Determination of spin compartment in ASL signal using TRUST-MRI

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INSTRUCTION: The ultimate goal of Arterial Spin Labeling (ASL) MRI is to be able to replace the gold-standard ^{15}O-PET as a standard technique for CBF measurement. However, unlike PET which specifically measures the labeled water that is exchanged into tissue, the signal origin of the ASL is more ambiguous. We do not know whether the measured signal (in the difference image) is in arteries, tissue or veins. This will cause difficulties in the quantification of CBF as well as uncertainty in choosing proper imaging parameters. This question cannot be answered by multi-delay ASL experiment as that approach only provides information about how long it takes for the labeled blood to reach the imaging slices, but once inside the imaging slice one cannot distinguish the labeled water in vessel or tissue. Crusher gradient cannot provide a definitive answer either, because the efficacy of the gradients on dephasing vessel signals is highly variable and is dependent on the vessel and gradient directions. Interestingly, the water spins in the different compartments have characteristic T2 values at 3T, with arterial T2 around 160 ms, venous T2 around 50 ms and tissue around 90 ms. Therefore, one can use the T2 value of the labeled spins to probe whether the detected ASL signal is located in artery, tissue or even vein, and investigate how this compartmental assignment changes with post-labeling delay time. Specifically, we combined two recently developed technique, pseudo-CASL (1-3) and TRUST MRI (4), to determine the flow-insensitive CPMG-T2 of the labeled spins in ASL.

METHODS: Eight healthy subjects (4 men and 4 women, 20-35 years of age) were studied on a Philips 3T MRI scanner. The TRUST-PCASL sequence was based on the PCASL technique but a non-slice-selective T2-preparation module was inserted before the slice excitation pulse to create T2-weighting. Similar technique has been used previously to measure venous T2 and oxygenation level (4). The non-slice-selective T2 preparation is critical to ensure that the measured T2 value is insensitive to the outflow effect, which would cause under-estimation in conventional T2 sequence. The entire scan consisted of interleaved acquisitions of label and control images with each image type acquired with multiple effective echo times (eTEs) (4). A single axial slice was positioned at 10 mm above the anterior-commissure (AC) posterior-commissure (PC) line. The labeling position is 84 mm distal to the AC-PC line. For each subject, images were obtained with post-labeling delay (w) of 200, 850, 1525 and 2000 ms. Other sequence parameters were: voxel size=3x3x10 mm^3, FOV=240x240x10 mm^3, TE=14 ms, labeling duration (τ) =1650 mm, T2 decay modulated by four eTE times: 0 ms, 40 ms, 80 ms and 160 ms, 16 repetitions. The duration of the scan depended on the delay time and ranged from 5-15 minutes. After motion correction, the CBF-weighted images were calculated for each eTE, and then segmented into vessel, gray matter and white matter ROIs based on intensity difference. The signal was fitted as a function of TE (ASL = S0*exp(-eTE/T2)) to yield the intensity of the labeled signal, S0, and the T2 value of the labeled spins.

RESULTS and DISCUSSION: A representative set of the CBF-weighted images (control–label) are displayed in figure 1. The image intensity decreases as eTE increases. The image intensity also decreases as delay time increases due to T1 relaxation, and becomes uniform as the labeled blood enters brain tissue from vessels. Figure 2 shows the labeled signal intensity (S0) as a function of post-labeling delay time for different voxels groups of vessel, gray matter and white matter (inset, Fig. 2). Signal from voxels containing large vessels decays rapidly with delay time and approaches the gray matter intensity at longer delays, while signal from regions containing predominantly gray matter or white matter decays much more slowly, consistent with the results of Alsop and Detre (5). Figure 3 shows the estimated T2 of ASL signal in gray and white matter ROIs at different delay times. The gray matter T2 decreases gradually from 161.78 ms at 200 ms delay to 136.42 ms at 850 ms delay, then to 97.49 ms at 1525 ms delay ($p<0.001$), suggesting that the labeled spins were primarily in blood at 200 ms delay, but enters the tissue compartment at longer delay times. The T2 value of ~160 ms is consistent with in vitro whole blood T2 measurement reported previously (6). Comparing T2 values between 1525 ms and 2000 ms delay times, there was not a significant difference ($p=0.37$), suggesting that the labeled spin has reached its "destination" and its environment (thus T2 value) does not change further. This is consistent with the comparison between T2 of the labeled spin and T2 of the whole voxel (Fig. 3), showing virtually the same values at longer delay times. For white matter ROI, the estimated T2 appears identical for delay times of 200 ms, 850 ms and 1525 ms, and the values are close to the blood T2, suggesting that all the labeled spins are still in the arterial compartment. At delay of 2000 ms, the T2 started to show a significant decrease ($p=0.02$), but the values were still higher than the whole voxel T2 (Fig. 3). We speculate that the labeled signal is located in both blood and tissue compartments at this delay. One can further fit the S0 and T2 values to a comprehensive ASL model proposed by Alsop and Detre which separately models the time for the labeled spin to reach the imaging slice and the time to actually enter the tissue space (5). Upon fitting our data to the model, the estimated parameters are: time taken for spin to travel from the labeling plane to the imaging slice $\delta a=0.67$ s, time taken for the spin to travel from the labeling plane to tissue $\delta=1.69$ s, and CBF=79 ml/100g tissue/min.

To our knowledge, this is the first study to determine spin compartment assignment in ASL. Our data suggest that, at typical delay time of 1.5 seconds, most of the detected spins in gray matter are already in the tissue space. For white matter, however, the spins are still virtually all in arteries. The averaged duration for a labeled spin to travel from the labeling plane to tissue/capillary is 1.69 second. Our data also suggest that virtually all blood spins are exchanged to tissue in capillary bed and very few directly entered the veins. This is consistent with the large volume ratio between tissue and capillary of more than 50 to 1.

REFERENCES: 1) Garcia ISMRM, 2005; 2) Wu et al. MRM, 58:1020, 2007; 3) Wong MRM, 58:1086, 2007; 4) Lu and Ge, MRM, 60:357, 2008; 5) Alsop and Detre, JCBFM 16:1236, 1996; 6) Chen and Pike, MRM, 61:249, 2009

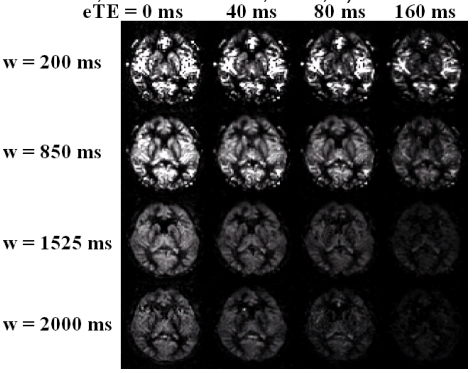

Fig. 1. The CBF-weighted images (control-label) from a representative subject acquired with post labeling delays from 200 to 2000 ms and effective echo times from 0 to 160 ms.

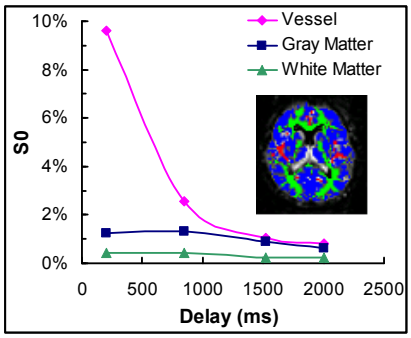

Fig. 2. Mean signal intensities in three types of brain tissue averaged across eight subjects. The inset shows the ROIs of these three types: vessel (red), gray matter (blue) and white matter (green).

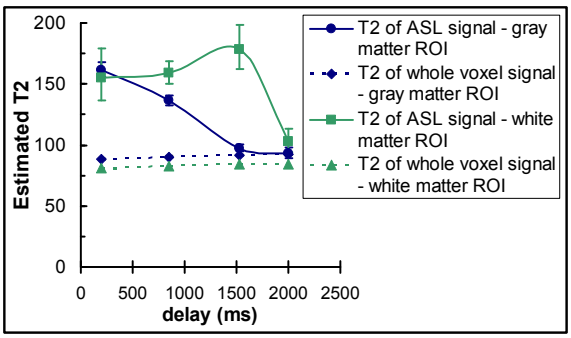

Fig. 3. Estimated T2 from the ASL signal and whole voxel signal of gray matter and white matter in experiment. ROIs of gray matter and white matter are defined in Fig. 2 (inset).