3D GRASE pseudo-continuous arterial spin labeling (pCASL) of preterm human brains

Minhui Ouyang[1], Peiying Liu[1], Hanzhang Lu[1], Tina Jeon[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, TX, United States*

Target audience: MR physicist, pediatric radiologist, neurologist and neonatologist

Purpose: Quantification of regional cerebral blood flow (CBF) is important for understanding the functional and behavioral development of human brain [1]. Arterial spin labeling (ASL) is a noninvasive perfusion imaging method for quantifying regional CBF using magnetically-labeled blood as an endogenous tracer. Limited studies on ASL for measuring CBF in neonates have been reported just recently [2~4]. However, accurate quantification of regional CBF in preterm neonates remains challenging due to extremely slow blood velocity in their brains comparing to that in adult brain, and therefore no standardized ASL protocol has been established for preterm brains. The 3rd trimester is characterized by rapid yet heterogeneous brain growth. Blood flow delivers both oxygen and glucose to different brain regions for supplying energy. Measuring the regional CBF in developmental brains provides the key information about local functional activity related to brain maturation. The purposes of our study are 1) to optimize 3D GRASE pseudo-continuous ASL (pCASL) protocol for reproducible and well validated ASL in preterm human brain; and 2) to explore the spatiotemporal CBF distribution and relationship between regional CBF and regional microstructural changes during the 3rd trimester.

Methods: *Participants:* 72 neonates (Age at scan: 30 to 43 *weeks of gestation (wg)*) were scanned with 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 read by a pediatric neuroradiologist. 14 of them were scanned with Phase-Contrast (PC) MRI, 12 of them were scanned with ASL. In addition, DTI of all 72 subjects was also acquired. *Data acquisition:* Cerebral perfusion images were acquired with pCASL method using 3D GRASE readout with background suppression, field of view = 140×140mm, acquisition matrix = 40×40, voxel size = 3.5×3.5mm, 13 slices acquired with slice thickness = 4 mm, no slice gap, labeling duration = 1650ms, post labeling delay = 2500ms, TR/TE = 4462/18ms. The center of the labeling plane was located at the tip of the pons with 16mm gap below the imaging slices. Global CBF was measured by applying PC MRI in the four feeding arteries of the brain, left/right internal carotid arteries (ICA) and left/right vertebral arteries (VA). In addition, an auxiliary scan for estimating the equilibrium magnetization of brain tissue (M^0_{brain}) was acquired with TR/TE = 1857/18ms and voxel size = 3.5×3.5×4 mm^3. The DTI parameters were: TE/TR=78/6850ms, in-plane imaging resolution=1.5x1.5mm^2, slice thickness=1.6mm, b-value = 1000 sec/mm^2, repetition=2. *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 divided by the value of M^0_{brain} to get relative CBF map. An absolute CBF map was estimated using the equation from Alsop et al. [5]. To correct the absolute CBF map, the M^0_{brain} was obtained from the auxiliary scan [6]. Fractional anisotropy (FA) was calculated with DTIStudio. Local CBF of 12 subjects and FA of 72 subjects were measured at the frontal and occipital cortical regions of interests (ROI). Intraclass correlation coefficient (ICC), defined as the proportion of the total variance due to the between-scan variance, was calculated to assess the reproducibility of ASL scans [7].

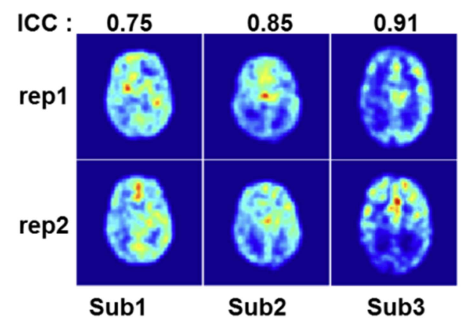

Fig. 1: (upper) Test-retest reliability of the experiment measure of CBF. Same slices of CBF maps from two repetitions of scans are shown as "rep1" and "rep2".

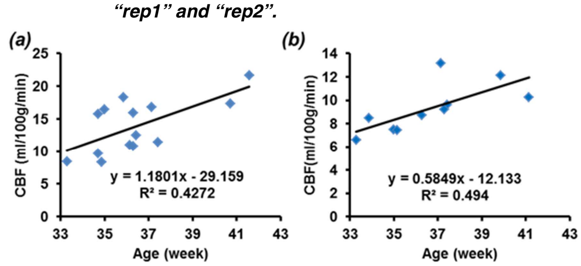

Fig. 2: (a) Whole brain average CBF measured by PC MRI increases significantly (p<0.01) with age. (b) Average CBF from slice at similar anatomical location measured by ASL increases significantly with age (p<0.05).

Results: In Fig. 1, ICC values of three subjects are 0.75, 0.85 and 0.91, indicating moderate-to-strong reliability (ICC=0.75~0.95) [8]. Fig. 2 shows that both whole brain CBF values obtained from PC MRI (Fig. 2a) and CBF values measured by ASL from a slice at similar anatomical location (Fig. 2b) increase significantly with age (p<0.05). Fig. 3b and Fig. 3c demonstrate the linear relationship between mean CBF values and age (Fig. 3b) and between FA values and age (Fig. 3c) in the frontal (blue) or occipital (red) lobe. Faster changes in frontal lobe, namely faster CBF increases and faster FA decreases, compared to those in occipital lobe can be appreciated in Fig. 3b and Fig. 3c.

Discussion and conclusion: We have optimized 3D GRASE pASL sequences to get reproducible regional CBF of the preterm brains. We found a longer post labeling delay time in pCASL is needed due to the small blood velocity. We also found that adding background suppression greatly enhanced signal-to-noise ratio (SNR) of the CBF map. Moderate to strong reliability of the optimized sequence has been revealed in Fig. 1. With significant age-dependent increase of CBF measured with PC MRI as the reference (Fig. 2a), significant age-dependent increase of ASL in typical 2D anatomical slice was also found (Fig. 2b). Despite significant age-dependent CBF increases from both measurements, further validation will be needed by directly correlating the CBF values measured from ASL to the CBF values obtained from PC MRI of the same group of subjects. The distribution of increased blood flow is demonstrated by relative CBF in Fig. 3. The regional neuronal growth including dendritic arborization can be characterized by local FA decrease and is fueled by the local CBF. Faster changes of both CBF and cortical FA were observed in frontal regions, suggesting a certain level of correlation of local neuronal microstructural changes and local blood flow. Data acquisition of more preterm neonates with this optimized 3D GRASE pCASL is underway.

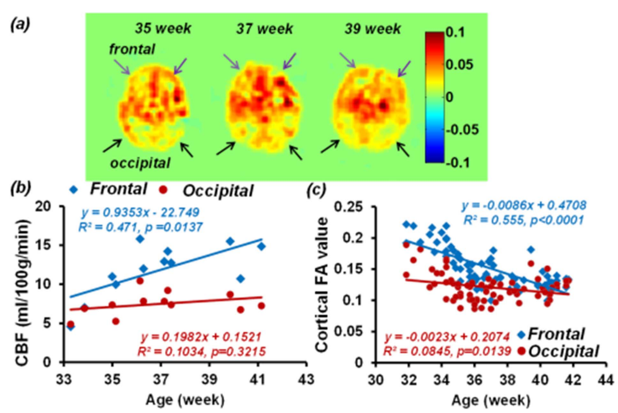

Fig. 3: Regional CBF and FA dynamics with ROI analysis. (a) Relative CBF map of representative subjects. Purple and black arrows in (a) indicate the frontal and occipital ROIs in regional CBF dynamics analysis. (b) Relationship of regional CBF value and gestational age (left) and relationship of regional FA value and gestational age (right).

References: [1] Chugani et al (1987) Annals of Neurology 22: 487. [2] Pienaar et al (2012) Neuroimage 63:1510. [3] Varela et al (2014) JMRI. [4] De Vis et al (2014) Eur Radiol. [5] Alsop et al (2013) MRM. [6]Aslan et al (2010) MRM 63: 765. [7] Shrout et al (1979) Psychological bulletin 86:420 [8] Mulcahey et al (2011) Spine 37:E797 **Acknowledgement:** This study is sponsored by NIH MH092535 and NIH MH092535-S1.