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Patient Information Sheet

LIFE-GlioB: Metabolic flux profiling of brain tumours by the new MR hyperpolarisation technology – Hyperpolarised MRI 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 will 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 using the contact details at the end of this document.

A member of the clinical team responsible for your care will ask if you are willing for a member of the research team to discuss this study with you, and if you verbally agree, your name and contact details will be passed on to the researchers to discuss the study with you. If you are satisfied with the information provided and would like 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 free to change your mind about taking part even after you have signed the consent form.

This information sheet is divided into 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?

The purpose of this study is to better understand in detail what is happening to patients with brain tumours by using a new imaging technique named 'Hyperpolarised Magnetic Resonance Imaging (MRI)'. We will image you before and after your normal radiotherapy, as decided by your clinical team ("standard-of-care"). We aim to find out whether we can predict who will have a better, more effective response to therapy and if this can be achieved at an earlier point. In addition to the before and after therapy scans, where possible, we may also image you before your surgery (if your clinical team decide you will have surgery). This before surgery imaging visit is **optional**. If you agree to this **optional** imaging visit, we would then like to compare the images from the imaging visit before surgery to tissue samples (e.g. biopsies) collected from your tumour at surgery (which is also **optional**). Where possible, we would also like to assess how reproducible this technique is by asking some patients to have an **optional** repeat imaging session at some of the stages in this study. This will allow us to increase our knowledge of what is happening inside your tumour.

Where possible, we may invite you to take part in the Deuterium Metabolic Imaging (DMI) part of this study. If you are being considered for this by the researcher, you will be given a separate information sheet to read and if you agree to take part you will sign a separate consent form. The DMI substudy would be performed on the same imaging visits as this substudy, where possible. Not taking part in the DMI substudy will not impact on your participation in this part of the study.

This study will also form part of a PhD thesis for a PhD student working in the research team.

What is Hyperpolarised MRI?
Hyperpolarised Carbon (^{13}C) MRI is very similar to a standard MRI, except that you will receive an injection of hyperpolarised pyruvate (pyruvate is a molecule which is found naturally in your body and is linked to how sugars are converted) through a small plastic tube (called a cannula). Hyperpolarised Pyruvate is not radioactive. The reason we hyperpolarise the pyruvate molecule is to greatly increase the signal strength above natural levels, so the MRI scanner can identify this in your body. This helps us to determine how tumour tissue processes and converts pyruvate which is considered to be at a higher rate in tumours to normal tissue and we can then compare this to other participants with similar disease to you and see if this technique could predict response to therapy.

Why have I been invited?
We are inviting up to 11 patients with suspected or known brain tumours and you have been identified by your clinical care team as a potential participant who meets the criteria for the research.

Do I have to take part?
No, taking part in this study is entirely voluntary. If you decide to participate, you are free to withdraw from the study at any time, without giving a reason. Withdrawal or refusal to participate will not in any way affect the standard or type of care you will receive from the clinical team who are looking after you.

Who is organising and funding the study?
The study is being conducted by the Department of Radiology, University of Cambridge and Cambridge University Hospitals NHS Foundation Trust. The study is being funded by the Lundbeck Foundation, who are a commercial foundation whose purpose is to strengthen brain health and are based in Denmark.

What will happen if I take part*?*
If you decide to take part, additional procedures will be performed beyond those normally required by your clinical team and are shown in the study flowchart on Page 4. Some of these events can occur during the same visit and wherever possible we will attempt to undertake these on the same day to avoid multiple visits to the hospital. To complete the study, you will be required to attend at least Visit 1, Visit 3a and Visit 4a (as shown in the study flowcharts on Pages 4 and 5). At any point during the study you can decide to not continue without affecting the care you would normally receive from the hospital. Study assessments may include, but are not limited to, checks of your blood pressure, heart rate, oxygen levels in your blood, blood samples (up to 50 mL per visit) and pregnancy test (where applicable). These will be kept to a minimum and will only be performed to ensure you are healthy enough and it is safe for you to continue the study.

You may be asked to fast for up to six hours before your scan (i.e. delaying breakfast if your scan is in the morning or delaying lunch if your scan is in the afternoon). Please let the researchers know if there are any reasons why this may be difficult for you and we will discuss what options you have. At the MRI scanning visits (shown on Page 4), you may be asked for a glucose measurement if you have not had a recent blood test at the hospital. We will use a finger prick method to acquire a small drop of blood prior to your imaging. This will be to determine whether it is safe for you to proceed with the study. At the same visit, you will have a standard MRI scan and a hyperpolarised MRI scan where you will receive an injection of hyperpolarised pyruvate while laying inside the MRI scanner. You will lie on the MRI bed; a member of staff will place your head inside a coil (see picture of example) and you will go into the scanner headfirst. The scans are performed to compare the information we gather from the standard MRI with the Hyperpolarised MRI. In total the examination (including pre and post study assessments) will last up to two hours (for standard MRI and Hyperpolarised MRI performed

Example of MRI coil used in this study (It gently slides over your head and remains in place whilst we scan). You will be faced up and will go head first into the scanner.

at the same visit). You will be able to get off the scanner between each MRI scan for a short break while the next scan is being set up.
No patient will be asked to have more than four Hyperpolarised MRI injections over the course of this study. You will be asked if you wish to have an **optional** scan and injection within five days of the first injection for testing the repeatability of the Hyperpolarised MRI technique. These repeat imaging sessions are identified as Visit "b" in the flow chart on Page 4.

If you have agreed to take part in the DMI substudy as well as this substudy, we will perform both techniques on the same imaging visit. You will be imaged for the Hyperpolarised MRI substudy first and then be asked to drink the deuterated glucose drink before completing this part of the study. If participating in both substudies, you will likely be with us for approximately three and a half hours.

Criteria that may exclude you from participating
If any of the below apply to you, please let a member of the research team know and we will discuss options with you (contact details at the end of this document).

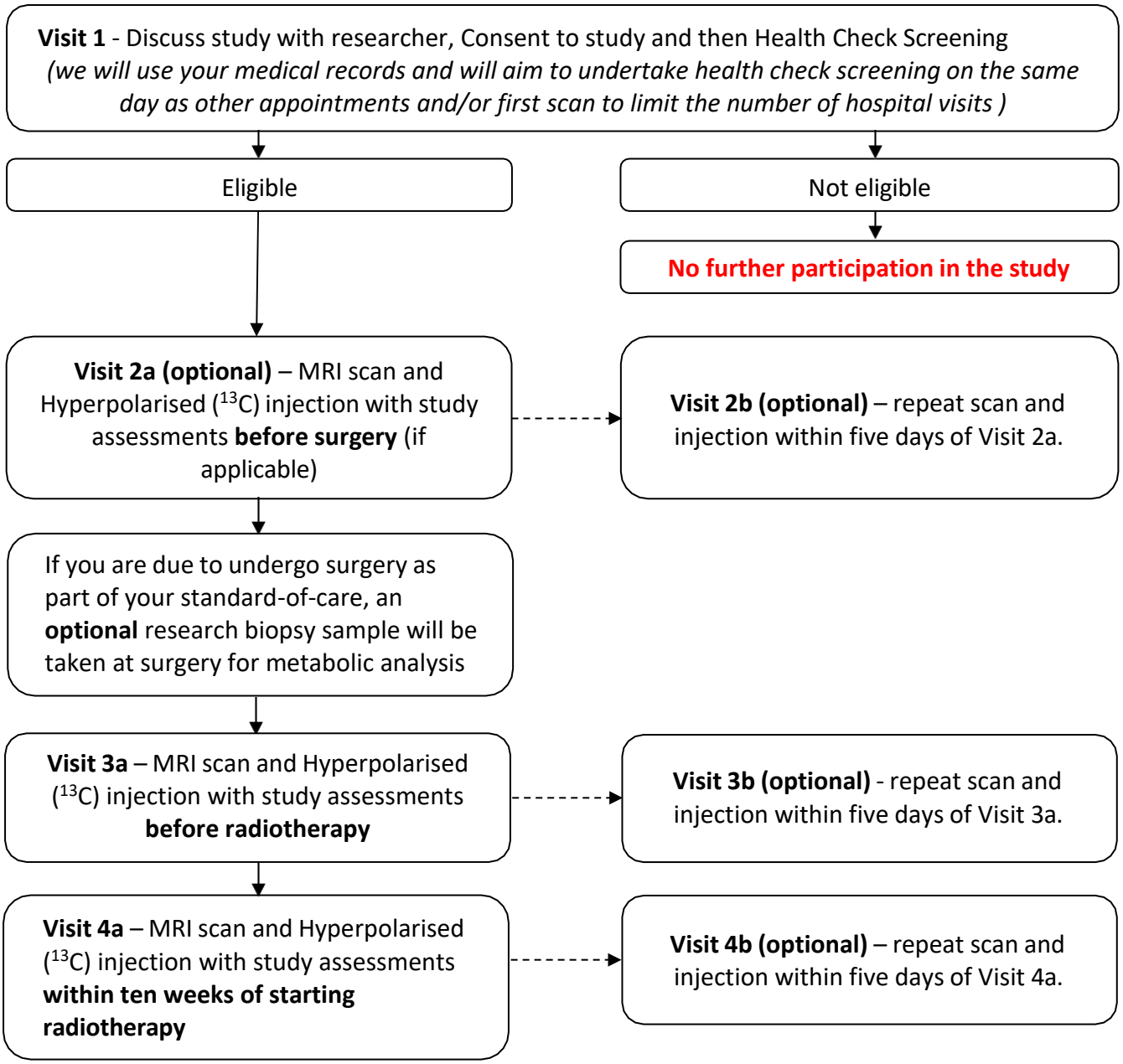
You may not be eligible to take part in the study if you:

- Have a heart pacemaker, a cardiac stent, an inner ear (cochlear) implant, or certain metallic devices such as a copper-coated intrauterine contraceptive device (coil).
- Have a known allergy to the MRI contrast agent (called Gadolinium)
- Have poor kidney function that would not allow you to have MRI contrast injected (this will be checked prior to the first scan, if needed, according to the clinical practice)
- Are pregnant, breast feeding or trying to get pregnant

As a precaution, women of childbearing potential are required to use adequate contraception for at least two weeks prior to each imaging visit and up to two weeks following each imaging visit and a pregnancy test will be performed prior to each scan. Men are also required to use adequate contraception (e.g. barrier methods such as condoms) for up to two weeks following each imaging visit. Details of what is classed as adequate contraception will be discussed with the researcher prior to consent.

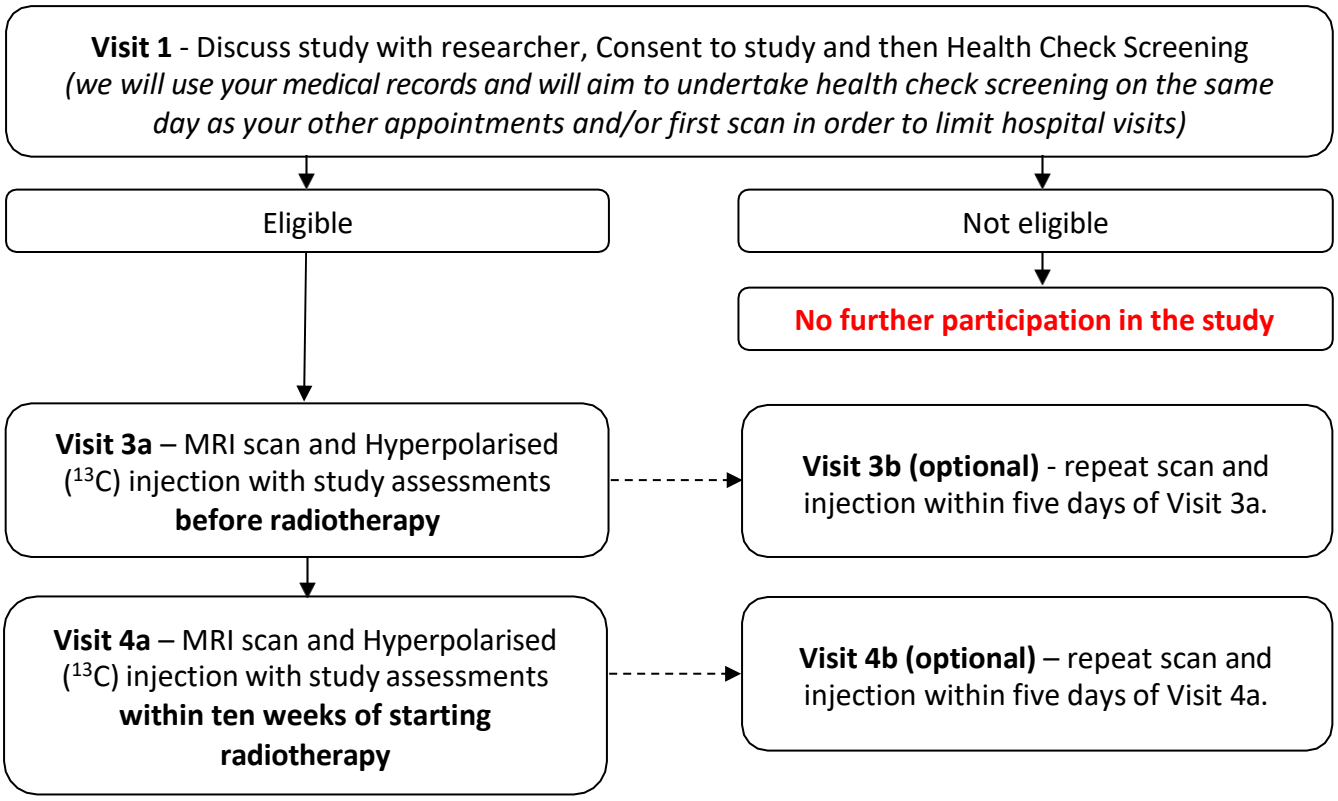
Study Flow chart for patients who have surgery planned as part of their care

Patients will not undergo more than four hyperpolarised injections. Therefore, you may not be asked to take part in all of the below study visits.



Study Flow chart for patients who will not have surgery

Patients will not undergo more than four hyperpolarised injections. Therefore, you may not be asked to take part in all of the below study visits.



What are the possible benefits of taking part?

We hope that this study will help develop new ways of imaging tumours and seeing how they respond to treatment, without patients having to have invasive procedures such as biopsies. This could also help to predict which patients will respond to which therapies with more accuracy. There are unlikely to be direct benefits to you from taking part. However, all images from the standard MRI acquired will be reviewed by a radiologist and any unanticipated findings will be reported to your clinical team to discuss if further investigations are needed.

Reimbursements

You will not receive any payment for participating in this study; however, we can reimburse any reasonable expenses such as travel and parking costs incurred by your participation in the study.

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

MRI

MRI scans do not involve X-rays or radioactivity. 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 5% or 1 in 20) experience a sense of being closed-in (claustrophobia). The MR system is 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. The radiographer conducting the scan will be able to see you, talk with you at all times and will stop the scan if necessary.

Cannulation

Placing a small plastic tube (cannula) into a vein can cause some discomfort and very rarely 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 Carbon MRI is a new technology, tests up to now with pyruvate have demonstrated no significant safety issues in Cambridge or at other sites around the world. Although it is unlikely that an allergic reaction or other side effects will occur, there are facilities in place within the MRI unit, and within the hospital, to manage these appropriately.

Gadolinium contrast injection

Patients are likely to require an injection of Gadolinium (contrast agent) through their cannula as part of standard-of-care imaging. The decision whether Gadolinium might be injected will be discussed with you prior to the scan by the researcher. Gadolinium may be given to patients during scans to help obtain a clearer image of the inside of the body. It is known that small amounts of Gadolinium may remain in the brain after a scan with this agent, although there is currently no evidence that these small amounts cause any harm. Gadolinium is essential for diagnosing a wide range of life-threatening and debilitating diseases and continues to be widely used in a large number of clinical MRI scans. If you need a scan with Gadolinium as part of a research study, your researcher will use the lowest dose required for a clear image. If you have any questions about your scan, please speak to the research team.

Optional research biopsy taken at surgery

If you have agreed to take part in the before surgery imaging visit, we would like your permission to take a research biopsy (sample of your tumour) when you are undergoing your surgery. The research team will only take the required amount of tissue for their analysis and any remaining will be kept according to standard NHS practice. We will not attempt to obtain these biopsies more than once and will only perform these procedures if the doctor undertaking them assesses it to be safe to do so. You will need to indicate if you agree to this in the consent form.

Risks and side effects from surgery will be discussed with your doctor and/or clinical team that are looking after you. The biopsy samples taken for this study would have a slight increase in risk as samples will be taken from the tumour during your surgery. However, it is likely that the surgeon will take samples for clinical diagnosis/use at the same time and the additional research biopsy samples would only require a few extra samples being taken.

Other Studies

It is possible that if you are already contributing to or plan to contribute to other research studies, being part of this study may affect these other studies and may increase the hospital visits required of you. We will try and limit any problems as much as possible. If you plan to or are enrolled on other research studies and are interested in participating in our study, please let us know, so we can discuss this and help as best we can. It is important for you to consider the time and other commitments required in participating in several studies simultaneously. We would be happy to discuss this with you and we can also talk with your family if required.

What happens at the end of the study?

The data from the images and tissue samples collected will be analysed and the results will be used to improve our understanding of tumours and hyperpolarised imaging. Your data, images and samples collected during the study may be transferred in an anonymised way to research collaborators working in a similar field on other ethically approved studies and this may include transfer abroad or to commercial companies. These will be labelled with a participant unique study code, which will not be able to identify as coming from you. On the consent form, you will be asked to give permission for research staff to consult your medical records collected. Your identity will be kept strictly confidential.

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 on NHS or University of Cambridge secure data storage in either partially anonymised or non-anonymised but encrypted form. Only the staff undertaking the study will have access to these non-anonymised scans and data. All images will be read by a board-certified radiologist. If any unexpected findings are identified by this review on the standard MRI images, these will be reported to the clinician that is leading your care who will decide whether any further investigations are required.

Will my consultant be informed?
Your consultant will be aware of your participation in the study.

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) to make them aware of your participation in this study. If you do agree to this, we may contact your GP (if you are not being seen in hospital) for an update on your progress at 36 months after your final research scan or earlier.

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 do not want to continue with the study?
You can withdraw from the study at any time without explanation. This will not affect any investigations or examinations that you might have in the future during the course of your routine health care. We would like your permission to continue to use the data and samples collected (without any personal details attached) up to the 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 (PALS) are available by telephone on (01223) 216756 and email at pals@addenbrookes.nhs.uk, regarding any formal complaints about the study.

Are there compensation arrangements if something goes wrong?
Cambridge University Hospitals NHS Foundation Trust, as a member of the NHS Clinical Negligence Scheme for Trusts, will accept full financial liability for harm caused to participants in the study caused through the negligence of its employees and honorary contract holders. There are no specific arrangements for compensation should a participant be harmed through participation in the study, but no-one has acted negligently.

The University of Cambridge will arrange insurance for negligent harm caused as a result of protocol design and for non-negligent harm arising through participation in the study.

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 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.

What are your choices about how your information is used?
You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Where can you find out more about how your information is used?
You can find out more about how we use your information:

- At www.hra.nhs.uk/information-about-patients/
- For Cambridge University Hospitals NHS Foundation Trust, please visit: https://www.cuh.nhs.uk/patient-privacy/, or email the Data Protection Officer 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.

Keeping information for future research
Information about you that is collected during a research study may be kept securely to be used in future research in any disease area, including research looking at social and economic factors affecting health. This may include combining it with information about you held by other health or government organisations such as NHS Digital. Usually the information is combined by matching information that has the same NHS number. Doing this makes maximum use of the information you have provided and allows researchers to discover more. Researchers may not be able to specify all the possible future uses of the information they keep. It could include providing the information to other researchers from NHS organisations, universities or companies developing new treatments or care. Wherever this happens it will be done under strict legal agreements. This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research and cannot be used to contact you or to affect your care.

What will happen to my samples?
All 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.

If you are due to take part in the before surgery imaging visit and have agreed to an **optional** biopsy sample taken at surgery, tissue samples (e.g. biopsies) will be processed and examined and compared to the results found at imaging visits. The processing and examination will be performed by suitably trained staff and may include genetic testing. This may include but not limited to growing cells for further experiments to look at cell metabolism (this will not require your involvement) and will be destroyed appropriately after the experiments have been completed. They will be stored for up to 15 years in a secure tissue storage facility before being destroyed. Blood samples collected for research will be stored and analysed for basic components of your blood (such as sugar levels) and destroyed when analysis is completed.

Some samples will be sent to third party companies or registered charities for analysis using the unique participant code, which may include sending abroad. The results from these samples may be used to support further studies working in a similar field in the UK and abroad, but you will not be identifiable to other researchers. These samples will either be destroyed following analysis or returned to the research group following completion of analysis.

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. Participant 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 with you directly. Please inform the researcher that consents you to the study if you wish to receive these and provide an email address on the consent form.

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 South Central - Oxford B Research Ethics Committee.

Contact details for further information

All of your questions should have been answered but if you have any further questions, you can contact the study team during office hours (9am to 5pm) who can provide further information regarding the study.

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.

Telephone: 01223 767926
Email: radiology.research@addenbrookes.nhs.uk

Out of Hours

If you decide to participate in this study, in the event of an emergency out of office hours, please contact:

Your own GP practice's telephone number. If the practice is closed, you will either be diverted to the out of hours surgery or a recorded message will provide further instructions to obtain help.

At any time

Failing to contact one of the above numbers at any time, please contact:

A&E department 01223 217118

For complaints

PALS (Patient Advice and Liaison Service):

Telephone 01223 216756
Email 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.