Arterial spin labeling perfusion imaging performed in acute perinatal stroke reveals hyperperfusion in association with cerebral ischemic injury

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PURPOSE: Stroke in neonates is common but its etiology, pathophysiology and optimum treatment remain elusive. To better understand perinatal stroke and potential of thrombolysis, knowledge of perfusion in the stroke core and penumbra would be instructive. To assess cerebral perfusion in neonates, noninvasive arterial spin labeling (ASL) is particularly attractive as bolus perfusion methods are invasive and require use of contrast agents which are not yet FDA approved for use in neonates. Perfusion magnetic resonance imaging (pMRI) in adult acute stroke often reveals a hypoperfused region in the fixed ischemic injury shown by diffusion weighted imaging (DWI) (the core) and occasionally in adjacent brain (the ischemic penumbra). However, unlike in adults, stroke perfusion has not been extensively studied in neonates with acute stroke. The purpose of this study was to evaluate the feasibility of acquiring ASL in neonates with acute stroke, and to determine qualitative perfusion patterns. We hypothesized that altered regional perfusion accompanies the ischemic injury in focal perinatal stroke.

METHODS: Experiment: Neonates (0-28 days of life) who presented with clinical features of acute stroke underwent MR imaging at 3T. pMRI employed a pseudo-continuous arterial spin labeling (PCASL) sequence with multi-slice echo planar readouts at 3x3x5mm^3 resolution with TE/TR = 12ms/3.5s, labeling time = 1.6s, a post-labeling delay = 1.5s, 9 axial slices, and scan time ~5 min. Forty label/control image pairs were acquired, subtracted, and averaged to obtain contrast maps proportional to cerebral blood flow (CBF). DWI, susceptibility weighted imaging (SWI), and T2-weighted series were also obtained with standard protocols.

Patient study: Data were collected on 33 neonates with acute stroke. A pediatric neurologist and pediatric neuroradiologist evaluated the images for stroke classification and perfusion signal pattern. Acute stroke was classified as either arterial or venous. Core infarction was considered to be the region of decreased signal on apparent diffusion coefficient (ADC) maps. Regional perfusion signal was in the ischemic core was compared to the homologous uninvolved region in the contralesional hemisphere. Differences in perfusion signal, presence of hemorrhage, and history of seizures across stroke types were determined using Fisher's exact test. Results were considered statistically significant at a level of $p < 0.05$.

RESULTS: Of the 33 datasets acquired, 10 were excluded due to poor data quality, leaving 23 for further analysis (15 male, mean gestational age = 38.9 weeks, median age at MRI = 3 days). The type of strokes were as follows: 13 (57%) were arterial ischemic stroke (AIS), 9 (39%) venous, and 1 (4%) both. Evidence of regional **hyperperfusion** existed in 10/13 (77%) with AIS and 1/9 (11%) with venous stroke. Figure 1 shows a patient with AIS and hyperperfusion on ASL. Hyperperfusion was part of a heterogeneous pattern of hypo- and hyperperfusion in 3 (23%) neonates with AIS and 1 (11%) with venous stroke. Hypoperfusion was present only in venous strokes (n=3; 33%). The difference in perfusion signal pattern across stroke types was statistically significant ($p < 0.001$). Hemorrhage occurred in 1/13 (8%) with AIS and 8/9 (89%) with venous stroke ($p < 0.001$). Electroencephalography (EEG) data obtained at presentation were available for 22 (96%) of patients. Twenty (87%) had either electrographic seizures or focal sharp waves in the same hemisphere as the infarction. Clinical seizures occurred in 13/13 (100%) with AIS and 06/9 (67%) with venous stroke ($p = 0.01$).

CONCLUSIONS: Arterial spin labeling pMRI can be successfully obtained in neonates who present with acute stroke. Unlike adults, pMRI in neonates often reveals hyperperfusion rather than hypoperfusion. This hyperperfusion may be due to early spontaneous reperfusion combined with increased neuronal demand due to stroke-associated seizure. Future work will assess whether or not perfusion signal in the acute stage after stroke is associated with neurological outcomes.

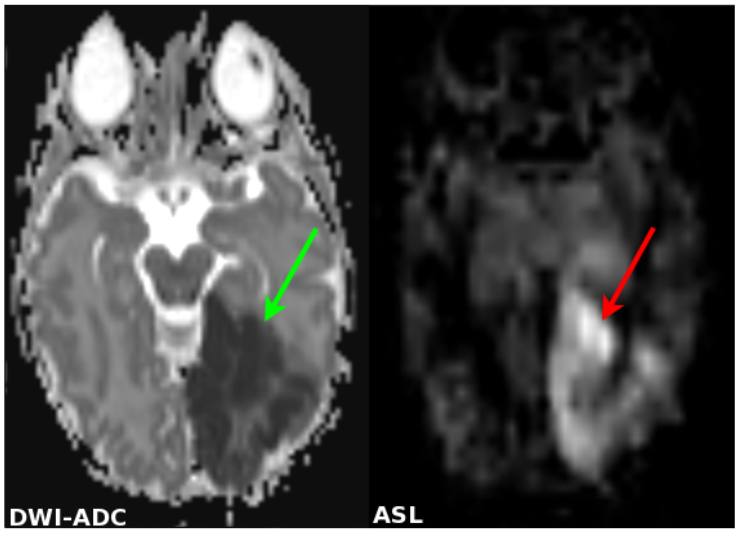

Figure 1: Axial slices showing region of arterial ischemic stroke with decreased diffusion on ADC (green arrow) and increased perfusion on ASL (red arrow).