injection will take place whilst you are inside the scanner, and has been done successfully and without incident in previous clinical trials. This preparation time before you enter the scanner, including the insertion of a cannula, should not take more than 15 minutes.

During the MRI examination, the pyruvate injected through a cannula placed in a vein in your arm. The cannula will be removed after the scan is complete. We would also like to take a blood sample (30 mL, or 2 tablespoons) to look at the levels of sugar, among other things, in your blood.

To participate in this study you will only be required to have one MRI scan, however, you may be invited to return within 14 days to have a repeat scan; this repeat scan may also take place on the same day as the initial scan. This repeat scan is **optional** and will not affect your participation if you choose not to return. The researcher taking your consent will talk to you about this.

We will invite you to allow your personal details to be kept on a volunteer database, should you wish to be contacted about participating in future studies. This is entirely **optional**.

**What are the possible benefits of taking part?**
We hope that this study will help develop non-invasive ways of assessing the response of multiple sclerosis to treatment, which could be used to help with treatment planning and to predict therapy outcomes in the future. There is no direct benefit to you from taking part in this study. The scans you will have are not

intended to be part of your medical history or designed to diagnose any illness you might have. However, there is a chance of less than 1:100 that a significant abnormality of which you are unaware becomes apparent in the research scan. In such circumstances, we may contact you (and if you agree, your GP also) to discuss with you what the scan shows and whether any further tests are required. Detection of such abnormalities may have the benefit of starting treatment early, but may also have detrimental implications for future employment and insurance. If you are not willing to be contacted in these circumstances, then we are unable to proceed with the scan. This does not affect your statutory rights.

**What are the possible risks/side effects of taking part?**

MRI

There are very few risks associated with having an MRI scan. MRI scanners have been used for the past 25 years on millions of patients worldwide and are considered very safe.

Some people (less than 1 in 20 people) experience a sense of being closed-in (claustrophobia). The radiographer conducting the scan will be able to see you and talk with you at all times, and will stop the scan if necessary. The MR system is a little noisy, but you will be provided with headphones or earplugs to wear. You will be provided with a 'squeeze-ball' alarm, which you are free to use if you feel any discomfort.

You will not be eligible to take part in the study if there are any recognised restrictions to having an MRI scan. This would include the presence of a heart pacemaker, a cardiac stent, an inner ear (cochlear) implant, or certain metallic devices. Please let the person discussing the study know if any of these apply.

Cannulation

Placing a small plastic tube (cannula) into a vein can cause some discomfort and very occasionally can lead to infection, but this is highly unlikely in the short time it will be in place. Some people may get bruising at the site where the cannula is inserted. This procedure is performed regularly in the hospital and is generally very safe. The cannula will be inserted just before the scan and will be removed immediately afterwards.

Pyruvate injection

Although hyperpolarised magnetic resonance is a new technology, tests have demonstrated no significant safety issues. Pyruvate is a naturally appearing molecule in the body. However, approximately 1 in 10 patients experienced some minor side effects noted, which included: a funny taste in the mouth or flushing, changes in smell, headaches, diarrhoea or dizziness.

Although it is unlikely that an allergic reaction or other side effect will occur, there are facilities in place within the MRI unit, and within the hospital, to manage this appropriately. There is a small possibility of discovering previously unknown additional abnormalities on your MRI examination. Any additional clinical information will be communicated to your GP who will then discuss the findings with you to determine if you should continue with the study or have any other investigations.

If you have private medical insurance you should check with the company before agreeing to take part in the study to ensure that your participation will not affect your insurance.

**What happens at the end of the study?**

The images collected from the examinations will be analysed, and the results will be compared with that of your blood results. Your identity will be kept strictly confidential.

**What if there is a problem?**
Any complaint about the way you have been dealt with in the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

**Who will have access to the scans and results?**
Any information and images collected during the study will be subject to the usual rules for medical confidentiality. Imaging data will be stored at the NHS or University of Cambridge in either pseudo-anonymised or non-anonymised and encrypted form. Only the staff undertaking the study will have access to the scans and data.

**Will my taking part in the study be kept confidential?**
Yes, all information about you will be handled in confidence. We will not inform anyone of your participation in the study without your consent. The details are included in Part 2.

**Will my GP be informed?**
We will not inform anyone of your involvement in the study without your consent; however we would recommend that you allow us to inform your General Practitioner (GP) in the case of unexpected findings.

**Will you provide expenses & payment?**
You will not receive any payment for participating in this study. However we can reimburse any reasonable travel and parking costs incurred by your participation in this study.

## If the information in Part 1 has interested you, and you are considering taking part, please read the additional information in Part 2 before making any decision.

## Part 2

**What will happen if I don't want to continue with the study?**
You can withdraw from the study at any time without explanation if you wish to do so. This will not affect any investigations or examinations that you might have in the future in the course of your routine health care. We would like your permission to use the data (without any personal details attached) that is collected up to time of your withdrawal.

**What if there is a problem?**
If you have concerns about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (see contact details at the end of this information sheet).

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure.

The Patient Advice and Liaison Service are available by telephone on (01223) 216756 and email at pals@addenbrookes.nhs.uk.

**Are there compensation arrangements if something goes wrong?**
In the unlikely event of something going wrong and your being harmed during the examination, this is covered by NHS and professional indemnity insurance. Problems related to the study design are also covered by insurance taken out by the University of Cambridge.

**How will we use information about you?**

We will need to use information from you and your medical records for this research project. This information will include (but not limited to) your NHS number, name and contact details. People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a unique code number instead. We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

**Where can you find out more about how your information is used?**

You can find out more about how we use your information at:

- At www.hra.nhs.uk/information-about-patients/
- For Cambridge University Hospitals NHS Foundation Trust, please visit: https://www.cuh.nhs.uk/corporate-information/about-us/our-responsibilities/looking-after-your-information, or email the Data Protection Office at: gdpr.enquiries@addenbrookes.nhs.uk
- For University of Cambridge, please visit: https://www.medschl.cam.ac.uk/research/information-governance, or email the Information Governance team at: researchgovernance@medschl.cam.ac.uk

**What will happen to my samples?**
All samples (e.g. blood samples) taken from an individual participant will be labelled with a code to allow them to be traced as coming from the same individual. These unique participant codes will be suitably anonymised so you as the participant are not identifiable, except to the core research team. Blood samples will be analysed for molecules in the blood and the results will be compared before and after the pyruvate injection to see if there are any differences. Blood samples will be discarded once analysis is completed.

**What will happen to the results of the study?**
Study results will be analysed for the purpose of publishing the results in medical journals and findings may be presented at both national and international scientific meetings. Confidentiality will be maintained at all times.

If you wish, a summary of the results of the study can be communicated to you in written form. We will not be able to share individual results.

**Who is organising and funding the research?**
Researchers from University Department of Radiology are organising the study. The NIHR Cambridge Biomedical Research Centre and the MS Society is funding this research.

**Who has reviewed the study?**
All research in the NHS is looked at by an independent Research Ethics Committee to protect your safety, rights, well-being and dignity. This study has been reviewed, and given a favourable opinion, by the Cambridge South Research Ethics Committee.

**Contact details for further information**

If you have any questions, you can contact the study team during office hours (Monday to Friday 9am to 5pm).

Please also contact the study team in the event of the following occurring:

- If you suffer an illness or a possible study related injury
- If you feel different in any way
- If you are admitted to hospital for any reason
- If you are seen at a casualty (accident/emergency department) for any reason.

Contact details are given below for the research team who can provide further information regarding the study:

During office hours (9am-5pm): 01223 767926 (secure voicemail)

Team email: radiology.research@addenbrookes.nhs.uk

**Out of Hours:**
Please contact your normal clinical telephone number

Failing to contact one of the above numbers, please contact:

**A&E department**
01223 217118

**For complaints**

**PALS (Patient Advice and Liaison Service)**
(01223) 216756
pals@addenbrookes.nhs.uk

***Thank you for considering taking part in this study. If you require any further information, please do not hesitate to contact us, we will be pleased to help you in any way we can. A copy of the consent form will be provided for you.***