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Protocol: Development of novel magnetic resonance techniques using volunteer participants

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Purpose and limitations

This research protocol relates to MR scans at UCLH for methodological research. It applies to normal volunteers and patients recruited as volunteers. The protocol applies only to MR scans with no interventional component and no additional drug administration except in some cases a standard dose of a Gadolinium-based contrast agent or inhalation of hyperpolarised xenon. Scans will take place using commercially available MR hardware at UCLH. MR itself has no known side-effects, and has been performed safely on millions of subjects worldwide.

Although scans may obtained as part of several research projects, in each case it is only the scanning technique (the programmed sequence of data acquisition and processing steps) which will vary, along with the body region to be imaged. The volunteer experience will be very similar, and all ethical issues, including the information sheet and consent form, will be identical. These scans are for methodological research on the MR techniques themselves, and will be never form part of the volunteer's own healthcare. Separate ethical permission is sought for any study which does not match the above criteria.

Procedure

Recruitment:
Healthy volunteers will normally be recruited by email from within departments at UCL and UCLH.

Volunteer patients will be identified by details on radiology request forms or by their clinical care team. A letter will be issued outlining the study and inviting participation. This will be followed up by a single phone call (by a named investigator) to gauge interest in the study. Volunteers will be greeted by a named investigator. The investigator will go through the information sheet and obtain signed consent prior to the research MRI being conducted. A medically qualified named investigator will have to give approval prior to any research imaging on a patient. Two recruitment pathways will be possible:

- Patients return for a separate scanning session.
- A routine clinical scan is extended.

For studies requiring additional contrast, potential participants will have the same renal function assessment as the standard out-patient assessment performed at UCLH.

Participation in studies requiring the consumption of normal quantities of consumer food or drink products and possibly fasting for up to 8 hours beforehand, will require the approval of a medically qualified named investigator.

Consent: participants will be consented by a researcher. A new consent form will be filed for each visit.

Exposure record: For each new volunteer, an 'exposure record' including duration and other details of scans will also be started, and an entry added for each subsequent visit involving that individual.

Metal check: the exclusion criteria for MR are well-established and will be applied for volunteers in the same way as for patients at UCLH. An MR radiographer or experienced MR physicist will work through the metal-check questionnaire with the volunteer before they enter the scanner. Only volunteers who do not meet any exclusion criteria will be scanned.

Clothing: depending on the body part scanned, the volunteer may be asked to change into non-metallic clothing, usually a hospital gown. Alternatively, volunteers may be encouraged to bring suitable clothing (eg jogging bottoms) with them. Clothing will always be checked for MR safety as part of the preparation for the scan.

Markers: occasionally, small markers (which are visible in the scans) will be placed on the volunteer's skin: these are usually ordinary cod liver oil capsules. They are temporary and can be removed straight after scanning.

Scan: The volunteer will lie on the scanner bed. One or more coils (panels which receive MR signal) may be placed over the areas of their body being scanned. They will also be given earplugs and/or headphones (MR scans can be quite noisy) and a communications buzzer which they can squeeze to attract the operator's attention. The scanner bed will then be moved into the scanner, and the operator will return to the control room. Scans will typically last up to one hour, and never more than two hours.
The headphones and a microphone in the scanner allow the volunteer and operator to remain in voice contact. The operator can also see the volunteer in the scanner. Occasionally the volunteer may be asked to briefly hold their breath or move in a particular way; for most of the time, however, they will just lie still in the scanner. The volunteer can terminate the scan at any time, with or without giving a reason, by talking to the operator. In particular, subjects occasionally find the scanner claustrophobic, or find the noise uncomfortable; if these aspects are intolerable for the volunteer the scan will be stopped immediately.

Inhaled hyperpolarised xenon:
Xenon (Xe) is an inert, non-toxic noble gas naturally occurring in trace amounts in the atmosphere. The stable isotope ^{129}Xe possesses nuclear spin, the essential property required for MRI detection. Hyperpolarisation is a process which transiently increases the nuclear spin polarisation, greatly increasing the potential signal detectable using MRI, without changing the other properties of the element / molecule. Following inhalation, hyperpolarised ^{129}xenon can cross the alveolar membrane and binds to haemoglobin in a similar fashion to oxygen, thus providing a surrogate marker of ventilation, gas exchange and lung perfusion.
Medical grade ^{129}Xe is hyperpolarised using a rubidium spin exchange optical pump hyperpolariser and supplied to the volunteer in a sealed, Tedler bag for inhalation *via* a sterile mouthpiece. Hyperpolarised ^{129}Xe has been extensively used in humans for more than fifteen years, both in healthy volunteers and those with pulmonary diseases, and there have been no significant adverse effects reported. Mild transient side effects included dizziness, paraesthesia and euphoria, which typically last for less than two minutes.

Data: All data will be fully anonymized, so that the volunteer cannot be identified from it, before analysis and any possible scientific publication.

Abnormalities: Research scans are not intended for diagnostic purposes. The images do not normally follow a diagnostic protocol, and are not routinely reviewed by a radiologist. However, occasionally a previously unknown abnormality is still detected in a volunteer scan. When this happens, a radiologist will review the films, and talk to the volunteer: consent is obtained in advance from the volunteer to be informed of any abnormalities detected. The radiologist may also contact the volunteer's GP to arrange follow-up assessment if appropriate.

Research support

This protocol covers several research studies. However, to demonstrate that independent peer review takes place for many of our studies, and to show that funding has been obtained, two current specific projects are outlined below.

Evaluating vascular properties of tumours in the presence of tissue motion: application to functional studies of liver tumours. This is a joint award to Prof D Hawkes at UCL's Centre for Medical Image Computing with Prof M O Leach at the Institute of Cancer Research. The UCL team are investigating ways of acquiring liver images during free breathing, including ways of modelling liver motion and of using this information to correct the artefacts that breathing causes in images. Volunteer studies at UCLH will involve imaging the liver with novel techniques to evaluate and refine these approaches. EPSRC grant GR/T20434/01; for details see http://gow.epsrc.ac.uk/ViewGrant.aspx?GrantRef=GR/T20434/01.

Integration of image derived information to guide breast cancer treatment. This is a joint DTI award to Prof D Hawkes with Kodak Ltd, investigating image fusion between ultrasound, X-ray mammograms and breast MR image. The current aspect of research relates to modelling breast deformation, and volunteer studies under this protocol would be used to define suitable imaging parameters for such assessment. (Separate ethical permission has already been obtained by Michael Douek, a UCLH breast surgeon, for actual breast compression experiments with MRI, ethics number 06/Q0505/99). For more detail see: http://www.dti.gov.uk/innovation/technologystrategy/successful_projects/page21525.html#breast