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Multi-cycle Reconstruction of Cardiac MRI for the Analysis of Inter-ventricular Septum Motion During Free Breathing

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Abstract

Small variations in left-ventricular preload due to respiration produce measurable changes in cardiac function in normal subjects. We show that this mechanism is altered in patients with reduced ejection fraction (EF), hypertrophy, or volume-loaded right ventricle (RV). We propose a multi-dimensional retrospective image reconstruction, based on an adaptive, soft classification of data into respiratory and cardiac phases, to study these effects.

Keywords

Cardiac function; Preload; Respiration

1 Introduction

Free-breathing cine MRI provides novel information on cardiac dynamics, extending routine cardiac function analysis to patients unable to hold their breath or suffering from arrhythmia. The recently developed XD-GRASP [1] (eXtra-Dimension-Golden-Angle-Radial-Sparse-Parallel) reconstruction technique enables the independent analysis of cardiac and respiratory motion within the same measurement, which can bring new insights into the normal and abnormal variability of cardiac function.

Breathing induces changes in the intrathoracic pressure, with associated variations in venous return. This causes small modulations in the interventricular septum position, including changes of the left ventricle (LV) diameter, reflecting normal preload variations in the corresponding cardiac cycles.

In this work, we investigate the relation between cardiac function and normal LV preload variations induced by respiration, in normal subjects and patients. We applied the XD-GRASP [1] technique to reconstruct the acquired data in a multi-dimensional image space composed of the spatial dimensions (X, Y) and two physiological dimensions (the cardiac

and respiratory cycle phases – Fig. 1). Using this data, we tracked the septum and measured its displacement over the two temporal dimensions to compute surrogate measures for preload and associated cardiac function response. This was applied to a small series of normal subjects and patients. We found significantly larger changes in diameter during the respiratory cycle for normal subjects compared to patients. We also found a significant correlation between preload and cardiac function for normal subjects, which was reduced for patients.

In the following section, we describe the image reconstruction approach that enabled us to evenly sample the respiratory physiological dimension, with a focus on data sorting and classification. In the remainder of the paper, we present the septum displacement analysis and its results.

2 Related Work

To reduce motion artifacts due to respiration, routine clinical MRI is typically performed during breath-hold [2]. However, not only is breath-holding sometimes too physically demanding for patients, but potentially important information about the influence of the respiratory cycle is lost. The presence of respiratory-synchronous fluctuations in stroke volume has been documented [3] and a quantitative assessment of the respiratory-related motion of the heart followed [4]. For the latter, subjects were imaged at different subjective respiratory positions, during several distinct measurements. A recent study found significant effects of free-breathing, compared to breath-held acquisition, on ventricular mechanics in patients with Duchenne muscular dystrophy and normal subjects [5]. However, artifacts due to respiratory motion still affected image quality. Common methods to reduce artifacts during free breathing include using a navigator [6] or respiratory bellows [7]. Nevertheless, data are conventionally still acquired for only a single respiratory state.

Recent rapid continuous non-Cartesian MRI techniques allow free-respiratory cine imaging [8]. However, they are still affected by motion artifacts, and respiratory states need to be determined separately in postprocessing. The recent XD-GRASP technique [1] enables the independent analysis of cardiac and respiratory physiological dimensions. This is achieved by populating a multi-dimensional image space by reconstruction from the continuously acquired radial spokes (incremented with the golden-angle scheme), based on separately determined cardiac and respiratory motion phases. This allows us to quantify the effect of respiration over different cardiac phases. The presented approach extends initial work on the analysis of septal motion [9] using adaptive data sorting, with automatic myocardium segmentation, and is applied to routine clinical data.

3 Methods

We considered 35 subjects: 11 normal (N), 9 with reduced EF (rEF), without left bundle branch block or infarction, 7 with volume-loaded RV (vIRV), 5 with asymmetric septal hypertrophy (aHyp), and 3 with diffuse hypertrophy (dHyp). We acquired single-slice images with the XD-GRASP technique, using a 2D radial golden-angle increment bSSFP readout with $TR/TE = 2.8/1.4$ ms, spatial resolution = 2×2 mm² and 8 mm slice thickness on

a 1.5T MRI scanner (Avanto, Siemens Healthcare, Erlangen, Germany). Images were acquired in a short-axis mid-ventricle position under free-breathing for an acquisition time of 23 s. Typically, between 6–9 respiratory cycles are sampled over around 20 consecutive hearts beats.

3.1 Multi-dimensional Reconstruction

Respiratory and cardiac motion-related time-phase curves were separately extracted from the image data during post-processing. The acquired data were resorted into $9 \text{ cardiac} \times 9 \text{ respiratory}$ states. The 4D dataset shown in Fig. 1 was reconstructed using a compressed sensing approach which employs sparsity priors along the cardiac and respiratory dimensions in an iterative reconstruction scheme [1].

Detecting Cardiac and Respiratory Phases—The continuous acquisition scheme allows for reconstruction of various temporal resolutions retrospectively. First, a low temporal resolution reconstruction R_0 is derived using the KWIC algorithm [10] in a sliding window approach. Although this results in an overly smooth image series, it mitigates the majority of undersampling artifacts. The frequency interval $H = 0.9\text{--}1.7 \text{ Hz}$ was used to represent the range of regular heartbeats; a lower interval $R = 0.2\text{--}0.4 \text{ Hz}$ was used for the respiratory cycles.

To extract cardiac motion, a mask was automatically constructed around the heart region, detected by first selecting the frequency responses in the heartbeat interval H , then summing the forward difference, and finally performing automatic thresholding [11]. The averaged temporal intensity curve over the cardiac mask represents the cardiac signal (Fig. 2-left). After some temporal filtering, the local maxima represent ED and local minima ES frames. Cardiac cycles are automatically segmented and corresponding k-space data are labeled based on their relative position within the cycles.

To extract respiratory motion, R_0 is further averaged over the temporal domain to reduce noise. The 2D image space is partitioned into partly overlapping rectangles of 15×15 pixels, over which average temporal frequency variations are computed. The sub-image block with the highest frequency response in the respiratory interval R , over the maximum frequency response in the cardiac interval H , represents the respiratory signal (Fig. 2-right).

The inspiration and expiration motion effects observed over the heart and diaphragm regions are different [12]. Therefore, it is desirable to distinguish between inspiration and expiration intervals, by mirroring the latter along the Y axis (Fig. 3-left). In practice, however, the sub-image block that produces the respiratory signal is usually located close to the diaphragm, where the presence of bright vessels or fat often causes large intensity variations, especially in the presence of through-plane motion. This makes it challenging to automatically distinguish whether local maxima represent end-expiration (Eexp) or end-inspiration (Einsp) phases by solely analyzing the temporal histogram. However, considering physiological mechanisms, we observed that, while inspiration can be varying in depth, Eexp phases are more similar (Fig. 2). Therefore, it can be derived that the set of local extrema (either minima or maxima) with the smallest standard deviation likely represents Eexp phases.

Adaptive Data Classification in Multidimensional Space—Based on the cardiac and respiratory motion information, the data was classified into 9×9 sets of cardio-respiratory phases. A relatively low number of bins was chosen, due to the short acquisition time, to account for the high undersampling, especially of the respiratory dimension. Since the analysis was focused on differences between systole and diastole, the low number of bins was sufficient.

To normalize cardiac cycle duration, we considered a fixed relative systolic time per patient, computed as the average duration between the occurrence of a local maximum of the cardiac signal and the subsequent minimum, and a variable-length diastole. Isolated arrhythmic cycles can be automatically detected based on their atypical length, and excluded from the reconstruction. As the acquired data is evenly distributed over the cardiac dimension, we performed a hard classification of the data into 9 equal bins corresponding to cardiac phases.

The respiratory time curves (with mirrored expiration phases) show that the data are not normally distributed, since inspiration and expiration often differ in duration and dynamics (Fig. 3). Particularly during irregular respiration, only few respiratory phases may be well-represented. Hard classification into equal bins therefore results in data subsets with heterogeneous motion states and, hence, may cause artifacts in the reconstruction (Fig. 4-top). An alternative is to seek an optimal classification into a fixed number of classes, based on standard clustering approaches, e.g., k-means. However, with such approaches, classes often contain too few k-space samples to allow a reconstruction with acceptable image quality, even using compressed sensing. In our approach, we propose using a Gaussian mixture model (GMM) [13] which produces a probabilistic (soft) classification along the respiratory dimension (Fig. 3-right). Data in similar respiratory phases are grouped together, but class sizes can be very different. The resulting probabilities are then used to weight the contribution of the data to their assigned class, and are used as weights in a soft-gated reconstruction scheme, as presented in [14]. Similarly, more information can be added to classes with few members in a strictly binary classification sense, by sharing the data from other classes in order of decreasing probability until a minimum threshold is met.

3.2 Septum Motion Analysis

We analyzed the variation of cardiac function with respiration by measuring the LV diameter perpendicular to the septum midpoint $d_{c,r}$ over the cardiac (c) and respiratory (r) phases. To ensure a consistent diameter computation, the myocardium was automatically segmented using an object-based approach [15], and manually corrected, as needed. The RV and the interventricular sulci were also automatically detected, to compute the midpoint of the septum (Fig. 5). The relative change in diameter between end-systole (d_{ES}) and end-diastole (d_{ED}) was computed for each respiratory phase, as a measure of the functional response (a 1D measure of cardiac function) $\nabla d_r = (d_{ED,r} - d_{ES,r}) / d_{ED,r}$.

4 Results and Discussion

The LV diameters d_{ED} and d_{ES} (Fig. 6-top), and the relative changes in diameter ∇d_r (Fig. 6-bottom) were plotted over the respiratory cycle, for N, rEF, vIRV, aHyp and dHyp. First, we observe that the relative position of the septum is modulated during respiration by the

normally varying preload, due to changes in intrathoracic pressure. The LV diameter at end-diastole d_{ED} varies most during the respiratory cycle, while the end-systolic diameter d_{ES} remains relatively constant. d_{ED} varies significantly with respiration for N ($p < 0.001$), providing a measure of LV preload (the blood volume in the LV at the beginning of the next beat). However, for an already dilated LV, as in the case of patients with reduced EF, or a thick and stiffer myocardium, different respiratory phases are associated with smaller changes in diameter, suggesting less variation in LV preload.

A second observation is that the relative change in LV diameter ∇d_r decreases during inspiration and increases during expiration for N. We found a significant correlation between ∇d_r (a measure of cardiac function) and respiratory phase for N ($r = 0.45$, $p < 0.001$), but a lower correlation for rEF ($r = 0.35$, $p = 0.001$) and for vLRV ($r = 0.35$, $p = 0.002$), and the two were not significantly correlated for hypertrophy patients. Assuming that through-plane motion is not significant at the mid-ventricular level, ∇d_r over the respiratory cycle could be interpreted as a measure of the LV functional response to the different respiratory states. The relative difference in ∇d_r between Eexp and Einsp phases, measuring the cardiac function response to the different respiratory states, was significantly larger for N compared to the set of all patients ($5.8 \pm 3.6\%$ vs. $2.5 \pm 3.4\%$, $p = 0.035$).

Finally, we can plot the functional response ∇d_r as a function of preload variation d_{ED} . In Fig. 7, d_{ED} is normalized to the average d_{ED} over the respiratory cycle. The slope of the relationship between ∇d_r (i.e. between a 1D EF measure) and the corresponding preload is greater for N, reduced for rEF and vLRV, and almost flat for the hypertrophic subgroups. This slope could be considered an equivalent to the Frank-Starling relationship, which is found to be altered for patients with reduced contractility, with a hypertrophic myocardium, or with volume-loaded RV.

Our hypothesis is that some patients with preserved EF may show reduced correlation between ∇d_r and d_{ED} , presumably due to hypertrophy, while for others this correlation is partially preserved despite a lower EF, possibly indicating an earlier stage of disease. This will be further investigated in a larger group of patients. Besides the small number of subjects, another limitation of our work is the restriction of image acquisition and analysis to a single mid-ventricular slice, as small variations in the slice position may affect the measurements. In the future, we plan to perform a 3D analysis of the septum relative displacement for a full stack of slices. The short acquisition time may also be a limitation when not enough respiratory cycles are recorded.

Limitations

Besides the relatively small number of subjects, an important limitation of this study is the restriction to a single mid-ventricular slice. In this work, we assumed that through-plane motion has a minimal impact on functional measurements, based on the constant wall thickness. However, it is possible that for other patients with local septal hypertrophy, through-plane motion may have a significant effect on the results, as a local bulge in the septum may move in and out of the plane. Furthermore, the relatively short acquisition time may not offer a sufficient sampling of different respiratory states, especially when breathing is not consistent. In the future, we will acquire longer datasets and also consider different

breathing patterns, such as Cheyne–Stokes respiration, which may have a different impact on cardiac function.

5 Conclusions

Free-breathing cardiac cine MRI provides novel information on cardiac dynamics. We demonstrated a new method for analyzing the influence of preload on cardiac function and function reserve, using the normal variation induced by respiration. For this, we devised a multi-dimensional reconstruction approach, using an adaptive soft classification of data into respiratory phases. The analysis revealed significant differences between normal subjects and patients with reduced EF and hypertrophy.

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Fig. 1. Multi-dimensional cardiac MRI with two physiological dimensions: cardiac (horizontal) and respiratory (vertical – arrows show displacement during inspiration and expiration).

Fig. 2.

Left – cardiac signal before and after smoothing. End-systole time-points marked (*). Right – respiratory signal. End-expiration time-points have less variation than end-inspiration.

Fig. 3.

Left – respiratory signal with mirrored expiration phases. Right – histogram of respiratory signal with overlaid GMM soft classification. Observe the different class sizes.

Fig. 4. Comparison between reconstructions using a hard classification into equal size respiratory bins (top), with associated artifacts (arrowheads), and using soft binning with variable bin size after a GMM classification (bottom) for different cardiac and respiratory phases.

Fig. 5. Segmented myocardium in a short-axis slice. The interventricular sulci are automatically detected in a polar coordinates representation and the septum midpoint and corresponding diameter (d) are computed.

Fig. 6.

$d_{ES,r}$ (red) and $d_{ED,r}$ (blue), normalized by $d_{ED,r}$ (Top), and ∇d_r (Bottom) for the respiratory cycle from end-expiration (EExp) to end-inspiration (EInsp) and back to EExp For the normal, reduced EF, asymmetric hypertrophy, diffuse hypertrophy, and volume loaded RV subgroups. Note the greater variation in the normal subjects. (Color figure online)

Fig. 7.

1D EF measure ∇d_r as a function of preload, measured as d_{ED} (normalized to the average d_{ED} during the respiratory cycle), for N, rEF, aHyp, vIRV, and dHyp subject groups. The corresponding 1D regressions are shown.