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 artifacts 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 $H_{ct} B_0 (1 - Y)$. As a spin moving near a cylinder, it experienced the field perturbation as follows:

$$\Delta B_0(r, \phi, \theta) = 2\pi H_{ct} B_0 (1 - Y) \left( \frac{r}{R} \right)^2 \cos 2\phi \sin \theta, \quad r \geq R$$

where $H_{ct} = 0.4$, $\phi = 0.27$ 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 $R \leq 100 \mu m$, and from 0.55 to 0.75 when $R > 100 \mu m$. 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 $1 \times 10^{-6}$ cm$^2$/s. In each time step (0.2 ms), the magnetization of each proton was calculated by considering a phase accrual by all the vessels, ($2 \pi$), and $T_1$ 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.


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 (~ 3% $\mu m$) 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 more prominent when TR is short; however, the overall percent signal change increases approximately linearly as TR increases. 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.

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 $R = 3 \mu m$ and 3% venule volume with $R = 100 \mu m$) and the other representing a voxel with large veins (20% venous volume with $R = 500 \mu m$ 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 performed. 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 = 2.2x2.4 mm$^2$, flip angle = 60°, TE/TR2/2, number of interleaves = 4, number of slices = 10, TR/TE = 4.16 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.

Reference

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

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