Quantification of the BOLD contrast mechanism, including its dynamic approach to steady state, for pass-band balanced-SSFP fMRI

S. Patterson[1,2], S. D. Beyea[1,2], and C. V. Bowen[1,2]

[1]Institute for Biodiagnostics (Atlantic), National Research Council, Halifax, NS, Canada, [2]Physics, Dalhousie University, Halifax, NS, Canada

Introduction: Recent work has investigated functional MRI (fMRI) using balanced steady-state free precession (b-SSFP) acquisitions. Methods exploiting the frequency-sensitive transition-band [1], the off-resonance phase profile [2], and the on-resonance pass-band [3] have all been implemented. Pass-band b-SSFP fMRI has attracted interest because of experimental evidence indicating reduced large vein sensitivity [3], robust performance in areas of magnetic field in-homogeneity [4], and reduced sensitivity to physiological noise [5]. Despite this growing interest, however, the contrast mechanism for pass-band b-SSFP fMRI remains unclear. Studies have implicated contrast mechanisms based primarily on diffusion sensitivity [6], intra-vascular T2 changes [7], and T2* [8]. Furthermore, experimental obstacles persist in the implementation of pass-band b-SSFP fMRI, as current whole brain 3D applications involve separate runs of the functional paradigm to acquire image volumes with different phase cycling, which are then combined to form artifact-free images [4]. These acquisitions can be several minutes apart, and so developing phase cycling methods that complete within a single acquisition volume is needed, which requires knowledge of the dynamic approach to steady state of BOLD contrast.

This study used a Monte-Carlo computer model to investigate the contrast mechanism in pass-band b-SSFP both in steady state and during the dynamic approach to steady state. The model permitted water self-diffusion, intra-vascular T2 changes, and susceptibility induced field offsets to be enabled in various combinations and for various vessel sizes, allowing a systematic investigation of the contributors to pass-band b-SSFP fMRI contrast. In addition to quantifying the relative strength of b-SSFP contrast sources, the simulations revealed strong peaks in BOLD CNR for high flip angles that occurred prior to the full development of the steady state. This implies that b-SSFP techniques could be accelerated, with higher BOLD contrast, by appropriate phase cycling and k-space ordering schemes.

Methods: Simulations of 4T α/2 catalyzed b-SSFP acquisitions with TE=TR/2 were conducted using Monte Carlo methods similar to [9-10]. However, unlike previous simulations [10], the effects of oxygenation dependent intravascular blood T2 relaxation changes were included [7,11]. Blood T2 values (s) were calculated at oxygenation saturation fraction Y and pulse separation τ (ms) using the Luz-Meiboom equation (eq. 1) with scaling parameters from [11]. The exchange time used, τ_{ex}, was 4.4 ms [7] and vessel water permeability was set to zero. Signal changes ($\Delta S/M_o$) between active (Y=0.85) and resting (Y=0.77) states were computed for four different cases: 1) field offsets from susceptibility changes only (F); 2) both field offsets and intra-vascular T2 changes (FT2); 3) field offsets and diffusion effects only (FD); and 4) full simulation including field offsets, diffusion and intra-vascular T2 changes (FDT2). The relative contribution of each contrast source was then computed by subtraction of $\Delta S/M_o$ from each simulation (eg. the intra-vascular T2 contrast contribution was calculated by subtraction of the FT2 and F runs). The separability of the individual contrast sources was supported by the near exact agreement of two methods for estimating the intra-vascular T2 contributions (FDT2-FD vs FT2-F) and diffusion contributions (FDT2-FT2 vs FD-F) (data not shown).

$$1/T_2 = 3.9 + 24.6(1-Y)^2(B_0/1.5)^2\left(1-\frac{2\tau_{ex}}{\tau}\tanh\frac{\tau}{2\tau_{ex}}\right)\Big/\left(1-\frac{2\tau_{ex}}{12}\tanh\frac{12}{2\tau_{ex}}\right) \quad [1]$$

Results/Discussion:

Figure 1

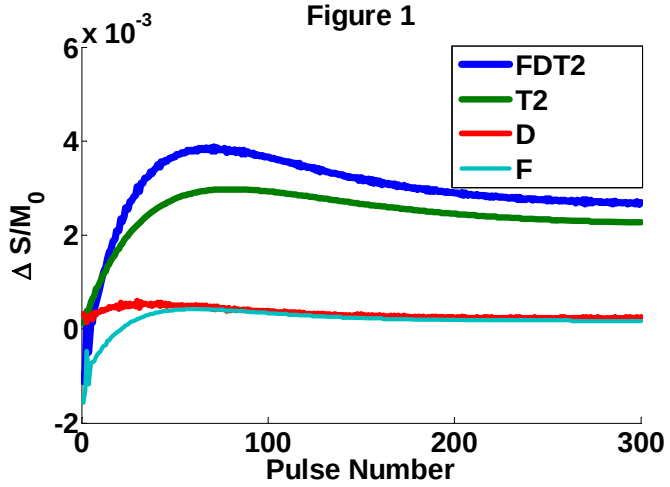

Figure 2

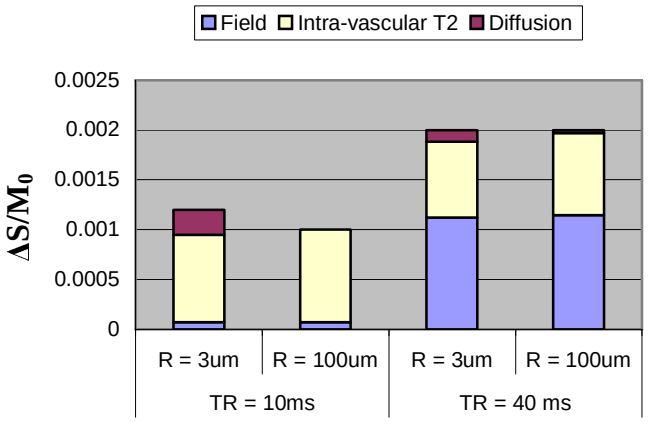

Fig. 1 shows normalized BOLD signal change ($\Delta S/M_o$) simulations for a grey matter voxel [10] as a function of RF pulse number (following α/2 catalyzation) for 10ms TR and 45° flip angle. These changes (peak $\Delta S/M_o$ of $4x10^{-3}$) are consistent with experimentally observed ΔS/S changes [3], with a 2.7% ΔS/S predicted for in vivo T1/T2 ratios (steady state signal of $0.15*M_o$). The FDT2 curve is the signal change resulting from all contrast sources combined, while the three remaining curves show the contrast resulting solely from intra-vascular T2 changes (T2), diffusion (D), and field offsets (F), respectively. Intravascular T2 effects dominate at short TR values for all pulse train lengths. Additionally, a 43% BOLD contrast increase over the steady state can be observed at short pulse train lengths (60 pulses in Fig. 1). These peaks occur for fewer pulses and are more prominent at higher flip angles (not shown). Fig. 2 shows the relative contributors to contrast, at steady state, for different vessel radii (all at 2% blood volume) and TR. For short TR (10ms), b-SSFP fMRI BOLD contrast is dominated by intra-vascular T2 changes, while at long TR (40ms), field offsets provide the majority of contrast consistent with gradient echo simulations (not shown). Vessel size also affects the contrast mechanism at short TR with diffusion being a significant though not dominant mechanism for capillaries (R=3uM). At short TR, b-SSFP simulations matched for blood volume show 20% greater contrast for capillary sized (3um) than venule sized (100um) calculations. This results from increased diffusion sensitivity and is consistent with experimental observations of large vessel [3] and physiological noise [5] suppression with b-SSFP fMRI.

Conclusion: The contrast mechanism in SSFP is dominated by intra-vascular T2 changes at low TR and by susceptibility induced field offsets at high TR, in agreement with Miller's experimental findings [5]. Shorter TR simulations show greater diffusion sensitivity and overall response to susceptibility changes in small, capillary-sized vessels. Simulations suggest a doubling of BOLD contrast can be achieved with high flip angles (60°) and short pulse trains (40), suggesting a re-ordering of k-space sampling to obtain optimal experimental b-SSFP fMRI BOLD CNR is feasible.

References: [1] Scheffler, NMR Biomed, 2001;14:490 [2] Miller, MRM, 2003;50(4):675 [3] Bowen, 13th ISMRM, 2005;p119 [4] Lee, 15th ISMRM, 2007;p694. [5] Miller, Neuroimage, 2007;34(4):1227 [6] Bowen, 14th ISMRM, 2006;p665 [7] Dharmakumar, MRM, 2005;53:574 [8] Zhong, MRM, 2007;57:67 [9] Boxerman, MRM, 1995;34:555 [10] Kim, 15th ISMRM 2007;p696 [11] Duong, MRM, 2003;49:1019