Detecting ACS and Identifying Acute Ischemic Territories with Cardiac Phase-Resolved BOLD MRI at Rest

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Introduction: Noninvasive imaging approaches that can rapidly assess an ongoing ischemia can be of great value in detecting and triaging patients experiencing acute coronary syndromes (ACS), particularly in cases of non ST elevation myocardial infarction (NSTEMI). Although a number of imaging approaches exist for the identification of myocardial territories supplied by stenotic coronary arteries, in general, all available imaging methods require provocative stress and/or exogenous contrast media. The most desirable imaging approach is also one that can identify ischemic territories and assess functional/volumetric status, while minimizing patient discomfort. We propose and test a new CMR method for a rapid assessment of ACS. Our approach relies on detecting systolic and diastolic SSFP signal changes related to perturbation in cardiac phase-dependent blood volume and oxygenation associated with severe coronary narrowing on the basis of cardiac phase-resolved Blood-Oxygen-Level-Dependent (CP-BOLD) imaging (1). We hypothesized that the proposed approach can assess functional/volumetric status and non-invasively identify ischemic territories under resting conditions in a single scan without any exogenous contrast media.

Methods: Imaging Studies: Flow and motion compensated 2D short-axis CP-BOLD (2) were acquired along the mid ventricle in 11 canines at baseline and under a severe LAD stenosis (in excess of ~90% flow reduction) as verified by Doppler flow velocities. Imaging studies were performed on a 1.5T Siemens System (Espree). Scan parameters were: resolution = 1.2x1.2x8 mm^3; flip-angle=70°; and T_R/T_E = 6.2/3.1 ms. Image Processing: End-systolic (ES) and end-diastolic (ED) images were identified automatically (3), and myocardial borders were traced (all phases) and segmented following the six-segment AHA model. Within the segmented myocardium, two regions 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, was computed for the remote and affected regions at baseline and stenosis conditions. In addition, Ejection Fraction (EF) was estimated based on the same endocardial delineations. Finally, myocardial wall thickening (WT) was estimated using the same delineations at 360 radial lines (chords) in ES (WT_S) and ED (WT_D). For each myocardial region, the segmental Wall Thickening (sWT), defined as the per-segment average of $[WT_S - WT_D]/WT_D$ was computed. Statistical Analysis: A paired t-test was used to test the null hypothesis that EF in baseline and stenosis are equal. Three Receiver Operating Characteristic (ROC) analyses were performed to demonstrate the diagnostic power of the proposed biomarker (S/D) in relation to EF and sWT, using various groupings of positive (+) and negative (-) diagnoses, shown in Table 1. A one-way repeated measurement ANOVA was used to test the effect of region (remote and affected) under stenosis on S/D and sWT.

Results: Fig. 1 shows segmental S/D ratios in a bulls eye plot. EF was markedly reduced ($p<0.01$) under stenosis (0.25±0.1) compared to baseline (0.45±0.1), in agreement with previous studies in canines (4). Fig. 2 shows the three ROC curves obtained with the grouping of Table 1. EF and sWT can reliably identify the presence of severe acute coronary stenosis at rest (Fig 2A); however, sWT cannot accurately identify the affected territory (Fig 2B,C). The proposed method (S/D) achieves comparable performance with EF in identifying ACS (Fig 2B,C). Furthermore, it can identify the affected territory solely relying on stenosis studies, while sWT performs poorly (Fig. 2C). This is also apparent from the results of the ANOVA test (Table 2).

Discussion & Conclusions: Our results demonstrate that S/D values, computed on the basis of CP-BOLD signal intensities, are significantly reduced with severe stenosis compared to baseline conditions. Since CP-BOLD generates cine images, the proposed approach can be used to generate a multitude of biomarkers (S/D, EF, sWT) for a comprehensive assessment of ACS from a single scan prescription. Although EF and sWT may be used to determine the presence/absence of ACS, they cannot reliably identify the ischemic territory when ACS is present, since EF is a gross volumetric measure and sWT changes are not regionally specific for identifying ischemic territories (5). The proposed biomarker (S/D) provides incremental information to aid in the identification of the ischemic territory and culprit artery, thus enabling guidance on revascularization efforts. Moreover, EF, sWT, and S/D may be linearly combined to further increase accuracy of ACS detection (6). While these results are encouraging and appear to be supported by the literature, further validation of the proposed method is required. Additional technical advances in sequence development, such as 3D CP-BOLD and in image processing, may be necessary prior to clinical translation.

Table 1. Grouping of positive and negative diagnoses for ROC analysis.

	biomarkers	Positive (+)	Negative (-)
A	EF, sWT	SS* affected$^{SS\,\#}$	BA affected^{BA}
B	S/D, sWT	affected^{SS}	affected^{BA} remote^{BA} remote^{SS}
C	S/D, sWT	affected^{SS}	remote^{SS}

Notes: * SS: Severe Stenosis; BA: Baseline
# denotes affected region under SS

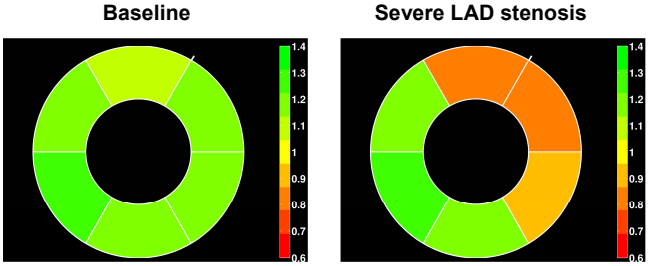

Fig.1 Circumferential polar plots (bulls eye) of systolic to diastolic ratios (S/D) under baseline (left) and stenosis (right) conditions. Observe that under baseline all S/D ratios are greater than 1. Under stenosis only the regions corresponding to the LAD territory have a markedly reduced S/D values.

Table 2. ANOVA results for S/D and sWT obtained under stenosis shown as mean ± std. errors. S/D is different between remote and affected territories ($p=0.012$); while no statistical difference is seen in sWT on the same territories.

	Remote	Affected
S/D	1.11 (0.025)*	1.01 (0.01)*
sWT	0.20 (0.063)	0.33 (0.08)

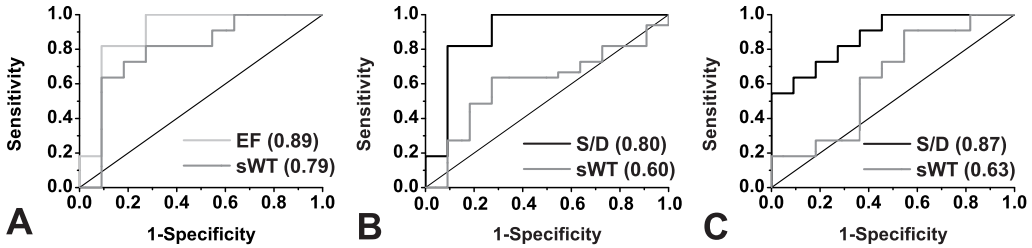

Fig. 2 ROC Curves in panels A, B, C corresponding to the biomarkers as in **Table 1**. In the legends of each plot AUC are given. Observe that the proposed biomarker (S/D) can provide comparable performance with EF (AUC=0.87 vs 0.89). The cut-off point that maximizes sensitivity and specificity for S/D is 1.07 (panel C).

References: (1) Tsaftaris et al., *ISMRM* #217 2011; (2) Zhou et al., *JMRI* 2010; (3) Tsaftaris et al., *ISMRM* #3715 2010; (4) Schneider et al., *Circ* 1985 72:632-638; (5) Guth et al, *Am Heart J.* 1984 107(3):458-64; (6) Pepe and Thompson, *Biostat* 2000 1 (2):123-140.