Unsupervised and Reproducible Image-based Identification of Cardiac Phases in Cine SSFP MRI

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Introduction: A critical component in computing quantitative diagnostic metrics, such as ejection fraction, as well as, image segmentation and registration is the accurate identification of the end-systolic (ES) and end-diastolic (ED) frames in cardiac cine MRI. Reliable identification of ES is also important in cardiac phase-resolved myocardial blood-oxygen-level-dependent (BOLD) MRI studies (1). An assessment of changes in myocardial oxygenation requires BOLD images to be collected at rest and stress, which is typically induced with intravenous infusion of adenosine. ES images at both states are compared to assess the presence of coronary artery stenosis. To increase reproducibility and eliminate variability it is desirable to automate this procedure. Most automated methods relying on trigger times do not account for anatomical correspondence, while methods based on identifying the minimum and maximum of the blood pool area in the Left Ventricle (LV) chamber, are computationally intensive, susceptible to noise, and require prior localization and segmentation of the LV. The purpose of this work is to develop automated methods to facilitate in the robust and reproducible evaluation of cardiac cine MRI studies.

Methods: Experimental Setup and Imaging: Short-axis cardiac cine MR images were acquired on Siemens 1.5T scanner from nine canines, which were sedated and mechanically ventilated. ECG-gated and breath-held SSFP acquisitions were prescribed over the mid-ventricle following scout scans at various temporal resolutions under rest and stress conditions. Scan parameters: voxel size=1.2x1.2x6mm^3; flip angle=60^o; TR/TE=3.5/1.8ms. Image Processing: Each image in a cine stack I(x,y,t) (t denotes cardiac phase out of F number of images/phases total) was convolved by a Gaussian filter (w=10 and σ=1). The normalized cross-correlation was computed between all possible image pairs I(x,y,i) and I(x,y,j), giving an FxF matrix C. The indices corresponding to the minimum of C are the ES, ED images, since they are uncorrelated due to cardiac motion. Data Analysis: Seventeen cine stacks under rest or stress conditions with different number of images were tested and additive-white-Gaussian-noise of zero mean and varying standard deviation (STD) was introduced to demonstrate robustness. Three expert users (R1, R2, R3), manually identified the ES and ED in the input stacks (which were duplicated, randomized, and loaded into ImageJ (4) without any additive noise.) (The reader was not aware that he/she was evaluating the duplicate stack.) The time to evaluate each stack was also recorded. The number of images away from the ES_m, ED_m images (*m* denotes the median of the experts' choice, indentified as R_m) was used to compare the proposed method when the entire image (suffix ALL) or just an area of interest (suffix ROI) around the heart is used, with an LV seeded-region-growing-segmentation-method (suffix SRGM) (3). For each noise STD , 20 trials were performed and the results were averaged. To compare the performance of all methods and assess intra- and inter- observer variability, Bland-Altman (BA) analysis (5) and ANOVA tests were used. Statistical significance was set at P<0.05.

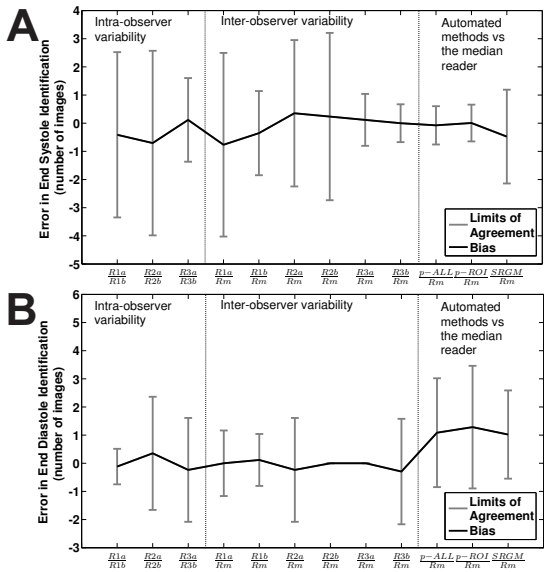

Fig. 1: Bias and limits of agreement (panel **A** for ES, panel **B** for ED).

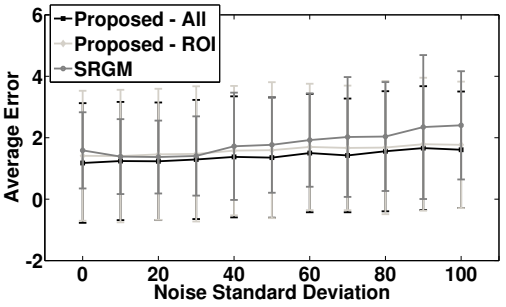

Fig. 2: Plots showing the combined error for ES and ED, (mean±STD) computed over all stacks as a function of noise.

Results: Fig. 1 summarizes graphically the bias and limits-of-agreement found with BA analysis (plots not shown for brevity) for all readers and automated methods. In the figure R(1/2/3/m)[a/b] denotes the rating from the first (a) or second (b) reading by reader 1, 2, or 3, and the median reader. Observe that the algorithms were within the limits of agreement found when the expert readers are compared against each other. Overall the average reading time/stack was 30±11 seconds. Fig. 2 illustrates the error defined as $|ES–ES_m| + |ED–ED_m|$, as a function of noise for the automated methods. At each noise level, a non-parametric Kruskal-Wallis ANOVA revealed no statistical difference among the three methods (P>0.1).

Discussion & Conclusions: A fully automated method for reliable and reproducible identification of key cardiac states (ES, ED) was presented. Expert readers deviated up to two images (limits-of-agreement > 2) in their choice of ES and ED images (Fig. 1). This variability demonstrates the need for reproducible, unbiased, and automated methods in identifying ES and ED images in cine stacks. Our analysis illustrates that all algorithms performed within (or even lower than) the observers variability (limits-of-agreement < 2) and that there were no statistical differences in error measurements when noise was added. According to our findings, pre-selection of an ROI does not offer any statistical advantage and is thus not necessary, which further simplifies the deployment of the proposed method. Segmentation of the myocardium in cine images based on pixel intensity may be challenging, most likely due to (i) the motion of blood within the cardiac chambers that increases the variability of the signal intensities within the blood pool, (ii) the presence of papillary muscles, and (iii) by the intensity variation of the myocardium, especially in the presence of stenosis, which forms the basis of myocardial BOLD. The proposed statistical identification method is robust against the above issues. On the other hand, SRGM, a segmentation-based method, underperforms due to these issues in some cases. As illustrated by the larger LAs and a positive bias, a potential limitation of our approach may be in the accurate identification of ED when the cardiac motion is significantly abnormal (due to underlying cardiac conditions) or the number of images is large; however, if the relevant locations of the images within the cardiac cycle (trigger-times) are added as another constraint the accuracy is expected to increase. The proposed method reliably identifies the cardiac phases, in an efficient manner, without the need for any parameterization and segmentation; therefore, making it ideal for on-line scanner implementations and integration into popular medical image analysis software.

References: (1) Dharmakumar et al., Inv. Rad. 42(3):180-188 (2007); **(2)** Codella et al. Radiology 248(3):1004-1012 (2008); **(3)** Bland & Altman, Lancet 1(8476):307-310 (1986).