Andrew Cooper

CoRIPS Research Grant 145

£4,590 awarded

Title: Upright open MRI for brain imaging in children – a pilot study

Principle Aim

To establish feasibility and acceptability of diagnostic brain imaging in young children using an upright MRI scanner.

Primary research question

Can diagnostic brain MRI be acquired in young children without sedation or anaesthesia using an upright MRI system for specified indications?

Secondary research questions

- How do young children who undergo brain MRI using upright MRI view the experience?
- How do the parents / carers of young children who undergo brain MRI using the upright MRI view the experience for their child and for themselves?
- How does image quality compare between brain MRI using the upright MRI scanner and the standard MRI scanner used in clinical practice?

Outcomes

Three specific outcomes are sought:

- Demonstration of feasibility of using an upright MRI system for brain scanning of young children without sedation or anaesthetic
- Demonstration of acceptability of the experience of upright brain MRI scanning as rated by child participants and their parents / carers
- Demonstration of diagnostic-quality image acquisition using an upright MRI system for specified paediatric neuroimaging indications

These outcomes will be used to support an application for a large follow-on grant (target funding source: NIHR Research for Patient Benefit) which is described under ‘Potential Impact’ (part 10g) below. The data acquired in this pilot study will

be used to inform sample size calculations for the large follow-on trial, and content and style of patient reported experience measures.

Review of literature and identification of current gap in knowledge

MRI is widely used in clinical practice to diagnose and monitor disease but remains problematic in young children due to anxiety caused by the confined space, loud noises, unfamiliar environment, and the need to lie still for an extended period of time (around 20-30 minutes for a typical clinical MRI scan) [1-3]. Anxiety and resultant poor compliance can lead to poor quality images or abandonment of the procedure. Various strategies have been developed to increase compliance of children having scans without sedation, including play therapy and mock MRI scans [3-6]. Internet-based delivery of preparatory materials provides an inexpensive, accessible and time efficient way to help prepare children for awake MRI, and Dr Dineen's group have previously developed and evaluated an animated educational video to prepare children for awake MRI showing this to improve knowledge and reduce anticipated anxiety of having an MRI scan [7].

Despite these strategies, young children (below the age of 7, sometimes older) typically require general anaesthetic (GA) to undergo MRI which is resource intensive (requiring specialist equipment, anaesthetic staff, rooms for induction and recovery and admission to a paediatric day-case facility) with consequent cost implications for the NHS. In addition GA adds a very small but real complication risk and hence alternative strategies should be sought [8].

We have recently installed a Paramed Medical Systems 0.5T open MRI scanner (figure 1) in the University of Nottingham Sir Peter Mansfield Imaging Centre (SPMIC) clinical facility in the Queen's Medical Centre, Nottingham. This system allows acquisition of commonly used brain structural imaging sequences including T1-weighted spin echo, T2-weighted spin echo, fluid attenuated inversion recovery (FLAIR) and 3D Gradient Balanced Steady State (3D-GBASS, heavily T2-weighted 3D acquisition equivalent to CISS or FIESTA by other manufacturers). The patient can be positioned lying flat, sitting semi-reclined or upright, or standing. The system therefore allows children to undergo MRI scanning while sitting up, which we anticipate will be more comfortable and less intimidating for the child. In the sitting position the child can watch an MRI compatible video screen for entertainment and distraction during the scan. Head immobilisation during the scan can be achieved using inflatable pads between the child's head and the head coil to minimise movement. With this approach we postulate that children

as young as 3 or 4 years of age will be able to undergo basic structural brain imaging without the need for GA or sedation.

Figure 1 (left): Paramed Medical Systems 0.5T open MRI scanner (figure 1) in the SPMIC clinical MRI facility in the Queen's Medical Centre, Nottingham, showing a child in the upright sitting position.

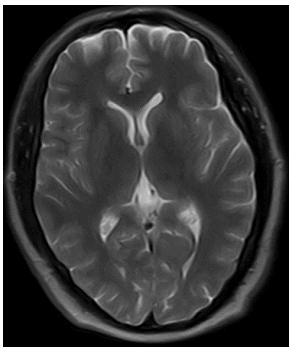


Figure 2 (right): Axial T2-weighted brain image from a healthy adult volunteer acquired on the upright

Two common clinical scenarios for which simple structural MRI scanning is performed in children are (i) symptoms or signs suggestive of brain tumour and (ii) symptoms or signs suggestive of shunt blockage in children with a ventriculoperitoneal (VP) shunt.

Children presenting with symptoms or signs suggestive of brain tumour require central nervous system imaging to identify or exclude intracranial tumour [9]. Thresholds for scanning children have lowered as a result of guidance for professionals and the University of Nottingham-led HeadSmart public awareness campaign which has resulted in reduced delays for diagnosis of paediatric brain tumours [10]. For most of these cases simple structural imaging is sufficient to exclude an intracranial tumour or other cause for the symptoms (although more detailed or targeted imaging may be required if certain features such as seizures, endocrine disturbance or visual disturbance are present). The increase in referrals for MRI, while important for allowing earlier diagnosis of paediatric brain tumours has led to an increase of young children having MRI under GA in our hospital unit.

Children presenting with symptoms or signs suggestive of shunt blockage in children with a VP shunt require imaging to look for change in ventricular dimension or migration of shunt position. Computed tomography allows a quick imaging modality for this indication, but carries a radiation burden. As some of these children have repeated scans throughout childhood, the cumulative burden of repeated CT scans is excessive. MRI provides an alternative imaging modality for visualising ventricular dimensions and shunt position without ionising radiation, but for young children this often requires GA.

We will address the aim and research questions given in parts 10(a-c) above by recruiting young children referred for structural imaging for these two clinical indications. To our knowledge this work is novel and we are unaware of any previous work that aim to exploit the child-friendly aspects of open upright MRI to for paediatric neuroimaging.

Methodology

Quantitative and Qualitative methodology will be applied as described below. The study will commence following Research Ethics Committee approval and in accordance with the principles of Good Clinical Practice.

We will recruit 20 young school-aged children (5to 10 years) referred for brain MRI at Nottingham University Hospitals NHS Trust (NUHT). We aim to recruit 10 children referred for brain MRI for symptoms and signs suggestive of brain tumour, and 10 with known VP shunts with a clinical suspicion of shunt dysfunction. Potential participants will be identified from MRI requests received in the MRI Department at NUHT. Prior to their scheduled clinical MRI scan, potential participants will be approached (via their parent or carer) and invited to join the study. The parent / carer and child will be receive an explanation of the study as well as an age-appropriate information sheet. Parent / carer consent and child assent will be obtained in all cases.

Standard clinical MRI scans will be conducted and reported as per routine standard of care, with or without GA or sedation as appropriate. Following the MRI scan child participants and parent / carers will complete questionnaires relating to their experience of routine clinical MRI scan. To record the child's experience we will offer a choice in terms of delivery of the set questions to suit the child; either the child can contribute their story by answering questions asked by their parent with responses recorded on the questionnaire, or the child can write down their experience in response to a few keys questions. Flexibility in approach will be guided by parents and the child, to ensure participation works for every child.

We will then arrange for the child to attend for the upright MRI scan within 72 hours of the clinical scan, except where the child has undergone neurosurgical or other medical intervention in the intervening period, which would exclude the child from the analysis. We will use the manufacturers CE marked sequences. Imaging protocols will be based on standard clinical protocols used at NUHT pragmatically adapted for the upright scanner including: axial T2, coronal T1 and sagittal FLAIR for exclusion of brain tumour, and axial T2 and sagittal CISS / FIESTA (or equivalent) for children with suspected shunt dysfunction. The upright scan will last no more than 30 minutes, including participant positioning and localisation scanning. Children will be able to watch a video on the MRI compatible monitor during the scan. Following the upright MRI scan child participants and parent / carers will again complete questionnaires documenting their experience of upright MRI scan as before.

Scan duration, challenges encountered and completion rates will be recorded. MRI images from both scans will be rated for diagnostic image quality and movement

artefact by two experienced neuroradiologists (Dr R Dineen and Prof D Auer) who will evaluate the images blinded to the scanner of acquisition. Technical image quality will also be compared between the scans from the two systems, using both the standard ACR phantom procedure, and a modified procedure to assess signal to noise ratio, contrast to noise ratio, and voxel dimensions. Questionnaires relating to participant experience and parent / carer views will contain age-appropriate rating scales as well as questions inviting free text response, allowing both quantitative and qualitative analyses of participant experience and parent / carer views.

Analysis: To address the principle aim (10a) and primary research question (10b) we will report completion rates and acceptability ratings for the upright MRI scan. Feasibility will defined as >75% of participants completing at least axial T2 brain imaging which is of acceptable diagnostic standard. Statistical comparison (by t-test or equivalent non-parametric test) of expert ratings of image quality and movement artefact, for standard MRI versus upright MRI scans.

Sample size considerations: The chosen sample size of 20 participants has not been derived from a formal power calculation as this is a pilot study, but has been chosen on pragmatic grounds as it is an achievable number for our unit, will allow us to establish the feasibility of this approach and provide pilot data on participant experience and image quality that we can use to support the argument and sample size calculations for the planned large follow-on grant described in section 10d.

Role of the co-investigators: **Dr Rob Dineen** (Clinical Associate Professor of Neuroimaging and Consultant Neuroradiologist) will act as the main supervisor and will oversee identification and recruitment of suitable participants. Both he and **Prof Dorothee Auer** (Professor of Neuroimaging, Consultant Neuroradiologist) have considerable experience of reporting paediatric neuroimaging, and will conduct the assessment of diagnostic image quality. **Prof Paul Morgan** (Head of Non-ionising Imaging Physics) will lead on technical assessment of image quality. **Prof Faith Gibson** (Professor of Child Health and Cancer Care) will oversee the development and analysis of questionnaires and other qualitative research tools for evaluating the child's experience.

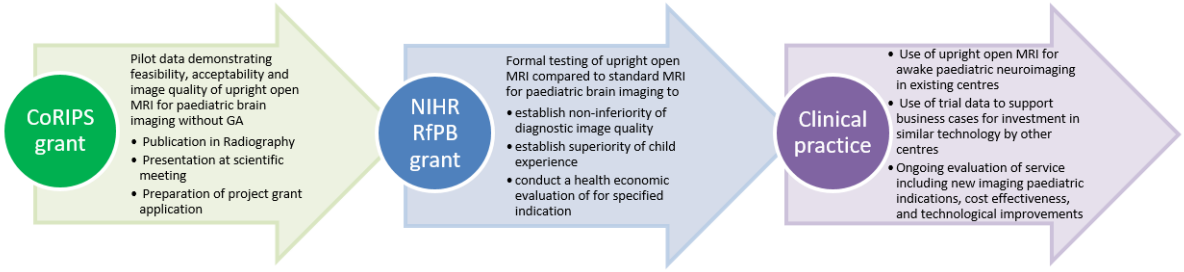
Research environment: The University of Nottingham and Nottingham University Hospitals NHS Trust have recently been awarded NIHR Biomedical Research Centre (BRC) status, which will strengthen the clinical research collaboration between these institutions. Biomedical imaging was identified as a particular strength and awarded funding as a cross-cutting theme within the BRC. The SPMIC, where this project will take place, is a multidisciplinary group of MRI researchers who continue the legacy of Nobel Laureate Sir Peter Mansfield in innovative MRI research at the University of Nottingham. The SPMIC facilities

have recently been upgraded following a £7.7M MRC infrastructure grant and include clinical 7T, 3T, 1.5T and upright MRI platforms. An exciting recent development is the installation of a child-friendly MRI suite which includes a children's waiting and preparation area (including a mock MRI scanner), and this facility is ideally suited to allow scanning of the children in my proposed project.

Potential impact

The pathway to impact is shown in the infographic below. The CoRIPS-funded study will form the basis of an application for a large follow-on grant (target funding source: NIHR Research for Patient Benefit) which will aim to (i) establish non-inferiority of diagnostic image quality, (ii) establish superiority of child experience, and (iii) conduct a health economic evaluation of upright MRI compared to standard MRI for paediatric brain imaging for specified indications.

This large study will, if successful, show that open upright MRI scanning allows diagnostic brain imaging in a child friendly manner with significant cost savings in terms of reduction of requirement for GA. Rapid translation into clinical practice will be possible at sites which have open upright MRI scanners such as the Queen's Medical Centre in Nottingham, where a region-wide service could be offered. At present only a small number of similar scanners are in operation in the UK which could limit widespread uptake, but Trusts considering investing in this technology for other purposes (for example for better established adult musculoskeletal imaging indications) could include paediatric imaging in their activity planning and business cases.



Dissemination Strategy

Study findings will be communicated to the scientific community via a publication Radiography as per the grant requirements. Results will also be presented to the UK medical imaging community at an event such as the UKRC and other specialist meetings such as the British Society of Paediatric Radiologists or British Society of Neuroradiologists meetings. In addition we will present study progress and findings to relevant patient groups, such as at our local Children's PPI group (which

we would ask for feedback and comments before applying for the large follow-on grant). We would also make us of the University of Nottingham Press Office to publicise this work to the general public through its various media channels.

References

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