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FULL PAPER

A qualitative comparison of arterial spin labelling and dynamic susceptibility contrast MRI in 52 children with a range of neurological conditions

¹PAUL A ARMITAGE, PhD, ²NICHOLAS SKIPPER, MBBS, FRCR, ²DANIEL J A CONNOLLY, MRCP, FRCR and
¹PAUL D GRIFFITHS, PhD, FRCR

¹Academic Unit of Radiology, University of Sheffield, Sheffield, UK

²Department of Radiology, Sheffield Children's Hospital, Sheffield, UK

Address correspondence to: Dr Paul A Armitage

E-mail: p.armitage@sheffield.ac.uk

Objective: To assess the usefulness of arterial spin labelling (ASL) compared with dynamic susceptibility contrast (DSC) perfusion MRI for typical paediatric neuroimaging applications at 1.5 T.

Methods: 52 children (age: 4 months–17 years) with a variety of neurological disorders were scanned using three-dimensional ASL and echoplanar imaging DSC sequences. All images were reviewed by an experienced neuroradiologist; image quality was recorded as “good”, “acceptable” or “poor” and diagnostic value was noted as being “greater”, “similar” or “less” for ASL when compared with DSC.

Results: ASL cerebral blood flow (CBF) images were judged to be acceptable in 89% of cases, poor in 11% of cases and good in 0% of cases, while DSC CBF images were acceptable in 88% of cases, poor in 12% of cases and

good in 0% of cases. ASL images were judged to have better diagnostic value than DSC images in 28% of cases, about the same in 58% of cases and worse in 14% of cases.

Conclusion: The results of this study suggest that ASL offers a realistic alternative to DSC in the paediatric setting for the majority of cases encountered in this study. However, there are some situations where DSC outperforms ASL; so, care is required to choose the most appropriate technique for the pathology under investigation. A larger study is required to corroborate these preliminary findings.

Advances in knowledge: ASL is a relatively new perfusion imaging technique whose use has not been explored extensively in the paediatric setting. This work is a preliminary study to evaluate its usefulness in paediatric neuroimaging.

INTRODUCTION

Cerebral blood flow (CBF) is a measure of the rate of blood delivery to the brain parenchyma. It is an important physiological parameter that is potentially useful in the characterization of many neurological diseases and can also be used as a surrogate measure of neuronal metabolic activity.

There are several perfusion imaging techniques which allow measurement of CBF, but most of these require the injection of an exogenous agent and/or the use of ionizing radiation and provide only relative CBF measurements. Dynamic susceptibility contrast (DSC) MRI is one such technique with an established value in the investigation of a number of pathologies of the central nervous system.^{1,2} Relative, or quantitative, estimates of CBF are determined by monitoring the change in T_2^* signal during the first pass of an i.v. injection of a gadolinium-containing contrast agent.

Arterial spin labelling (ASL) MRI negates the need for i.v. injection, instead using radiofrequency pulses to non-invasively label endogenous protons within the arterial blood, in order to measure CBF. It uses no ionizing radiation, allows an estimation of absolute values of CBF and has recently become commercially available.^{2,3} However, ASL does have disadvantages, including its susceptibility to a number of artefacts and low signal-to-noise ratio.⁴

ASL has potential applications in many neurological conditions, such as acute ischaemic stroke, chronic cerebral ischaemia, localization of epileptogenic foci, tumour characterization, tumour grading and detection of regional hypoperfusion patterns in neurodegenerative diseases.⁵ Non-invasive imaging techniques are particularly desirable in the paediatric population, as invasive techniques may be technically challenging, tolerated poorly or deemed unjustifiable. Examples where ASL has found application in the paediatric population include patients with temporal

lobe epilepsy,⁶ acute ischaemic stroke,⁷ brain tumours,⁸ sickle cell disease,^{9–11} neurotuberculosis,¹² focal cortical dysplasia,^{13,14} arteriovenous malformations,¹⁵ traumatic brain injury¹⁶ and moyamoya disease.¹⁷ There have been several studies performed that compare perfusion measurements obtained from ASL with those from DSC,^{18–23} particularly in stroke and brain tumour populations, but few have been performed in a paediatric population.¹⁷

The purpose of this study was to make a qualitative comparison between CBF images produced by traditional DSC MRI and those produced using ASL MRI in a group of paediatric patients imaged as part of the routine investigation of a variety of neurological conditions.

METHODS AND MATERIALS

Patients

A three-dimensional (3D) pulsed continuous ASL sequence was included in the routine imaging protocol for 52 paediatric patients undergoing investigation for a variety of disorders over a 9-month period from October 2011 to July 2012. 40 patients were imaged on 1 occasion, 11 patients on 2 occasions and 1 patient on 3 occasions, resulting in a total of 65 3D ASL scans. 57 of the 65 3D ASL scans were accompanied by DSC imaging at the same imaging session. All patients underwent T_1 weighted and T_2 weighted imaging in addition to other sequences selected on the basis of clinical need. Informed consent for MRI was obtained from parents and, where appropriate, from patients prior to scanning.

Ethical approval

This work was performed in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki); approval was granted by the local research and development office as a service development project and informed consent was obtained by all patients, or their parents, as appropriate.

Imaging

All MRI data were acquired on a GE Signa Horizon HDXT 1.5-T whole-body clinical system (General Electric, Milwaukee, WI), using a manufacturer-supplied head coil. The MRI protocol included the following sequences (all acquired in the axial plane): T_1 weighted spin echo [repetition time (TR)/echo time (TE) = 400/9 ms, $\alpha = 73^\circ$, 512×512 matrix, 230×23 -mm field of view (FOV), 4-mm-thick slices, 1-mm gap], T_2 weighted fast spin echo (TR/TE = 4660/113 ms, $\alpha = 90^\circ$, 512×512 matrix, 230×230 -mm FOV, echo train length = 12, 4-mm-thick slices, 1-mm gap), 3D pulsed continuous ASL (TR/TE = 4322/10.97 ms, post-label delay = 1025 ms, $\alpha = 155^\circ$, 128×128 matrix, 240×240 -mm FOV, 4-mm-thick slices, number of excitations = 3) and DSC gradient-echo (GE) echoplanar imaging (EPI) (TR/TE = 1600/30 ms, $\alpha = 90^\circ$, 128×128 matrix, 240×240 -mm FOV, 5-mm-thick slices, no slice gap).

All images were transferred in digital imaging and communications in medicine format onto a standard personal computer workstation and converted into the Analyze 7.5 file format using custom software. DSC images were processed using standard methods that involved voxel-by-voxel gamma-variate curve fitting, with cerebral blood volume estimated from the area under

the curve, mean transit time from its first moment and CBF calculated by dividing cerebral blood volume by mean transit time.²⁴ Only relative perfusion metrics were calculated with no attempt being made to correct for the arterial input *via* deconvolution. The calculated relative CBF image obtained using DSC MRI was compared with the ASL mean subtraction image ($\approx$ CBF) calculated automatically by the GE scanner from the labelled/unlabelled image pairs. All images were displayed and interpreted using standard greyscale mapping to ensure consistency.

Visual assessment

Image quality was assessed using consensus review by an experienced paediatric neuroradiologist (DC) and an MR physicist (PA), who classified the image quality of the 65 ASL and 57 DSC CBF images as “good”, “acceptable” or “poor”. Image quality was assessed in two separate sessions for ASL and DSC images, performed several months apart and blind to the imaging and assessment outcome of the other method. In addition, for the 57 cases where both types of images were available, the ASL CBF images were viewed side by side with the DSC CBF images and the neuroradiologist classified the ASL images as being of “greater”, “similar” or “less” diagnostic value.

RESULTS

A total of 30 males and 22 females were scanned with an age range of 4 months–17 years (mean age: 9.6 ± 4.5 years). The pathology under investigation and the number of patients with each pathology are shown in Table 1, along with patient demographics.

Consensus review

Of the 65 ASL CBF images, 58 (89%) images were classified as having acceptable image quality, 7 (11%) images as poor and none as good. The seven poor-quality ASL images could be broadly classified into three groups (Figure 1): two images had failed reconstruction with considerable ghosting and loss of detail, one image had areas of significant signal drop out and four images had minimal parenchymal signal with high signal returned from the major intracranial vessels. This latter group were likely the result of either raised intracranial pressure causing delayed arrival of the tagged bolus or high arterial flow rates associated with patients who are younger (<2 years).

Of the 57 DSC CBF images, 50 (88%) images were classified as having acceptable image quality, 7 (12%) images as poor and none as good. The seven poor-quality DSC images resulted from: two images had large areas of corrupted signal owing to the presence of *in situ* ventricular drainage devices, three images had contrast agent administration failures, one image had large areas of signal drop out and artefact, possibly owing to motion, and one image exhibited high contrast with little white matter signal owing to their young age (4 months).

Of the seven poor-quality ASL images, five were imaged under general anaesthesia (GA) compared with four of the seven poor-quality DSC images. However, there was a significant difference in the age distribution of those patients undergoing GA (6.6 ± 3.6 years, $N = 31$) compared with those scanned without an

Table 1. Summary of patient demographics by pathology

Pathology	Frequency	Age, mean $\pm$ SD (years)	Sex
Brain tumour	29	10.7 $\pm$ 3.8	8 F, 21 M
Stroke	6	11.0 $\pm$ 3.5	4 F, 2 M
Neurofibromatosis Type 1	4	6.7 $\pm$ 5.5	4 F
Moyamoya	2	4.5 $\pm$ 0.7	2 F
Focal cortical dysplasia	1	4	1 M
Sickle cell disease	1	8	1 M
Birth asphyxia	1	4	1 M
Tuberous sclerosis	1	15	1 F
Sturge-Weber	1	0.33	1 F
Neonatal encephalitis (follow-up)	1	7	1 F
No abnormality identified	5	6.4 $\pm$ 5.2	1 F, 4 M

F, female; M, male; SD, standard deviation.

anaesthetic (12.4 $\pm$ 3.1 years, $N = 34$) and it was felt that this had a greater influence on the success of a scan, particularly for ASL where the default timing parameters were suboptimal for very young children. Clearly, the small sample size and the consequent small number of poor-quality images makes it difficult to definitively characterize the dependence of image quality on age or anaesthetic status.

The absence of any ASL images deemed to be of good quality was primarily owing to their general low resolution and the tendency for images to exhibit high contrast between grey and white matter with low signal in the white matter and seemingly random areas of high signal within the cortex. These areas of high cortical signal were generally non-uniform and it was not possible to predict which patient images would be most affected. Several images exhibited particularly high cortical signal within the posterior cerebral hemispheres and occasionally left-to-right heterogeneity, which could potentially lead to diagnostic uncertainty (Figure 2).

Similarly, no DSC images were deemed to be of good quality. This was primarily owing to the low resolution of the EPI acquisition, excessive signal resulting from the intravascular contrast agent exaggerated by the GE acquisition and scattered voxels with no signal owing to failure of the gamma-variate fitting algorithm and subsequent estimation of relative CBF.

Of the 57 cases with both ASL and DSC sequences included in the imaging protocol, 16 (28%) ASL images were judged to be of greater diagnostic value, 33 (58%) images were judged to be of similar diagnostic value and 8 (14%) images were judged to be of less diagnostic value compared with the corresponding DSC images.

In general, the ASL images appeared less sharp and of lower spatial resolution than the DSC images, despite both being 128 $\times$ 128 matrix acquisitions. This presumably resulted from the differences in k -space trajectory and reconstruction used in the 3D ASL acquisition compared with the EPI sequence used

Figure 1. Examples of image artefacts observed in poor-quality arterial spin labelling cerebral blood flow images: (a) failed image reconstruction with ghosting, (b) significant signal drop out and (c) low parenchymal signal with most of the signal originating from the major intracranial arteries.

Figure 2. Examples of spurious high cortical signal (a) in the posterior cerebral hemispheres and (b) in the posterior cerebral hemispheres but more marked on the left.

for the DSC acquisition. However, this apparent lower spatial resolution was not felt to have been deleterious to the diagnostic value of the images in the cases acquired in this study.

The 16 ASL images judged to be of more diagnostic value than the corresponding DSC images could be classified into 5 groups: 2 images had ventricular drainage devices *in situ*, which produced less artefacts on ASL, 6 images contained small areas of low-flow pathology within the grey matter, which produced greater contrast against the adjacent high signal grey matter on ASL, 3 images had large areas of hypoperfusion owing to stroke or moyamoya, 4 images had brainstem tumours and in 1 case, the DSC contrast administration had failed. Some typical examples where ASL was deemed to be of greater diagnostic value are provided in Figure 3. Figure 4 gives an example of a case where the ASL images were deemed to be of similar diagnostic value to the DSC images.

Of the eight ASL images judged to be of less diagnostic value than the corresponding DSC images, 7 images had very low white matter signal or very high cortical signal, making lesion identification more challenging or in some cases impossible (Figure 5). The other case involved a patient with raised intracranial pressure, which resulted in little parenchymal signal with the default timing parameters of the ASL image acquisition.

DISCUSSION

All cerebral perfusion imaging techniques have associated advantages and disadvantages, which have been extensively described in the literature.¹ The absence of ionizing radiation and the lack of need for i.v. injection make ASL a particularly attractive method for imaging in the paediatric population. In addition, one of the disadvantages of ASL, its intrinsically low signal-to-noise ratio, is less of an issue in young children, by virtue of their higher baseline CBF and longer blood and parenchymal T_1 relaxation times.²⁵

In this study, image quality was judged to be adequate in 89% of ASL acquisitions and 86% of ASL acquisitions were judged to be of similar or greater diagnostic usefulness compared with the corresponding DSC acquisitions. These initial cases suggest that

ASL may be of particular value in the identification of brainstem perfusion abnormalities and areas of impaired cortical perfusion. The ASL sequence also appears to be less sensitive to large vessel contamination, although the choice of a GE, rather than a spin-echo, echoplanar acquisition will certainly have influenced this finding.²³

The EPI sequence used in the DSC acquisition is also more prone to artefact from foreign materials (e.g. ventricular drainage devices), the bone of the skull base and air within the paranasal sinuses. As expected, the 3D ASL acquisitions were much less affected by these susceptibility artefacts.

Our ASL protocol used a fixed time delay of 1025 ms between image tagging and acquisition. This was the recommended delay time suggested by the manufacturer for use in the paediatric setting, but obviously it will not be optimum in all subjects. In patients less than 2 years of age and in those with suspected raised intracranial pressure, the non-optimal delay time resulted in a poor image quality and a reduction in perfusion signal from brain parenchyma. A low-resolution scout sequence to guide delay time setting on an individual basis, or a separate ASL protocol with a shorter time delay, could prove effective for imaging patients who are young, where high CBF is expected.

Two ASL images suffered from failed image reconstruction and signal drop out. This is likely to have been due, at least in part, to patient movement and it may have been possible to produce useable images through retrospective or prospective motion correction.^{4,26}

A number of images suffered from scattered foci of high signal intensity within the peripheral cerebral cortex, which may actually have originated from small cortical vessels containing labelled blood.^{4,27} Other images showed high signal within the cortex of the occipital lobes and in some cases left-to-right heterogeneity. This has been described elsewhere and may relate to increased perfusion of the occipital cortex owing to visual stimulation during image acquisition.²⁷ Stimulation of the visual cortex would be reduced by blindfolding, but some patients may not tolerate this.

Figure 3. Examples of arterial spin labelling (ASL) images judged to be of greater diagnostic value than the corresponding dynamic susceptibility contrast (DSC) images: T_1 weighted, T_2 weighted, DSC and ASL images are given for comparison—(a) less artefacts from a ventricular drainage device in the ASL image; (b) a brainstem perfusion abnormality is more obvious on the ASL image; (c) hypoperfusion primarily in the left cerebral hemisphere in a patient with moyamoya, more clearly visualized on ASL; and (d) marked perfusion asymmetry in a patient with moyamoya, only visible on the ASL image.

Compared with DSC images, ASL generally exhibits higher signal in grey matter and lower signal in white matter. While this may be beneficial in some instances, it may mask pathology in others; specifically, low-flow white matter lesions and high-flow grey matter lesions may be more difficult to identify.

The ASL acquisition at 4 min 10 s is significantly longer than the 90-s DSC acquisition used in this study. GA would therefore be

prolonged and perfusion images in children being imaged without GA may be more prone to movement artefact and poor image quality. Nevertheless, we did not see any obvious tendency towards increased motion artefact in the ASL acquisition in the present study. The increased acquisition time may be compensated somewhat in children not requiring cannulation for GA or for other contrast-enhanced sequences, as there may be no requirement to gain i.v. access or administer contrast.

Figure 4. An example of dynamic susceptibility contrast (DSC) and arterial spin labelling (ASL) images judged to be of similar diagnostic value: T_1 weighted, T_2 weighted, DSC and ASL images are given for comparison—a low-flow cortical lesion is clearly visualized on ASL and DSC imaging.

The present study has several potential limitations. Firstly, the overall study sample was small and analysis of the value of ASL CBF imaging in each particular pathology was precluded by the small number of patients. Clearly, a larger study assessing the use of ASL in the general paediatric setting would be a worthwhile future aim, as well as studies looking specifically at individual pathologies. Secondly, the assessment of the images produced and their diagnostic value was subjectively performed with no attempt to assess intraobserver or interobserver variability. The method used is reasonably consistent with how the images are used in practice, as they tend to be used to provide a subjective assessment of perfusion, rather than relying on defined quantitative thresholds to characterize perfusion abnormalities. Thirdly, the diagnostic performance of the perfusion techniques was assessed simultaneously with no blinding. However, blinding of techniques would be difficult to perform, as the differences between the techniques are immediately obvious from the image characteristics. Given the limited number of patients in this study, it was felt likely to be more sensitive to compare the techniques side by side. Lastly, relative CBF maps were used throughout the study for assessing both ASL and DSC acquisitions, rather than performing quantitative modelling

of CBF. While there is clear value in having quantitative perfusion measures, it should not make a significant difference to the qualitative assessments performed in this study, as both relative CBF maps are proportional to the absolute CBF value. Quantitative perfusion maps also make a number of assumptions in their modelling that are not always valid, and many clinical sites do not have the expertise or software necessary to perform the analysis.

CONCLUSION

The results of this study suggest that in the majority of cases, ASL perfusion imaging offers a viable alternative to DSC perfusion imaging of the paediatric brain in clinical practice at 1.5 T. There are, however, some instances where DSC clearly remains the superior technique and for the moment, both techniques will be employed alongside each other at our institution until further refinements and an evaluation of a larger cohort of patients have been made.

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Figure 5. An example of an arterial spin labelling (ASL) image judged to be of less diagnostic value than the corresponding dynamic susceptibility contrast (DSC) image: T_1 weighted, T_2 weighted, DSC and ASL images are given for comparison—a low-flow white matter lesion is not visible on the ASL image owing to lack of contrast with the surrounding low-signal white matter. The lesion is clearly visualized on the DSC image.

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