The diagnosis of left ventricular mechanical dyssynchrony (LVMD) and identifying cardiac resynchronization therapy (CRT) candidates are challenging problems due to the limitation of the currently applied regional volume-curve analysis. In this study, four-dimensional (4D, 3D+time) left ventricle (LV) regional shape models of 26 LVMD patients were constructed from pre- and/or post-CRT real-time 3D echocardiography (RT3DE) datasets that include 9,900 traced slices on 663 cardiac phases. The shape model analysis based on principal components were compared to volume curve model analysis. The results suggested that the 4D shape modal indices correctly capture LVMD motion patterns and their relative changes after CRT, comparably to the volume curve analysis, and they are also likely to capture unique LVMD shape and motion features that cannot be found by volume curve analysis.

**Index Terms**— Real-time 3D echocardiography, left-ventricular shape and motion modeling, four-dimensional statistical shape model, regional volume curves, principal component analysis

1. **INTRODUCTION**

Cardiac resynchronization therapy (CRT) involves bi-ventricular pacing as treatment for left ventricular mechanical dyssynchrony (LVMD) in order to coordinate or synchronize the left ventricle (LV) motion patterns in symptomatic heart failure. Its invasive nature, high cost, and a high rate of non-responsiveness (20% to 30%) have made the candidate selection a crucial issue [1]. Real-time 3D echocardiography (RT3DE) provides dynamic information about the full LV and has become one of the preferred modalities for detecting LVMD prior to CRT. Whether or not a patient benefits from CRT can often be determined by comparing the regional volume curves derived from pre- and post-CRT RT3DE datasets. Current clinical analysis of RT3DE dataset obtains the semi-automated endocardial segmentation, from which regional volume curves are derived for 16 myocardial LV subvolumes as recommended by the American Heart Association (AHA) [2]. Regional correspondence of the maximum contraction (i.e., the minimum regional volume) is used as an indicator for dyssynchrony. A systolic dyssynchrony index derived from the regional volumes has been proposed and preliminarily validated as a new method of quantifying global LVMD [3]. The main limitation of regional volumes is the lack of shape information about the endocardial surface prevents it from utilizing all information provided by RT3DE to fully describe the changes introduced by CRT. Therefore, the analysis of regional volume curves may not be sufficient to capture the unique features of CRT responders or non-responders and to predict the outcome of CRT. We hypothesize that quantitative analysis of the shape and motion features unique to LVMD is essential for improving CRT candidate selection and the assessment of its effectiveness.

A statistical shape model (point distribution model) [4] describes the shape variation of a training set of objects. A four-dimensional (4D = 3D+time) shape model describes shape and motion variations. In a previous cardiac study on tetralogy of Fallot patients, we have shown that the modal indices (weights of principal components) of the 4D shape model can be used as cardiac functional indices, thus providing more insight about the unique features and progression of a condition than traditional volume-based indices [5]. Similar methodology will likely to be successful in the assessment of LVMD and provide important additional information to determine the likelihood of CRT success in a patient prior to implantation.

The objective of this study is to test the feasibility and capability of using 4D shape modal indices to capture the changes in shape and motion patterns of LVMD from pre- and post-CRT RT3DE datasets and compare them with those of the regional volume curves.

![Fig. 1. A screen shot of the manual tracing application showing orthogonal slices of reorientated RT3DE dataset.](image_url)
use of the original tracings allows us to more conclusively determine the accuracy of the model without potential artifacts from a prior segmentation step.

A custom-designed application is used to perform reorientation recommended by AHA [2] and manual tracing on RT3DE datasets (Fig. 1). The LV endocardial border is traced on roughly equidistant user-selected short-axis slices of the reoriented dataset. This application is capable of creating LV 3D surface from traced contours by linear shape interpolation and displaying the volume curve over the cardiac cycle. The 2D tracing contour is defined by spline control points which can be easily modified based on 3D/4D context acquired from observing the cine movie of image and created shape. To construct a 4D shape model, the RT3DE datasets are normalized along the time axis so that they have the same number of phases (frames) that cover a whole cardiac cycle. Such normalization is performed on 3D shapes and volumes using linear interpolation.

2.2. 4D Shape Model Construcion

The landmarks (in the point distribution model context) for the LV are selected on a fixed number of equally spaced short-axis slices. On each short-axis slice, the landmarks are surface points that are sampled using fixed angle increments based on the long axis. On each cardiac phase, the coordinates of the landmarks are concatenated to form a 3D shape vector. The 4D shape vector is formed by concatenating 3D shape vectors of all cardiac phases. The correspondence of landmarks between phases is guaranteed by selecting same number of landmarks on each phase with respect to the 3D anatomical context. Therefore, the 4D shape vector has motion information embedded. In this study, 20 4D shape models are constructed: 16 individual regional models for AHA-recommended regions as shown in Fig. 2, one basal model, one mid-cavity model, one apical model, and one whole-LV model.

![Fig. 2. Sixteen left ventricular regions.](image)

The reorientation described in Section 2.1 removes the variability in rotation, therefore the Procrustes Analysis that aligns all 4D shapes into a common reference frame is limited to translation and isotropic scaling. To keep shape and motion features of individual regions intact, a single set of translation and scaling parameters is found by aligning all whole-LV 4D shapes and used for constructing all 20 4D shape models.

The statistical properties of the aligned 4D shapes are identified via Principal Component Analysis (PCA) that finds the mean shape \( \bar{s} \) of the training set and \( \Phi \) contains PCA modes (a.k.a. eigenvectors) ordered by their significance. The variation of the training set along the \( i \)th component is \( \sigma_i = 2\sqrt{\lambda_i} \), where \( \lambda_i \) is the \( i \)th eigenvalue. The \( K \) most significant modes are kept to cover 97% of the variations,

\[
\sum_{i=1}^{K} \frac{\lambda_i}{\sum_j \lambda_j} < 0.97 , \quad (1)
\]

and any shape \( s \) in the training set can be approximated as

\[
s \approx \bar{s} + \Phi b , \quad (2)
\]

where the weight vector \( b \) (modal indices) can be used as compact alternative representation of \( s \).

2.3. Volume Curve Model Analysis

Replacing \( s \) in Eq. (2) with a vector that contains the LV volumes of all cardiac phases, PCA can be used to create a statistical model for the volume curves. The measured regional volumes are first normalized with respect to the LV end-diastolic volume and then analyzed by PCA. This provides a measure for the variation of the regional volume rather than the regional shape, therefore presents an additional layer of consolidation.

3. RESULTS

The left ventricles of 26 LVMD patients were scanned before CRT and/or 2–5 months after CRT using a Philips Sonos 7500 Live RT3DE machine equipped with an X4 matrix array transducer to obtain a pyramidal volume in real time. The 3D data size was 160×144×208 with average resolution of 1.43×1.46×0.93 mm.

The acquired number of phases per cardiac cycle was 10 to 22 (15±3). A total of 44 RT3DE datasets were acquired. Independent of our shape and volume analysis, a cardiologist identified the CRT responder/non-responder status based on chart review and physiological parameters before and after CRT was performed. Among the 26 patients, 11 are clinically identified as CRT responders, 4 are non-responders, 3 have undetermined status, 7 have no post-CRT scan yet, 1 has post-CRT data but the pre-CRT data is excluded due to quality issue. The number of patients with known CRT outcome corresponds to the expected distribution of responders versus non-responders.

![Fig. 3. Shape variation on the first cardiac phase introduced by changing the 1st, 2nd, and 3rd modal indices of the 4D LV shape model within \([−2\sigma, +2\sigma]\) (0: mean shape).](image)
landmarked LV surface topology is shown in Fig. 3. All 44 RT3DE datasets were used as the training set for the statistical models of 4D shapes and regional volumes.

Fig. 3 also shows the shape variations on the first (end-diastolic) cardiac phase associated with the three most significant shape modal indices. The shrinking and bulging of the LV are mainly modeled by the first and second indices. In addition, these two indices also model the bending of the LV along the long axis. The third index mainly models the local deformation of the basal and mid-cavity regions. Note that in addition to the 3D shape variations, these indices also model motion variations along the time axis over the cardiac cycle.

Fig. 4. Volume curve variations introduced by changing the first to third (top to bottom) modal indices of the volume curve models within $[-2\sigma, +2\sigma]$ (solid line: mean; dashed lines: $-2\sigma$ and $+2\sigma$).

The volume-time curves partially describe the ventricular motion patterns. Fig. 4(a) indicates that the main motion variation of the LV is in the systole stage and it can lead to changes in ejection fraction and the timing of end-systole. Fig. 4(b) indicates that region 3 exhibits larger variation in the basal-inferoseptal ejection fraction.

To test the feasibility of shape modal indices capturing LVMD shape and motion features, especially when pre-CRT and post-CRT are compared, the shape and volume curve modal indices of all patients and the displacements of indices between pre-CRT and post-CRT were plotted for all analyzed regions and for two pairs of the most significant indices. Some of the plots are shown in Fig. 5.

In all plots of Fig. 5, changing the value of any modal index introduces shape and motion variations (see Figs. 3 and 4) that otherwise cannot be described by a simple parameter such as ejection fraction or isotropic scaling. The values of the modal indices in the plots were scaled with respect to $\sigma$, such that they indicate variations in the context of the study population. The $n$th modes of different shape or volume curve models represent different types of shape and motion variation, their weights are not directly comparable. Therefore, we chose to compare the relative magnitude of pre- to post-CRT displacements in the context of the population. In the volume curve model space, a large displacement means the patient exhibits clear changes in cardiac volume and shapeless motion. In the shape model space, a large displacement means the shape and motion pattern of a patient is clearly changed after CRT.

From observing the plots for all analyzed 20 regions, several common characteristics were found. For 4D shape modal indices: 1) the post-CRT data often have clustered distribution and it is possible to distinguish them from pre-CRT data; 2) CRT responders are more likely to have larger index displacements than non-responders; 3) A responder can have small displacement and a non-responder can have large displacement in certain regions, which suggest that CRT may not substantially change the shape and motion of such regions; 4) For a certain patient, the displacements for all regions are not always large or small, which suggests CRT introduce different amounts of changes to different regions. The plots for volume curve modal indices showed no clustering of pre- or post-CRT data and they have no clear distinction. The observations 2–4 for shape modal indices are also true for volume curve modal indices.

4. DISCUSSION

Further comparison of relative displacement magnitudes of a certain patient in shape and volume modal indices showed that: 1) a patient with large displacement in volume modal indices often exhibits large displacement in shape modal indices. Such results suggest that any apparent changes in cardiac function (measured by cardiac volumes) can be captured by the shape model; 2) A patient with small displacement in volume modal indices does not always have small displacement in shape modal indices. Such results suggest that the shape model may capture some unique changes in shape and motion that are not reflected in the regional volumes.

The current results of shape modal indices show possible clustering of pre-CRT data and distinction between pre-CRT and post-CRT data, therefore these indices may potentially provide more information that can be used to achieve LVMD diagnosis and CRT outcome prediction. However, identifying the capabilities and limitations of these modal indices in classification requires larger study population.

In this study, other LVMD related symptoms such as orthopnea, edema and chest pain are used together with ejection fraction to determine the CRT outcome. CRT responders were mainly identified due to improved ejection fraction after CRT. They often show large displacements in modal indices. In contrast, several patients showed no clear improvement in ejection fraction after CRT, but reported disappearing of orthopnea and chest pain and therefore were identified as responders. They often show small displacements of volume modal indices. Because the outcome is not determined by motion patterns, there exist some uncertainties which caused 3 patients in the study population to have undetermined outcome. Further quantitative analysis on the shape and motion features of LVMD need to be performed based on different types of responders and non-responders, as well as undetermined cases.

5. CONCLUSION

In this study, the LV regional shape and motion patterns of 26 LVMD patients, as imaged before and/or after CRT, were derived from RT3DE datasets. These datasets were analyzed by 4D shape model and volume curve model, and the two approaches were compared. Our results suggest that the 4D shape modal indices can correctly capture LVMD motion patterns, especially their changes after CRT, as well as the traditional volume curve analysis. In addition, the 4D shape modal indices can potentially capture some unique LVMD shape and motion features that cannot be found by volume curve analysis. Therefore, we anticipate that such 4D shape modal indices will increase the accuracy in LVMD diagnosis and CRT candidate identification in the future.

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7. REFERENCES


