Is cerebral microvascular flow anisotropic - preliminary evidence from multi-directional diffusion weighted perfusion MRI

A. K. Priya[1], L. Yan[1], and D. J. Wang[1]
[1]Neurology, UCLA, Los Angeles, CA, United States

Introduction: While microvascular flow in the brain is commonly thought to be isotropic, recent evidence suggests that anisotropic capillary structures may exist in the cerebral vasculature. For instance, capillary network may lie perpendicular or parallel to the sulcus surface depending on the cortical depth (1), and deep white matter arteries may align parallel to white matter tracts (2). These intriguing findings triggered the development of new MRI methods to quantify the orientational information of microvascular flow or perfusion in the brain and other organs such as skeletal muscle. In a way similar to diffusion tensor imaging (DTI), directional flow in feeding arteries or arterioles to an imaging voxel can be quantified using velocity selective arterial spin labeling (VS-ASL) along that direction, and performing VS-ASL along multiple non-collinear directions (n≥6) allows so called perfusion tensor imaging (PTI) (3). While initial results demonstrated directional flow in the brain and skeletal muscle using PTI, the encoded flow velocity was on the order a few cm/s, which corresponded to arteriolar flow. In the present study, we employed an alternative technique termed multi-directional diffusion-weighted (DW) ASL with appropriate post-labeling delay and b value to specifically target and derive directional information of capillary flow.

Methods: Five healthy volunteers were scanned on a Siemens TIM Trio scanner at 3T, using 12ch head coil. The DW-ASL sequence combined pseudo-continuous ASL with a twice-refocused spin-echo diffusion weighted EPI sequence (4). Two non-selective HS inversion pulses were applied during the post-labeling delay (PLD) to suppress the background EPI signal (5). Multi-directional DW was implemented using 2 pairs of bipolar gradients along 6 non-collinear directions (gradient table in Fig. 1), with the refocusing pulses dividing each bipolar pair. It has been shown that DW-ASL signal can be characterized using a bi-exponential model, with the slow and fast decaying components corresponding to labeled signals in the vascular and tissue compartments (4). These 2 components can be well separated by a b value of 50s/mm^2, which was adopted in the present study along with a PLD of 1200ms that allowed the labeled spins to flow into the microvasculature. Imaging parameters were: FOV=22cm, matrix=64x64, TR=3.5s, TE=43ms, 10 slices of 8mm thickness with 2mm gap, labeling duration=1.5s. 30 pairs of tag and control images were acquired for b=0, and b=50s/mm^2 along 6 directions, respectively. In each subject, the 6 multi-directional DW-ASL perfusion images along with the b0 image were analyzed using FDT in FSL to generate maps of fractional anisotropy (FA) and eigenvectors. Gray matter (GM) and white matter (WM) masks were generated by segmenting the raw EPI image using SPM. Wilcoxon signed-rank test was used to test statistical significance.

Results: Figure 1 displays the set of 7 perfusion images from a representative subject. Applying DW with b=50s/mm^2 attenuated the perfusion signal almost equally along the 6 directions (Fig. 2). The calculated FA values were relatively uniform but high throughout the brain (see Fig. 1&Table 1). The mean FA value in WM, nevertheless, was significantly greater than that in GM (p=0.043). The primary eigenvectors (V1) showed random patterns throughout the brain. To investigate whether the relatively high FA values were due to low SNR, the perfusion images were spatially smoothed with a 5 and 10mm FWHM kernel respectively. As expected, the mean FA values decreased with heavier smoothing (Table 1, p=0.043). Yet the FA difference between GM and WM was still significant, and no organized pattern of the primary eigenvector was observed.

Discussion: Compared to VS-ASL which selectively labels blood spins in feeding arteries and arterioles with a cut-off velocity of a few cm/s, the DW-ASL method primarily targets labeled blood within the capillaries with a PLD of 1.2s and a b value of 50s/mm^2 (i.e., encoded velocity= ~2mm/s). No evidence of consistent anisotropy of microvascular flow was found using the above parameters. The difference between GM and WM FA may be due to anisotropic microvascular flow along white matter tracks, which requires further validation. Anisotropic perfusion within GM may not be detectable using the current spatial resolution. Nevertheless, the largely isotropic microvascular flow or perfusion in the brain implies that a single ASL scan may be enough to quantify cerebral perfusion.

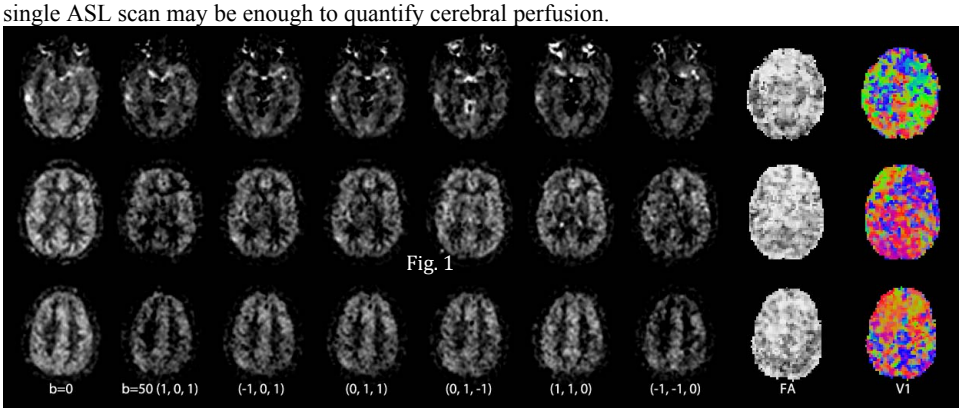

Fig. 1

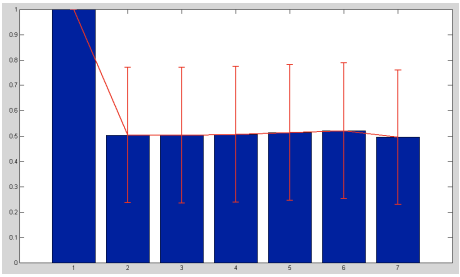
Figure2: Average fractional DW-ASL signals for the 6 directions (whole brain)

Table 1: Variation of mean FA in the gray matter (GM) and white matter (WM) with smoothing for the five volunteers

Smoothing kernel size	Volunteer1		Volunteer2		Volunteer3		Volunteer4		Volunteer5	
	GM	WM	GM	WM	GM	WM	GM	WM	GM	WM
5mm	0.9034	0.9889	0.8511	0.9689	0.9640	0.9880	0.8300	0.8921	0.7255	0.9536
10mm	0.8628	0.9407	0.7438	0.8426	0.9248	0.9393	0.7424	0.7871	0.6029	0.8054

References: (1) Cassot et al, *Microcirculation,* 13, 1, 2006; (2) Nonaka et al, *Neuropathology,* 23, 111, 2003; (3) Frank et al, *MRM*, 60, 1284, 2008; (4) Wang et al, *JCBFM*, 27, 839, 2007; (5) St Lawrence et al, *Proc ISMRM*, 16, 188, 2008