Arterial Spin-Labeling Perfusion MRI in Pediatric Arterial Ischemic Stroke

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Introduction

Pediatric stroke has been a chronically underestimated and poorly understood brain disorder with no accepted protocol for patient treatment and management [1]. The difficulty resides in the diverse etiology and clinical manifestations of pediatric stroke as well as the lack of suitable evaluation technology. Existing cerebral blood flow (CBF) measurements in adults cannot be easily applied on children due to safety concerns related to the use of radioisotopes and the logistical difficulties in rapidly injecting contrast agents in pediatric patients. Arterial spin labeling (ASL) perfusion MR is ideally suited to measure CBF in the pediatric population, because it is entirely noninvasive and provides improved image quality due to specific physiologic properties of the child brain [2, 3]. The purpose of this study was: 1) to evaluate the feasibility and efficacy of a pulsed arterial spin-labeling (PASL) technique in pediatric stroke; 2) to determine the prevalence of regional CBF abnormalities in pediatric patients with acute and subacute stages of arterial ischemic stroke (AIS); and 3) to explore the clinical significance of ASL perfusion MRI by correlating the degree of perfusion deficit with clinical symptom and outcome.

Methods

From Feb 03 to Oct 06, 9 patients (6 M, 3 F, age range 14months-16years, mean 8.88 years) with presentation of AIS syndromes from any cause were recruited. Patients with prior stroke, hemorrhage or infratentorial lesions were excluded. AIS patients were diagnosed based on clinical assessments by two neurologists (DL & RI) at the Children's Hospital of Philadelphia (CHOP). All patients were scanned at 4-125 hours, mean 60.35 hours after symptom onset. MRI was obtained on Siemens whole-body 1.5T (Vision, Sonata, or Avanto) or 3T (Trio) systems. Written informed consent was obtained from parents or guardians of all participating children. An identical PASL sequence, modified from FAIR with inferior saturation pulses to determine the bolus duration for quantification [3], was added to clinically indicated MRI scans (including diffusion, T1, T2, FLAIR and MRA). A delay time (1-1.5s) was applied between the saturation and excitation pulses to reduce transit artifacts. Imaging parameters were: FOV=20cm, 64x64 matrix, TR/TE=3000/19ms, slice thickness= 8 mm, 2 mm gap for 1.5 T; 5 mm, 1mm gap for 3 T. Eight (1.5T) or 16 (3.0T) slices were acquired using a gradient echo EPI sequence. An M0 image was acquired after the perfusion scans. The raw EPI image series were pairwise subtracted and then averaged to form the mean ASL perfusion images, which were converted into absolute CBF maps based on a PASL perfusion model [3]. Follow-up images were performed in 8 patients 3-12 months later.

Two image analysis methods were employed: 1) Lesion ROI was traced on diffusion images and then was superimposed on CBF images for quantifying mean CBF values within the ROI. 2) A template (SPM2 Pickatlas Toolbox) was used for automatic segmentation of CBF maps (after normalization) into vascular territories within which mean CBF values were obtained. Percentage difference of perfusion between the affected and unaffected hemispheres (= (affected-unaffected)/unaffected x 100%) was calculated in both ROIs and vascular territories. Infarct volume was manually traced on follow up T2 or CT images by a neuroradiologist (JC) using MRICRO.

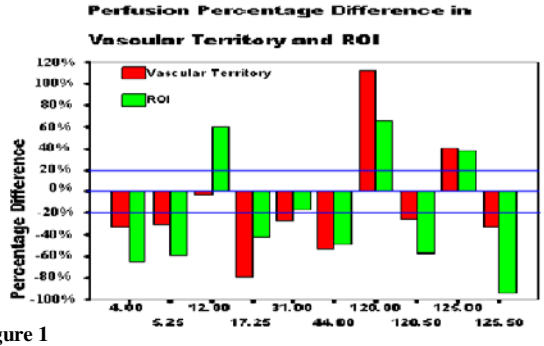

Figure 1

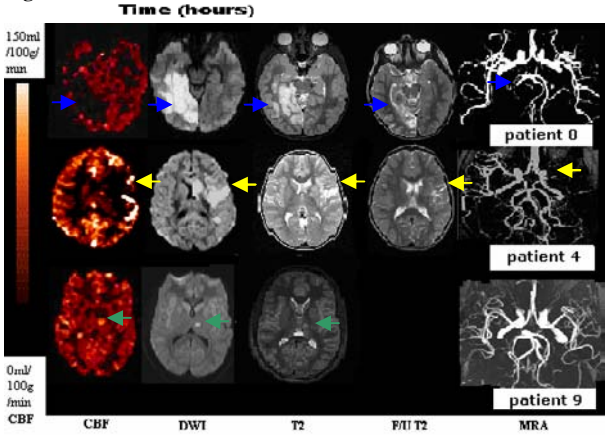

Figure 2.

Patient 8 showed a hypoperfusion lesion (blue arrows) in the right occipital lobe in a 5 yo boy. Imaged at 44h. A follow-up T_2 image showed a large final infarct. MRA showed narrowing of R PCA.

Patient 4 showed a hypoperfusion lesion (yellow arrows) in the left MCA territory in a 10.33 yo girl. Imaged at 31h. A follow-up T_2 image showed a small final infarct. MRA showed occlusion of L M1.

Patient 9 showed a hyperperfused region (green arrows) in the left thalamus in a 13 yo boy. Imaged at 12h. Clinically recovered before being imaged. MRA showed normal signal. (* no follow-up images)

Results

Totally there were 10 ischemic lesions (1 patient had 2 lesions), 7 showed relative hypoperfusion in the affected hemispheres, and 3 showed relative hyperperfusion, 7 in MCA territories and 3 in PCA territories. Percentage differences of perfusion between the affected and unaffected sides measured in ROIs and vascular territories were highly correlated (P=0.012, r=0.754). Figure 1 shows the percentage perfusion differences in ROIs and vascular territories as a function of imaging time from symptom onset in the 10 lesions. By visual inspection, perfusion deficits are compatible with DWI, T2 and follow-up images in all cases.

Moderate to severe hypoperfusion, defined as perfusion difference between the affected and unaffected hemispheres $\geqslant$20% [4], was present in 6 lesions. These lesions are associated with relatively large infarct volumes in follow up images (40.75 ± 37cc). (Fig 2 (patient 8) and Table 1).

Hyperperfusion and ***mild hypoperfusion***: hyperperfusion found in 3 lesions (affected > unaffected hemisphere) (Fig 2 (patient 9) and Table 1) and mild hypoperfusion found in 1 lesion (perfusion difference between the affected and unaffected hemispheres <20%) are associated with small infarct volume (4.61 ± 0.94cc) (one tail T test, P=0.07 compared to hypoperfusion cases) (Fig 2 (patient 4) and Table 1). In particular, patient 9's symptom was spontaneously resolved during MRI session.

Discussion

Our results demonstrate feasibility of PASL in detecting perfusion deficits in the acute and subacute stages of pediatric stroke, with an excellent agreement of ASL perfusion maps with DWI and T2 findings both for hypo- and hyperperfusion. Adult studies have suggested that hyperperfused areas in acute ischemic stroke are consistent with postrecanalization hyperperfusion, vasodilatation, and luxury perfusion [4], and hyperperfusion is correlated with better outcome after acute stroke despite a significant DWI lesion [5,6]. We hypothesize that hyperperfusion or mild hypoperfusion detected using ASL may predict a good clinical outcome in pediatric patients with AIS. The use of ASL is advantageous since it is noninvasive and repeatable, and it provides clinically valid information within reasonable acquisition times.

Table 1	CBF (ml/100g/min)		% of Perfusion Difference in ROI	FU infarct volume (cc)
	ROI	Contralatral		
Pat 8	12.36	24.33	-49%	30.82
Pat 4	26.84	32.49	-17%	3.58
Pat 9	71.44	44.75	60%	*

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