Initial Experience with pseudo-continuous Arterial Spin Labeling (pCASL) in the Infant Brain

M. Dehaes[1,2], R. Pienaar[2], J. S. Soul[3], and P. E. Grant[1,2]

[1]Division of Newborn Medicine, Department of Medicine, Children's Hospital Boston, Harvard Medical School, Boston, Massachusetts, United States, [2]Center for Fetal-Neonatal Neuroimaging & Developmental Science, Boston, Massachusetts, United States, [3]Department of Neurolory, Children's Hospital Boston, Harvard Medical School, Boston, Massachusetts, United States

Objectives & Hypothesis

Cerebral perfusion is correlated with cerebral glucose metabolism and provides important physiological information. Cerebral perfusion has the potential to better characterize normal development and improve our understanding of metabolic changes that occur with injury. Pseudo-continuous Arterial Spin Labeling (pCASL) provides quantitative information on cerebral blood flow (CBF) in mL/100g/min and compared to pulsed ASL (PASL) has increased signal to noise and less sensitivity to delays in arrival times **[1]**. The increased SNR allows faster scan times making pCASL more clinically feasible and the relative insensitivity to arrival times makes pCASL more robust in infancy given the changing blood flow during early development and changes in blood flow that occur with therapeutic hypothermia. Here we report our initial experience with pCASL in the first four months of life.

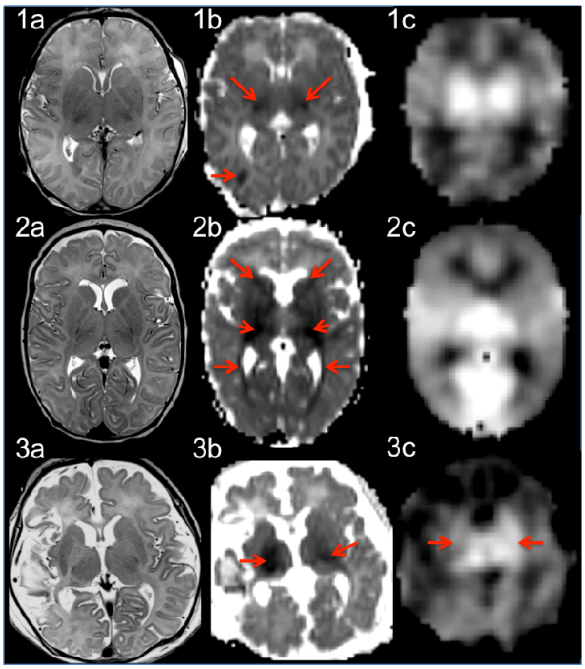
Methods

All MR images were acquired on a Siemens Trio 3T with a 32-channel head coil. In particular, structural images were acquired using a MPRAGE sequence with motion correction enabled **[2]**. pCASL was obtained in 13 subjects < 4months. This study was IRB approved. The pCASL sequence was similar to that of **[3]**. Imaging parameters of the scan were label time = 1.5 s, delay time = 1.2 s, TR/TE = 7740/20 ms. The pixel bandwidth was 3005 Hz and the slice thickness was 5 mm. The label location was individually optimized to be in the neck region. In neonates, this typically resulted in the label being placed 5 cm below the imaging slices. Scan time was 3 minutes 58 seconds. Each slice was acquired using a 2D EPI sequence. DTI images were acquired with TR/TE = 8000/88 ms, b = 1000 s/mm^2, FOV = 256 x 256 and acquisition matrix = 128 x 128, while structural T2 images with TR/TE = 11000/90 ms, FOV = 146 x 180 and acquisition matrix = 291 x 512. Pre-processing operations included resetting of the orientation of structural and functional images as well as alignment to the AC-PC (anterior and posterior commissures) line. Functional images were realigned and co-registered to the anatomical images using SMP8 (Wellcome Trust Centre for Neuroimaging, University College London, UK). Functional images were also smoothed before the analysis. Analysis of pCASL images was performed using a specific toolbox developed at U. of Pennsylvania **[4]**. Label images were simply subtracted with control images. Quantitative CBF estimates were computed using eq. (1) from **[5]**.

Results

Table 1 Clinical summary from subjects and averaged whole brain CBF estimations [mL/100g/min]. Subjects with bold ID numbers are depicted in **Fig. 1**.

ID	Age	Clinical Summary	Whole Brain CBF
Neonates ≤ 7 days			
n1	7 days	37 wk GA, desaturations, normal clinical MRI (discharged without O_2 requirements)	31
n2	0 days	40 wk GA, hypoxic ischemic encephalopathy, receiving therapeutic hypothermia while scanned, profound hypoxic ischemic injury pattern on MRI (died)	48
Infants ≤ 16 wks			
i1	15 wks	26 + 3/7 wk GA, post hemorrhagic hydrocephalus, white matter injury of prematurity (hypertonicity at 18 wks)	25
i2	7 wks	40 wk GA, hypotonia, acute cardiac arrest within 24 hours of MRI (died)	98
i3	7 wks	Fever, meningitis, seizures, tiny venous infarct on MRI (discharged with normal exam)	61
i4	3 wks	Prior ECMO, chronic right MCA stroke, acute arrest with cardiac arrest pattern on MRI	30



Acceptable image quality was obtained in six of thirteen subjects (**Table 2**). Quantitative CBF were computed for 2 neonates (≤ 7 days) and 4 infants (> 7 days but ≤ 16 wks). No signal was identified in the arteries or veins. Three subjects were imaged within 24 hours of cardiac arrest and 2 of 3 showed marked whole brain elevated CBF (**n2** and **i2**) indicating rebound hyperperfusion even with therapeutic hypothermia in the neonate. Both neonates showed elevations in CBF compared to reported normal PASL 3T values (16 ± 6 mL/100g/min) **[6]** but normal values with pCASL have not been established in the 0 to 4 month age group. In these three cases ADC abnormalities were similar or larger than T2 abnormalities and ASL abnormalities were similar or larger than the ADC abnormalities as shown on **Fig. 1**. The high CBF in i3 may be related to seizure activity.

Fig. 1 a) T2, b) ADC map, c) pCASL. **Row 1:** Term newborn on first day of life with history of hypoxic ischemic encephalopathy (HIE). Imaging shows a pattern of profound HI injury or cardiac arrest with diffusely increased T2 in deep gray nuclei and decreased diffusion in VL thalamus and in the right occipital lobe (arrows). pCASL shows marked increased CBF most marked in the deep gray nuclei but also in the cerebral cortex with a mean CBF of 48 mL/100mg/min. Thus despite hypothermia the CBF is high. The neonate died a few days later. **Row 2:** 7 week old former term infant with respiratory distress followed by cardiac arrest, imaged within 24 hours of the arrest. Imaging shows a pattern of cardiac arrest with diffusely increased T2 and decreased diffusion throughout the deep gray nuclei but most prominently in the VL thalamus extending into optic radiations (arrows). pCASL shows marked increased CBF most marked in the deep gray nuclei but also in the cerebral cortex with a mean CBF of 98 mL/100g/min. In both cases the CBF abnormalities are far more diffuse than the ADC abnormalities. **Row 3:** 3 week old neonate with seizures post ECMO, chronic right hemispheric stroke. Imaging shows new pattern of cardiac arrest with diffusely increased and decreased diffusion throughout the deep gray nuclei most marked in VL thalamus (arrows). pCASL as expected shows decreased CBF in the encephalomalic region but increased CBF in the deep gray nuclei (arrows) with a whole brain mean CBF of 30 mL/100g/min.

Discussion & Conclusion

pCASL has tremendous potential in improving our understanding of physiological changes with injury and often show more extensive changes than ADC abnormalities. Better characterization of normal subject is needed to determine if there are more subtle increases in CBF in cases where there are no ADC abnormalities, such as the case of meningitis (i3). Follow-up studies are needed to determine if hyperfusion alone can be associated with volume loss and is a potential marker for impending apoptosis.

Acknowledgements & References

This work was supported by the NIH/NICHD grant #R21-HD058725. **[1]** Wu WC *et al.* Magn Reson Med. 2007 Nov; 58(5):1020-7 **[2]** Tisdall MD *et al.* In proceeding of ISMRM 2010. **[3]** Durduran T *et al.* J biomed Opt. 2010 May;15(3): 037004. **[4]** Wang Z *et al.* Magn Reson Imaging, 2008;26(2):261-9. **[5]** Wang J *et al.* Magn Reson Med. 2003 May;50(3):599-607. **[6]** Miranda MJ *et al.* Pediatr Res. 2006 April; 60(3):359-63.