Detecting Myocardial Ischemia at Rest with Cardiac Phase-Resolved BOLD MRI: Early Findings

S. A. Tsaftaris[1,2], V. Rundell[2], X. Zhou[2], Y. Liu[2], R. Tang[2], D. Li[2], and R. Dharmakumar[2]
[1]Electrical Engineering and Computer Science, Northwestern University, Evanston, IL, United States, [2]Radiology, Northwestern University, Chicago, IL, United States

Introduction: Vasodilatory stress is the standard paradigm for probing myocardial oxygenation (O_2) changes due to coronary artery stenosis on the basis of BOLD MRI (1-3). However, since vasodilation is typically achieved with provocative stress, approaches that can identify the presence of stenosis on the basis of microvascular alterations at rest are highly desirable. It is known that myocardial blood volume (MBV) varies throughout the cardiac cycle; MBV increases during diastole and decreases during systole (4,5). It has also been shown that changes in MBV lead to increased O_2 extraction by cardiomyocytes (6). Thus, MBV and O_2 are expected to vary at different parts of the cardiac cycle. In particular, in diastole, it is expected that MBV and O_2 extraction are maximal, while in systole, MBV and O_2 extraction are minimal. In addition, as MBV increases, even at a stable level of O_2, the number of deoxygenated hemoglobin molecules within a voxel increases, causing a proportionate elevation in the local magnetic field inhomogeneities (7). Moreover, with increasing grade of stenosis, the MBV in the myocardial territory supplied by a stenotic artery increases in systole (8-11). Thus, the relative MBV and O_2 changes between systole and diastole are expected to be different between myocardial territories supplied by healthy and stenotic coronary arteries. Moreover, it is also known that T_1 of myocardium is dependent on MBV and that the apparent T_2 is dependent on blood O_2. Since SSFP signals are approximately T_2/T_1 weighted, it is hypothesized that cardiac phase-resolved BOLD SSFP (CP-BOLD) (12) signal intensities at systole and diastole may reflect changes in MBV and blood O_2. In addition, since stenosis leads to an increase in systolic MBV and is accompanied by a reduction in blood O_2, it is hypothesized that systolic and diastolic CP-BOLD signal intensities may be used to detect the ischemic territories at resting states. These hypotheses were tested with simulations and canine experiments.

Methods: Theory: To establish the theoretical foundation and to lend additional support to our hypothesis that MBV and O_2 synergistically contribute to cardiac phase-dependent myocardial signal changes, numerical simulations were performed using a two-pool exchange model (13). T_1, T_2, and SSFP signal changes were computed assuming that the relative MBV is 9% (systole) and 15% (diastole) (14) and myocardial O_2 is 30% (systole) and 80% (diastole) (15). Systolic and diastolic T_1 changes were computed from the simulations of the dual flip angle technique (16) with flip angles = 3° and 15°. The cardiac phase-dependent changes in T_2 were computed from simulations of the T_2-preparation method (17) with T_2-preparation durations of 24 ms and 48 ms. SSFP signals were computed assuming T_R = 6.2 ms and flip angle of 70°. To evaluate phasic changes in T_1, T_2, and SSFP signal intensities, relative changes in T_1, T_2, and SSFP signal intensities were computed between systole and diastole, and used to define Systolic to Diastolic Ratios (S/D). Imaging Studies: Flow and motion compensated 2D short-axis CP-BOLD (12) were acquired along the mid ventricle in 10 canines under rest without stenosis (baseline) and with a severe LAD stenosis controlled by a surgically implanted hydraulic occluder. Doppler flow was used to determine the extent of stenosis. Imaging studies were performed at 1.5T (Siemens Espree); and scan parameters were: resolution = 1.2x1.2x8 mm^3; flip-angle=70°; and T_R/T_E = 6.2/3.1 ms. First-pass perfusion (FPP) and late-enhancement scans were performed to visually confirm perfusion deficits and absence of infarction. Image Processing: End-systolic (ES) and end-diastolic (ED) images were identified automatically (18), myocardial borders were traced in all images of the cardiac cycle, and the myocardium was segmented following the six-segment AHA model. On the basis of the FPP images two regions of myocardial segments were defined: "affected" as those affected by the LAD stenosis and "remote" as LCX territory. S/D, defined as a quotient of the mean intensity at ES and ED of a region under baseline and stenosis conditions were computed. A two-way repeated measurement ANOVA was used to test the effects of region (LAD and LCX) and condition (baseline or stenosis) and their interaction on S/D.

Results: Fig. 1 shows normalized regional mean intensities for remote and affected regions under both conditions obtained from a canine study. Observe that under LAD stenosis, the S/D of the LAD region was below 1, while the remote (LCX) region was larger than 1, while this discrepancy was not observed under baseline conditions. Fig. 2 shows both theoretical and experimental findings for baseline and experimental results from stenosis studies. Statistically significant differences in S/D were found between LCX and LAD regions under stenosis (p=0.01).

Discussion & Conclusions: Our results suggest that the ratio of ES and ED myocardial signal intensities from CP-BOLD is decreased in the presence of stenosis compared to healthy conditions under rest. While these results are encouraging and appear to be supported by the literature and our theoretical results, further validation of the proposed method is required. Moreover, technical advances in sequence development on 3D CP-BOLD (for minimizing potential signal variations due to through-plane motion) and in image processing, may be necessary prior to clinical translation.

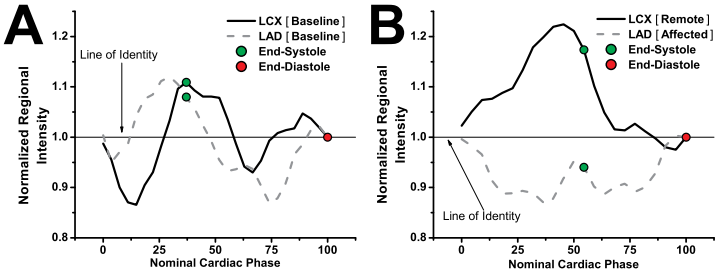

Fig. 1 Regional mean intensities from LAD and LCX regions under baseline (**panel A**) and LAD stenosis (**panel B**) conditions (obtained from canine studies) normalized by the regional mean intensities at ED (shown with red circles) as a function of nominal percentage of cardiac cycle are shown. Green circles indicate end-systole. A line of identity (between ES and ED, i.e. S/D =1) is also shown for reference. Observe that during baseline conditions, both regions have S/Ds that are higher than 1 (1.1 and 1.07, for LCX and LAD respectively). Under stenosis, however, only the LCX region (remote territory) maintained a S/D greater than 1 (at 1.17). Conversely, the S/D for the LAD region decreased significantly below 1 (at 0.93), in line with the hypothesis.

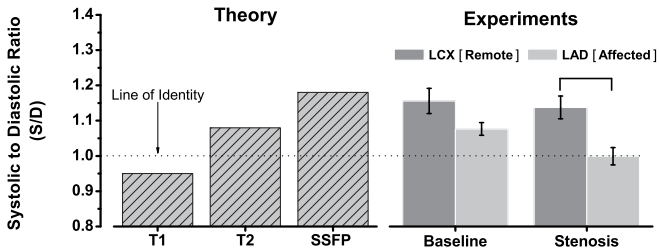

Fig. 2 Bar plots showing an agreement between theoretical and experimental findings on S/D. Observe that in line with the hypothesis, theoretical and experimental S/Ds are greater than 1 in the absence of stenosis (t-test; p<0.001), except in affected regions under stenosis, where S/D is below 1 (p>0.05). The ANOVA test indicated that 'region' had a significant overall effect on S/D (p=0.006). Tukey post-hoc comparisons with Bonferroni correction, showed that under stenosis, the LAD region exhibited statistically significant lower S/D compared to the LCX (remote) region under the same condition (indicated by a bracket on the figure; p=0.01). Between-subject effects were not significant (p=0.99). Experimental data are reported as mean ± SEM.

References: (1) Friedrich et al., *Circ* 2003; (2) Karamitsos et al., *Circ Imag*; 2010; (3) Jahnke C et al., *JACC CV Imag* 2010; (4) Wu et al., *JMRI* 2004; (5) Wansapura et al., *MRI* 2006; (6) Bai et al. *AJP* 1994; (7) Klocke et al., *JACC* 2003; (8) Wei et al., *Circ* 2005; (9) Wei et al., *Circ* 2002; (10) Wacker et al., *JACC* 2003; (11) Lindner et al., *AJP* 1997; (12) Zhou et al., *JMRI* 2010; (13) Dharmakumar et al., *MRM* 2006; (14) Judd et al., *Circ Res* 1991; (15) Li et al., in *Cardiovascular Magnetic Resonance* 2001; (16) Deoni et al., *MRM* 2003; (17) Wright et al., *JMRI* 1991; (18) Tsaftaris et al., *ISMRM* #3715 2010.