Spin-lock functional MRI at low locking fields shows improved microvascular specificity

Swati Rane[1], John T Spear[1], Carlos Faraco[1], Manus Donahue[1,2], and John C Gore[1,3]

[1]*Radiology and Radiological Sciences, Vanderbilt University, Nashville, TN, United States,* [2]*Neurology, Vanderbilt University, Nashville, TN, United States,* [3]*Biomedical Engineering, Vanderbilt University, Nashville, TN, United States*

TARGET AUDIENCE: Investigators interested in functional MRI of the brain and/or T1-rho contrast mechanisms

INTRODUCTION: This study was undertaken to demonstrate that spin lock prepped MR images can provide superior depictions of functional activations, with greater specificity for microvascular BOLD effects, than conventional fMRI sequences. BOLD fMRI detects oxygenation related transverse relaxation changes usually using spin echo (SE: *R2*) or gradient echo (GE: *R2**) sequences. The major contributors to changes in *R2* or *R2** are changes in local static field inhomogeneities as well as diffusion effects within local field gradients. Static effects are dominated by larger veins but are reversible with a spin-echo, whereas contributions of diffusion in the extravascular gradients around large veins persist. We have recently shown how diffusion losses in inhomogeneous media may be reduced by using spin-lock prepped ($T1_\rho$ weighted) acquisitions, and that the reduction depends on the magnitude of the locking field relative to spatial frequency of local gradients. In particular, dephasing caused by larger structures may be selectively reduced using relatively low amplitude locking pulses. [1,2]. We applied this approach to measure evoked BOLD responses in the visual cortex[3]. Here, we sought to evaluate the specificity of spin-lock prepared fMRI ($T1_\rho$ fMRI) at low locking fields (ω_1 = 80Hz) for emphasizing diffusion effects in oxygenation-related local magnetic field changes in the microvasculature (size ~ 14μm). We hypothesized that relative to gray matter, BOLD signal changes caused by large vessels will be reduced with $T1_\rho$ fMRI at ω_1 = 80Hz compared to GE and SE BOLD fMRI signal changes owing to a de-emphasis of diffusion effects from large venous structures (~ 100μm).

METHODS: ***Experiment:*** Nine subjects provided written informed consent and were scanned on a 3T Philips Achieva scanner with a 32 channel receiver head coil. A 3D MPRAGE sequence was used to select a slice parallel to the AC-PC line and tangential to the corpus callosum. We performed a hyperoxia experiment to induce only oxygenation changes. Subjects wore a gas mask with the reservoir closed for 100% oxygen delivery at 12L/min during 2 blocks of 2.5 min each separated by a 2.5 min block of room-air delivery. We applied a Fast Spin Echo acquisition with spin-lock preparation[4,5] comprised of a 90° pulse, a pair of locking pulses separated by a 180° pulse, and a -90° flip; ω_1=80Hz, spin lock duration = 50 ms, single slice, TR/TE=2200/6.2 ms, SPIR fat suppression, voxel size=1x1x4 mm^3. Multi-echo GE and SE data were acquired with TR/TE=2200/22,64,106 ms and TR/TE=2200/44,90 ms respectively. Additionally, we acquired an angiography scan to identify large vessels (TR/TE=17/24 ms, voxel size = 0.8x0.8x0.8 mm^3, 240 slices). ***Analysis:*** **(1)** The anatomical slice was segmented into gray and white matter using FSL[6]. Five slices covering the imaging slice were combined with a minimum intensity projection (MinIP) to obtain a map of large vessels. This vessel map was then subtracted from the gray and white matter mask to obtain a mask of gray and white matter tissue containing mostly microvasculature. **(2)** fMRI data were corrected for baseline drift, head motion, and registered to the T1 slice. A generalized linear model (GLM) design was used in FSL to determine BOLD signal increases. Ratios of BOLD signal increases in the vessel mask to that in the gray matter mask were compared between the GE (TE=64 ms), SE (TE=90 ms) and $T1_\rho$ fMRI. **(3)** To ensure an absence of inflow-effects, the multi-echo GE and SE data were fit to a log ($-ln(S/S_0)/TE$) linear data to evaluate *R2,* $S0_{GE}$, *R2**, and $S0_{SE}$ maps at each TR, where $S0_{GE}$ and $S0_{SE}$ reflect changes in blood volume or inflowing blood. The same GLM was applied to the $S0_{GE}$ and $S0_{SE}$ maps as in **(2).**

RESULTS: **Figures 1(a-f)** show the imaging slice, segmentation result, GE, SE, and $T1_\rho$ BOLD maps for a representative subject. The average BOLD signal changes with GE, SE, and $T1_\rho$ were 4.46±0.71%, 2.77±0.57%, and 1.18±0.16% respectively in the vasculature and 3.33±0.69%, 2.45±0.21%, and 1.12±0.15% respectively in the gray matter tissue while the ratio of BOLD signal increases in the vasculature to gray matter tissue were 1.37±0.24, 1.14±0.08, and 1.07±0.09 respectively (**1g**). This ratio showed a significant decreasing trend between GE and SE BOLD data in accordance with the literature ($p<0.005$) as well as between SE and $T1_\rho$ BOLD data ($p<0.05$). $S0_{GE}$ and $S0_{SE}$ changes were minimal (0.20±0.07%, 0.22±0.13% respectively). Z-scores for the signal changes in gray matter were higher for the $T1_\rho$ sequence.

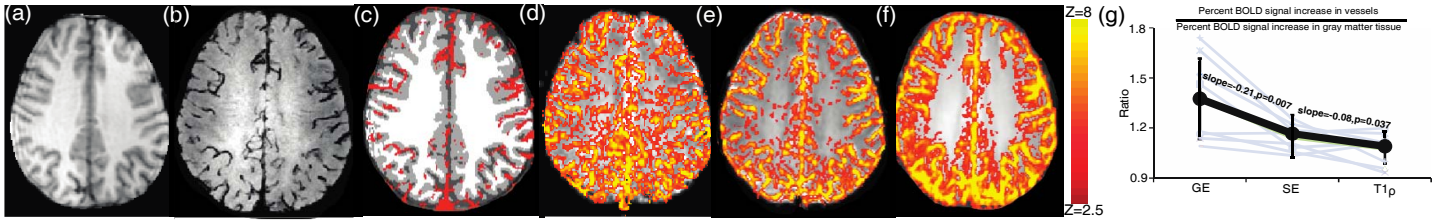

Figure 1: *(a) T1, (b) angiography, and subsequent (c) segmentation into gray matter (light gray), white matter (white), and vessels (red) for the imaging slice. (d-f) BOLD maps for GE, SE, and $T1_\rho$ fMRI respectively following hyperoxia. GE signal changes are more spurious while the SE and $T1_\rho$ signals are confined to the cortex. Also the Z scores in the gray matter are the highest for $T1_\rho$ fMRI. (g) BOLD contrast from large vessels is reduced in SE compared to GE fMRI ($p<0.005$) and further reduced with $T1_\rho$ fMRI ($p<0.05$)*

DISCUSSION: Relative BOLD signal change in large vessels compared to gray matter is further reduced with $T1_\rho$ compared to SE fMRI likely due to a lack of sensitivity to diffusion effects across large structures at ω_1 = 80Hz which persist in SE fMRI. BOLD signals in the MinIP vessel mask represent large vessels and the surrounding extravascular tissue but even with the higher resolution fMRI and PCA scans, difficulty to resolve vasculature clearly in the gray matter may affect BOLD measurements. Future work will involve extension of the $T1_\rho$ approach to whole brain coverage to improve its utility.

CONCLUSION: We show that $T1_\rho$ fMRI with low locking fields can detect BOLD contrast similar to SE fMRI, but $T1_\rho$ fMRI with low locking fields de-emphasizes non-specific BOLD contrast signals from large vascular structures to a greater extent than GE and SE BOLD fMRI.

REFERENCES: 1. Spear J., MRM, (2014), 71(5):1906, 2. Spear J., JMR, (2014), ahead of press, 3. Rane S., MRI, (2014), 32(7):813, 4. Zeng H., ISMRM (2006), 5.Witschey W., JMR, (2007), 186:75, 6. Zhang Y., IEEE TMI (2001), 20(1):45, 7. Beckmann C., HBM (2006), 27:380