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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)

Deuterium Metabolic Imaging (DMI) 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 substudy?
As one of the most active organs in the human body, the brain requires a large amount of energy, which is drawn from the metabolism of glucose. Being able to monitor the rate at which the brain uses glucose would allow us to crucially understand various brain conditions. For example, it is well known that tumours tend to metabolise glucose differently compared to normal brain tissue. Being able to accurately measure altered glucose metabolism would therefore allow for better characterisation of tumours.

One method for imaging glucose activity in the brain is Hyperpolarised Carbon MRI (this is another part of this study and is explained in more detail in a separate information sheet). "Deuterium metabolic imaging" can also be performed with an MRI scan, which can be compared with Hyperpolarised Carbon MRI. Deuterium is a hydrogen atom with an additional neutron in its nucleus compared to a normal hydrogen atom and when found in water, this is sometimes termed "heavy water". Importantly, deuterium is not radioactive and a small percentage of the natural hydrogen in your body is already found in the form of deuterium. We can detect both forms of hydrogen using special type of MRI.

We wish to image healthy volunteers with both Hyperpolarised Carbon and Deuterium MRI techniques, in order to measure fast and slow glucose metabolism with each respective technique.

This substudy will allow us to compare the information obtained with the two techniques to determine the specific advantages of each method.

What is Deuterium MRI?
Deuterium MRI is very similar to a standard MRI, except you will be asked to drink an oral solution of either sugar labelled with deuterium (deuterated glucose) or heavy water (deuterated water) diluted in water. This will be determined by the research team and you will be made aware of this prior to consenting to the study. Glucose is a sugar found naturally in the body and in many foods, as very small amounts of both natural glucose and water are labelled with deuterium. Increasing the percentage labelling of the glucose or water with deuterium allows for the MRI scanner to identify how healthy tissue in the brain processes both these molecules.

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.

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.

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 question you may have and 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, to reduce the number of visits to the hospital, you will be asked to give your informed consent to participate via a telephone call with one of the research team and will sign the informed consent form prior to your imaging appointment. The imaging 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. If you are due to receive the deuterated glucose drink (discussed with the researcher), you will be asked to fast for at least six hours prior to your imaging appointment, which may include either missing breakfast or lunch, depending on when your imaging appointment is. This is to avoid any effects on the imaging results from potential sugars within food or drink that you consume, as these can affect the uptake of the deuterated glucose. We will try to book imaging appointments around your schedule and also to minimise the impact fasting has on your day. You will not be allowed to eat and you will only be allowed to take small sips of water during this fasting period. This will be discussed with you at the time of booking your appointment. If you have concerns about this, please let the study team know.

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. For women of child-bearing potential, you will be asked to have a pregnancy test prior to the examination. We would also like to take a small amount of blood (up to 50 mL or approximately 3 tablespoons) over the course of your study visit at the scanning facility. This would be taken from a cannula (or small plastic tube) that is placed in a vein in your arm or hand and we would try to use the same cannula for all time points. Blood will be analysed for a number of chemicals in your blood and will be compared prior to deuterated drink and after to see if there is any changes. This is **optional** and will not affect your participation in the study if you decline. After you have consented to the study in writing, you will then be asked to drink a solution containing either deuterated water or deuterated glucose, diluted with 200 to

300 mL of water and may have to wait up to 90 minutes before being scanned. The choice of solution will be made by the research team and will be explained prior to consenting to the study.

After this time, you will 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 will 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.

To participate in this study you will only be required to have one MRI scan after drinking the deuterated solution, however, you may be invited to take part in the Hyperpolarised Carbon MRI substudy as well. This scan may take place at the same occasion as the Deuterium MRI and you will be given a separate information sheet explaining this substudy. This is **optional** and will not affect your participation in the DMI substudy if you choose not to take part. 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 substudy will allow us to identify and develop more sensitive and specific techniques for imaging brain metabolism which could improve recognition and treatment of different brain issues. 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.

Deuterated drink
Glucose is a naturally occurring molecule in the body. Deuterium is a stable version of hydrogen and is not radioactive. It is also found in very small amounts in the body. Previous studies with deuterium labelled water and glucose have been performed on humans previously with no documented significant safety issues.

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 you or 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. If you agree to take part in the Hyperpolarised Carbon MRI, these will be compared with the DMI images. 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 substudy?
You can withdraw from the substudy 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. If you are enrolled in the Hyperpolarised Carbon MRI substudy, you may also withdraw from this substudy without affecting the other substudy (and vice versa). 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 various chemicals in the blood and the results will be compared before and after the deuterated drink 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.