Participant Information Sheet A

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Nigrosomal Iron Imaging in Parkinson's Disease (N3iPD)

Name of Researcher(s): **Prof. DP Auer, Dr. N. Bajaj, Dr A. Martin-Bastida, Dr. S. Naidu, Prof P. Piccini, Dr. S. Schwarz, Dr. Y. Xing, Dr. Xingfeng Li.**

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. You can talk to others about the study if you wish. Do ask us if there is anything that is not clear.

Why perform a Magnetic Resonance Scan in Parkinson's disease?

There is more and more evidence showing that Magnetic Resonance Imaging (MRI), a commonly used medical imaging method not requiring any x-rays, can demonstrate changes in the brain related to Parkinson's disease. DaTScan™ is a different type of imaging which is the current gold standard to establish the diagnosis of Parkinson's disease if there is any doubt after clinical examination by a specialist doctor. However, DaTScan™ involves injection of a radioactive substance and is more expensive than a MRI scan and takes much longer to perform. In this study we want to investigate whether a new MRI test developed in Nottingham is as good as a DaTScan™ to help the diagnosis of Parkinson's.

Why have I been invited?

You are being invited to take part because your doctor thinks you could possibly be affected by Parkinson's disease and referred you for a DaTScan™ as an established diagnostic test to investigate further. We are inviting 145 participants like you to take part in this study to undergo an alternative MRI test to establish whether it could replace DaTScan™ in the future.

What does it involve for you to participate in this study?

We will arrange an appointment for you on a day convenient to you to visit the research MRI unit on the University of Nottingham campus or the Imperial College of London campus. In case your doctor has started you on medication to help symptoms of Parkinson's disease you may be asked to stop this antiparkinsonian therapeutic regime one day prior to the MRI scan and then to continue to take your usual medication after completion of the scan. When you arrive you will be asked to sign a consent form and we will check your eligibility for the study and ask you to complete a MR Volunteer Safety Screening Questionnaire. This is to ensure your safety in the MRI scanner and it asks you to answer a series of simple questions aimed to ensure that you do not have any metal implant (such as a pacemaker or surgical implants) in your body.
One of the questions will ask you if you have ever worked in a machine tool shop without eye protection and/or could possibly have any metal in your eye. If yes, we will have to ensure that there are no traces left in your eyes before we scan you. We will check your x-ray records to see if you have any previous results, which show that your eyes are free from

metal. If you have not had an x-ray taken previously for this or your x-ray was taken some time ago and at the time you still had traces of metal, we will give you an x-ray to check that your eyes are now clear. Please note; if you already have a previous x-ray result confirming that your eyes are free from metal, then, you will not be required to have another one and it will be safe for you to go into the MRI scanner.
The MRI scan will last approximately 30 - 45 minutes. Also, a clinically qualified person will examine you before or after the scan (for up to 1.5 - 2 hours with a break of up to 15 min after one hour if necessary). The clinical examination will involve the use of standard tools to assess a range of, brain functions and signs of Parkinson's disease. All information you will be giving is strictly confidential and unauthorized personal outside the research team will not have access to this information without your specific prior authorization.

We will compare the findings of the MRI scan with the findings of a clinical examination, which is scheduled for 12 months after the initial visit. This follow up visit can either be performed as part of your usual NHS care, or if this is not feasible we will invite you for a follow up visit to the research department to assess you for clinical signs and symptoms of Parkinson's disease (lasting for up to 1.5 – 2 hours). Just like for the first visit, in case your doctor has started you on medication to help symptoms of Parkinson's disease you may be asked to stop this antiparkinsonian therapeutic regime one day prior to follow up visit and then to continue to take your usual medication after your visit.

What are the possible disadvantages and risks of taking part?

None of the procedures are painful.

The scanner environment can cause anxiety in subjects who are not comfortable in enclosed spaces. The scan involves the placement in a tunnel and the wearing of a helmet-like coil fitted with a mirror to allow seeing past one's feet. In addition, some people may also feel dizzy when they move into and out of the scanner. During the MRI, the scanner will make loud beeping noises and vibrate slightly, however this should not cause any pain or discomfort as both earplugs and ear defenders will be provided.

What is Magnetic Resonance?

Magnetic Resonance Imaging (MRI) is a powerful method for diagnosing diseases and investigating physiological (normal) and pathological (abnormal) processes inside the brain. MRI is used to demonstrate the structure and contents of the brain, and can examine different brain tissues, nerve fibres or even the chemical composition of some brain areas. The newly developed test is an optimised MRI with very high resolution and sensitive to iron that tends to increase in two very small areas in the brain of people with Parkinson's.

Do I have to take part in this Imaging study?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This would not affect your legal rights.

Expenses and payments

Participants will not be paid to participate in the study. Travel expenses will be offered for any visits incurred as a result of participation.

Are there any risks?

Magnetic Resonance Imaging (MRI) uses radio waves similar to those used in radio and TV transmission. These have a much lower energy than X-rays and as such are considered biologically safe. We will be following strict national safety guidelines, which are designed to prevent the potential hazards of MRI.

While there is no evidence to suggest that MRI is harmful during pregnancy, the Medicines and Healthcare products Regulatory Agency (MHRA) advises against scanning pregnant women in the first three months of pregnancy or at magnetic field strengths above 2.5 Tesla. As we are intending to use a MRI scanner with a field strength of 3 Tesla we would not include you in this MRI study if there is a possibility you could be pregnant.

The strong magnetic field of the scanner can damage implanted electrical devices or move other metallic objects. As part of a routine pre-scan safety check (which is also standard before every clinical MRI scan) we will enquire about prosthesis, implanted electrical devices or metallic foreign bodies. In case there is a possibility of you having a metallic foreign body in your eyes we would like to perform a x-ray of your head to ensure that you do not have a metallic foreign body.

Radiation risk

MRI does not use ionizing radiation and does therefore not carry any radiation risk.
In up to 1 in 15 people it may be necessary to perform an x-ray of the head to exclude a metallic foreign body in the eyes prior to the MRI scan.

Orbital x-ray require you to be exposed to ionising radiation; however some of these procedures would be performed as part of your normal care, whether or not you agree to take part in this study.
Radiation is around us all the time in small amounts, from rocks in the ground and cosmic rays coming through our atmosphere. The dose you will receive from participating in the trial if you had to undergo an x-ray of the orbit has been estimated to be equivalent of two days of natural radiation exposure received by a typical UK resident.

What will we do if we notice something abnormal on your scans?

In healthy volunteers of all ages between 10-47 % of the examined participants may show some abnormality that may vary from a normal anatomical variation to a pathological finding which in the absence of any symptoms we call chance finding.

We have local protocols that we follow to deal with such 'chance findings', i.e. if anything abnormal is suspected on the scan. The local protocols may vary slightly between sites, but follow general consensus in the scientific community and the following principles:

- The MRI scans are not being carried out for diagnostic purposes and due to the large volume of research scans and their specific purpose to answer a research question rather than a clinical question, scans will not be routinely reviewed by a specialist

radiologist. Therefore abnormalities may be recorded on the research MRI but may not be uncovered.

- In case the scanner operator or image analysis researcher notices or suspects such a chance finding, the scan will then be reviewed by a more experienced person to decide whether this is of potential significance, and in that case only your GP or responsible physician will be informed.
- Your GP or responsible physician will then take appropriate action if needed and inform you. This might have the benefit of allowing you to start treatment earlier than you would have otherwise, but it may also have implications for your future ability to find employment and obtain insurance.
- As part of the enrolment into the study we will inform your GP of your participation.

What are the possible benefits of taking part?

There is normally no direct benefit for you to participate in the study. The only remote benefit could arise in the rare event of a chance finding that is being picked up and may allow earlier treatment. The main anticipated benefit of the study is a better and less invasive diagnostic test for people like you in the future, as they will be offered a simpler, completely non-invasive test to find out whether they have Parkinson's.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. The researchers contact details are given at the end of this information sheet. If you remain unhappy and wish to complain formally, you can do this by contacting [Contact details of PALS for the hospital Complaints of ICL or NUH will be added]

Will my taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence.

If you join the study, some parts of your medical records and the data collected for the study will be looked at by authorised persons from the respective study sites who are organising the research. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

All information, which is collected about you during the course of the research, will be kept **strictly confidential**, stored in a secure and locked office, and on a password-protected database. Any information about you, which leaves the hospital will have your name and address removed (pseudo anonymised) and substituted by a unique code of randomly assigned numbers/letters so that you cannot be recognised from it. The key to the code is held securely by authorised persons from the University of Nottingham (or Imperial College London) campus who are organising the research prior to the completion of this study.

Your personal data (address, telephone number) will be kept for 2 years after the end of the study so that we are able to contact you about *possible follow-up studies* (unless you advise us that you do not wish to be contacted).

To maximise the benefit of your taking part in this study we would like to use the anonymised imaging and clinical data, which we record from you (DaTSCAN and MRI) in this study for comparative studies conducted at the University of Nottingham. In addition, after the completion of this study we will pass on core clinical and imaging data recorded from you to the Michael J Fox Foundation who has funded this study and is based in the US. The Michael J Fox Foundation wants to make all research data they fund available to other researchers in the field across the world. This will ensure that we can maximise the benefit of your contribution of your data to research. Before data transfer from the University of Nottingham (or Imperial College London) to Michael J Fox Foundation, your data will be fully anonymised and to further ensure that you will also not be identifiable by chance from more refined reconstructions of parts of your head MRI scans, we will strip the skull and potentially identifiable facial features from the images that will be uploaded on such a research repository.

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

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you withdraw then the information collected so far cannot be erased and this information may still be used in the project analysis.
The standard of any future care will not be affected by a decision to withdraw from the study.

What will happen to the results of the research study?

We plan to publish any results in scientific journals and will also present the findings in annual meetings to inform the scientific and expert groups dealing with Parkinson's as early and completely as possible. Your name would not be mentioned in any publication. The results of this study may be written up as part of a higher academic degree (e.g. PhD, MD or MSc) at the University of Nottingham or Imperial College London. We will make regular reports to funding bodies and to patient groups. If you are interested in the outcome of this study please let us know and we will send you a brief summary of the findings after the end of this study.

Who is organising and funding the research?

This research is being organised ('sponsored') by the University of Nottingham and is being funded the Michael J Fox Foundation.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by Derby Research Ethics Committee.

Further information and contact details

The chief investigator of this study is Prof. Dorothee Auer, Head of Radiological Sciences Research Group, University of Nottingham (Tel.: 01158 231178, Email: dorothee.auer@nottingham.ac.uk)

The contact details for the Imperial College Principal investigator are: Prof. Paola Piccini, Head of Neurodegeneration and Neuroinflammation Department, Imperial College London (Tel.: 02083833172, Email: paola.piccini@imperial.ac.uk)

We will give you a copy of the information sheet and signed consent form to keep. If you would like more information about the MRI study and feel free to ask the person who gave you this sheet or contact the local investigator [contact details of local study investigator in London or Nottingham will be added]