Functional MRI Using Spin-Lock Sequences to Modulate BOLD Activation

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Target Audience: Investigators performing fMRI of brain function or interested in novel methods of characterizing vasculature.

Purpose: Functional MRI is well-established as an important modality for mapping the functional architecture of the brain based on detecting BOLD signal changes caused by the hemodynamic response to changes in neural activity. Nearly all fMRI is performed using sequences that are sensitive to R_2* ($=1/T_2$*) and typically also using single shot acquisitions such as echo planar imaging. The major contributions to the observed decreases in R_2*, that accompany activation come from changes in the magnitudes and distributions of local magnetic fields experienced by water molecules (so-called static field effects) as well as reductions in dephasing caused by diffusion through local field gradients[1]. The static effects are reversible using a spin-echo, and may be dominated by larger venous structures. Asymmetric spin echo sequences provide one means to manipulate the relative contributions of these processes[2], but the ability to "tune" for specific sizes of susceptibility variation is very limited. Here we demonstrate the ability of spin-locking preparation pulses to modulate BOLD effects and specifically to be able to explicitly emphasize diffusion losses through gradients of a selected spatial scale. This approach allows acquisitions with any rapid imaging sequence, including single shot methods, but with minimal echo time, so that the resultant images are much less prone to geometric distortion. The method may be used to emphasize activation due to microvascular changes and to remove larger scale effects.

Methods: *Theory:* Our approach is based on a theoretical analysis of the effects of diffusion through periodic variations of magnetic susceptibility on the behavior of rates of spin-lattice relaxation in the rotating frame $R_{1\rho}$ ($=1/T_{1\rho}$). Magnetic susceptibility variations induce local field gradients that scale with field strength, and diffusion through such gradients is well known to increase transverse relaxation rates. $R_{1\rho}$ is also affected by diffusion effects to a degree that depends on the magnitude of the locking field used for measurements. We recently derived an expression for quantifying the influence of diffusion on $R_{1\rho}$ in the presence of a sinusoidally varying local field $b(x) = A\sin qx$, where q is a spatial frequency, and g is the mean gradient amplitude i.e. $g^2 = A^2q^2/2$. The contribution to $R_{1\rho}$ from diffusion in this gradient during a spin-locking experiment can be shown to be

$$R_{1\rho}^{diff} = \frac{\gamma^2 g^2 D}{(q^2 D)^2 + \omega_1^2}$$

where γ is the gyromagnetic ratio, ω_1 is the spin-lock amplitude, and D is the self-diffusion coefficient[3]. The decrease of $R_{1\rho}$ with increasing locking field provides information about the spatial scales and magnitudes of the gradient pattern, and the ability to vary ω_1 allows for selection of structures of specific spatial frequencies. The above expression provides useful insights and an approximate theoretical description of the effects of arrays of microvessels whose internal susceptibility differs from the surround, the case for BOLD effects.

Experiment: To demonstrate the ability to perform fMRI studies, we implemented a spin-lock preparation pulse cluster[4,5] directly in front of a FSE acquisition with minimal TE = 5.7ms. The cluster consisted of an initial 90 degree flip, a pair of locking pulses with selectable strength (separated by a refocusing pulse), followed by a -90 flip back to the z direction. The spin lock amplitude ω_1 was selected to be either 0, 80 Hz or 400 Hz, and the pulse was applied for durations (TSL) of 0, 50 and 80 ms. Functional imaging acquisitions were acquired on a Philips Achieva 3T scanner using an 8 channel head coil. Different acquisition sequences were implemented in a standard block design visual activation experiment. An 8 Hz full-field flickering checkerboard was presented in blocks of 36 seconds, alternated with blank presentations of 36 seconds, and repeated 5 times per run. Images were acquired with the following parameters: single slice TR/TE = 2200/5.7 ms, SPIR fat suppression, voxel size 2.3 x 2.3 x 4 mm^3. 7 runs were performed, one for each combination of ω_1 and TSL. Conventional BOLD data were also acquired with TR/TE = 2200/35 ms, with only 3 blocks of stimulation and blank presentations per run. *Analysis:* The three TSL data at ω_1 = 80 and 400 Hz were fit to a monoexponential decay to produce maps of $R_{1\rho}$ at each lock amplitude. Activation maps were derived in FSL using a GLM analysis using (i) the conventional BOLD acquisitions (ii) the $R_{1\rho}$-weighted images at TSL = 50ms for each of the three values of the locking field and (iii) the calculated $R_{1\rho}$ maps at each locking field. Mean time courses and % signal changes for activated (visual cortex) and reference (frontal) regions were also calculated.

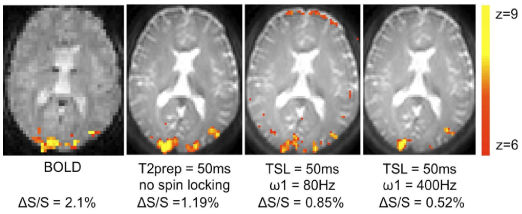

Figure 1: *Activation maps for (a) BOLD, preparation pulse (TSL = 50 ms) with (b) ω_1 = 0, (c) ω_1 =80, (d) ω_1 = 400 Hz*

Results: Figure 1 shows **(a)** a conventional BOLD activation map using single shot EPI with TE = 35ms **(b)** the activation map produced with TSL = 50 ms with ω_1 = 0 and (c) and (d) the maps with TSL = 50ms and ω_1 corresponding to 80Hz and 400Hz respectively. Figure 1 also shows how the % change in signal from activation varied for different sequences. Figure 2 shows activation map for the calculated $R_{1\rho}$ map and the % change in $R_{1\rho}$ during activation (-1.55%) at ω_1 = 80 Hz. The % change in $R_{1\rho}$ during activation at ω_1 = 400 Hz was (-0.14%).

Discussion: The spin-lock preparation includes a 180 pulse that refocuses static dephasing effects but does not compensate for the effects of diffusion through field gradients. When the spin-lock amplitude = 0, significant signal losses accrue during the preparation interval and the relaxation rate $R_{1\rho}$ varies as ~ q^{-4} i.e. may be dominated by large scale structures such as draining veins. The activation pattern resembles that produced by a standard T_2*-weighted BOLD image. At high values of the locking field, the contribution of diffusion to $R_{1\rho}$ is removed so there is little difference between the activated and baseline conditions. However, in the presence of a locking field of 80 Hz, $R_{1\rho}$ will show maximal rate of change to susceptibility variations for which $q \approx 4400$ cm^{-1}, corresponding to susceptibility variations spaced ≈ 14 μm. Compared to their contributions when the locking field is 0, the contributions to $R_{1\rho}$ from diffusion for objects of dimension ≈ 1000 μm are reduced by $>10^8$, for 100 μm by more than 10^3, whereas for 10 μm only by 0.7 i.e. the locking field dramatically enhances the relative contribution of microvascular structures of interest compared to other structures.

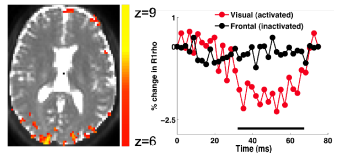

Figure 2:*Activation maps for $R1_\rho$ at $\omega 1$ = 80 Hz. Plot shows % change in $R1_\rho$ during activation (defined by black line)*

Conclusion: FMRI can be successfully performed using a spin-lock prepared acquisition with minimal TE. The effects of diffusion amongst field gradients contribute to spin-lattice relaxation rates in the rotating frame differently in a baseline compared to an activated condition as with conventional BOLD imaging. However, by judicious choice of the spin-locking field, the contribution to the activation signal changes from susceptibility variations of specific spatial scales can be dramatically emphasized, and by acquiring an appropriate set of measurements at different locking fields, their magnitudes and dimensions can be estimated. This approach also has considerable potential for characterization of vascular structures in normal and abnormal tissues.

References:[1] RP Kennan et al., Magn. Reson. Med. 31, 9-21, 1994 [2] LA Stables et al., Mag. Res. Med. 40, 432-442, 1998 [3] JC Cobb et al., Magn Reson Med. 2012 Jul 12 [4] H Zeng et al, Proc ISMRM Annual Meeting, Seattle, WA 2006 [5] WR Witschey et al., J Magn Reson 186, 75-85 2007.