Magnetization "reset" for non-steady-state blood spins in Vascular-Space-Occupancy (VASO) fMRI

H. Lu[1]

[1]Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, United States

INTRODUCTION: Vascular-Space-Occupancy (VASO) fMRI is a technique targeting for Cerebral-Blood-Volume (CBV) based functional brain mapping (1), which can be used for understanding BOLD fMRI signal, estimating cerebral metabolic rate of oxygen (CMRO2), and better localization of parenchymal activation (2,3). However, recent evidences have suggested that the mechanism of VASO signal may contain contributions from factors other than CBV changes, depending on imaging parameters used (4,5,6). Donahue et al. showed that, when a short TR (<5s) is used, the VASO signal has a significant contribution from flow-related effects, particularly from blood spins whose magnetizations have not reached a steady state (5). Since the VASO formulation assumed a steady state magnetization, these non-steady-state "fresh spins" will cause the signal to deviate from what is expected from a pure CBV contrast, most often resulting in an over-estimation. Here we aim to eliminate non-steady-state spins and "reset" the magnetization by adding a non-slice-selective 90º saturation RF pulse immediately after the image acquisition (post-sat), followed by dephasing gradients. Experiments and numerical simulations were performed, showing that the post-sat pulse can eliminate virtually all fresh spins and bring the VASO signal back to a level consistent with predominantly CBV-contrast for a TR range of 1-1.6s. At intermediate TR range (1.7-5s), the post-sat reduced the flow contribution, but is not able to completely remove the effect.

METHODS: The modified VASO sequence is shown in Fig. 1. Compared to the original VASO sequence, the key modification is a post-sat pulse (green rectangle). The timing of the post-sat pulse is chosen such that it does not interfere with the signal evolution for steady-state situation (neglecting the short time between the excitation pulse and the post-sat pulse): 1) for the tissue and blood spins inside the imaging slice, they have just experienced the 90º excitation pulse, so the post-sat has no effect; 2) for the blood spins outside the imaging slice, their magnetization is at zero-crossing (assuming steady-state), so the post-sat has no effect; 3) for tissue outside the imaging slice, their magnetization will be affected, but since they are static spins and do not enter the imaging slice so the signal in the imaging slice is not affected. It is important to point out that the post-sat pulse can reset the magnetization for fresh spins currently inside the body coil coverage. However, new fresh spins can still come into the body coil coverage after the post-sat pulse and enter the imaging slice by the time of data acquisition. The time interval is one TR. Thus, for long TR values, there will still be some residual fresh-spin effects even with the post-sat pulse. For TR values shorter than the arrival time ("trailing time" in ASL term (7)), on the other hand, no fresh spins are expected to be present in the imaging slice at the time of RF excitation.

MR experiments (3T Achieva, Philips) were performed on a total of 7 healthy subjects with informed consent. Five fMRI were performed: conventional (no post-sat) VASO and post-sat VASO at TR=2s, conventional VASO and post-sat VASO at TR=1s, and post-sat VASO at TR=6s to provide a "gold standard" signal amplitude. Other parameters: FOV 240mm, matrix 64x64, 1 slice with thickness of 6mm, single-shot gradient-echo EPI, SENSE factor 2, TE=7.8ms, TI was based on individual TR (1). FMRI paradigm used flashing checkerboard with 30s ON and 30s OFF, and repeated 4 times, resulting a duration of 4.5 min. All five fMRI experiments had the same paradigm and duration. Activation detection used cross-correlation (cc) with a box-car function and cluster size of 3. A p=0.05 was used as the cc threshold, corresponding to cc=0.25, 0.14 and 0.10 for TR=6s, 2s and 1s, respectively, because the number of images are dependent on TR for a given scan duration.

Simulations were performed for the magnetizations. The magnetizations of non-steady-state blood spins were calculated according to how long they have been inside the body coil coverage, thereby determining how many RF pulses they have experienced. The status of the non-steady-state spins inside the imaging slice was estimated based on the arrival time and dwelling time of the blood spins. Capillary exchange effect is not included, as the effect was previously shown to be relatively small (1).

RESULTS and DISCUSSION: VASO fMRI with a long TR (6s) yielded 63±7 activated voxels in the occipital cortex with a signal change of -0.9±0.1%, consistent with previous reports (1). These same voxels were then masked onto the other fMRI data to obtain time-courses for TR of 1s and 2s with and without the post-sat pulse. For TR=2s data and with-sat TR=1s data, visual stimulation resulted in a signal decrease, as expected. For TR=1s without post-sat, however, the signal increased with stimulation. This can be verified from the cc maps (Fig. 2). Activation detection was then applied using the appropriate signs for thresholding (i.e. positive for TR=1s without post-sat; negative for all others). Fig. 3 plots the signal time-courses. TR=2s without post-sat (conventional VASO) shows a large signal change, greater than what is expected from a pure-CBV effect (TR=6s). The addition of post-sat reduces the amplitude to some extent, but does not completely bring it back to the TR=6s amplitude. At TR=1s, on the other hand, the post-sat pulse restore the VASO amplitude to match excellently with the TR=6s case. The experimental data can be explained by simulations. At steady state, a blood spin should have no signal (zero-crossing) at the time of acquisition in VASO. At non-steady state, the blood signal can be either positive or negative depending on the history of magnetization. Fig. 4a shows the magnetization evolution for several spins that entered the body coil coverage 1,2,3,4s before the acquisition time-point. The post-sat pulse resets all the spins that arrived one TR ago or longer to the steady state (black curve). In a brain voxel, the blood spins will have a range of entry times, assumed to be 1.8-6.8s (evenly distributed) in our simulation (7). With this assumption, the simulated signal (in %) as a function of TR is shown in Fig. 4b. Under conventional VASO (blue curve in Fig. 4b), the signal becomes more negative as TR shortens and, consistent with the experimental data, turns positive at a TR of 1s. The post-sat pulse is able to normalize the signal amplitude completely at TR<1.6s (red curve in Fig. 4b). In summary, the addition of a non-selective saturation pulse appears to be able to reduce the fresh spin effects at intermediate TR and, moreover, can completely eliminate the effect at short TR (<1.6s). This helps to bring the VASO fMRI contrast back to a predominantly CBV-weighted technique for brain mapping.

REFERENCES: 1) Lu et al. MRM 50: 263, (2003); 2) Yang et al. MRM 52: 1407, (2004); 3) Tuunanen et al. MRI 24:993, (2006); 4) Donahue et al. MRM 56:1261, (2006); 5) Zimine et al. ISMRM 493, (2005); 6) Scouten et al. MRM 58:306, (2007); 7) Hendriske MRM 50:429(2003).

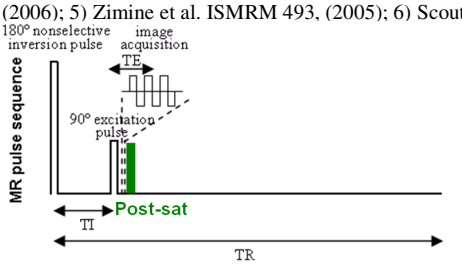

Fig. 1: VASO sequence with a post-saturation pulse (green) to reset magnetization of non-steady-state spins.

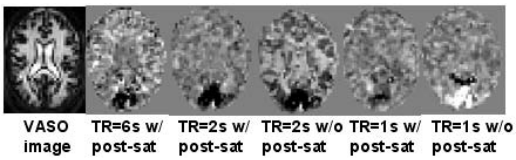

Fig. 2: Map of cross-correlation coefficients between signal time-courses and a box-car function. A VASO image is also shown for anatomical reference.

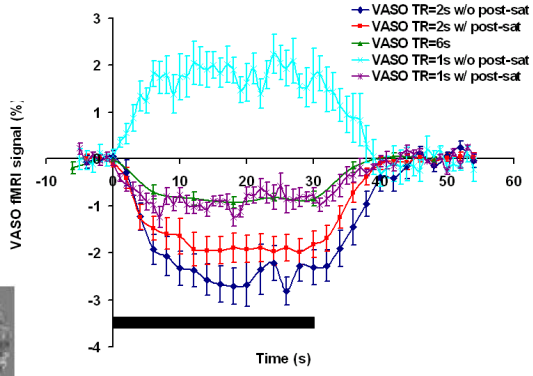

Fig. 3: VASO signal time-courses with and without the post-sat pulse at different TRs. TR=6s is used as the reference signal as it has minimal fresh spin effects. Error bars indicate the standard errors from all subjects.

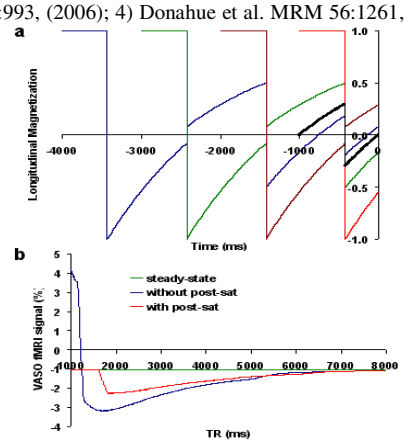

Fig. 4: (a) Simulation of magnetization for spins entering the body coil coverage at different times. The magnetization at time 0 determines the acquired signal amplitude. (b) VASO fMRI signal as a function of TR for different spins states.