The Effect of Blood Inflow on Vascular-space-occupancy (VASO) Contrast

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Background and Objective. Vascular-space-occupancy (VASO) fMRI is gaining popularity as a method for non-invasively measuring cerebral blood volume (CBV) changes accompanying brain activity [1-5]. In VASO, a non-selective inversion pulse is applied, after which an image is acquired at an inversion time (TI) when the longitudinal magnetization (M_z) of blood is zero, yet M_z of tissue is positive. By acquiring multiple images at a repetition time (TR) interval, and adjusting TI so as to keep steady-state blood signal nulled, VASO fMRI can be performed in a time-efficient manner. A negative VASO signal change (ΔS/S) has been observed during increased neuronal activity, which was originally attributed to a decrease in tissue signal consequential to CBV increases. More recently, it has been shown that inverted blood water will exchange with tissue water and attenuate tissue M_z in a cerebral blood flow (CBF)-dependent manner [3], similar to arterial spin labeling (ASL) experiments [6]. This CBF effect is only detectable at short TR≤3000 ms, where inverted blood water is sufficiently far from equilibrium. The ability to accurately and separately quantify both CBV and CBF contributions would be extremely valuable for studying cerebral physiology. However, one important uncertainty preventing this goal is that it is unknown whether blood in the steady-state VASO experiment is entirely nulled. A body-coil will invert only a finite volume of thickness (450-700 mm), which may allow for some blood which is not in steady-state to enter the imaging volume. It has previously been simulated that such *fresh* blood will cause VASO ΔS/S to become significantly more negative [3], especially at short TR, and may mimic or even eclipse the TR-dependent CBF effect. Here, we investigate this possibility in detail by measuring VASO ΔS/S as a function of inversion volume thickness.

Methods. The body coil-administered adiabatic inversion pulse in VASO experiments is non-selective. The local MR engineer determined the length of our current body coil to be 650 mm and therefore an adiabatic pulse is expected to invert no less than this volume. Here, we introduced a gradient associated with the adiabatic inversion to allow for a finite volume thickness (δ) of water to be inverted. VASO fMRI experiments were performed for a non-selective inversion pulse, as well as δ=10, 100, 200, 300, 400, 500, 600 mm, each at a short TR=2000 ms and long TR=5000 ms. These 16 experiments were pseudo-randomized and repeated on four healthy volunteers (age=27±3 yrs), all of whom provided informed, written consent in accordance with IRB and HIPAA guidelines. *Scan parameters*: Philips 3.0T MR scanner (Philips, Best, The Netherlands), 3.75x3.75x5 mm^3 spatial resolution, FOV=240x240, reconstruction matrix=256x256, single-shot gradient echo EPI, TE=12.7 ms, SENSE=2.5, TR/TI=2000/711 ms or TR/TI=5000/1054 ms. The fMRI paradigm consisted of 30s/30s cross-hair fixation/flashing checkerboard (8 Hz) repeated three times. An additional 30s of data acquired before the paradigm block began were not analyzed. Positive and negative VASO ΔS/S was calculated from voxels meeting activation criteria in a z-hypothesis test; activation criteria were: z≤-3 (p<0.05) or z≥3(p<0.05), SNR≥20, cluster size≥4. Parenchymal ΔS/S was calculated from the measured ΔS/S assuming a CSF voxel fraction of 15% [3]. To assess how parenchymal ΔS/S varied with δ, time courses were calculated for each δ scan for voxels meeting activation criteria in the non-selective VASO experiment; this assured that common voxels were analyzed in all scans.

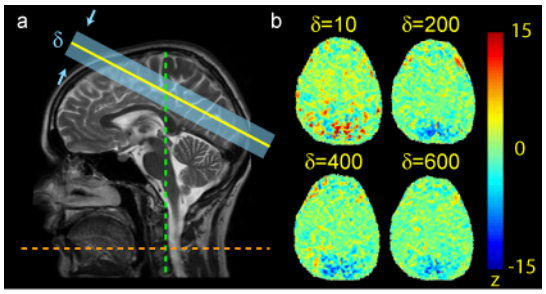

Fig. 1. The VASO inversion slab (blue) is varied in thickness δ around the imaging slice (yellow) (a). The green line is approximately 210 mm and the orange line shows the scanner isocenter. In (b), *z*-maps are shown for varying δ.

Results and Discussion. Fig. 1a shows how the VASO inversion thickness (δ, blue) was varied. The green line is approximately 210 mm and the orange line shows the location of the scanner isocenter. Representative *z*-maps are shown for δ=10, 200, 400, and 600 mm (Fig. 1b). Notice that for small δ=10 mm, the visual cortex shows a positive z, suggestive of blood in equilibrium and T_2*-induced blood-oxygenation-level-dependent [7] (BOLD) and/or inflow effects. Number of voxels with positive (blue) and negative (black) *z* are shown in Fig. 2a for TR=2000 ms (solid line) and TR=5000 ms (dashed line). Notice that for δ≥200 mm, significantly more voxels with negative *z* (-ΔS/S) are apparent, indicating that VASO effects outweigh BOLD and inflow effects here. Fig. 2b shows parenchymal ΔS/S as a function of δ. For TR=2000 ms, ΔS/S is most negative for 100≤δ≤300 mm (ΔS/S=-2.7±0.6%), indicating some fresh blood here, but ΔS/S approximately plateaus for δ≥500 mm (ΔS/S=-1.8±0.0%), which we believe is within the adiabatic inversion range of the present body coil. ΔS/S was consistently and statistically (p=0.0007) more negative at short TR=2000 ms. Finally, Fig. 2c shows a surface map depicting the relationship between the time, δ, and ΔS/S for TR=2000 ms fMRI data. In all three task periods, ΔS/S is most negative for small δ (dark blue) and becomes approximately equal in all task periods for δ≥500 mm. Several important conclusions can be taken from this study. First, at TR=5000 ms, VASO ΔS/S is approximately constant for δ≥200 mm (ΔS/S=-1.2±0.4%). This is likely due to the TI for blood nulling at TR=5000 ms (1054 ms) being similar to the null time for fresh blood which sees only a single inversion pulse (1126 ms). At short TR=2000 ms, ΔS/S does not plateau until δ≥500 mm, which we attribute to blood which is not in steady-state entering the imaging voxel. This effect is more pronounced at TR=2000 ms since TI here (711 ms) is much shorter than the fresh blood nulling TI (1126 ms). This consideration should be taken into account when performing VASO experiments using scanners with a coil inversion volume thickness less than 500 mm. Note that only a volume of δ/2 is inverted below the isocenter; when the isocenter is centered on the imaging slice, this is the thickness that is relevant for inversion of blood-water in feeding arteries. Finally, short TR ΔS/S (ΔS/S=-1.8±0.0%) is more negative than long TR ΔS/S (ΔS/S=-1.1±0.3%), which we attribute to a TR-induced CBF effect [3].

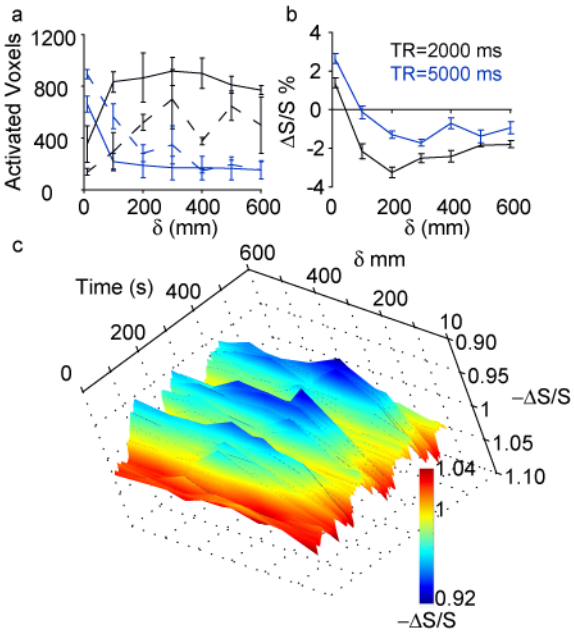

Fig. 2. Number of voxels meeting positive (blue) and negative (black) activation criteria for TR=2000 ms (solid) and TR=5000 ms (dashed). In (b), parenchymal ΔS/S is shown as a function of δ. A surface plot shows that for δ≥500 mm, TR=2000 ms ΔS/S is approximately constant in all task periods (c).

Conclusions. This work shows how VASO ΔS/S varies with inversion volume and suggests that for large body coils, inflow-independent CBF effects are present in short TR VASO data for δ≥500 mm. However, care should be taken when interpreting VASO ΔS/S on smaller body coil systems, or when head coils are used for transmission, due to possible inflow of fresh blood.

References. [1] Lu H, et al. *MRM*;50:263-74. [2] Poser BA, et al. *MAGMA*;20:63-7. [3] Donahue MJ, et al. *MRM*;56:1261-73. [4]Yang Y, et al. *MRM*;52:1407-17. [5] Scouten A. *MRM*;58:306-15. [6] Williams DS, et al. *PNAS*;89:212-6. [7] Ogawa S, et al. *PNAS*;87:9868-72.