Dependence of Myocardial BOLD Contrast on Imaging Parameters at 1.5T: Monte Carlo Simulation and Experiments

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Introduction: Previous studies have shown that the dependence of SSFP signals on microcirculatory oxygenation may be modeled as a two-site exchange of spins between the intravascular space (IVS) and extravascular space (EVS) [1]. However, these studies have largely neglected the spin diffusion effects within IVS and EVS and approximated the diffusion between IVS and EVS as an exchange phenomenon. To develop a rigorous understanding of SSFP BOLD imaging in the myocardium it is imperative to consider the SSFP signal dependence on spin diffusion in a field variation. This is particularly important in the heart muscle since most of the blood is in the capillaries [2], where the diffusion-mediated effects is expected to play a central role [3] in the development of SSFP-based BOLD contrast. Moreover, previous non-cardiac studies have also shown that the SSFP BOLD sensitivity is strongly dependent on repetition time (TR) and flip angle (FA) [4]. This work investigates the effects of TR and FA on SSFP-based myocardial BOLD sensitivity through Monte-Carlo simulations accounting for diffusion in a field variation and validates the finding in a canine model with controllable coronary artery stenosis.

Methods Monte-Carlo Simulations (MCS): Approximating capillaries as infinite cylinders (3), the magnetic field variation (ΔB_z) inside and outside the capillary vessel due to oxygenation changes were computed using: $\Delta B_z = B_0\Delta\chi(R/r)^2\cos(2\varphi)\sin^2\theta/2$ (outside) and $\Delta B_z = B_0\Delta\chi(\cos^2\theta\text{-}1/3)/2$ (inside), where R is the vessel radius; (r, θ, φ) is a field point in spherical co-ordinates; B_0 is the main magnetic field; $\Delta\chi$ is the susceptibility difference between IVS and EVS and is defined as: $\Delta\chi = Hct(1\text{-}Y)\Delta\chi_d$, where $\Delta\chi_d$ = 3.39 ppm [5] is the $\Delta\chi$ between fully oxygenated and fully deoxygenated hemoglobin, Hct is the hematocrit (assumed to be 0.4), and Y is oxygen saturation (allowed to vary between 20% and 80%, typical myocardial oxygenation under severe coronary stenosis and in health, respectively, in the presence of adenosine stress). Spin diffusion was modeled as Brownian motion in a Cartesian grid with 5000 spins with Monte-Carlo method. Change in position of each spin after a time step of (Δt =50μs) along each dimension within the cubic box was determined as $(2D\Delta t)^{0.5}$, where D is the diffusion coefficient of protons ($1.5x10^{-9}m^2/s$). Phase changes, $\Delta\Phi$, from diffusion in a field variation over Δt for each spin was computed as $\Delta\Phi = \gamma\Delta B_z\Delta t$, where γ is the gyro-magnetic ratio of proton. The vessel radius R and blood volume fraction were set to 6 μm and 9%, respectively. A total of 2000 pulses were used to ensure steady state condition is met and the TR and FA were allowed to vary between 3.5ms to 6.0ms and 30°-70°, respectively. Experiments: A canine model (n=4) with a hydraulic occluder placed around the left circumflex coronary (LCX) was used to validate the theoretical findings. Following recovery after surgery (1 week), animals were sedated, ventilated and placed on the scanner table (at a 1.5T Siemens Espree). ECG-gated and multiple breath-held 2D Cine SSFP sequences were prescribed under adenosine stress (continuous infusion rate of 140 mg/kg/min) with and without LCX stenosis over the left ventricle (LV). Three short-axis images with centre slice positioned over the mid LV were acquired for each study. Scan parameters were: in-plane resolution = 1.2 x $1.2mm^2$; slice thickness = 5mm; TR/TE = 3.5ms/1.75ms, 4.7ms/2.35ms, 6.0ms/3.0ms; FA = 30°, 50°, 70°; and segments/cardiac-phase were adjusted to achieve an optimal temporal resolution (10ms to 20ms) that minimize motion and flow artifacts. Regional SSFP BOLD Contrast defined as $[I_{LAD}\text{-}I_{LCX}]/I_{LAD}$ was used to assess the SSFP BOLD sensitivity at different TR and FA, where I_{LAD} and I_{LCX} are average SSFP signal intensities measured within the LAD and LCX territories.

Results: Figure 1 shows a set of typical 2D late diastolic short-axis cardiac images from SSFP cine scans of a dog with severe stenosis under adenosine stress for different TR and FA combinations, LCX regions are the shorter arcs subtended by arrows. Note that the global and regional signal intensities are strongly dependent on imaging parameters. Figure 2 shows the SSFP BOLD signal contrast obtained from MCS and experimental studies. The regional BOLD signal contrast between LAD and LCX supplying regions compared well with the MCS. MCS and experiments showed that increasing TR and FA, leads to increases in regional myocardial contrast.

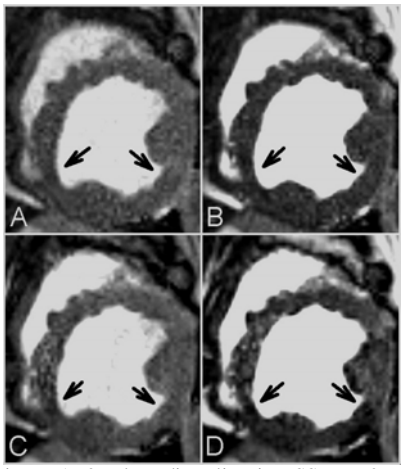

Figure 1. 2D late diastolic cine SSFP BOLD images of a dog with severe LCX stenosis and adenosine infusion at different TR and FA combination: TR/FA=3.5ms/30° (A); 3.5ms/70° (B); 6.0ms/30° (C); and 6.0ms/70° (D).

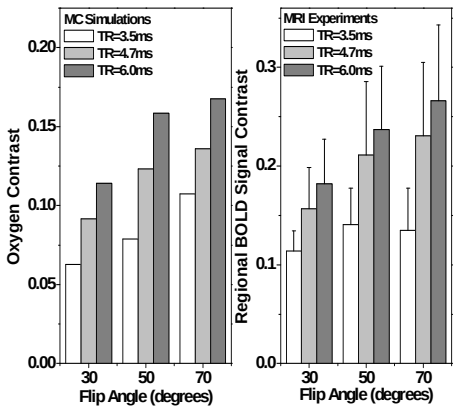

Figure 2. SSFP-based Myocardial BOLD contrast obtained from MCS and experimental studies with the same parameters (TR = 3.5ms, 4.7ms, 6.0ms; Flip angle = 30°, 50°, 70°).

Discussion: Results from MCS and experimental studies showed that TR and FA play a significant role in determining SSFP-based myocardial BOLD contrast. In particular, both MCS and experiments showed that increasing the FA or TR gave a concomitant increase in SSFP-based myocardial BOLD contrast, consistent with previous studies in other tissues [4]. We found that that a combination of TR/FA= 6.0ms/70° gave the highest oxygen contrast among all the parameter sets studied, although more artifacts were observed in certain cardiac phases as TR was increased from 3.5 ms to 6.0ms. It is expected that in order to enable the entire cine image set to be able to provide reliable and optimal regional BOLD contrast, robust artifact correction methods need to be developed.

References: [1] Dharmakumar R et al. MRM 2006; [2] Kassab GS et al. AJP 1994; [3] Boxerman JL et al. MRM 1995; [4] Arumana JM et al. MRM 2008; [5] Martindale J et al. MRM 2008.