SPECT Validation of Pseudo-continuous Arterial Spin Labeling MRI

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INTRODUCTION: Pseudo-continuous Arterial Spin Labeling (PCASL) as a new arterial spin labeling (ASL) technique has shown great promise in terms of sensitivity and practicality (1,2). Validation of this technique with a gold-standard method would provide a critical step toward wider applications in neurological and brain mapping studies. Like other ASL techniques, the quantification of CBF from PCASL signal requires the knowledge of arterial transit times, δa, (i.e. the time it takes for the blood to travel from the labeling site to the imaging slice), which is not well established for gray matter and has not been explored for white matter. Therefore, the purpose of this work is two-fold. First, we determined the arterial transit times (δa) by measuring the time difference between the appearance of Gd-DTPA bolus in the labeling and imaging slices, respectively. Second, we conducted a validation study of PCASL using a radiotracer-based single photon emission computer tomography (SPECT) method. The CBF map obtained with SPECT was compared to simple PCASL signal, PCASL-derived CBF map using a one-compartment kinetic model (3), and that using a two-compartment model (4).

METHODS: All MRI scans were performed on a Philips 3T system (Best, the Netherlands). The two components of the study were performed on separate cohorts. *Transit time study:* Five subjects (4 females, 34.4±6.1 years old) participated in a bolus tracking MRI experiment. To achieve a relatively high temporal accuracy in the transit time estimation, the MR images were acquired at TR=100ms while 15ml of Gd-DTPA (Magnevist®) was injected intravenously at 5ml/s., Two slices were acquired, one at 84mm distal to the anterior-commissure (AC) posterior–commissure (PC) line corresponding to the optimal PCASL labeling plane (5) and the other at 10mm above AC-PC line corresponding to typical imaging slice (see Fig 1a). The scan duration was 200sec (giving 2000 measurements), and Gd-DTPA injection took place at 1 min after the start of scan. δa was determined as the relative time shift between the onset of the signal drop (Fig. 1d) in Internal carotid arteries (ICA, ROI shown in fig. 1c) and tissues in the brain (gray and white matter ROIs shown in fig 1b). *Validation study:* Ten subjects (7 females, 40.6±10.0 years old) underwent both a PCASL MRI scan and a SPECT scan using a Technetium-99m hexamethylpropyleneamine oxime (^{99m}Tc-HMPAO) radiotracer. Both PCASL and SPECT images covered the whole brain. The PCASL MRI scans used the following parameters: labeling duration 1650ms, labeling RF flip angle 18º, RF interval 1ms, TR/TE/TI=4151ms/14ms/1500ms, matrix size 80x80, 27 slices with 5mm thickness, duration 4.1 minutes. The SPECT image was acquired with a PRISM 3000S three-headed SPECT camera (Picker International, Cleveland) with ultra-high-resolution fanbeam collimators (reconstructed resolution of 6.5mm). Both the PCASL and SPECT data were spatially transformed to the standard MNI space to facilitate region-specific comparison. Images were smoothed so that the final resolutions are matched. Three maps were obtained from the PCASL data for comparison with SPECT: simple control-label image, CBF map using a one-compartment model, and CBF map using a two-compartment model that separately considers blood and tissue compartments. Gray matter to white matter ratio was evaluated by ROI analysis.

RESULTS and DISCUSSION: Fig. 1d shows representative time courses of the bolus tracking experiment. ROI containing feeding arteries shows an early and large signal drop due to high blood content, but it also manifests greater signal fluctuation due to cardiac pulsation. The signal change in the tissue occurs at a later time with the white matter ROI showing the largest latency (Fig. 1d). Fig. 2 shows a representative δa map and demonstrates the heterogeneity of arterial transit times across brain regions. The splenium of the corpus callosum seems to have the longest δa while the frontal gray matter regions showed the shortest δa. Average gray and white matter δa from the ROI analysis was 1.18±0.22 s and 1.87±0.19 s, respectively. The transit time from artery to vein was also assessed comparing ICA to sagittal sinus and was found to be 4.88±0.50 s. Fig. 3a shows SPECT CBF map and three CBF images derived from the PCASL data. A general agreement between the modalities can be seen. However, the gray/white contrast in the PCASL control-label image was greater than that in SPECT, as quantitatively revealed in the Fig. 3b. One possible reason is that the arterial transit time in the white matter is longer thus the CBF signal is underestimated. Therefore, absolute CBF values were obtained with a one-compartment kinetic model utilizing δa values determined in Study 1. As seen in Fig. 3b, the one-compartment model helps to reduce the gray/white ratio but it is still considerably greater than the SPECT ratio (P<0.001). Another possible factor is that the gray matter CBF in PCASL may be over-estimated with a one-compartment model because the blood may remain inside the vessel for a period of time in the imaging voxel, causing an enhancement of ASL signal (because blood T1 > tissue T1) (6). We therefore also used a two-compartment model to quantify CBF by assuming that, after reaching the voxel, the blood stays in the arteries for 1 second before entering gray matter tissue. The results (Fig. 3b) showed that the gray/white ratio now became more comparable to SPECT (P=0.15). Our results suggest that differences between PCASL and radiotracer-derived CBF maps are present even using a long post-labeling delay time of 1.5 seconds. This discrepancy is partly attributed to an underestimation in white matter CBF using ASL and could be corrected by accounting for arterial transit times. A second source for the difference may be the over-estimation in gray matter CBF due to blood/tissue T1 difference and could be corrected by using a two-compartment kinetic model. Another confounding factor, not investigated in our study, was the large vessel contributions to PCASL, which may be the reason for the "hot spots" in the PCASL CBF map (arrows in Fig. 3a). The use of crusher gradients may be helpful in mitigating this problem. Despite these discrepancies, PCASL has the potential to become a fast, reliable, and noninvasive method for CBF measurements in humans.

REFERENCES: 1) Garcia et al., ISMRM, 2005; 2) Wong, MRM, 58:1086, 2007; 3) Alsop and Detre, JCBFM, 16:1236, 1996; 4)Wang et al., MRM, 48:242, 2002; 5) Aslan et al. MRM 63:765, 2010; 6) Liu et al., MRM, in press. FUNDING: NIH DA023203, EB007821.

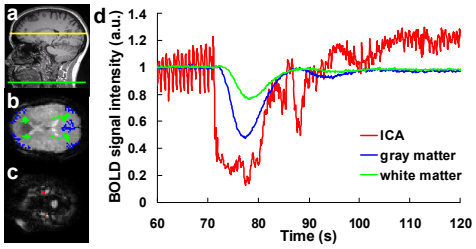

Fig. 1: Bolus-tracking experiment of a representative subject. (a) Two slices were acquired in each measurement, corresponding to the labeling plane (green) and imaging slice (yellow) in PCASL. (b) gray matter (blue) and white matter (green) ROIs defined on the upper slice. (c) ICA ROI (red) defined on the lower slice. (d) Signal time courses in the three ROIs. The signals have been normalized to the pre-injection signals for each ROI.

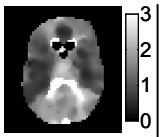

Fig. 2: An example of arterial transit time map obtained by bolus tracking. Data was from the same subject shown in Fig.1.

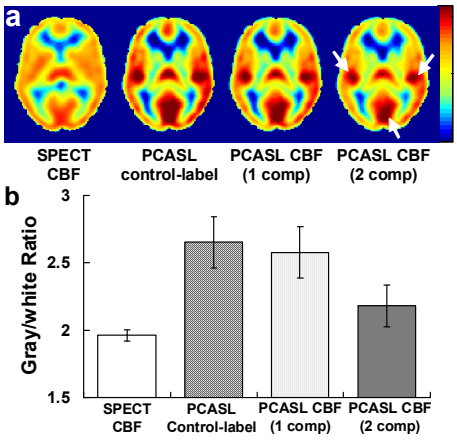

Fig. 3: (a) A representative slice of the averaged CBF maps from SPECT, simple control-label PCASL image, CBF map derived from PCASL data using one-compartment model (1 comp) and CBF map derived from PCASL data using two-compartment model (2 comp), respectively. (b) Gray matter to white matter ratio from the ROI analysis on the four CBF maps. The result is the averaged value across10 subjects. Error bar indicates standard error.