Automated synchronization of cardiac phases for Myocardial BOLD MRI

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Introduction: Cardiac phase-resolved myocardial Blood-Oxygen-Level-Dependent (BOLD) MRI is expected to increase the diagnostic confidence for identifying the myocardial territories with reduced perfusion reserves (1). However, an accurate assessment of pathological changes in myocardial perfusion reserve using this approach requires an accurate alignment of phase-resolved images acquired at rest and under provocative stress, typically at different heart rates. Manual alignment of the rest and stress images is time consuming and can be subject to intra- and/or inter-observer variability. An automated approach that can robustly and reproducibly synchronizes images acquired at rest and stress is highly desirable. One such method may be reached on the basis of the segmentation of the blood pool area in the Left Ventricle (LV) chamber to derive area curves for matching images according to their position in the curve. However, this approach is computationally intensive, susceptible to noise, and requires prior localization and segmentation of the LV. Another alternative may be to synchronize the images based on trigger times; however, while this approach can provide an estimate of the position of each image within the cardiac cycle, it does not necessarily provide the correct anatomical correspondence. The purpose of this work is to develop an automated statistical method that can reliably evaluate cardiac phase-resolved myocardial BOLD MRI through temporal synchronization of rest and stress images acquired at different heart rates, without resorting to LV segmentation algorithms.

Methods: Experimental Setup and Imaging: Short-axis BOLD cine cardiac images were acquired on Siemens 1.5T scanner from 4 canines, that were sedated and mechanically ventilated and instrumented with a hydraulic occluder placed around the left circumflex coronary artery (LCX) to control the patency (stenosis) of LCX. Following scout scans,. ECG-gated and breath-held bSSFP acquisitions were prescribed over the mid-ventricle under rest (baseline) and adenosine stress. Stress scans typically resulted in nearly 20% increase in heart rate. Scan parameters: voxel size=1.2x1.2x6mm^3; flip angle=60^o; TR/TE=3.5/1.8ms. Image Processing: The goal of this process is to align two input stacks **X** (baseline) and **Y** (stress) with L and K images ($L>K$), respectively. This translates to finding a stack **Z** by replicating images in **Y**, such that it has L images and that when **Z** is viewed simultaneously with **X**, it appears synchronized, permitting phase-to-phase comparison between the rest and stress stacks. The proposed method achieves this goal by first identifying the ES and ED of **X** and **Y** using the methods in (2) denoted as $ES_{\mathbf{X}}$, $ES_{\mathbf{Y}}$, $ED_{\mathbf{X}}$, and $ED_{\mathbf{Y}}$, respectively. It proceeds by finding the similarity of all image pairs in **X** and **Y** and by using a dynamic programming algorithm (4,5) to decide which images of **Y** to replicate to create **Z**, such that **X** and **Z** have the maximum similarity. The cross-correlation matrix, $\mathbf{R_{YX}}$, between each image in the two stacks, found according to (2), is used as a measure of image similarity. $\mathbf{R_{YX}}$, is transformed into an exponential cost function $\mathbf{d}_o=\exp(1-\mathbf{R_{YX}})$. Subsequently, the values $\mathbf{d}_o[ES_{\mathbf{Y}},ES_{\mathbf{X}}]$, $\mathbf{d}_o[ED_{\mathbf{Y}},ED_{\mathbf{X}}]$ are set to zero (assuring that ES and ED images will be matched exactly), and $\mathbf{d}_o$ is circularly shifted by $ES_{\mathbf{Y}}$, $ES_{\mathbf{X}}$ forming **d**, such that the entry **d**[1,1]=0. The problem at hand reduces to form a stack **Z** by duplicating images Y that minimizes the trace of the matrix $\exp(1-\mathbf{R_{ZX}})$. A dynamic programming algorithm (DP) formulation (4,5) can be used to efficiently find the optimal solution of the recursion $\mathbf{D}[i,j] = \min(\mathbf{D}[i-1,j-1]+\mathbf{d}[i,j], \mathbf{D}[i,j-1]+\mathbf{d}[i,j])$ for $2\le i\le K$, $2\le j\le L$, with basis conditions $\mathbf{D}[i,1] = \mathbf{d}[i,1]$ and $\mathbf{D}[1,j] = \mathbf{D}[1,j-1]+\mathbf{d}[1,j]$, for all i and $j>1$, respectively. Data analysis: To assess the validity of the proposed approach, each image in the stack (**X**, **Y**, and **Z**) was segmented using the seeded-region-growing-method (SRGM) in (3) and the size of the LV blood pool per cardiac phase, i.e. LV volume curve, was recorded for each stack, denoted as $v_{\mathbf{X}}$, $v_{\mathbf{Y}}$, and $v_{\mathbf{Z}}$. The mean-squared errors (MSE) of the differences $|v_{\mathbf{X}}-v_{\mathbf{Z}}|$ and $|v_{\mathbf{X}}-v_{\mathbf{Y}}|$ were computed and the ratio $R_M=|v_{\mathbf{X}}-v_{\mathbf{Y}}| \,/\, |v_{\mathbf{X}}-v_{\mathbf{Z}}|$ was used as a metric of performance. Since stacks **X** and **Y** have different number of images, to ensure accurate computation of the differences, all curves were interpolated to have $2L$ number of points. Overall four baseline, six stress without, and six stress with LCX stenosis studies were examined. A total of twelve synchronizations were performed and their respective R_M's were collected and a Wilcoxon Signed rank test was performed to the test the null hypothesis that the median of R_M was less than 1.

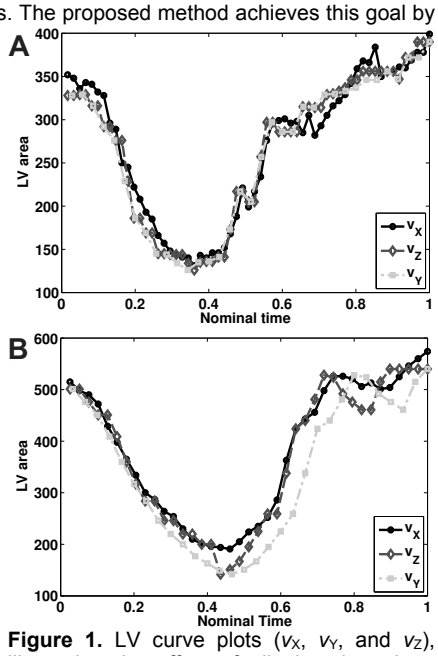

Figure 1. LV curve plots (v_X, v_Y, and v_Z), illustrating the effect of aligning, based on similarity, stack Y to X to produce a stack Z for two cases in panel A and B (see text for details).

Results: Figure 1, illustrates two examples of the blood area curves $v_{\mathbf{X}}$, $v_{\mathbf{Y}}$, and $v_{\mathbf{Z}}$, when the alignment procedure was used in two different cases. Panel **A** corresponds to a case where stack X is a baseline scan and stack Y is a stress scan (X: 61 images, Y: 55 images). Panel **B** corresponds to the case where stack X is a baseline scan and stack Y is a stress scan in a canine with severe LCX stenosis (X: 39 images, Y:30 images). The LV curves were calculated using the SRGM method. Mean squared error (MSE), Panel **A**: MSE (v_X - v_Y) = 306, MSE (v_X - v_Z) = 245; Panel **B**: MSE (v_X - v_Y) = 2828, MSE (v_X - v_Z) = 607; MSE reduction was 20% and 70%, respectively. The Wilcoxon test failed to accept the null hypothesis ($P<0.05$), thus the median of $R_M > 1$.

Discussion & Conclusions: The cardiac phase synchronization method presented relies on correlation to measure the similarity between images obtained at rest and stress which is later used as a cost metric to drive a DP minimization routine. The particular algorithmic formulation is adopted from the bioinformatics and audio processing community where it is used to align DNA (4) and speech sequences (5), respectively, and preserves the order of the images in the stack. It is particularly efficient and relies on the accurate identification of ES and ED presented previously (2). Although direct metrics of comparison are not available, using the LV volume curves as grounds for comparison illustrated that the proposed method achieves the goal of aligning cardiac phases without need for LV segmentation. A segmentation-based approach would involve segmentation of the LV, measurement of the blood volume in X and Y, and then use of a DP formulation, such as the one proposed here, to match the two time-series of the LV blood curves. However, this would involve full segmentation of the LV, a task that is laborious if not done automatically, or if performed automatically, it can be either computationally intensive or inaccurate. As Figure 1 (Panel B) demonstrates, the LV curves computed with SRGM for the rest and severe stenosis cases are not smooth, indicating that blood flow within the myocardium or the appearance of papillary muscles affects the accuracy of pixel-intensity-based segmentation methods. For a LV-volume-curve-based synchronization algorithm to succeed, accurate and smooth LV curves are necessary, which imply that expert feedback and/or more sophisticated segmentation algorithms may be necessary.

References: (1) Dharmakumar et al., *Inv. Rad.* 42(3):180-188 (2007); (2) Tsaftaris et al., *ISMRM p*#3748 (2009); (3) Codella et al., *Radiology* 248(3):1004-1012 (1986); (4) Needleman & Wunsch, *J Mol Bio*, 48(3):443-453 (1970); (5) Sakoe & Chiba, *IEEE Trans Acc. Sp. Sig. Proc.*, 26(1):43-49 (1990).