Pulsed Arterial Spin Labeling Perfusion MR in Neonates with Severe Congenital Heart Defects –-Feasibility, Reliability and Repeatability

J. Wang[1], D. J. Licht[2], D. W. Silverstre[2], S. C. Nicolson[2], L. M. Montenegro[2], S. Tabbutt[2], S. M. Durning[2], M. Shabbout[2], D. M. Shera[2], J. W. Gaynor[2], T. L. Spray[2], R. R. Clancy[2], R. A. Zimmerman[2], J. A. Detre[1]

[1]University of Pennsylvania, Philadelphia, PA, United States, [2]the Children's Hospital of Philadelphia, Philadelphia, PA, United States

Introduction Arterial spin labeling (ASL) perfusion MR is idealy suited to measure cerebral blood flow (CBF) in the pediatric population, because it is entirely noninvasive and provides improved image quality due to normally increased blood flow and water content of the child brain. While preliminary data demonstrated a substantial (70%) improvement in the signal-to-noise ratio (SNR) of pediatric perfusion images as compared to adult images (1), the feasibility of ASL perfusion MR in neonates and infants has not been exploited. Particularly, diminshed CBF has been suspected to be a major etiology for impaired neurological outcome of neonatal patients undergoing surgeries for congenital heart defects (CHD). The purpose of this study was to test the feasibility of perfusion imaging in neonates with severe forms of CHD using a pulsed ASL (PASL) technique at 1.5T. The PASL method was validated with perfusion scans before and after hypercapnia stimulation. The precision of the perfusion measurement was assessed using repeated scans under the same physiological condition.

Methods 25 infants (13 female, mean weight=3.1kg range 2.4-4kg; mean age=4.4days range 1–25days) underwent MR scanning on a 1.5T Siemens Sonata system, using the product head coil as receiver and body coil as transmitter. All patients were intubated and received similar sedation and muscle relaxation. The PASL sequence was a modified FAIR technique, as described previously (1). A gradient-echo EPI sequence was used for image acquisition (FOV=17cm, 64x64matrix, TR/TE=3000/19ms, 8 slices of 8mm thickness with 2mm gap). Each PASL scan with 80 acquisitions took 4min. Three PASL scans with inversion times (TI, duration between the labeling pulse and image acquisition) of 1.4, 1.7 and 2.0s were carried out immediately before surgery, under standard ventilator settings ($PaCO_2$=40.7±5.4). PASL scans with TI of 1.7s were carried out under conditions of increased carbon dioxide ($PaCO_2$=61.6±7.0), and was repeated in 17 patients to test the repeaibility (2). M_0 images were acquired after PASL scans for CBF quantification. T1 and T2 weighted structural MR images were also obtained. PASL image series were pair-wise subtracted and then averaged to generate the mean difference perfusion images. These images were converted into absolute CBF maps based on a PASL perfusion model (1), assuming a blood T1 of 1.5s (3) and a blood brain water partition coefficient of 1.1ml/g (4). At baseline, a considerable amount of (average 40%) brain pixels of the neonatal perfusion images showed negative values, leading to spuriously negative global CBF values in 5 neonates. As discussed below, these negative signals arised primarily from special physiological conditions in this patient group, and a reasonable estimation of the global mean CBF was achieved by clipping these negative pixel values to 0. The global CBF values acquired with TI=1.7s pre- and post-hypercapnia were used for statistical analyses..

Results and Discussion The measured global CBF values were 18.1±8.5 and 36.9±18.7ml/100g/min pre- and post-hypercapnia conditions (p<0.001), with an average signal change of 99.1±50% (Fig. 1). This phenomenon was seen in every patient. Vascular effects were observed in the baseline perfusion images acquired with a long TI of 2.0s, suggesting prolonged arterial transit time in this patient group. The two repeated post-hypercapnia PASL scans showed a high repeatability of 4.1% (4.0ml/100g/min) at 95% confidence interval. In addition, the neonatal perfusion images show higher blood flow in brain stem, thalamus, basal ganglia and sensorimotor cortex, which are in excellent agreement with FDG PET results (5). Univariate analysis found a lower hemoglobin was associated with higher baseline CBF (p=0.04). A larger fractional CBF change induced by hypercapnia was associated with a lower hemoglobin (p=0.012) and higher mean arterial pressure (p=0.004) (Fig. 2). Several special physiological conditions may affect the accuracy of perfusion measurements in neonates with severe CHD. In this study, the body coil was used as transmitter resulting in a labeling volume that covers the whole neonate body. Because the blood flow in neonates with CHD is extremely slow and tracer life time (blood T1) is very long, a considerable amount of labeled spins still stay in the brain tissue when the subsequent (control) acquisition is carried out, leading to cross-contamination of the label and control acquisitions and negative signals in the baseline perfusion images. The bypass (shunt) between the pulmonary and systemic circulations present in CHD infants may also be a factor since the labeled blood from the body may be shunted to the brain instead of relaxing during the pulmonary circulation. We tested this hypothesis by scanning 3 neonatal CHD patients using PASL scans with increased TR of 4s and with confined tagging region above possible shunt locations, respectively. In both cases, the negative values were greatly reduced and the global CBF values were similar to those obtained using the original PASL method with clipped negative values (Fig. 3). Post-hypercapnia measurements did not change with the different techniques. Due to the severely prolonged transit time and the mix of label and control signals, the baseline CBF values may be underestimated in the present study whereas the perfusion increase in response to CO_2 is very robust. The feasibility, reliability and repeatability of PASL perfusion MR in neonates with CHD were demonstrated. However, the accuracy of severely low CBF measurements in the presence of prolonged transit time along with their physiologic significance require continued investigation.

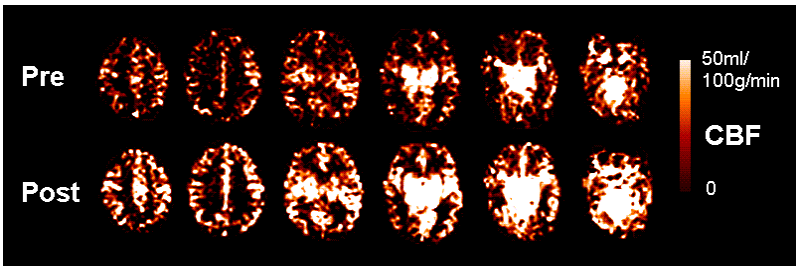

Fig. 1 CBF images of a neonate (5 days) with CHD pre- and post-hypercapnia.

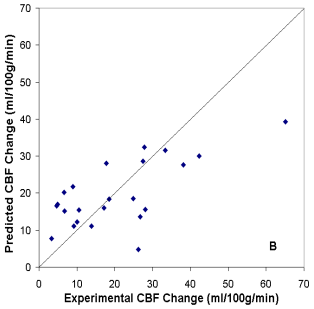

Fig. 2 Predicted vs. measured CBF change with hypercapnia. Equation is ΔCBF=43.3+0.48xMAP–3.4xHb

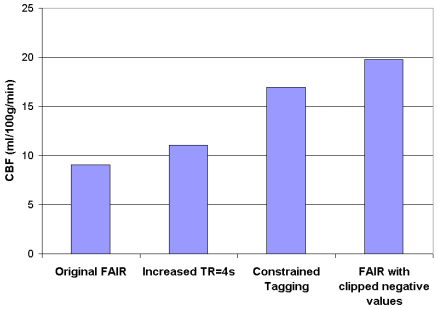

Fig. 3 Comparison of CBF values by various PASL techniques.

References (1) Wang J et al. *JMRI* **18**: 404-13; 2003. (2) Bland JM & Altman DG. *BMJ* **313**:744; 1996 (3) van der Knaap MS et al. *Neuroradiology* **31**:459-470; 1990. (4) Herscovitch P & Raichle ME. *JCBFM* **5**:65-9; 1985 (5) Chugani HT *Prev Med* **27**:184-188; 1998