Functional MRI Using Arteriolar Cerebral Blood Volume Changes

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Introduction: Changes in functional brain activity cause changes in vascular diameter, predominantly in the arterioles. An MRI method sensitive to changes in arteriolar blood volume (CBV_a) should improve spatial specificity and perhaps hemodynamic response time for fMRI. Vascular space occupancy (VASO) MRI (1) is a blood nulling approach employing a spatially non-selective inversion recovery (IR) pulse to assess micro-vascular cerebral blood volume (CBV) changes without contrast agent. In order to make VASO specific for the arterioles, we designed an experiment in which a spatially selective inversion of the blood water spins is applied outside the imaging slice, and images are acquired when the spins flowing into the slice are nulled. This new approach is dubbed *inflow VASO (iVASO)*. As the arterial transit time (400-1400 ms) (2,3) is in the range of TI (300-1150 ms) used in VASO MRI (4), iVASO is expected to achieve predominantly arteriolar-selective blood nulling. Contrary to VASO, which has low SNR because the nonselective inversion pulse leaves only 10-20% gray matter signal, iVASO has full signal at the time of nulling. Using iVASO to study visual stimulation in humans, we validate the expected increase in SNR and CNR with respect to VASO, and show the faster response.

Methods: Visual simulation with black/white flashing checkerboard (30s/30s off/on; 4 repetitions) was performed (n=7). Three iVASO experiments with different preparatory inversion schemes and one conventional VASO experiment were conducted in a pseudo-randomized order: 1) Seq. I (slab-selective iVASO): A slab-selective adiabatic inversion pulse inverts a slab (150 mm) beneath the imaging slice; 2) Seq. IIa (flip-back iVASO): A non-selective adiabatic inversion pulse is followed by a slice-selective adiabatic inversion pulse (23 mm) that flips back the spins within the imaging slice; 3) Seq. IIb: same as Seq. IIa except that a larger area covering the slice and the brain above it (80 mm) is flipped back; 4) VASO: non-selective inversion. In the iVASO experiments, the gap between the leading edge of the inverted spins and the bottom of the imaging slice was 10 mm. Three different TR/TIs were used: TR/TI=5000/1054ms, 2000/711ms, 1000/424ms. Single-shot turbo spin echo (TSE) with centric readout order was used to minimize SE BOLD effects. Other imaging parameters: TE=5.9ms, flip angle=90˚, matrix=64x64, voxel=3x3x3 mm^3, single-slice, SENSE=2.5. Requirements for voxel activation were z-score<-2.5, p-value<0.01, SNR>20, and cluster size>4.

Results & Discussion: Fig. 1 shows activation maps superimposed on the iVASO and VASO images as well as the time courses of the relative signal changes (ΔS/S) upon neuronal stimulation averaged over all subjects (n=7) for TR of 5s. The activated brain areas and signal changes are very reproducible for all sequences. Results for ΔS/S are summarized in Table 1. For iVASO, ΔS/S was -0.47~-0.69%, which corresponds to a 30-50% CBV_a increase during neuronal activation, in line with literature values (5,6). ΔS/S in conventional VASO is bigger (P<0.01), mainly because it reflects total CBV change. Using iVASO, activation could still be reliably detected at TR of 1s, while activated voxels could barely be seen in VASO at such short TR, due presumably to interference from the negative signal of inflowing blood. The magnitude of ΔS/S in iVASO decreased with TR/TI (P<0.1), which implies less inflowing blood at shorter TI. No significant differences in ΔS/S or activated voxel numbers were found between iVASO sequences at any TR (P>0.1). Averaged over all iVASO sequences, SNR values were 3.04±0.11 and 4.41±0.11 times that of VASO at TR of 5s and 2s, respectively. This can be expected for the static tissue signal in the imaging slice in iVASO is unaffected or flipped back to ~100% while it is only 10-20% in VASO. CNR, defined as SNR*ΔS/S*√(number of images acquired per minute), was 41±2% (TR=5s) and 25±2% (TR=2s) greater in iVASO than in VASO. Fig. 2 compares the hemodynamic responses detected by iVASO (average from all three sequences) and VASO at a temporal resolution of 2s. The time courses were averaged to one block and scaled by the ratio of mean ΔS/S between VASO and iVASO. A paired Student T-test was conducted for each pair of the transition points (labeled by error bars). The P-values (n=7) were (in order of time): 0.0008, 0.016, 0.192, 0.026, 0.030, 0.272. Thus, the hemodynamic response detected by iVASO proceeds the one measured by conventional VASO, which is in line with recent high-resolution optical imaging results, showing faster response in arterioles than in capillaries and venules (6). Note that while using similar pulse sequences, iVASO is fundamentally different from ASL. The signal difference in ASL is assumed to be due to exchange of blood label to tissue in capillaries. In iVASO, we use the fact that arterial vessels are impermeable. Besides, iVASO does not need a control scan and image is acquired only at the blood nulling time, which furnishes a higher SNR than the subtraction method used in ASL.

Table 1 TR/TI (ms)	Method	Activated Voxels	ΔS/S (%)	SNR	CNR
5000/1054	Seq. I	2731±204	-0.62±0.04	347±8	7.59±0.50
	Seq. IIa	2388±224	-0.66±0.06	308±16	7.25±0.35
	Seq. IIb	2698±220	-0.69±0.04	308±16	7.35±0.37
	VASO	1910±213	-1.46±0.15	104±4	5.18±0.57
2000/711	Seq. I	2219±183	-0.59±0.06	319±9	10.14±1.03
	Seq. IIa	2286±168	-0.60±0.07	288±8	9.75±0.91
	Seq. IIb	2102±230	-0.59±0.05	302±7	10.01±0.91
	VASO	2252±216	-2.16±0.32	66±3	7.98±0.92
1000/424	Seq. I	2294±108	-0.47±0.03	227±9	8.23±0.47
	Seq. IIa	2053±211	-0.48±0.03	207±6	7.91±0.59
	Seq. IIb	2210±134	-0.51±0.03	196±6	8.03±0.43
	VASO	893±131	N/A	N/A	N/A

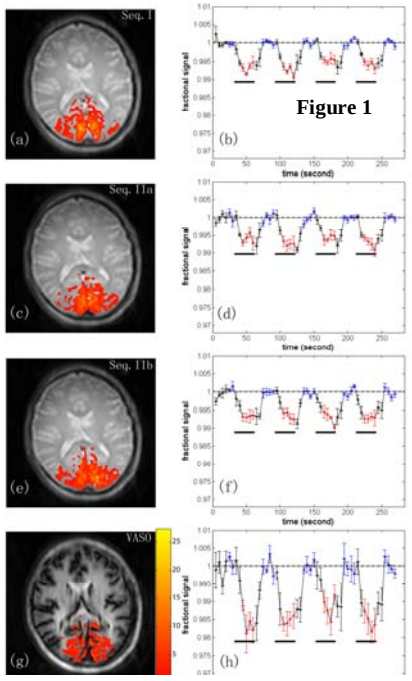

Figure 1

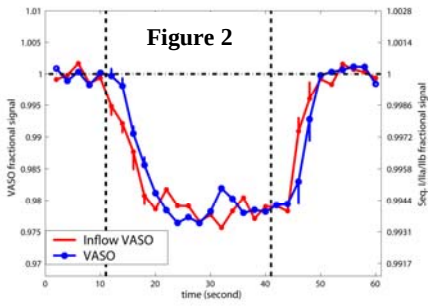

Figure 2

Conclusion: A new fMRI approach was introduced that is sensitive predominantly to changes in arteriolar blood volume. It employs principles similar to the VASO approach for detecting total CBV changes, but has improved SNR and reduced partial volume effects with white matter and CSF. The new approach showed an immediate hemodynamic response to visual activation, which was faster than the VASO response, which is known to be faster than the BOLD response. The signal changes measured with iVASO depend on the arterial transit time, which complicates interpretation but also opens up new avenues for research.

(1) Lu et al. MRM 2003;50:263. (2) Francis et al. MRM 2008;59:316. (3) Gonzales et al. MRM 2000;44:739. (4) Donahue et al. MRM 2006;56:1261. (5) Kim et al. JCBFM 2007;27:1235. (6) Hillman et al. Neuroimage 2007;35:89.