Feasibility of Longitudinal Study using Arterial Spin-Labeling Perfusion MRI in Pediatric Arterial Ischemic Stroke

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Introduction

Cerebrovascular disorders are among the top 10 causes of death in children (1). Brain infarction is a dynamic process and the extent of the lesion determines the clinical prognosis. Detailed knowledge about the hemodynamic and neuroanatomical development of an infarct lesion is fundamental for stroke management, however in pediatrics it is unclear how perfusion and diffusion lesions evolve beyond the acute stage (2). The aim of this study was to investigate the feasibility and utility of pulse arterial spin labeling (PASL) perfusion imaging to follow perfusion deficits and their relation to volumetric changes that occur in the infarct lesion over time. Further aims were to investigate novel pixel-based methods to study perfusion within an acute stroke lesion.

Methods

Three children diagnosed with acute arterial ischemic stroke (AIS) underwent acute MRI examination with PASL perfusion imaging and serial follow-up PASL scans were studied. Repeated PASL scans were performed 11 days - 41 months following symptom onset. All MRIs were obtained on Siemens whole-body 1.5T (Sonata, or Avanto) or 3T (Trio) systems. Written informed consent was obtained from parents or guardians of all participating children. Identical PASL sequences, modified from FAIR with inferior saturation pulses to determine the bolus duration for quantification (3), were added to clinically indicated MRI scans (including diffusion, T1, T2, FLAIR and MRA, Fig. 1). 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). Serial follow-up MRI examinations obtained for clinical indications were used to calculate chronic infarct volume. Two image analysis methods were employed. 1) Lesion ROI was traced on acute diffusion or follow-up T2 images. These were then superimposed on CBF images for quantifying mean CBF values within the ROI at each time point. Inter-hemispheric perfusion deficit (IHPD) was calculated as [(unaffected-affected)/ unaffected] × 100%. Changes in lesion volume over time were tracked and expressed as a percentage of the DWI ROI volume from the acute imaging . 2) Pixel-by-pixel scatterplot of the CBF and ADC values from the initial scan was analyzed to evaluate the distribution of voxels within each ROI. ROIs from different time points are presented in different colors.

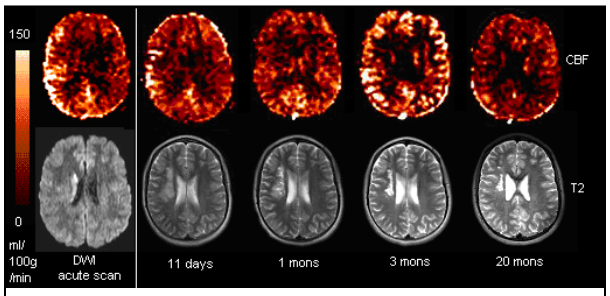

Figure 1.

Results

All 3 patients presented with focal neurological deficits consistent with the DWI abnormalities on the acute imaging. Patients had either 3 (2/3 patients) or 4 (1/3 patients) follow up scans. Ischemic lesions showed an early increase in volume followed by a robust and exponential decrease over time ($r = 0.58$, $p = 0.034$), (Fig. 1 and 2). The mean infarction size for these 3 patients was 9.77 mL at 0-2 months after stroke onset, 2.95 mL at 3-6 months, 1.67 mL at 7-12 months and 1.5 mL at ≥ 1year. Infarct volumes stabilized after 12 months. Changes in lesion volume over time were negatively correlated with changes in IHPD ($r = -0.446$, $p = 0.063$). Furthermore, there was a trend towards a positive correlation between temporal changes in lesion volume and absolute CBF ($r = 0.399$, $p = 0.088$) (both lesion size and CBF within the lesion decrease with time). Figure 3 displays voxel-based scatterplot of changes in CBF (y-axis) and ADC (x-axis) values of one patient over time (5 scans). Viable tissue within regions of restricted diffusion (low ADC values, $< 120 \times 10^{-5} mm^2/s$) were seen to have relatively higher CBF (upper left quadrant) and than those within the ischemic core (lower left quadrant) during the initial scan (Hotelling's T square test, $P<0.001$).

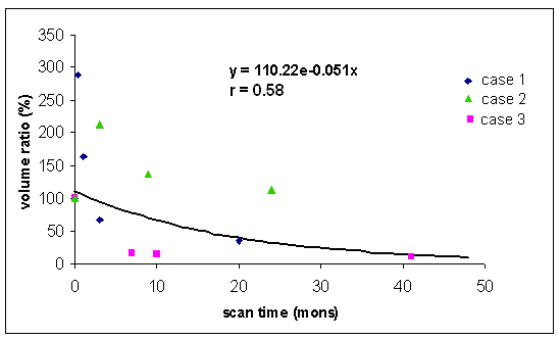

Figure 2.

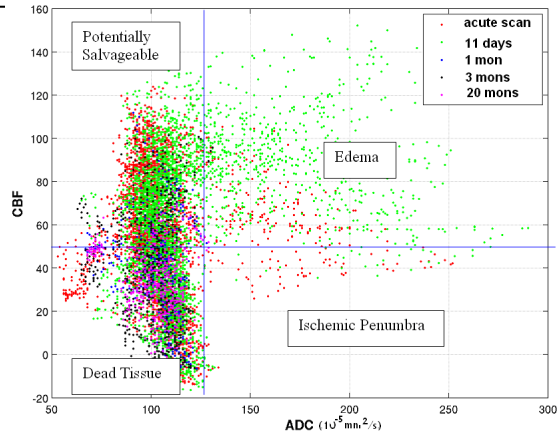

Figure 3.

Discussion

This data from a small cohort of pediatric stroke patients demonstrates a decrease in lesion volume over time outside of the subacute time window. This reduction in lesion volume may be due, in part, to resolution of edema and lesion consolidation with dismantling of necrotic brain tissue, resulting in pseudocyst formation. The correlation between temporal changes in lesion volume and CBF supports the clinical validity of longitudinal PASL scans to follow stroke development. Furthermore, voxel-based analyses indicated that there is a wide range of CBF within tissue that has restricted diffusion. Regions of tissue within a lesion that demonstrate a combination of robust CBF and low ADC values may be potentially salvageable. These regions of potentially salvageable tissue may explain the constriction of a lesion volume over time. Longitudinal ASL scans performed in conjunction with diffusion and conventional MRI, may provide a means to track the evolution of an ischemic lesion and provide novel insight to the dynamic physiology within an ischemic injury.

References:

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