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Participant Information Sheet

LIFE-GlioB: Using Advanced MRI to Study Brain Tumor Metabolism – Glucose (DMI) substudy

Chief Investigator: Prof Ferdia Gallagher

Sponsor: Cambridge University Hospitals NHS Foundation Trust and University of Cambridge

SCAN ME

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Introduction

We're inviting you to join a research study, and it's important that you understand why and what it will mean for you. Please take your time to read this document, discuss it with others, and feel free to ask us any questions. Signing the consent form is your choice and you can change your mind at any time.

This study is conducted by the Department of Radiology at the University of Cambridge and Cambridge University Hospitals NHS Foundation Trust, with funding from the Denmark-based Lundbeck Foundation, which focuses on brain health and Cambridge Research UK.

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LUNDBECK FOUNDATION

What is the purpose of this study?

We are a group of doctors and medical scientists looking to increase the amount of information we can gather from a commonly used type of scan called an MRI (Magnetic Resonance Imaging). Conventional MRI can show us what is happening inside the body, and we use it to detect the presence, size, and spread of cancers. Sometimes, this information is not enough to make accurate clinical diagnoses. We believe there may be a way to increase the amount of information we can capture.

Our idea involves using techniques called **Deuterium Metabolic Imaging (DMI) and Chemical Exchange Saturation Transfer (CEST) imaging.** DMI is a special type of MRI scan that involves ingestion of a labeled substance called glucose (sugar). The MRI tracks how glucose moves and changes inside the body, providing detailed pictures of how tissues and organs are working. CEST imaging is very similar to a standard MRI and might give us similar information as DMI but without a need for a glucose drink. Our hypothesis is that brain tumor processes labelled glucose in a different way than healthy tissue. We may see these differences in the imaging, which may help us better characterise cancer, and better predict how well patients respond to therapy.

We will take images before and after your regular radiotherapy to see if we can predict who will respond better to the treatment, and possibly sooner. If you're scheduled for surgery, we may also take images before your operation and compare these images to tissue samples taken during surgery, but this is optional. We might ask some patients to have a repeat imaging session to check the technique's reliability. You might be invited to join a related study called Hyperpolarised Carbon-13 MRI, which will involve separate consent.

Why have I been invited?

We are asking you to help us because you have been identified by your cancer clinical care team as a person who meets our criteria for participation.

Do I have to take part?

You do not have to agree to take part. Your care will continue regardless and even if you change your mind later that will be fine, and you do not have to give a reason why you wish to withdraw from this study.

Criteria that may exclude you from participating

You might not be eligible if…

…you have a heart pacemaker, cardiac stent, cochlear implant, or certain metal devices such as a copper-coated intrauterine contraceptive device (coil).

…you're expecting, nursing, or planning for a baby, please inform us.

…you have a known allergy to the MRI contrast agent (called Gadolinium).

…you 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).

Your wellbeing is our priority!

What will happen if I take part?

If you choose to help us, when you arrive for your planned scan, we will carry out certain study procedures. We anticipate your visit will take approximate **two hours**.

Consent Process:

- If you decide to participate after reading this information sheet and having an opportunity to talk to us, you'll be asked to provide your informed consent.
- Some research activates are optional and opting out of these won't affect your participation in others.
- You might need to fast for **up to six hours** before your scan.

Appointment Booking:

- We will schedule your research MRI scan at the same time as your clinical MRI either at the Department of Magnetic Resonance Imaging and Spectroscopy (MRIS) or the Wolfson Brain Imaging Centre (WBIC) in Addenbrooke's hospital (map **page 17**).
- Appointments are usually in the afternoon (1-4 PM). We do our best to find the most suitable day and time.

Safety Checklist:

- Please remove metal items before the scan.
- Before the MRI scan, a qualified team member will go through a safety metal checklist with you.
- We may perform some health checks to ensure your wellbeing, for example finger prick glucose test, pregnancy test, blood pressure, heart rate, oxygen level and temperature. This is to ensure it is safe for you to participate in the study.

What will happen if I take part?

MRI Scans:

- You will be guided to the MRI scanner and asked to lie on a movable bed. We will place your head inside a coil which is used to send and receive radio waves that interact with the body's tissues.

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 headfirst into the scanner.

- The radiographer will operate the scanner from the control room, maintaining constant observation through a two-way intercom.
- For a standard MRI scan, you might need a special dye called **Gadolinium** injected through the same tube in your vein. This is a standard clinical practice.
- For DMI, we'll ask you to drink approximately 200 mL of water with **labeled glucose**[1] before you are scanned.
- CEST imaging is very similar to a standard MRI. It does not involve any contrast injection or drink, and takes 7 minutes.
- The entire study visit will last **up to two hours.** This visit includes pre- and post-scan assessments, glucose drink, your standard clinical MRI scan, and research MRI scan. You can take short breaks between each MRI scan while the next one is being set up.
- More details about the scans are provided on **page 16**.

[1]Labeled glucose is a type of sugar that has been modified to make it visible during scans. It contains deuterium (heavy hydrogen), which is stable and naturally occurs in small amounts in water and other substances.

What will happen if I take part?

Optional Tissue and Blood Samples:

- With your agreement, we may take a small blood sample (two tablespoons) before and after the scan.
- With your agreement, we may use your tissue sample from biopsies or surgery already taken for clinical use. We will only take the required amount of tissue for our analysis and any remaining will be kept according to standard NHS practice.

Optional Repeat Scan:

- There are two research scan visits (page 16). We might ask you to help us further by having an extra MRI scan within five days of the main scan. We will not ask you to have more than **four** scans for this study.

This process aims to ensure your comfort, safety, and active participation. Feel free to ask any questions or share concerns at any point.

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

MRI:

MRI scans are safe and don't involve X-rays or radioactivity. Some of the equipment used is meant for research, not routine diagnosis. Some people may feel 'closed in' (**claustrophobic**). You'll have a 'squeeze-ball' alarm, and we can stop the scan at any point if you ask us. An MRI machine makes **loud noises** such as banging, clicking, whirring, clanging, beeping. This is normal. We will provide headphones and earplugs. You're always visible and can communicate with the staff during the scan.

Cannulation:

This safe and routine procedure involves inserting a small tube in a vein just for the scan. It might cause some **discomfort** and very **rarely** can lead to **infection** or **bruising** at the site where the cannula is inserted, which will disappear after a few days.

Gadolinium dye injection:

Gadolinium is used in many 'standard-of-care' clinical MRI scans. Patients often report a warm, flushed feeling throughout their body, including a sensation of warmth between the legs, mimicking the feeling of urination. Some people may experience side effects such as **pain** at the injection site, feeling or being **sick, itching, rash, headache**, skin sensation, such as **prickling, burning or tingling**. These are usually mild and short lasting. After the scan, a little bit of Gadolinium might stay in your brain, skin or other organs but there's no proof it causes harm.

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

Deuterated Glucose Drink:
Glucose drinks are safe; deuterium isn't radioactive. While **allergic reactions** are rare, we're prepared to manage them.

Incidental Findings:
Your scans **are not** for diagnosis but may reveal unexpected observations. If we find something important, we'll discuss it with you and your GP. It may identify something you weren't aware of which may affect employment and insurance. If you cannot consent to being informed of an unexpected finding, you will be ineligible to take part in this study. Your rights remain unaffected.

Optional Biopsy:
A biopsy is a straightforward procedure, where we remove a small (a grain of rice) sample of tissue from the site of your cancer with a thin needle under local anesthesia. After having a biopsy, you may feel a dull **ache** or some slight **discomfort**. It's rare for serious **bleeding**, **infection**, **bruising** and **swelling** to occur after having a biopsy, but if it does, you may need to have an operation or a blood transfusion.

Other studies:
Taking part in this study while participating in other studies might be difficult for you and research teams. If you're already in another study or are thinking about joining one, please let us know.

What are the possible benefits of taking part?

We don't anticipate you will have any direct benefit from helping us, but what you do will help many others in the future.

This study aims to develop new imaging techniques for tumours to monitor treatment responses without requiring invasive procedures like biopsies. We also aim to improve the accuracy of predicting patient responses to different therapies.

Reimbursements

We'll cover travel and parking expenses related to your study participation if the visit is outside your clinical appointment.

What if there is a problem?

If you have any concerns about how you have been treated or any potential issues, we are here to help. Our contact details are on **page 15**. And if things still are not quite right, you can make a formal complaint through the NHS Complaints Procedure (page 15).

What happens at the end of the study?

We will analyse the information we collect from the images and the blood and tissue samples. This helps us learn more about how our bodies work and figure out the best ways to use MRI scans for diagnosis.

Who will have access to the scans and results?

We will **store data securely** and the security will be overseen by independent people. There is no risk that you will be identified by helping us. Only the study team will have access to the non-anonymous scans and data.

We may share **pseudonymised**[2] data with others working in a similar field, and this may include research organisations and companies working abroad.

Will my taking part in the study be kept confidential?

Yes, we'll keep your details confidential. We'll not share that you are part of the study with anyone without your consent.

Will my GP be informed?

It is your choice, but we recommend that your GP is kept informed particularly of any unexpected observations.

[2]Pseudonymization is a process where personal information in a data record is replaced with unique codes, making the data less identifiable but still possible to link back to the original person if needed.

What will happen if I do not want to continue with the study?

Feel free to step back from the study anytime – no need to explain why. Just let us know through phone, letter, or email. It will not affect your future healthcare. With your permission, we'd like to keep using the pseudonymised data and samples up to the point you decide to step out.

Are there compensation arrangements if something goes wrong?

If anything goes wrong because of a mistake on our part, Cambridge University Hospitals NHS Foundation Trust will take full financial responsibility.

The University of Cambridge has insurance to cover any harm related to how the study is set up or any unintentional problems during your participation.

How will we use information about you?

For our research, we'll use some information from you and your medical records. The team will use this data to carry out the research properly, but rest assured, your personal details won't be visible to those who don't need to know. We'll assign a unique code to your data, keeping everything about you safe and secure.

After the study ends, we'll keep some data needed to check results. Our reports will be written in a way that protects your privacy, making sure no one can figure out you took part in the study.

What are your choices about how your information is used?

You can step back from the study anytime, without giving a reason, but we'll keep information about you that we already have.

We need to manage study 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.

You have a say in whether your samples, data, and information are used for future ethical research – feel free to agree or disagree as you see fit.

You can visit the following websites to find out more about how your information is used:

Health Research Authority:
www.hra.nhs.uk/information-about-patients

Cambridge University Hospitals NHS Foundation Trust:
https://www.cuh.nhs.uk/patient-privacy
or email the Data Protection Officer at: cuh.gdpr@nhs.net

University of Cambridge:
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?

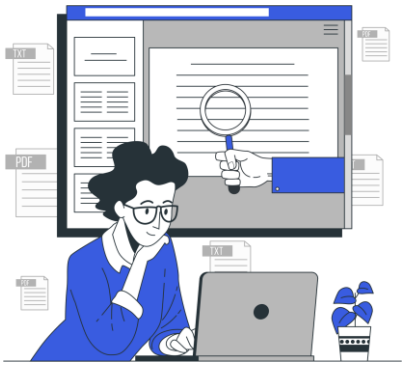
We'll label all your samples with a special code to keep track of them, but your identity stays private, known only to our core research team. We'll keep your samples safe in a secure University lab until we process them. We'll analyze your blood for certain molecules and compare the results with your MRI scans. Once we finish the analysis, we'll dispose the blood samples appropriately.

What will happen to the results of the study?

We plan to share our study findings by publishing in medical journals and presenting at scientific meetings, both nationally and internationally. This research might be included in a PhD thesis for a student on our research team.
If you agree, we might share pseudonymized data with collaborators in similar studies, keeping your privacy intact. Additionally, we're happy to send you a written summary of the study results, though we can't provide individual results directly. If you're interested, let the researcher who got your consent know, and share your email address on the consent form.

Who has reviewed the study?

All NHS research, including our study, is assessed by an independent committee to ensure your safety, rights, and wellbeing. Our study has been thoroughly reviewed and earned a positive opinion from the Research Ethics Committee.



Contact details for further information

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

If you're unwell, feel different, end up in the hospital, or visit the emergency department, please let the study team know.

Telephone: **01223 256989** or **01223 767926**
Email: cuh.radiologyresearch@nhs.net

Out of Hours
If you join the study and need help after hours, call your GP's number. If they're closed, you will get redirected or receive guidance via a recorded message.

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 cuh.pals@nhs.net

Thank you for thinking about joining the study. If you need more information, just reach out – we are here to assist.

A copy of the consent form will be provided for you.

Additional information

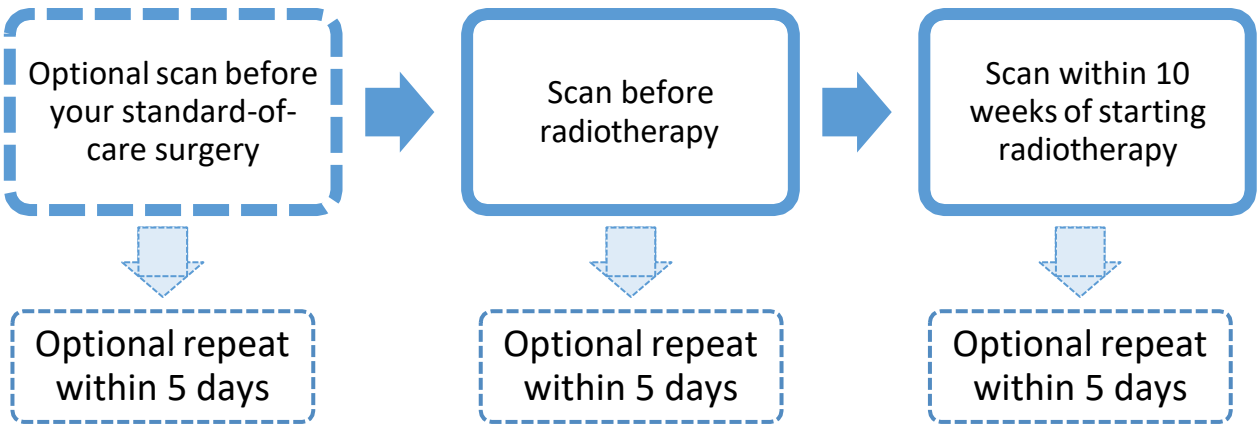
You will be asked to attend **minimum 2 visits**. If you are willing you might be asked to attend **additional 2 visits (optional).** You might not have a standard-of-care surgery. Your cancer clinical care team will advise the most appropriate treatment pathway for you. We anticipate the appointment will take approximate two hours: 45 minutes consenting and preparation for the scan including having a glucose drink, 60 minutes scan, 15 minutes post-scan checks.

Useful links:

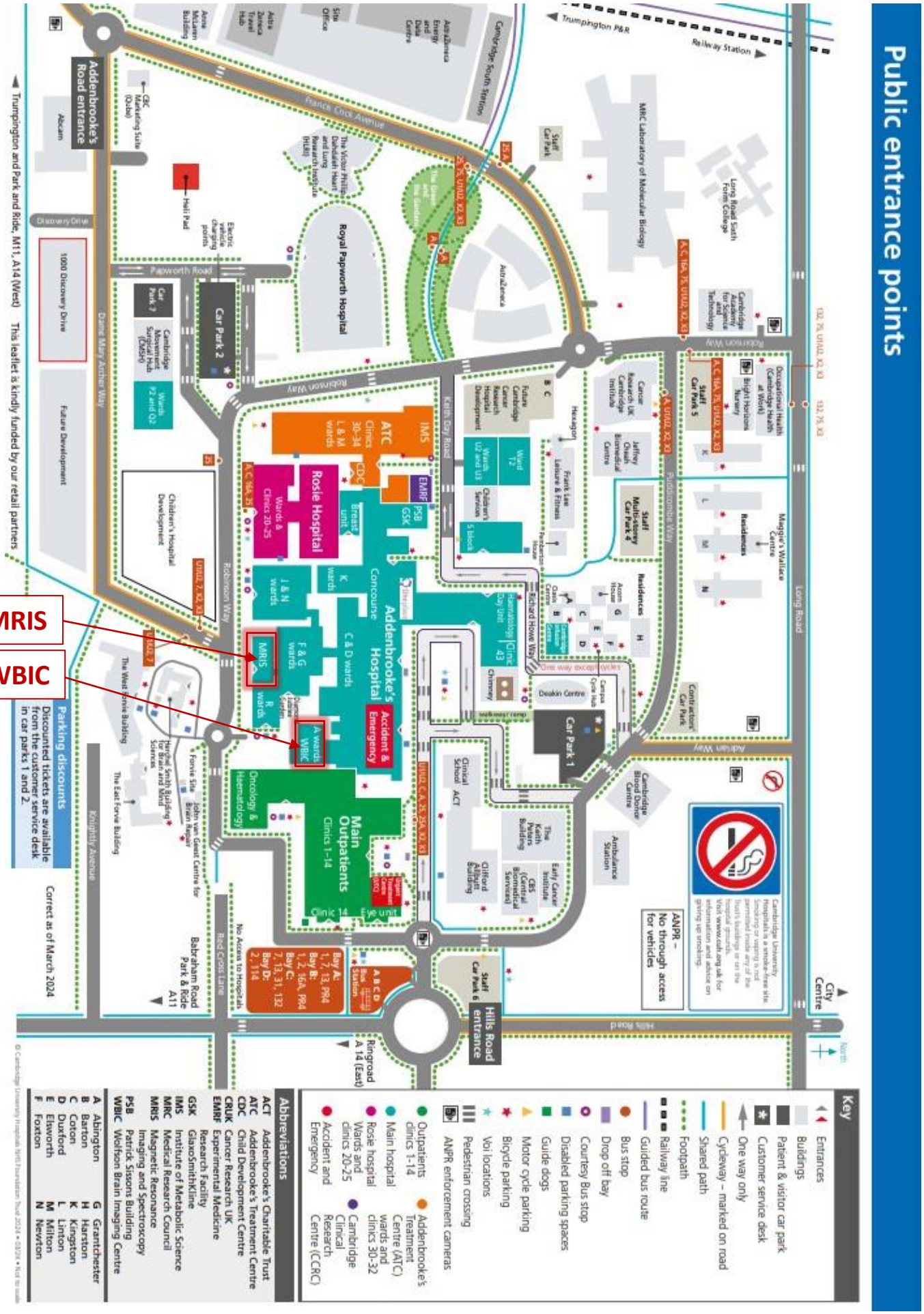
Gadolinium contrast agent: https://www.guysandstthomas.nhs.uk/health-information/gadolinium-contrast-injection

Study registration website: https://www.isrctn.com/ISRCTN12155285

Study Flowchart



Public entrance points



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Participant Consent Form

LIFE-GlioB: Using Advanced MRI to Study Brain Tumor Metabolism – Glucose (DMI) substudy

Chief Investigator: Prof Ferdia Gallagher

Patient Identification Number for this study: _____

If you agree with each sentence below, please initial the box	Initials
1. I confirm that I have read and understand the information sheet version _ . _ , dated _ _/_ _ _/ _ _ _ _ , for the above study, have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my medical care or legal rights being affected.	
3. I agree that if I withdraw, all identifiable information collected will be destroyed, but non-identifiable data will be kept and used for analysis.	
4. I understand that data collected as part of this study and sections of any of my medical records (where they are relevant to my taking part in this study) may be looked at by members of the research team, and also made available to the Trust Research & Development Department for audit and monitoring purposes. I give permission for these individuals to have access to my records in accordance with GDPR and the Data Protection Act 2018 and medical confidentiality rules.	
5. I understand that this research scan is not a clinical scan and will not be explicitly screened for medical disorders or diagnostic purposes; however, if a significant abnormality is noticed, I agree that myself, my clinician and my GP are informed of the result.	
6. I understand the data, images and samples collected as part of this study will be stored and used as described in the participant information sheet.	
7. I understand samples may include transferring to research collaborators working in a similar field as part of an ethically approved study and this may include transfer abroad or to a commercial company all in anonymised fashion.	
8. I understand the risks associated with taking part in the study that are detailed in the participant information sheet.	
9. I agree to take part in the above study.	

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OPTIONAL Consent

If you agree with each sentence below, please initial the box

10. I give permission for the research team on this study to have access to any remaining biopsy samples that have been taken during the course of my clinical assessment or as part of another research study as described in the participant information sheet.	Yes / No
11. I give permission for the research team on this study to collect research blood samples as described in the participant information sheet.	Yes / No
12. I give permission for the research team to discuss the optional additional biopsy. I understand that if consenting, this will be discussed before each imaging visit to see if I continue to consent to this.	Yes / No
13. I give permission for the research team to discuss the optional repeatability scan within 5 days. I understand that if consenting, this will be discussed before each imaging visit to see if I continue to consent to this.	Yes / No
14. I give permission for my General Practitioner (GP) to be informed of my participation in this research.	Yes / No
15. I give permission for my samples, data and information collected about me to be used in other ethically approved research in the future and may be shared anonymously with other academic and commercial researchers external to this study, within the UK and abroad.	Yes / No
16. I am interested in participating in further radiology research studies and I can be contacted in this regard.	Yes / No

Name of Research Participant *(Please print)*	Date	Signature
Name of Research Team member *(Please print)*	Date	Signature

Optional – please insert GP details below:

Name of GP: _____

Address: _____

If you wish to be contacted with a summary of the overall findings from this study, please provide an email address here: _____

3 copies required: top copy for researcher; one copy for participant, one in file