Exploring spatiotemporal dynamics of the cerebral blood flow of perinatal human brains with arterial spin labeling

Minhui Ouyang[1], Peiying Liu[1], Hanzhang Lu[1], Lina Chalak[2], Jonathan M Chia[3], Andrea Wiethoff[1], Nancy K Rollins[4], and Hao Huang[1]

[1]*Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, TX, United States,* [2]*Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, TX, United States,* [3]*Philips Healthcare, Cleveland, Ohio, United States,* [4]*Radiology, Children's Medical Center, Dallas, Texas, United States*

Target audience: Clinicians, MR physicists and neuroscientists interested in measuring regional cerebral blood flow of perinatal brains from 30 to 45 weeks of gestation.

Purpose: Cerebral blood flow (CBF, mL/100g/min) couples to neural activity and can be used to characterize normal brain development [1]. The 3rd trimester is characterized by rapid brain growth. However, little is known about spatiotemporal changes of CBF of human brain during this period. Previously, positron emission tomography (PET) studies of human brain development suggested that local cerebral metabolic rates for glucose (LCMRglc) increase rapidly and are regionally heterogeneous from birth to 2 years-of-age [2]. We hypothesized that the rapid and heterogeneous brain development in early postnatal years is the extension of the heterogeneous brain development in the 3rd trimester. Arterial spin labeling (ASL) is a noninvasive perfusion imaging method for quantifying regional CBF using labeled blood as an endogenous tracer. ASL perfusion imaging of perinatal brains can be found only recently in the literature [3-6], most of which are conference publications. Slower CBF in perinatal brains from 30 to 45 weeks of gestation (wg) compared to that in adult brain makes ASL of perinatal brains difficult due to the balance between the use of a longer post labeling delay time [3] and the signal-to-noise ratio (SNR) of ASL data. In this study, we aim to acquire highly reproducible and well validated ASL data of perinatal brains in the 3rd trimester with sequence optimization as well as explore the CBF dynamics during this period.

Methods: *Participants:*9 newborn babies (Gestational age at scan: 32 to 45 *wg*) were scanned on a 3T MR system (Achieva, Philips Healthcare, Best, The Netherlands). These neonates were pre-term or term, carefully screened by neonatologists as normal babies with no brain pathology confirmed by clinical MR images. *Data acquisition:* Cerebral perfusion images were acquired with a pseudo-continuous arterial spin labeling (pCASL) method using single-shot gradient-echo echo-planar imaging, field of view = 160×160mm, acquisition matrix = 44×46, voxel size = 3.64×3.48mm, 16 slices acquired in ascending order, slice thickness = 3.5 mm, no slice gap, labeling duration = 1650ms, post labeling delay = 2500ms, TR/TE = 4380/7.34ms. The center of the labeling plane is located at the tip of the pons with 8mm gap below the imaging slices. In addition, a high resolution T2-weighted image was acquired with following parameters: turbo spin echo sequence, TR/TE = 3000/135ms, 65 slices, voxel size =1.5×1.5×1.6 mm^3, field of view = 160×160×104 mm^3. *Data analysis:* Motion correction was applied to pCASL data using SPM8. Difference images between control and label images were calculated using an in-house MATLAB program and corrected for each imaging slice's delay time to get a CBF-weighted image. An absolute CBF map was estimated using the equation from Alsop and Detre [7]. T2-weighted images were co-registered to the pCASL mean control image for anatomical reference.

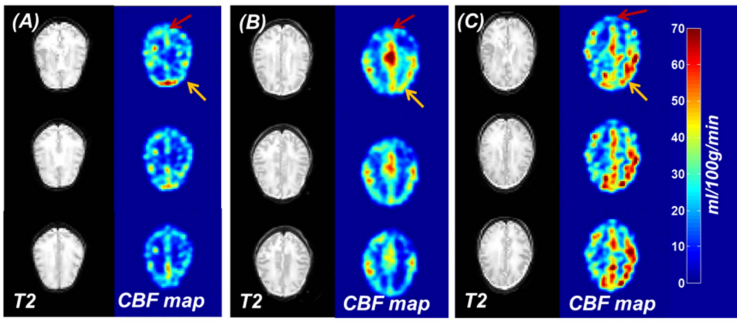

Fig. 1: ***CBF distribution maps and corresponding T2 weighted image in different axial planes of neonate brains at 32.71 wg (A), 35.86 wg (B) and 45 wg (C).***

Results: Figs. 1A, 1B and 1C show the typical CBF distribution maps at early (32.71 week), middle (35.86 week) and the late (45 week) time point of 3rd trimester, respectively. The corresponding T2-weighted images are displayed for anatomical guidance. By comparison of CBF maps at these three different time points in Fig. 1, consistently low CBF in the occipital lobe (red arrows) and apparently higher CBF in some areas of the frontal lobe (yellow arrows) can be appreciated. Fig.2 shows the regional CBF dynamics with ASL acquired from perinatal brains of a comprehensive age range (9 neonates from 32.71 to 45 weeks). The upper panel in the Fig. 2A shows the T2-weighted images as anatomical reference and lower panel shows corresponding CBF maps. For each subject, two regions-of-interest (ROI) in the occipital lobe (red arrows) and two ROIs in the frontal lobe (green arrows) were selected (Fig. 2A). Fig. 2B demonstrates the linear relationship between mean CBF value in the frontal (green) or occipital (red) lobe and age. Fig. 2B indicated that the CBF values in the frontal lobe increase with age significantly (P =0.0247) while CBF values in the occipital lobe show no significant age-related difference (p=0.4529).

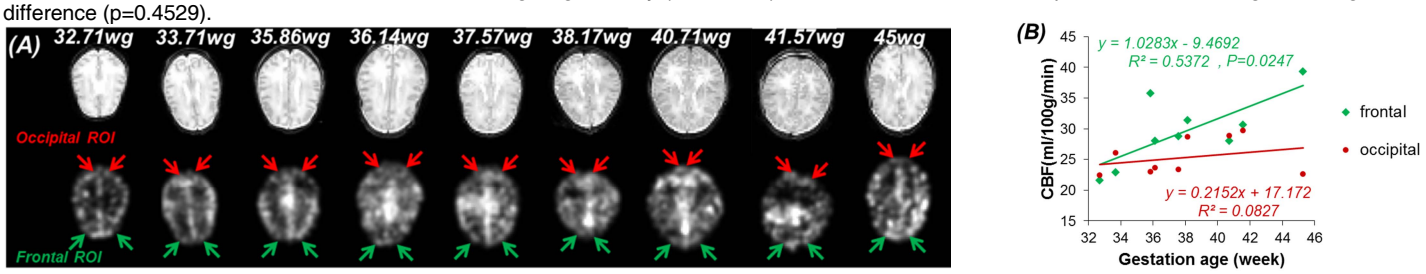

Fig. 2: Regional CBF dynamics with ROI analysis. (A)T2-weighted image (upper) and corresponding CBF map (lower) of each subject; (B) Relationship of regional CBF values and gestation ages. Red and green arrows in (A) indicate the occipital and frontal ROIs, respectively.

Discussion and conclusion: During the 3rd trimester, the brain is developing rapidly yet heterogeneously. Oxygen and glucose are the main substrates supplying energy for the complicated molecular and cellular processes that take place in the brain and are essential for brain maturation. Both oxygen and glucose are delivered to different brain regions by blood flow. Measuring the regional CBF in the brain during the maturation process provides the key information about local functional activity related to brain development. Previous investigations with PET [e.g. 2,8], histology [e.g. 9] and DTI [e.g. 10] have suggested heterogeneous metabolism, synaptogenesis and dendrite growth in early developing cerebral cortex. Although the underlying mechanism of significant CBF increases in the frontal area and relatively constant CBF in the visual cortex as shown in Fig. 2 is not known, it has been found in the literature [11] that primary visual cortex develops earlier than prefrontal cortex in prenatal stage. The heterogeneity of the CBF dynamics between these brain regions is clear in Fig. 2. Noninvasive pCASL of perinatal brains could offer new information of regional CBF to better understand the rapid and complicated processes in this vital developmental stage. In the future, we will confirm the reproducibility of neonate pCASL scan and validate of the measured absolute CBF values. With inclusion of more samples, our ultimate goal is to reveal the accurate regional CBF dynamics of the perinatal brains.

References: [1]Detre et al (2012). JMRI 35:1026. [2] Chugani et al (1987) Annals of Neurology 22: 487. [3] O'Gorman et al (2011). Proc. Intl. Soc. Mag. Reson. Med. [4] O'Gorman et al (2012) Proc. Intl. Soc. Mag. Reson. Med. [5] Dehaes et al (2011). Proc. Intl. Soc. Mag. Reson. Med. [6] Pienaar et al (2012) Neuroimage 63:1510. [7] Alsop et al (1996) J Cereb Blood Flow Metab 16: 1236. [8]Ghugani and Phelps, (1986) Science 231:840. [9] Huttenlocher and Dabholkar (1997) J Comp Neurol 387: 167. [10] Huang et al. (2013) Cereb Cortex 23: 2620. [11] Tau and Peterson (2010) Neuropsychopharmacology 35: 147. **Acknowledgement:** This study is sponsored by NIH MH092535 and NIH MH092535-S