Three-dimensional acquisition of cerebral blood volume, blood flow and blood oxygenation-weighted responses during functional stimulation in a single scan

Ying Cheng[1,2], Qin Qin[1,3], Peter C. M. van Zijl[1,3], James J. Pekar[1,3], and Jun Hua[1,3]

[1]F.M. Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, Maryland, United States, [2]Dept. of Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland, United States, [3]Neurosection, Div. of MRI Research, Dept. of Radiology and Radiological Science, Johns Hopkins University, Baltimore, Maryland, United States

Purpose: The blood-oxygenation-level-dependent (BOLD) effect reflects ensemble changes in several physiological parameters such as cerebral blood volume (CBV), blood flow (CBF), and cerebral metabolic rate of oxygen (CMRO2). Quantitative approaches have been developed to estimate CMRO2 dynamics from BOLD, CBF, and CBV responses[1,2,3]. Most studies acquire BOLD, CBF, and CBV images in separate scans. The ability to measure BOLD, CBF, and CBV signals in one single scan would be potentially useful to improve the efficiency of image acquisition, and to reduce temporal variations due to factors such as subject head motion, task performance, and physiologic changes between scans. Yang *et al* previously devised a single-slice technique for concurrently measuring those three modalities during functional stimulation[4]. This technique was further modified and applied at 7T[5]. Recently, a 3D whole-brain MRI "VASO-FAIR" approach was proposed that combines the vascular-space-occupancy (VASO)[6] and flow-sensitive alternating inversion recovery (FAIR) arterial spin labeling (ASL)[7,8] techniques to measure CBV and CBF responses in one single scan[9]. Here, we extend this method by adding a third acquisition module for BOLD images in the pulse sequence, which allows the measurement of BOLD, CBV, and CBF responses in one scan with 3D whole-brain coverage. The recently developed 3D T2prep BOLD method was employed, which uses a T2-preparation module to induce T2-weighted BOLD contrast[10]. Functional experiments with visual stimulation were performed in human brain using both the combined sequence and original separate scans, and the results were compared.

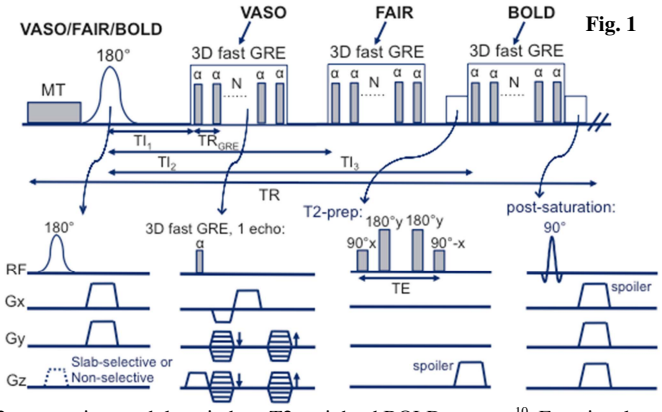
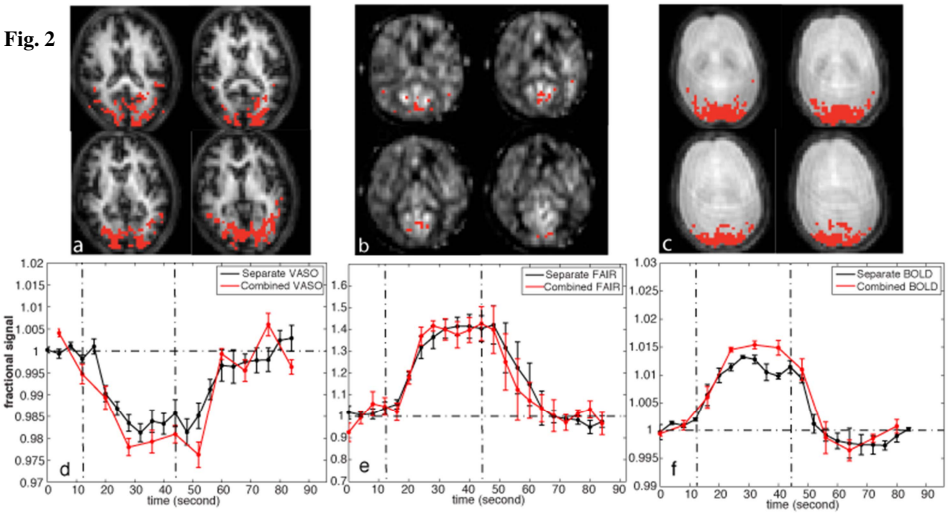


Fig. 1

Fig. 2



Methods: The combined pulse sequence (Fig. 1) consists of interleaved slab-selective (SS) and non-selective (NS) inversion preparations. CBV-weighted VASO images are obtained at TI_1 after NS inversion when blood signal is nulled, while CBF-weighted FAIR images are collected at TI_2 after both SS and NS inversion; BOLD images are acquired at TI_3 after the T2-preparation module. Studies were performed on a 3T Philips Achieva system (Philips Healthcare, Best, The Netherlands) using a body coil for RF transmission and a 32-channel head coil for reception. Four fMRI scans with visual stimulation (yellow/blue flashing checkerboard, 56s/32s off/on; 4 repetitions) were performed on each participant (n=4): 1) VASO-FAIR-BOLD ($TR/TI_1/TI_2/TI_3$=4.0/0.6/1.5/2.4s, effective TE = 60ms); 2) VASO (TR/TI=4.0/0.88s); 3) FAIR (TR/TI=4.0/1.5s); 4) 3D T2prep BOLD (TR = 4.0s, effective TE = 60ms). The order of the experiments was randomized across participants. Optimal blood-nulling times were calculated for both VASO-FAIR-BOLD (TI_1) and the separate VASO scan (TI). A magnetization transfer (MT) pulse was applied immediately before the inversion pulse to enhance tissue signals[11,12]. Single-shot 3D fast gradient echo (GRE, also called Turbo Field Echo, TFE) with centric phase encoding profile was used for all scans (flip angle=7°, FOV=192x192cm^2,voxel=5x5x5mm^3, 16 slices, SENSE factor=3x2). A post-saturation module[11,13] was employed to suppress blood inflow effects in VASO and guarantee that in VASO-FAIR-BOLD, blood spins inside and outside the imaging slab have the same steady-state magnetization[9]. *Data analysis:* All fMRI analysis was performed in SPM12. Activation detection: VASO, t-score<-1.5, SNR>20; FAIR, t-score>1.5, SNR>1; BOLD, t-score>1.5, SNR>20; all, adjusted p<0.01, cluster size>3. Temporal SNR (tSNR) was calculated as the voxel-wise average baseline signal divided by the standard deviation along the time course during the baseline period. Contrast-to-noise ratio (CNR) per scan = (ΔS/S) x tSNR. CNR per unit time = CNR per scan x square root of number of image volumes acquired during the entire scan.

Results & Discussion: Fig.2 shows the activation maps overlayed on the respective VASO/FAIR/BOLD images from the combined method. From the activation maps (16 slices acquired, 4 slices shown), the activated voxels were well localized in the visual cortex as expected. The time courses averaged over voxels activated in all three methods in all slices and all subjects (Fig. 2 bottom) matched well between the combined and separate scans. The error bars represent inter-subject variations. The vertical dotted lines indicate the start and end of visual stimulation. Quantitative results are summarized in Table 1. Average ΔS/S, tSNR, and CNR did not differ significantly (P>0.05) between combined and individual scans.

Conclusion: A pulse sequence was introduced to perform 3D acquisition of BOLD, CBV, and CBF responses in one single scan during functional stimulation. We demonstrated that the proposed method achieved image quality and activation patterns comparable with the individual scans as well as tSNR and CNR similar to the original separate scans.

Reference: (1) Davis *et al*. PNAS 1998;95:1834 (2) Lu *et al*. JCBFM 2004;24:764. (3) Blockley et al. NMR Biomed 2013;26:987. (4) Yang et al. MRM 2004;52:1407. (5) Krieger *et al.* MRM 2014; Early View. (6) Lu *et al*. MRM 2003;50:263. (7) Kim *et al*. MRM 1995;34:293. (8) Kwong *et al*. MRM 1995;34:878. (9) Cheng *et al*. NeuroImage 2014. (10) Hua *et al*. MRM 2013; Early View. (11) Hua *et al*. MRM 2013;69:1003. (12) Hua *et al*. MRM 2009;61;944. (13) Lu. ISMRM p406, 2008.
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Table 1.	VASO in combined scan	Separate VASO	FAIR in combined scan	Separate FAIR	BOLD in combined scan	Separate BOLD
ΔS/S(%)	-2.06±0.33	-1.65±0.45	40.4±8.1	40.0±8.9	1.49±0.15	1.16±0.08
tSNR	60.9±8.1	46.6±7.2	1.34±0.13	1.83±0.49	139±15	154±21
CNR per scan	1.24±0.14	0.74±0.10	0.55±0.16	0.73±0.26	2.07±0.27	1.78±0.13
CNR per unit time	8.88±1.00	7.52±0.98	5.55±1.57	7.38±2.68	14.8±1.9	18.0±1.3