Minimizing BOLD contamination in VASO fMRI with SE-EPI

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Introduction

The recently proposed Vascular Space Occupancy (VASO) functional MRI (fMRI) method detects changes in cerebral blood volume (CBV) by nulling the blood signal, causing negative signal changes during brain activation [1]. However, because VASO typically uses IR-GRE-EPI which is sensitive to opposing (positive) T_2^* BOLD changes, quantification will significantly underestimate CBV changes, even at the shortest possible TE. Spin echo (SE) sequences are less sensitive to BOLD changes, which will have a T_2 (instead of T_2^*) dependence [2]. VASO acquisitions based on IR-SE-EPI may therefore suffer less from BOLD contamination; however, the longer TE associated with achieving a spin echo may reduce the advantage of SE over GRE. In general, SE-based VASO has not been explored, despite these potential advantages. This work demonstrates the feasibility of SE-EPI VASO, and uses multi-TE measurements to determine the amount of BOLD contamination in GRE-EPI VASO and SE-EPI.

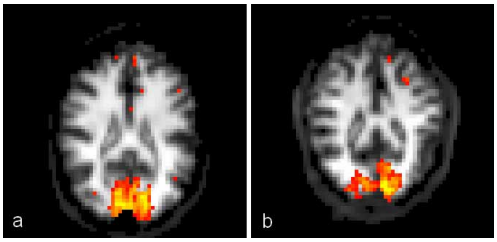

Figure 1 *VASO activation maps; threshold at $z \geq |3.5|$. **a)** IR-GRE-EPI (TE=12 ms) **b)** IR-SE-EPI (TE=20 ms)*

Methods

VASO fMRI experiments were conducted on ten healthy volunteers (n = 5 each for GRE-EPI and SE-EPI) on a 3T whole body scanner (Siemens, Germany). Each subject was presented with a series of visual stimuli in a block paradigm consisting of 4 blocks of 15s of rest interleaved with 15s of visual stimulation. Single-slice VASO data with a non-slice-selective inversion pulse was acquired at 5 different TEs for IR-GRE-EPI (TE = 12, 20, 30, 50, 75ms) and IR-SE-EPI (TE = 20, 30, 50, 70, 90 ms), with TR/TI = 3000 ms/890 ms, in-plane matrix size = 64x64 (resolution = 3.2×3.2×5mm) and flip angle $\alpha = 90^0$. GRE-EPI BOLD and SE-EPI BOLD runs were also acquired with the same parameters and slice location as VASO, but without the inversion recovery pulse. The latter scans can be used to assess the BOLD contamination in the matched VASO data. Fractional signal changes were determined by their averaged values within the ROIs, which were defined as the subset of BOLD-activated voxels overlapping with VASO-activated voxels to localize the ROI mainly in the microvasculature. The activated voxels were identified by thresholding the correlation ($|z| \geq 3.5$) and cluster significance ($p \geq 0.05$). The contrast-to-noise-ratio (CNR) was calculated by averaging the z-statistic values within the defined ROIs. The BOLD contamination and volume change were estimated from a line fit of the fractional signal change vs. TE. The slope of the fitted line reflects the BOLD component (ΔR_2^* or ΔR_2), and the intercept (extrapolation to TE=0) provides an estimate of ΔCBV [3]. Given that the true VASO signal contains no BOLD contribution, we calculated the underestimation of ΔCBV at the shortest possible TE for both IR-GRE-EPI and IR-SE-EPI.

Results and Discussion

At the shortest TE, the average CNR of IR-SE-EPI (5.0±0.5) was comparable to IR-GRE-EPI (4.9±0.3), suggesting that the sensitivity is similar for both sequences. The localization of the activated voxels is also similar for the two acquisitions (Fig 1). As expected, the BOLD contribution, denoted by the slopes of the linear fit (Fig 2), was considerably reduced for SE VASO as compared to GRE VASO. The transverse relaxation rates decreased from ΔR_2^*=0.61±0.15 for IR-GRE-EPI to ΔR_2=0.14±0.09 for IR-SE-EPI. The TE=0 intercept indicates fractional CBV change of 3.5±0.3% and 2.5±0.6% for GRE and SE, respectively, a difference which was not significant (Student's t-test, p<0.01). Because the amount of BOLD contribution is directly related to the amount of underestimation in ΔCBV, minimizing the ΔR_2 will improve the accuracy of estimating ΔCBV when a single-echo acquisition is performed and extrapolation to TE=0 is not possible. Based on our fits, we calculate the amount of underestimation to be 24% for IR-GRE-EPI (at TE=12 ms), whereas IR-SE-EPI underestimated ΔCBV by only 5% (at TE=20 ms). Finally, when comparing the slopes of the BOLD fits to the VASO curves it is seen that for GRE-EPI, the VASO curves have smaller slopes compared to the BOLD curves. This agrees with previous work that predicted that the non-IR curve reflects intra- and extravascular BOLD, whereas the IR-prepped VASO signal reflects only extravascular BOLD effects [3]. For SE-EPI, the IR and non-IR curves have similar slopes, which may suggest that the intravascular BOLD effects are heavily reduced for SE-EPI BOLD. However, our data are not sufficient to conclusively infer intra- vs. extravascular changes, and it is important to note that the isolation of extravascular effects in VASO is crucially dependent on achieving perfect nulling of the blood. If IR-SE and IR-GRE are sensitive to different vascular compartments, this may explain the tendency toward different extrapolated ΔCBV values (which, as described above, were not significant).

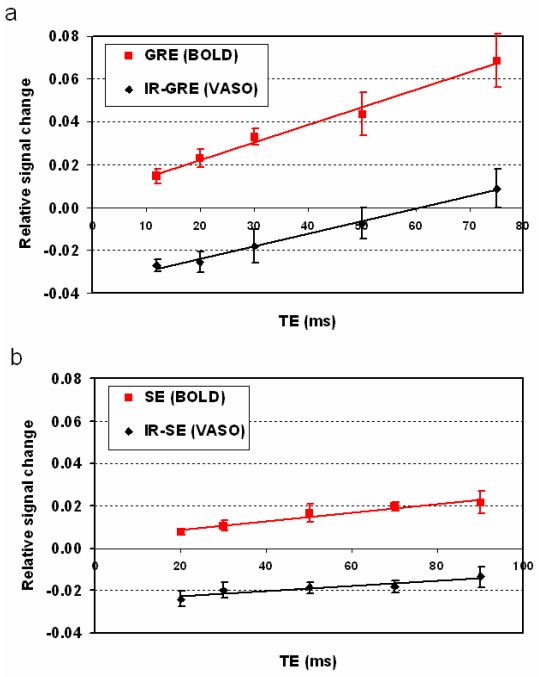

Figure 2 *Relative signal changes as function of TE. **a)** GRE-EPI BOLD and VASO **b)** SE-EPI BOLD and VASO*

Conclusions

Our data indicates that SE-EPI VASO is less prone to BOLD contamination than GRE-EPI VASO. As a result, underestimation of ΔCBV was reduced for TE>0. Moreover it is found that SE VASO has similar CNR compared to IR-GRE-EPI.

[1] Lu H, Golay X, Pekar JJ, van Zijl PCM. *Magn Res Med*, 2003;50(2):263-274. [2] Parkes LM et al, *Magn Res Med 2005*,Dec;54(6):1465-72. [3] Lu H, van Zijl PCM. *Magn Res Med*, 53(4):808-816,2005