Experimental separation of intra and extravascular BOLD effects using multi-echo VASO and BOLD fMRI at 1.5T and 3.0T

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INTRODUCTION: Separation of intravascular and extravascular contributions to the BOLD effect is important for understanding BOLD fMRI signal changes and, therefore, for the interpretation of activation results. It is essential for accurate determination of physiological parameters such as venous oxygenation (Yv) and oxygen extraction fraction (OEF) of tissue. Extravascular theoretical models and simulations have been used to study these two components in BOLD fMRI and their dependence on oxygenation and field strength (1, 2). However, except for long TE experiments at very high fields (3), present experimental methods do not allow effective determination of extravascular BOLD effects. In the recently developed VASO technique (4), intravascular signal is nulled, allowing measurement of changes in extravascular R2* using multi-gradient-echo experiments. By comparing these with the total R2* changes from BOLD fMRI during visual activation, we determined intra and extravascular BOLD contributions for 1.5T and 3.0T. Activation changes in Yv and OEF were found to be in excellent agreement with literature expectations.

METHODS Experiment: Studies were performed on a 1.5 T and a 3.0T MR scanner (Philips Medical Systems) using body coil transmission and SENSE head coil reception. Subjects (n=5, written consent) participated in both a 1.5T and 3.0T session. FMRI of visual stimulation (checkerboard, visual angle=25º, frequency=8Hz, block design: 30 ON, 30 OFF, 4 repetitions) was performed with: TR=3s, FA=90º, matrix=112x112, SENSE factor 2.5, FOV=220mm, single slice (5mm). For VASO, TI=797ms at 1.5T and 889ms at 3.0T. Multiple gradient-echo images were collected at four TEs in two different experiments: 14.0ms and 55.0ms in one and 34.5ms and 75.9ms in the other. VASO fMRI was repeated once to improve the SNR and to study the reproducibility. **Data processing:** VASO activation results were based on TE=14ms data; BOLD results on TE=34.5ms data. Detection criteria: cross-correlation, |cc|>0.22, cluster>3, p<0.005, SNR>10. In order to localize activated voxels located predominantly in microvasculatures, only voxels activated in both techniques were studied for extravascular contributions. The averaged voxel signal was fitted as a function of TE to obtain S0 and R2* for both resting and activated states. Yv was calculated using (2): $R^*_{2t,Hb} = f_v \cdot \gamma \cdot B_0 \cdot \frac{4}{3}\pi \cdot \Delta\chi \cdot Hct \cdot CBV \cdot (1-Y_v)$, in which $R^*_{2t,Hb}$ is the extravascular R2* effect caused by blood, f_v =0.7 the venular cerebral blood volume (CBV) fraction, and $\Delta\chi$ the susceptibility difference between fully oxygenated and deoxygenated blood (0.31ppm, (5)); *Hct*=0.42*85%=0.357 is the hematocrit in microvasculature. OEF was calculated from $(1-Y_v) = 1 - Y_a + OEF \cdot Y_a$, where Ya=0.98 is the arterial oxygenation.

RESULTS and DISCUSSION: Fig. 1 and Table 1 show activation maps for VASO and BOLD. Fig. 2 shows VASO and BOLD fMRI signal changes as a function of TE. The straight lines show the results of model fitting. Note that the intercepts and slopes of the VASO curves give information about CBV changes and extravascular ΔR2*, respectively, whereas the slopes of the BOLD curves give information about total ΔR2*. Table 2 shows the results for extravascular and total BOLD effects. The total ΔR2* at 1.5T agrees well with literature values (6). It can be seen that the contribution of extravascular BOLD to total BOLD increases at higher field, in agreement with predictions in the literature based on reduction of the intravascular venous and venular components with higher field. In addition, the amplitude of extravascular ΔR2* at 3.0T is 1.82 times the 1.5T value, close to the theoretical prediction by Yablonskiy's (2) and Ogawa's (1) equations (see Methods) that extravascular R2* change is proportional to B0. Interestingly, the total R2* does not increase significantly at 3.0T, which may be due to the very short T2* of venous blood at 3.0T (~20ms) leading to significant attenuation of intravascular BOLD signal at the TE used for detection (34.5ms). The VASO signal changes have similar amplitudes at 1.5T and 3.0T, because they reflect CBV changes, a physiological parameter that is independent of field strength. Using extravascular ΔR2* and CBV changes, Yv and OEF during activation was calculated and, again, gave similar values at 1.5T and 3.0T. Contrary to previous work where OEF was measured in draining veins (7), this OEF value was determined in parenchymal regions highly localized to activation sites, as judged based on the VASO signal origin (4). The determined effects are in excellent agreement with PET literature results (8), showing a 31% decrease in OEF upon activation. The present approach provides a non-invasive means to determine parenchymal OEF in situ.

REFERENCES: 1) Ogawa Biophys J 64: 803 1993; 2) Yablonskiy MRM 32: 749 1994; 3) Duong MRM 49: 1019 2003; 4) Lu MRM 50: 263 2003; 5) Golay MRM 46: 282 2001; 6) Bandettini NMR Biomed 7: 12 1994; 7) Oja JCBFM 19: 1289 1999; 8) Fox Science 241: 462 1988.

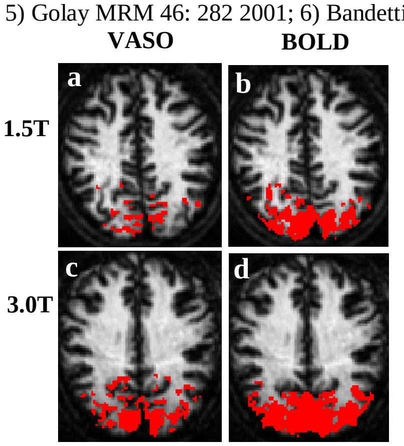

Fig. 1: Activation maps overlaid on VASO EPI images. 3.0T provides higher CNR for both techniques compared to 1.5T.

Table 1: Comparison of VASO and BOLD fMRI results and contrast-to-noise ratio (n=5, mean ± SEM). CNR = {(fMRI signal change) / noise SD} * sqrt(number of images).

	VASO		BOLD	
Field	1.5T	3.0T	1.5T	3.0T
Number of activated voxels	171±39	421±83	452±44	685±39
CNR	5.03	8.55	9.57	15.03

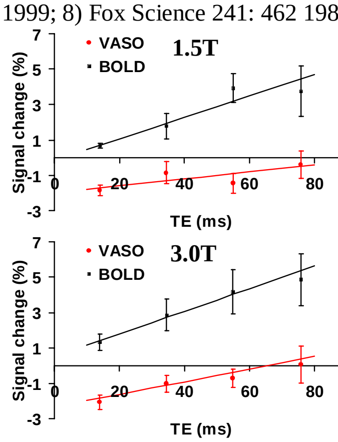

Fig. 2: FMRI signal changes vs TE in voxels that showed activation in both VASO and BOLD experiments. Error bar=SD, n=5.

Table 2: Data summary (n=5, mean±SEM) of multi-echo VASO and BOLD experiments. Yv,act and OEFact was calculated with assumptions below: CBVrest=4.7%, Yv,rest=0.61. OEFrest=0.380.

	extrav. ΔR2* (s-1)	total ΔR2* (s-1)	extrav. ΔR2* fraction	VASO signal change	Yv (activated)	OEF (activated)
1.5T	-0.198±0.055	-0.591±0.084	37.5±10.9%	1.85±0.14%	0.747±0.010	0.238±0.010
3.0T	-0.360±0.042	-0.619±0.076	60.9±7.7%	2.07±0.18%	0.761±0.009	0.223±0.009