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PATIENT INFORMATION SHEET

[^{18}F]Fluorodopa PET and Oxygen Enhanced MR Imaging in Glioma: Feasibility Study for Advanced Imaging Guided Brain Biopsy (FIG Study)

Chief Investigator: Professor Geoffrey Higgins

You are being asked to take part in this study as you have been diagnosed with low-grade glioma based on clinical imaging. Your surgeon has recommended primary surgical resection of the glioma.

Glioma is a type of brain tumour, where there has been no significant change in recent survival trends. The distinction between high-grade and low-grade glioma is important as treatments are different depending on the grade of tumour. This distinction between high-grade and low-grade glioma is normally made by taking a sample of the tumour and looking at it closely with other types of medical imaging. However, there is a risk that current sampling methods may not identify some high-grade gliomas.

In a number of recent studies, the use of a certain type of medical imaging called amino acid Positron Emission Tomography (PET) in glioma imaging has been shown to be better in distinguishing between high and low grade gliomas. A type of novel MRI technique, called oxygen enhanced MRI (OEMRI), has the ability to detect areas of hypoxia (low oxygen levels) within solid tumours which would potentially detect more aggressive high-grade areas within gliomas. Hence, there is a growing interest to see if this can be confirmed in patients.
This information sheet describes a clinical study for assessing new types of imaging using [^{18}F]fluorodopa, a radio tracer which helps doctors to look at images taken of the body and or oxygen enhanced MRI, a MRI scan performed whilst breathing oxygen. One of our study team will go through the information sheet with you to explain the study and answer any questions you have. The study only includes people who choose to take part and have signed a consent form, after carefully reading this information sheet.

PART 1 tells you the purpose of this study and what will happen if you choose to take part.
PART 2 gives you more detailed information about the conduct of the study.

Before you decide whether or not to take part in this study, we would like you to understand why the research is being done and what it would involve for you. Please ask questions if there is anything that is not clear or if you would like to have more information. Please talk to your family, friends and your doctor about the study if you wish, to help you make your decision. You can take your time to decide to take part.

You do not have to take part in the study. This is entirely voluntary. If you do decide to take part, you will be asked to sign study consent form to show that you agree. You will also be given a copy of the signed consent form to keep.

PART 1

1. What is the purpose of the study?

The main purpose of this study is to assess the feasibility of using advanced imaging techniques to guide biopsies. The information from the study may form the basis of future clinical application and further research into these methods.

2. What is MRI and PET/CT?

Magnetic resonance imaging (MRI) is a type of scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body. It is non-invasive and does not involve any ionizing radiation such as x-rays. You will have MRIs as part of the study.

PET/CT is similar to MRI but also uses a mildly radioactive drug, called a radio-tracer, and x-rays to produce detailed images of the inside of the body.

You will lie on a flat bed and be moved into the scanner head first. The scan itself can be noisy so you will be offered earplugs or headphones to wear during the scan. It's important you remain still throughout the scan so high-quality images can be taken. You **must not**:

- Suffer from claustrophobia
- Have any metal implantable devices e.g. pacemaker, cardioverter-defibrillator, brain aneurysm clips, hip replacement or other implant.

3. What will happen to me if I take part in the study?

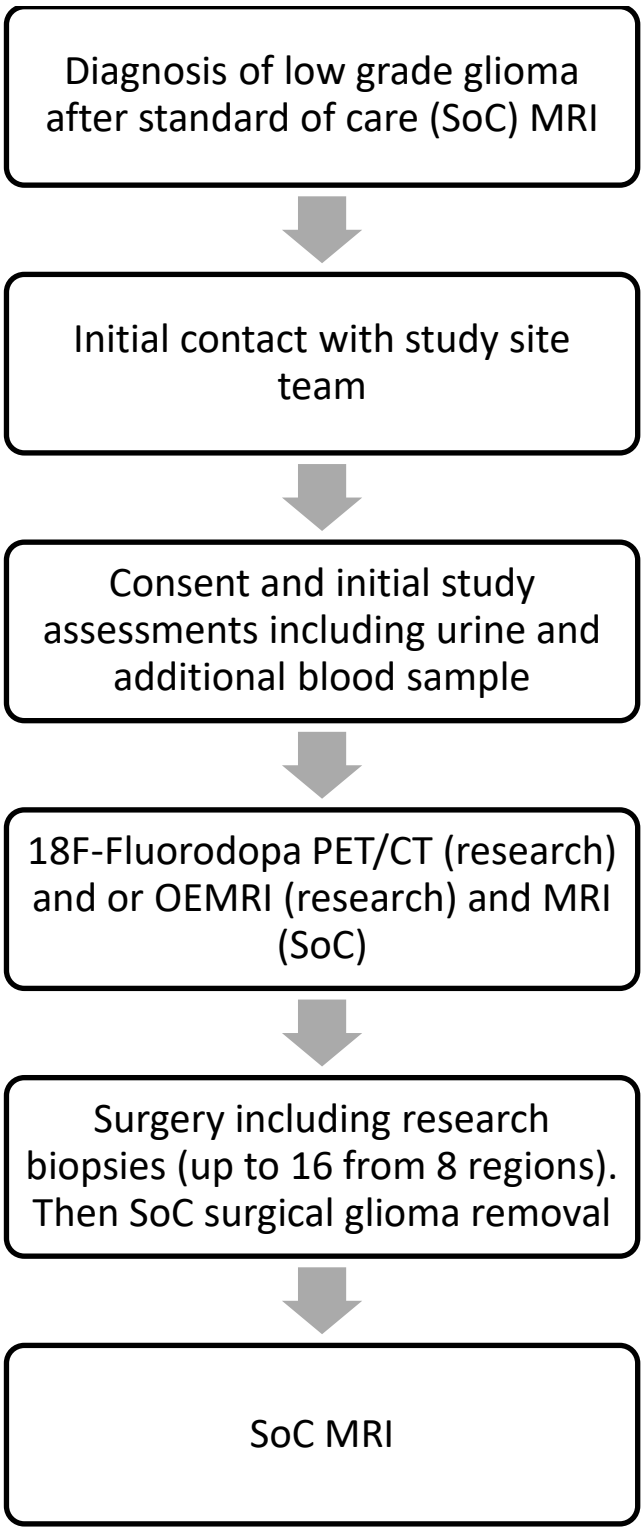
If you agree to take part in the study, we will ask you a number of questions about your medical history and current medications to ensure that you are eligible to take part. In female patients of child bearing potential we will ask you to have a pregnancy test. Pregnant women cannot take part in this study.

At two separate occasions during the study, you will be asked to undergo research assessments. Both sets of the assessments will occur at the visits when you are due to attend the hospital appointments and imaging centre for standard tests or surgery. Thus, you will not require any additional hospital visits.

At this visit we will:

- Collect information about the MRI scan of your brain performed as part of your standard of care. (Standard of care means the routine investigations that would be carried out if you were not part of the study)
- Undertake the [^{18}F]fluorodopa PET/CT and or oxygen enhanced MRI scan of the brain. The research scans will be either done locally or by a subcontractor called GenesisCare.
- Collect information about your biopsy and other lab sample results, if applicable.
- You will be given the option to provide a blood and a urine sample at your first face to face visit for involvement in the translational sub-study. The amount of blood is small, approximately two teaspoons. This option might not be available at all sites. These samples will be used to study small molecules within cells to inform us on what is happening at a biological system level. Involvement in this sub-study is optional and not required to take part in the main study.

The flow chart provides details of the study visits and procedures. You will be in the study for approximately 2 weeks depending on the timelines for the scan and surgery scheduling. Following the end of study visit, you will receive standard care and there will be no further study follow-up.



Study Visit 1 – PET scan and MRI scan at imaging centre

You will undergo a research PET/CT scan and or an oxygen enhanced MRI. The PET/CT scan will last approximately 60 minutes. A mildly radioactive dye tracer [^{18}F]fluorodopa will be injected into a vein to highlight parts of your tumour. This will be performed either locally or, at Oxford only, by a subcontractor (GenesisCare).

For the oxygen enhanced MRI you will be asked to wear a face mask, similar to those worn by patients in hospital for the MRI scan. For technical reasons this might be done on two separate MRI scanners either locally or for Oxford only, by a subcontractor (GenesisCare). The oxygen enhanced MRI will last approximately 60 minutes. The mask will be connected to two types of gas which you will breathe throughout the scan. These are air and 100% (pure) oxygen. During the scan, we will alter which gas is being supplied to you, which will allow measurements of tumour oxygen levels to be taken. You should not experience any discomfort with the mask, and the gases will allow you to breathe normally. You will receive either the normal amount of oxygen in the air or more.

You will be monitored at all times and also you will be able to talk with the study team directly during the scan. You will be allowed to leave the hospital after the scan. The scans will not delay or interfere with any of the appointments you are having in preparation for your surgery.

Within 48 hours of the PET/CT, you will have a standard care, pre-surgery MRI which will last approximately 30 minutes.

Study Visit 2 – Biopsy from gliomas at surgery

Your last visit will be on the day of your surgery. This will happen approximately 0-4 weeks after your first visit. During surgery, your neurosurgeon will use the images taken from your MRI and PET/CT scans to guide and take biopsies from the glioma tumour. The biopsy samples will be taken from tumour that will subsequently be removed during surgery. As part of standard clinical care, your tumour tissue will be sent for local histology analysis, in addition some will be sent for research analysis at the University of Oxford. This information will be available within a few weeks after your surgery.

It is important to note that the OEMRI and PET/CT scans are not carried out for diagnostic purposes. Therefore, unlike any routine standard scans you will be receiving, these scans are not routinely looked at by your doctor. Research scans are intended for research purposes only.

4. What should I consider?

Pregnancy and breast feeding

If you are pregnant or breastfeeding, you cannot take part in this study. We will discuss appropriate means of contraception if you agree to take part in the study.

If you decide to take part in this study, you must commit to continue true abstinence from heterosexual contact if it is in line with your preferred and usual lifestyle, or agree to use contraception as discussed and approved with the study doctor. This must be without interruption up to 30 days after your treatment.

You must tell us at once if you become aware that you are pregnant while in this study or within 30 days of your last treatment. This is because [^{18}F]fluorodopa has not been specifically tested for effects during pregnancy or breastfeeding and as it is radioactive, it may cause adverse effects to an early pregnancy. The study doctor will follow you and your pregnancy to birth, even if you discontinue from the study.

Males

If you have a partner who can become pregnant, you should avoid fathering a child while receiving study medication and for 30 days after your last treatment. You must agree to continue true abstinence from

heterosexual contact if it is in line with your preferred and usual lifestyle, or agree to use contraception approved by the study doctor. This is because [^{18}F]fluorodopa has not been specifically tested for effects during pregnancy or breastfeeding. As it is radioactive it may cause adverse effects to an early pregnancy.

If your partner becomes pregnant within 30 days after you last took your study medication, you must tell the study doctor right away. The study doctor will follow your partner's pregnancy to birth, even if you discontinue from the study.

5. Do I have to take part?

You do not have to take part in the study. This is entirely voluntary. If you do decide to take part, you will be asked to sign study consent form to show that you agree. You will also be given a copy of the signed consent form to keep.

If you choose not to take part in the study, no further action is required. Your care with your doctor will be continued without affecting the care you receive in the future.

6. What are the possible benefits of taking part?

We cannot guarantee any specific treatment benefits. However, the information we obtain from this study could improve the future diagnosis and treatment of people with gliomas.

7. What are the possible disadvantages and risks of taking part?

MRI is a safe technique that has no known risks used in a routine clinical practice. MRI does not involve any ionizing radiation such as X-rays. Therefore, the MRI scans will not involve any additional exposure to radiation. There are certain precautions that we undertake to ensure that the individuals having the MRI scan can do so safely. We will perform a safety assessment before you are allowed to enter the MRI scanner room.

Some people find that the scanner makes them feel uncomfortable (because they have to keep still for a long time), gives them vertigo (dizziness) or claustrophobia (nervous in small spaces). Such feelings will go away once you are outside the scanner. If you know that you are claustrophobic, you may wish to discuss this with the study team beforehand.

The PET/CT scan of your brain will be an additional imaging test to those examinations that you would have as part of your standard care. This procedure uses ionising radiation to form images of your body and provide us with other clinical information. A radioactive tracer is injected to allow further imaging of disease sites. Ionising radiation can cause cell damage that may, after many years or decades turn cancerous. The chances of this happening to you as a consequence of taking part in this study are 0.03%.

To date, [^{18}F]fluorodopa has been found to be well-tolerated, with all drug related side effects reported in patients to be mild, with none requiring treatment. Reported side effects considered possibly related to receiving [^{18}F]fluorodopa include injection site reactions (redness, pain, bruising), change in sense of taste or smell, headache and constipation.

As for all injections, it is possible that rare or unforeseeable side effects may occur, for example, an allergic reaction to [^{18}F]fluorodopa. You will be closely monitored while having the scan and if an allergic reaction does occur the radiology department staff members are trained in how to diagnose and treat this.

[^{18}F]fluorodopa has not been specifically tested for effects during pregnancy or breastfeeding. However, as it is radioactive it may cause adverse effects to an early pregnancy. For women of childbearing potential, it is very important that you use effective contraception during the study and throughout your cancer treatment, as advised by the glioma care team. The scan will only go ahead if there is no chance that you may be pregnant.

The main risk associated with biopsy of glioma is hemorrhage (bleeding). However, in this setting, biopsy of the tumour during surgery should not carry any significant increased risk as your tumour will be operated on immediately after the biopsies are taken.

PART 2

8. What happens if relevant new information becomes available?

New information about the treatment being studied may be found during the study. If this happens, your research doctor will tell you and discuss whether you should continue in the study. If you decide to continue in the study you may be asked to sign an updated consent form.

If the study is stopped for any other reason, you will be told why and your research doctor will arrange for your continuing care. If any relevant new information becomes available after you have had all of your procedures, it will not affect you as you will no longer be in the study.

9. What will happen if I don't want to carry on with the study

You are free to withdraw at any time without giving a reason and without affecting the care you receive in the future. The research team will respect your decision and we will happily answer any questions you might have at the time.

If you do decide to withdraw, you should inform your research doctor of your decision so that appropriate follow up can be arranged.

10. What if there are any problems?

If you have any problems during the study or would like to discuss the study, you can contact any of the research investigators. You can find their contact details on the last page of this information sheet. Every care will be taken in the course of this study. However, in the unlikely event that you come to harm as a result of you taking part in the study, compensation may be available. If you suspect that the injury is the result of the Sponsor's negligence (University College London), then you may be able to claim compensation. After discussing with your clinical study doctor, please make the claim in writing to Professor Geoffrey Higgins who is the Chief Investigator for the study. The Chief Investigator will then pass the claim to the Sponsor and on to Sponsor's Insurers. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the study, the normal National Health Service complaints mechanisms are available to you. Please ask your clinical study doctor if you would like more information on this. Details

can be obtained from the NHS website. You can also speak to the Patient Advice and Liaison Service (PALS). When contacting them, please quote the study number that can be found on the first page of this information sheet. Details can also be obtained from the Department of Health and Social Care website: http://www.dh.gov.uk (see question 18 for all the relevant contact details).

How will we use information about you?

We will need to use information from your medical records for this research project.

This information will include your:

- Name
- NHS number
- Date of birth
- 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 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 or samples 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.

What happens to the biopsy samples?

Your biopsy samples will be analysed as per standard of care. The research samples will be anonymised and transported to Oxford University for analysis. Samples will be transferred using a third party courier service.

What happens to the blood and urine samples?

Your urine and blood samples will be anonymised, transferred to Oxford University and analysed.

What happens to the imaging results?

Your imaging results will be anonymised and uploaded to the NCITA Repository Unit by the local hospital or subcontractor (GenesisCare, at Oxford only) for analysis by Oxford University.

11. Will my taking part be kept confidential?

All information, including personal information, which is collected about you during the course of the research, will be kept strictly confidential. Your information will be identified only by a unique study number so that you cannot be recognised from this number and there are strict laws which safeguard patients' privacy at every stage.

Only the researchers, study monitors on behalf of the Sponsor and representatives of regulatory authorities and research ethics committees may have direct access to it. Anonymised information collected about you during the study will be stored by the NCITA Clinical Trials Unit. This information would only be transferred to other researchers after all necessary approvals were in place.

In order to monitor and audit the study we will ask for your consent to access your medical records and data collected during the study, where it is relevant to taking part in this research.

As your images and study information may be useful for other research, we will retain your images and study information in an anonymised form for other research in the future that has been approved (as appropriate) by an ethics committee, for up to 25 years. Names will not be used in any of the study records or in reports and publications.

12. Involvement of your General Practitioner (GP)/family doctor

Your consent to participate will allow your study doctor to inform your GP of your participation in this study, unless otherwise asked not to.

13. What happens when the study is finished?

After your participation in the study is complete, the routine standard care will continue as normal.

14. What will happen to the results of the research study?

The whole study is expected to take 2 years. Once the results of the study are available if you wish to have the results of the study, we will provide you a summarised version of the main findings of the study. Please contact us.

We may wish to publish the results of the study in a scientific paper, through medical publications and websites. You will not be identified in any report or publication. Some of the data from this study may be used for the purposes of obtaining a research degree and qualification (e.g. a doctoral degree).

Your information, images and samples collected by this study may be used to support other research in future in an anonymous form. However, individual patients will not be identifiable in any data format.

In the unlikely event that standard clinical testing determines that your tumour is not a glioma, but some other form of tumour, we would still like to retain your anonymised data as they may be useful to a future study in a different disease area.

Local Data Protection Privacy Notice

The controller for this project will be University College London (UCL). The UCL Data Protection Officer provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk. This 'local' privacy notice sets out the information that applies to this particular study. Further information on how UCL uses participant information can be found in our 'general' privacy notice.
The information that is required to be provided to participants under data protection legislation (GDPR and DPA 2018) is provided across both the 'local' and 'general' privacy notices. The lawful basis that will be used to process your personal data are: 'Public task' for personal data. Your personal data will be processed so long as it is required for the research project. If we are able to anonymise or pseudonymise the personal data you provide we will undertake this and will endeavour to minimise the processing of personal data wherever possible. If you are concerned about how your personal data is being processed, or if you would like to contact us about your rights, please contact UCL in the first instance at data-protection@ucl.ac.uk. The pseudonymised data from the FIG Study will be used as part of a doctoral qualification.

15. Who is organising and funding the research?

UCL is sponsoring the research, however, funding of this research is provided by Cancer Research UK. This means that UCL is legally responsible for the study organisation and for overseeing the work of the study team.

16. Expenses and Payments

There is no remuneration for taking part in this study. The majority of the research study visits are planned to be at the same time as your standard of care visits. Therefore, it is expected that you will have a maximum of one extra visit to the hospital imaging centre for the research assessments.

You will be reimbursed for the cost of travelling to your extra visits beyond your routine clinical care upon presentation of receipts or a mileage allowance provided as appropriate.

17. Who has reviewed the study?

All research in the NHS is reviewed by an independent Research Ethics Committee, which is there to protect your safety, rights and wellbeing. A favourable ethical opinion has been obtained from the London Bridge Research Ethics Committee. The study has also been approved by local NHS Research and Development Departments at each site. It has also been reviewed by Patient and Public Involvement (PPI) organisation.

18. Contacts for further information

If you would like further information or have any questions about this study, please discuss them with the research staff or your study doctor.

FIG study team contact details:

Chief Investigator
Prof. Geoffrey Higgins
Address: Department of Oncology, Old Road Research Campus, Oxford
Tel: 01865 617311
Email: geoffrey.higgins@oncology.ox.ac.uk

Principal Investigator at local site
Prof. Geoffrey Higgins
Address: Department of Oncology, Old Road Research Campus, Oxford
Tel: 01865 617311
Email: geoffrey.higgins@oncology.ox.ac.uk

Trial Coordinator/or Point-of-contact research team at Local Site
Miss Joy Roach
Address: Department of Oncology, Old Road Research Campus, Oxford
Email: joy.roach@oncology.ox.ac.uk

If you wish to make a complaint about the study please contact:

Patient Advice Liaison Services (PALS)
Tel: **01865 221473**
Email: PALS@ouh.nhs.uk

If you would like some independent advice, you can contact either of the following:
Macmillan Cancer Support, which is an independent charity providing support and information to help people with cancer; www.macmillan.org.uk ; http://brainstrust.org.uk/ or https://www.thebraintumourcharity.org/

Alternatively, you can call Macmillan Cancer Support on 0808 808 0000 (Freephone), and they will send you information leaflets in the post free of charge.

If you would like to know more about how patients help initiate, design, support and monitor research, you will find information on the websites for the National Institute for Health Research (NIHR) (www.crncc.nihr.ac.uk), the National Cancer Research Institute (NCRI) (https://www.ncri.org.uk/patient-and-public-involvement/) or the NHS (www.invo.org.uk)

We will give you a copy of this information and a copy of the signed consent form to keep.

Thank you for taking the time to read the information about the study.