Elimination of non-steady-state blood spins in Vascular-Space-Occupancy (VASO) fMRI

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TARGET AUDIENCE: MR physicists and clinicians who are interested in fMRI acquisition methods and cerebral blood volume (CBV) imaging.

PURPOSE: Vascular-space-occupancy (VASO) MRI measures cerebral blood volume (CBV) changes through extravascular tissue signal changes. Based on the difference between blood and tissue T1, inversion recovery is employed to null blood signal while keeping substantial tissue signal for detection. The choice of inversion time (TI) is based on the assumption that all blood spins within the imaging volume have reached the inversion steady state of approximately nulled signal before image acquisition. However, this assumption may not hold if TR is short relative to blood T1 and/or if the inversion volume (determined by transmit coil coverage) is small so that some fast flowing blood spins are not inverted sufficiently often before image acquisition to reach the steady state[1,2]. The non-steady-state inflowing blood spins can be categorized into three types[3] based on the time when they flow into the transmit coil: I) spins flowing in before the end of readout of the previous TR; II) spins flowing in between the readout of previous TR and the inversion pulse of current TR; III) spins flowing in after the inversion pulse of current TR. Type I non-steady-state blood spins can be eliminated by a spatially nonselective saturation module (90º RF pulse followed by spoiler gradients) applied immediately after each readout. This "magnetization reset" technique[1] establishes the steady state for all spins within the transmit coil for the next scan. However, it is not effective for spins flowing into the coil after the saturation module (type II and III spins). Those spins, provided they flow fast enough to reach the imaging volume before next acquisition, will still have non-steady-state effects on the overall VASO signal. In this study, we show that contaminations from type II and III non-steady-state spins can be eliminated using motion-sensitized crushing gradients[3]. It can be implemented with bipolar gradients in a 2D sequence such as 2D gradient echo (GRE) echo-planar-imaging (EPI), or a motion-sensitized driven equilibrium (MSDE) spin preparation module immediately before a 3D sequence such as 3D fast GRE.

METHODS: Seven subjects were scanned on a 7T Philips MRI scanner. A 32-channel phased-array head coil (Nova Medical) was used for RF reception and a head-only quadrature coil for transmit. fMRI was performed using flashing checkerboard (40s off/24s on, 4 repetitions, 1 extra off period in the end). Two sets of experiments using magnetization transfer enhanced (MT-VASO) with different imaging sequences were carried out on each subject. *Experiment set I* uses a single slice GRE EPI readout. Three pseudo-randomized fMRI experiments were performed: (a) MT-VASO with GRE EPI (single shot, voxel=2mm isotropic, TR/TI=4s/1294ms, 3 echoes, TE/echo spacing (ES)=15/20ms, FA=70º, SENSE=4, partial Fourier fraction=0.7, fat suppression). (b) MT-VASO with GRE EPI and magnetization rest. (c) MT-VASO with GRE EPI, magnetization rest and bipolar gradients Venc=3cm/s. The multi-echo data were used to extrapolate to effective TE=0 to remove BOLD contamination. *Experiment set II* uses a 3D spoiled fast GRE (also known as T1-enhanced TFE or TurboFLASH) readout: voxel=2mm isotropic, 21 slices, TR_{GRE}/TE=3.9/1.8ms, FA=7º, TR=4s, turbo direction=radial, SENSE=3x2(APxFH),low-high phase encoding. A MSDE module, which consists of a spatially nonselective Carr–Purcell–Meiboom–Gill (CPMG) based T2 preparation module with inserted motion-sensitized crushing gradients in the z-direction (two refocusing pulses, effective TE=15ms, inter-echo spacing (τ_{CPMG})=7.5ms, Venc=3cm/s), was applied immediately before the readout. Four pseudo-randomized fMRI experiments were performed: (a) MT-VASO with 3D fast GRE, TR/TI=4s/892ms; (b) MT-VASO with 3D fast GRE, TR/TI=4s/892ms, with magnetization reset but no MSDE; (c) MT-VASO with 3D fast GRE, TR/TI=4s/903ms, with magnetization reset and the T2 preparation pulses in MSDE, but no crushing gradients; (d) MT-VASO with 3D fast GRE, TR/TI=4s/903ms, with magnetization reset and MSDE. The single slice in (I) was aligned with the center of the 3D volume in (II). A general linear model was employed to detect functional activation in fMRI scans (P=0.05, t-score<-2, cluster size≥4, and SNR>5).

RESULTS: Figs. 1a,b show typical activation maps in the visual cortex detected with the single slice GRE EPI (Experiment set I) and 3D fast GRE (Experiment set II, middle slice) MT-VASO sequences, respectively. The activation pattern and number of activated voxels were comparable (n=7, P>0.1) among all scans in Experiment set I (Table 1) and II (Table 2, all slices included), respectively. Only voxels that were activated in all scans of each Experiment set were selected to calculate the average time courses and signal changes during visual stimulation. The general trend of the time courses shown in Figs. 1c,d from Experiment set I and II, respectively, was similar, consistent with the VASO time courses in the literature. In Experiment set I, the relative signal changes (ΔS/S) during visual stimulation (Table 1) were the largest (P<0.01) in scan (a), became smaller in (b), and further decreased (P<0.01) in (c). In Experiment set II, ΔS/S were the largest (P<0.01) in scan (a), comparable (P>0.1) between (b) and (c), and smallest (P<0.01) in (d).

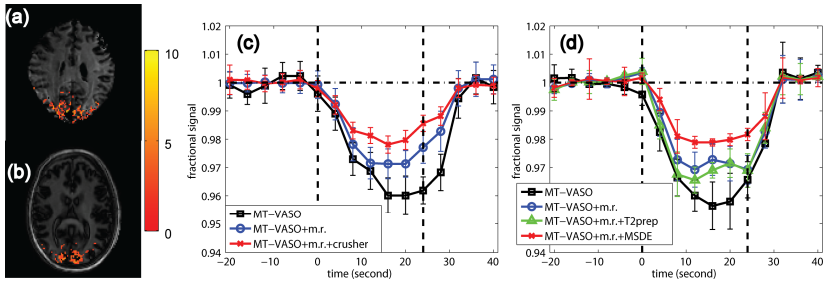

Table 1. *Exp. set I: single slice EPI*	**MT-VASO**	**MT-VASO +m.r.**	**MT-VASO +m.r.+crusher**
#activated voxels	161±33	148±33	154±38
ΔS/S (%)	-3.81±0.68	-2.82±0.58	-1.95±0.31

Table 2. *Exp. set II: 3D fast GRE*	**MT-VASO**	**MT-VASO +m.r.**	**MT-VASO +m.r.+T2prep**	**MT-VASO +m.r.+MSDE**
#activated voxels	942 ±382	1129 ± 518	1147 ± 544	819 ± 359
ΔS/S (%)	-3.98 ± 0.75	-2.94 ± 0.61	-3.16 ± 0.45	-2.04 ± 0.19

DISCUSSION: Previous studies[1,2] have demonstrated that type I and II non-steady-state blood spins would furnish a larger (more negative) VASO signal change during vasodilation, while type III spins have the opposite effect. Our data from both the single slice GRE EPI and 3D fast GRE MT-VASO experiments show that with magnetization reset, VASO signal changes decreased, indicating that type I non-steady-state spins were suppressed. This result is consistent with a previous study[1] at 3T. After adding bipolar gradients in the single slice GRE EPI and MSDE module in the 3D fast GRE MT-VASO sequences, the VASO signal changes further decreased, which indicates that effects from type II non-steady-state spins were also suppressed. Note that only spins reaching the imaging volume before acquisition contribute to the measurable MR signal. Therefore, type III spins are expected to have much less impact than the other two types, as they enter the transmit coil at a later time and thus are less likely to arrive at the imaging volume before acquisition. If there were some type III spins flowing fast enough to contribute, their velocities should be greater than those of type II spins, and thus should be suppressed by the crushing gradients. The VASO signal change measured with magnetization reset and crushing gradients agrees reasonably with theoretical calculations, which predicted about -1.5% VASO signal change at 7T assuming a 25% CBV increase during activation. Note that the T2 preparation pulses in MSDE may introduce some unwanted BOLD effects. This can be evaluated by comparing results from scans (b) and (c) in Experiment set II. However, the number and pattern of activated voxels, as well as the signal changes and time courses from common voxels (Table 2, Fig. 1d) in these two scans were all comparable (P>0.1), implying that there was little BOLD effect resulting from the T2 preparation module. A reasonable explanation is that when a short effective TE (15ms, closer to venous blood T2, but much shorter than tissue T2 at 7T) is used, the T2-weighted BOLD effect is mainly in the intravascular compartment, which is nulled in VASO MRI.

CONCLUSION: We show that by combining the magnetization reset technique and crushing gradients, non-steady-state blood spins in VASO fMRI can be suppressed.

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