Analysis of the BOLD Signal Characteristics in balanced SSFP fMRI: a Monte-Carlo Simulation

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Introduction Recently, balanced SSFP (Steady State Free Precession) has been proposed as an alternative method to measure the BOLD contrast [1-3]. Two different contrast mechanisms have been explored experimentally: (1) transition-band SSFP fMRI (BOSS fMRI) that detects the BOLD induced frequency shift near the transition part of the SSFP profile [1,2], and (2) pass-band SSFP fMRI that is believed to utilize the T_2 sensitivity (or spin diffusion effects) of balanced SSFP in a relatively wide and flat off-resonance frequency band in the SSFP profile [3]. Both of them provide a higher SNR efficiency with reduced imaging artefacts compared to conventional methods providing a great opportunity for high-resolution functional studies. Moreover, the pass-band method is believed to possess the spin-echo characteristic [4], potentially providing a reduced signal contribution from large veins [3]. The previous experimental results suggest that the level of the functional contrast and its characteristics are significantly influenced by the sequence parameters [5,6]. However, none of these pass-band contrast characteristics have been investigated systematically, and even the contrast mechanism has not fully understood. In this study, we utilized a Monte-Carlo simulation technique to demonstrate that the spin diffusion effects (T_2 change) account for a large portion of the functional contrast in pass-band SSFP fMRI. We also investigated various parameters (TR, flip angle, off-resonance and field strength) to show the characteristics of the functional contrast and to find optimize scan parameters for the pass-band SSFP fMRI. The preliminary experiments were performed to validate the simulation results.

Methods In the simulation, the BOLD signal was decomposed into the intravascular and extravascular parts. The extravascular contribution was investigated using the Monte-Carlo method similar to [7], whereas the intravascular contribution was calculated by the modified Luz-Meiboom model [8]. This intravascular model is particularly important in SSFP fMRI because it allows us to include the spin exchange effects between RBC and plasma pools; hence it provides a more realistic model when TR becomes short.

Extravascular simulation: For the Monte-Carlo simulation, the blood vessels were modelled as infinite cylinders whose magnetic susceptibility are different by $Hct\Delta\chi\ B_0(1\text{-}Y)$. As a spin moving near a cylinder, it experienced the field perturbation as follows:

$$\Delta B_z(r,\varphi) = 2\pi\gamma Hct\Delta\chi B_0(1-Y)(R/r)^2\cos 2\varphi\sin^2\theta, \quad r \geq R$$

where Hct = 0.4, $\Delta\chi$ = 0.27 ppm and the other parameters can be found in [7]. The Y value was assumed to change from 0.77 (resting state) to 0.85 (activation state) when R ≤ 100 μm, and from 0.55 to 0.75 when R > 100 μm. A large number of cylinders were generated in random orientations, filling 2% of the total volume. A total of 1000 protons, starting at random locations (only in the extravascular space), were generated and performed random walks with an apparent diffusion coefficient of 1×10^{-5} cm^2/s. In each time step (0.2 ms), the magnetization of each proton was calculated by considering (1) a phase accrual by all the vessels, (2) T_1 and T_2 relaxations, and (3) the phase-cycled RF pulse applied in every TR by solving the Bloch-Torrey equation. The signal decay was measured after 2 sec to ensure a steady-state, and averaged over the next 30 TRs. The whole simulation was repeated to measure the percent signal changes between the two states and also repeated for the various parameters.

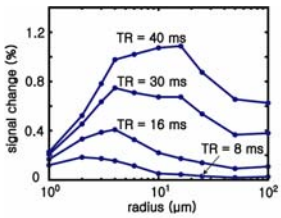

FIG. 1. Signal change with TR and cylinder size. B_0 = 3 T, α = 60°.

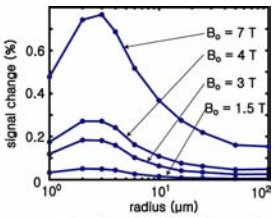

FIG. 2. Signal change with B_0 and cylinder size. TR = 8 ms, α = 60°.

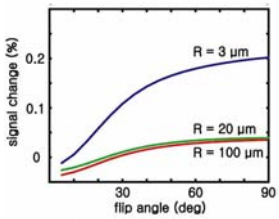

FIG. 3. Signal change with flip angle. B0 = 3 T, TR = 8 ms.

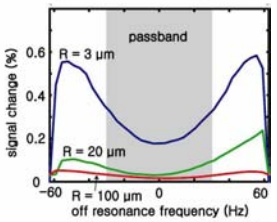

FIG. 4. Signal change with off-resonance. B0 = 3 T, TR = 8 ms.

Intravascular simulation: In SSFP, when TR is close the mean exchange time (τ_{ex}, 1 ~ 10 ms, [9]), the RF excitation can refocus some of the diffusion effects, resulting in a reduced T_2 sensitivity. This T_2 change can be modeled as $1/T_2 = 1/T_{2o} + K(1\text{-}Y)^2$ (see [8] for the parameters) and Y is the same as in the extravascular case. For different TRs, the K values were estimated from [8] by calculating other parameters from the measured values. After calculating the T_2 values for the resting and activation states, the intravascular signal was calculated by the SSFP signal equation.

These intra- and extravascular contributions were combined together [9] to generate the percent signal change. Two simplified voxels, one representing a grey matter voxel (2% capillary volume with R = 3 μm and 3% venule volume with R = 100 μm) and the other representing a voxel with large veins (20% venous volume with R = 500 μm in addition to 2% capillary and 3 % venule volumes) were assumed to compare the signal change levels with the experimental results.

Experiment: To validate the simulation results, preliminary experiments were preformed. Three subjects were scanned at a 1.5T GE scanner using a 3-inch surface coil. For pass-band SSFP fMRI sequence, a 3D stack-of-spirals sequence (FOV = 16 cm^2, resolution = 2x2x4 mm^3, flip angle = 60°, TE = TR/2, number of interleaves = 4, number of slices = 10, and readout duration = 8.48 ms) was used for three different TRs (20.8, 31.3, and 41.6 ms). Each 3D volume was acquired every 1 sec (TR = 20.8 ms), 1.5 sec (TR = 31.3 ms), and 2 sec (TR = 41.6 ms). A visual stimulation with a flashing checkerboard was used (20 sec on/off for 3 minutes in each scan). For the analysis, FEAT FSL was used with a threshold z > 2.33. After generating each activation map, commonly activated voxels were chosen and the mean percent signal changes were calculated to compare with the simulation results.

Results & Discussion The Monte Carlo simulation results for the extravascular signal changes are shown in Fig. 1-4. In Fig. 1, the percent signal change dependence is plotted for various vessel sizes and TRs. As expected, the pass-band balanced SSFP possesses the spin-echo behaviour: the signal change is higher in capillaries (~ 3μm) compared to large veins. This effect is more prominent when TR is short; however, the overall percent signal change increases approximately linearly as TR increases with increasing plateau toward larger size veins. This linear increase is also clearly observed in the experimental results shown in Fig. 5, validating our simulation results. Figure 2 reveals the field strength dependence on a range of vessel sizes. As the field strength increases, the signal changes increase approximately quadratically. These results suggest that higher field strengths with short TRs will provide a good localized activation in capillaries in SSFP fMRI. The RF flip angle also affects the contrast levels as shown in Fig. 3. As the flip angle increases, the percent signal changes also increase. This flip angle dependency agrees with the previous experimental results shown by Bowen et al. [5] where a linear increase was observed. In our simulation, the slopes of the curves become lower after approximately 45°, resulting in smooth plateaus. Therefore, the use of the flip angle 45° is suggested in high field strength systems when the SAR becomes a major problem. Depending on the off-resonance frequency, the extravascular contrasts can vary up to 50% (R = 3 μm) when the bandwidth of the spatial coverage is assumed to be the half of 1/TR (Hz). The significant increase in the percent signal change when f_{off} < -40 Hz and f_{off} > 40 Hz (Fig. 4) is due to the decreased baseline signals because the percent signal change is defined as $100\cdot(S_{active}\text{-}S_{base})/S_{base}$. The experimental results at 1.5 T show, on average, 1 ~ 3.3 % signal activation (circles) with increasing signal changes as TR becomes longer (Fig. 5). The mean z-score of the commonly activated voxel was 5.16. The upper (triangles) and lower (rectangulars) marks shown in the plot represents the mean of the top 25% and the mean of the bottom 25% from the selected voxels (commonly activated voxels in all TR) in all the subjects. Both the simulation plots and the experimental results agree well: increasing percent signal changes when TR becomes longer. The experimental results lie between the simulated grey matter voxel and the large vein voxel as expected. For this experiment, the TRs were relatively long to acquired functional contrast at a low field strength system. Therefore the large vein contribution was unavoidable. However, the simulation results suggest that at high field strength with a short TR, the large vein signal change can be reduced by this pass-band SSFP fMRI method.

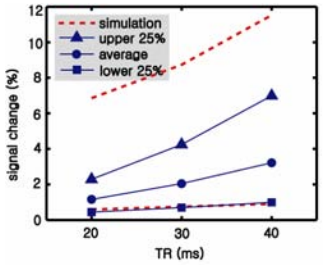

FIG. 5. Comparison between simulation and experimental result. Dotted red line is simulation result and solid blue line is experimental result.

Reference [1] Scheffler, NMR Biomed, 2001;14:490 [2] Miller, MRM, 2003;50(4):675 [3] Bowen, 13th ISMRM, 2005;p119 [4] Scheffler, MRM, 2002;48:633 [5] Bowen 14th ISMRM, 2006;p665 [6] Zhong, 14th ISMRM, 2006;p3296 [7] Boxerman, MRM, 1995;34:555 [8] Dharmakumar, MRM, 2005;53:574 [9] Jin, MRM, 2006;55:1281 [10] Miller, MRM, 2006;55(1):161