

Cardiac Motion Analysis to Improve Pacing Site Selection in CRT¹

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Rationale and Objectives: The aim of the study is to build cardiac wall motion models to characterize mechanical dyssynchrony and predict pacing sites for the left ventricle of the heart in cardiac resynchronization therapy (CRT).

Materials and Methods: Cardiac magnetic resonance imaging data from 20 patients are used, in which half have heart failure problems. We propose two spatio-temporal ventricular motion models to analyze the mechanical dyssynchrony of heart: radial motion series and wall motion series (a time series of radial length or wall thickness change). The hierarchical agglomerative clustering technique is applied to the motion series to find candidate pacing sites. All experiments are performed separately on each ventricular motion model to facilitate performance comparison among models.

Results: The experimental results demonstrate that the proposed methods perform as well as we expect. Our techniques not only effectively generate the candidate pacing sites list that can help guide CRT, but also derive clustering results that can distinguish the heart conditions between patients and normals perfectly to help medical diagnosis and prognosis. After comparing the results between two different ventricular motion models, the wall motion series model shows a better performance.

Conclusion: In a traditional CRT device deployment, pacing sites are selected without efficient prediction, which runs the risk of suboptimal benefits. Our techniques can extract useful wall motion information from ventricular mechanical dyssynchrony and identify the candidate pacing sites with maximum contraction delay to assist pacemaker implantation in CRT.

Key Words: Computer-aided diagnosis; cardiac resynchronization therapy; time series analysis; medical image computing; heart failure.

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Heart failure, also called congestive heart failure, is a major health problem that continues to increase in prevalence. It is a disorder in which the heart loses its ability to pump blood efficiently. Low cardiac output resulting from heart failure may cause the body's organ systems to fail. As part of the problems, the walls of the left ventri-

cle (LV) are unable to contract synchronously. Thus there exist contraction delays (intraventricular dyssynchrony) in a portion of the LV, which may damage the heart's pumping action and lead to blood accumulation into other areas of the body that may cause the body's organ systems to fail. Figure 1 shows sample of contraction delays on the LV.

Over the past decade, investigators (1) have established the feasibility of placing multiple pacing leads of pacemaker to improve the activation synchrony (sameness of activation time) of the LV and biventricle. As a result, the pump function efficiency is increased (2–4). Based on these studies, a promising therapeutic option, called cardiac resynchronization therapy (CRT), has been proposed

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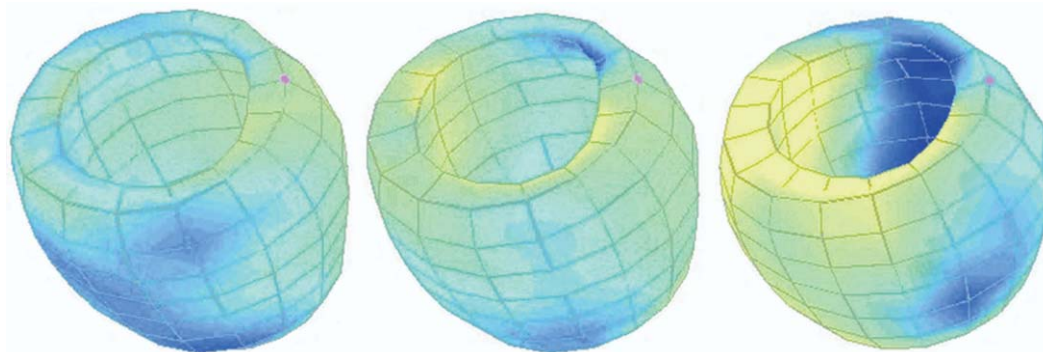


Figure 1. Sample simulation of a failing left ventricle at three different timing phases during a heartbeat. Color coding shows the contracting (yellow) and neutral (blue) regions based on their regional wall thickness. Yellow regions have a high value of wall thickness and blue ones own the low value. In this sample, the right wall contracts first (early activated) and the left wall contracts after a timing delay (activated late).

as an alternative treatment in patients with severe, drug-refractory heart failure. It is aimed at correcting contraction delays that result in different regions of the heart not working optimally in concert (5). A successful CRT will synchronize the wall contraction so that left ventricular ejection fraction is maximized. Therefore, the improvement in cardiac performance is highly dependent on the pacing site that changes the sequence of ventricular activation in a manner that translates to an improvement in cardiac performance.

As an important medical device, the pacemaker is used to speed up the patient's heart rate when the rate is too slow. It sends out tiny electrical impulses, which travel through the insulated wires of a pacing lead until they reach the metal electrode at the tip of the lead, to cause the heart to beat if the heart itself fails to generate an electrical impulse. CRT uses a specialized pacemaker to recoordinate (resynchronize) the action of the ventricles in patients with heart failure to increase pumping action and improve blood flow.

In early studies, because of familiarity with and demonstrated safety of the right ventricle (RV) pacing lead, CRT was accomplished by pacing both ventricles simultaneously. However, RV pacing was not required for hemodynamic benefit in many patients (6). Many research results already demonstrated LV pacing alone achieves a similar benefit and persistence (7–9). Thus, in our research, we focus on the CRT with LV pacing sites.

Optimal LV site selection is one of major clinical considerations for CRT device implantation. De Teresa and colleagues (10) demonstrated that cardiac function can be improved by changing the sequence of the ventricular electrical activation using pacing. They noted that the left

ventricular ejection fraction (an important index for cardiac function) was maximal when wall contractions were simultaneous (6). Murphy and colleagues (11) found that reverse remodeling and increase in ejection fraction were more likely to occur if the pacing site was concordant with the maximum electromechanical delay. Improvements in the techniques for determining and guiding the optimal placement of pacing leads are needed.

Many ultrasound techniques (12–14) (eg, M-mode echocardiography, tissue Doppler techniques) are employed for measuring cardiac dyssynchrony to facilitate the selection of patients and pacing sites for CRT, but CRT studies based on these techniques are limited in both radial (using M-mode echocardiography) and longitudinal wall motion (using tissue Doppler velocities), and ultrasonic techniques are also very sensitive to noise. Compared with ultrasound and other imaging techniques, magnetic resonance imaging (MRI) provides high spatial and temporal resolutions imaging of the anatomy of the heart in tomographic planes of any desired position and orientation. Because MRI can provide an in-depth understanding of anatomy, structure, global and regional function, and contraction patterns in patient's heart (15), it is an effective and practical way to define the optimal pacing sites for patients with heart failure.

Because the ventricular wall thickening and motion reflect mechanical activation, we explore two spatio-temporal ventricular motion models to analyze the mechanical dyssynchrony of heart. Our models allow determination of the most delayed contraction sites of the LV that are effective places for implanting the pacemaker to achieve a more likely optimal CRT result (11). In these two models, radial motion series and wall motion series

are used as indicators of the ventricular wall change. The hierarchical agglomerative clustering method (16) is applied on these time series to find candidate pacing sites with abnormal local motion. Meanwhile, the contraction time delays between each region of LV wall are obtained by calculating the crossing correlation of the targets' motion to quantify the mechanical dyssynchrony of LV. Our experiments also show that this study can be used to distinguish patients and normals. At the end of this article, we will compare these two models by a series experiments on cardiac MRI.

MATERIALS AND METHODS

Imaging Technique

In our study, cardiac MRI is used to capture three-dimensional (3D) images of a heart in the short-axis or long-axis orientation during its normal operation. With acquisition timed according to heartbeat frequency, a fixed number of images can be acquired during each heartbeat. In this work, imaging was performed on a GE twin gradient Excite at 1.5 T with an eight-element phased-array cardiac receive coil (GE Healthcare Technologies: Waukesha, WI) and the following pulse sequences:

- real-time motion imaging (parallel acquisition asset = 4, repetition time [TR]/echo time [TE] = 2.394/0.986, FA (flip angle) = 45, Nex (Number of excitations) = 0.5, matrix = 128×72 , ST (slice thickness) = 8 mm);
- bright blood movie series (asset = 2, TR/TE = 3.161/1.422, FA = 45, Nex = 0.5, matrix = 192×224 , ST = 8 mm);
- high-signal bright blood movie series (steady-state recalled gradient echo = FIESTA, TR/TE = 3.001/1.016, FA = 45, Nex = 1, matrix = 192×128 , ST = 8 mm);
- strain maps (end-diastolic magnetization inversion recovery grid pattern tracking, prospective triggered phase advance, 20 phases/RR, TR/TE = 8.948/5.272, FA = 60, Nex = 1, matrix = 256×128 , ST = 8 mm);
- velocity map movies (two-dimensional, phase-encoded velocity sensitivity adjusted to shy of aliasing, triggered for 20 progressive phases/RR, TR/TE = 11.684/4.312, FA = 20, Nex = 1, matrix = 256×128 , ST = 10 mm);
- scar maps (inversion recovery adjusted 250–300 milli-

seconds to null non-contrast myocardium, imaging 10 minutes after 0.2 mM/kg Gd-DTPA for retention by scar, TR/TE = 7.116/3.368, FA = 20, Nex = 2, matrix = 256×192 , ST = 10 mm).

The heart orientation was determined by the operator from four-chamber scout views and optimized for perpendicularity to the cardiac wall. The sequences of heart images were produced in the Digital Imaging and Communications in Medicine (DICOM) format with 256×256 pixel size. Each sequence consists of 17 volume images that together represent one complete heart cycle (17). Endocardial and epicardial contours were semiautomatically traced by an experienced observer using space-time segmentation software developed in our lab (Fig 2).

To determine the orientation of the cross-sectional images, the DICOM standard protocol is used for cardiac model reconstruction (18). DICOM plane attribute descriptions (eg, patient orientation, image position, image orientation) are read from DICOM file header. The x, y, and z coordinates of the upper left hand corner of every image are read from "Image Position (0020, 0032)" in the DICOM file header and it is the center of the first voxel transmitted. These coordinates specify the origin of the image with respect to the patient-based coordinate system. In each image, the direction cosines of the first row and the first column with respect to the patient are read from "Image Orientation (0020, 0037)." Row value for the x, y, and z axis, respectively, is followed by the column value for the x, y, and z axis, respectively (18). The point (i, j) (unit is pixel) on the image plane is mapped to the reference coordinate system as follows:

$$\begin{pmatrix} x_{3d} \\ y_{3d} \\ z_{3d} \end{pmatrix} = \begin{pmatrix} OX_x & OY_x & P_x \\ OX_y & OY_y & P_y \\ OX_z & OY_z & P_z \end{pmatrix} \times \begin{pmatrix} i \times unit \\ j \times unit \\ 1 \end{pmatrix} \quad (1)$$

Where (x_{3d} , y_{3d} , z_{3d}) are the coordinates of voxel (i, j) in the reference coordinate system (unit is mm); (OX_x , OX_y , OX_z) are the row direction cosine values, (OY_x , OY_y , OY_z) are the column direction cosine value, and both of them come from "Image Orientation (0020, 0037)"; (P_x , P_y , P_z) are the position values of image in the reference coordinate system (unit is mm) and read from "Image Position (0020,0032)"; and unit is the transformation from pixel resolution to millimeter resolution.

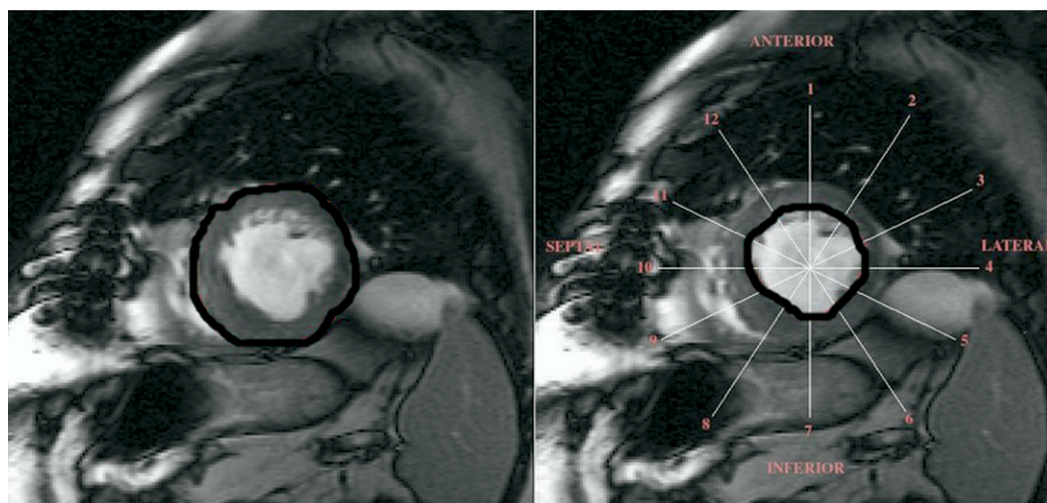


Figure 2. Short-axis magnetic resonance imaging. (Left) Segmentation for epicardium of left ventricle and calculate the center of the border. After segmenting the endocardium (right), we draw 12 radii with equal angles between 2 neighboring radii. They are marked from 1 to 12.

Ventricular Motion Descriptors

In CRT, electrical impulses go into the myocardium by the pacing lead tip anchored in the muscle and stimulate the electrical activation of the LV to get a synchronous wall motion. The stimulation by electrical impulses is instantaneous at the contact location during each heart cycle, not after the contracting myocardium.

To quantify the ventricular mechanical asynchrony, which is important for the diagnosis and the prognosis and can help determine optimal treatment, we develop two spatio-temporal models to describe the left ventricular wall change during a heart cycle: radial motion series (19) and wall motion series (20).

Radial motion series.—At first, we used surface tracking techniques (21,22) to create temporal sequence descriptions for points on the left ventricular endocardial surface throughout each heart cycle (19). In the first step, we calculated the centers of epicardial borders on every MRI slice and used these centers as origin points of radii on each image slice. In the second step, for each image slice, we acquired a number of radii by connecting the center to sampled points on each endocardial border. In our study, 12 radii were used for each MRI slice. Figure 2 shows the entire process for retrieving the radii from LV. In previous work (23,24), researchers used a similar model (using 16 segments with radial lines) to deduce the left ventricular radius and wall thickness from the geometry of the ventricle on two consecutive short-axis slices. Compared with their 16 radial lines, our 12 radii included 4 directions of anterior, lateral, inferior, and septal wall;

the other 8 radii are uniformly interpolated among them. Although more detailed information could be found after increasing the number of radii, the computational time of pacing sites prediction also increased. We performed several experiments with varying number of radii and found that 12 radii is a good choice for our modeling purpose. Thus, in this article, we report the results using 12 uniformly distributed radii in each image slice.

Each MRI sequence holds 17 temporal phases per heartbeat, in which each temporal phase consists of a stack of image slices that forms a 3D heart image at the corresponding time point. Thus each heartbeat corresponds to a spatio-temporal image sequence. For convenience, we use P_i to denote the i -th temporal phase and S_j to denote the j -th spatial image slice. For example, $\{P_1S_6, P_2S_6, \dots, P_{17}S_6\}$ represents a temporal sequence of the i -th image slice with 17 phases. The radii are grouped in the same way, and $\{P_1S_6R_8, P_2S_6R_8, \dots, P_{17}S_6R_8\}$ represents a sample radial motion series for the 8-th radius (R_8) in slice 6 (S_6). A radial motion series includes all the length values of a radius during a heart cycle, from end-systolic phase to next end-systolic one. Because the left ventricular wall is oriented into perpendicularity for the MRI scan process, a radial motion profile represents relative contraction between endocardium and epicardium and reflects the wall's activation. For a normal heart, all the radial motions are approximately similar to one another because different LV parts tend to contract synchronously. However, for a failing heart, different LV parts may have different contraction behaviors, which may re-

sult in different radial motions. Thus, in our study, we use radial motions to characterize local contraction behaviors of left ventricular wall. Given a radius r , we use $r = \{r_1, r_2, \dots, r_{17}\}$ to denote its radial motion series, where r_i is the value of radius r at the time phase i .

Wall motion series.—Because the heart contracts and dilates along both the long and short axes of the image stack, the radial motion series only can approximately describe the spatio-temporal wall motion from two-dimensional view. Therefore, we use the wall thickness change of LV instead as the wall motion descriptor, because it directly shows the wall motion in 3D space during a heart cycle. In this new model, we combine spherical harmonic (SPHARM) description (25) and surface alignment method (26) to offer a set of spatio-temporal surface correspondences to build the wall motion descriptor (20).

Surface reconstruction.—We reconstructed both endocardium and epicardium of the LV by using the SPHARM method, which was introduced by Brechbühler and colleagues (25) for modeling any simply connected 3D object. The object surface is parameterized as $v(\theta, \varphi) = (x(\theta, \varphi), y(\theta, \varphi), z(\theta, \varphi))^T$ using a pair of spherical coordinates (θ, φ) , where the parameterization aims to preserve the area and minimize the angle distortion. Thus $v(\theta, \varphi)$ becomes a vector of three spherical functions that can be expanded using spherical harmonics $Y_l^m(\theta, \varphi)$ as follows,

$$v(\theta, \varphi) = \sum_{l=0}^{\infty} \sum_{m=-l}^l c_l^m Y_l^m(\theta, \varphi), \text{ where } c_l^m = (c_{lx}^m, c_{ly}^m, c_{lz}^m)^T.$$

SPHARM has been used by Gerig and Styner in many medical imaging applications (eg, shape analysis of brain structures) (27,28). Because SPHARM provides an implicit correspondence between surfaces of 3D objects, it is suitable to be used to analyze the LV wall motion during a heart cycle.

In our cardiac MRI data sets, each MRI sequence holds seventeen temporal phases per heartbeat. Because the LV deformation is exhibited by the thickness change of the wall between endocardium and epicardium, we use 17 reconstructed SPHARM surface pairs (including both endocardium and epicardium) to describe the LV contraction and dilation during a whole heart cycle.

Surface correspondence.—To measure the wall thickness at each surface location and compare thickness changes between different time points, a registration step is necessary for aligning all the reconstructed epicardial surfaces together. Given two SPHARM models, we established their surface correspondence by minimizing the

Euclidean distances between their corresponding surface locations. Formally, for two surfaces given by $v_1(s)$ and $v_2(s)$, their distance $D(v_1, v_2)$ is defined as (27):

$$D(v_1, v_2) = (\oint \|v_1(s) - v_2(s)\|^2 ds)^{1/2} \\ = \left(\sum_{f \in \{x, y, z\}} \sum_{l=0}^L \sum_{m=-l}^l (c_{lf_1}^m - c_{lf_2}^m)^2 \right)^{1/2}.$$

The epicardial surface in the first time phase of the heart beat (diastolic phase in our MRI data) is used as the template. For any other epicardial surface in the same sequence, we align it to the template by rotating its parameter net (26) so that the surface distances $D(v_1, v_i)$, ($i = 2, \dots, 17$) between them (between the considered surface and the template) is minimized. Given an aligned surface sequence, we used the same method to align the endocardium to the epicardium in the same time phase.

Wall thickness change.—Most of previous studies on wall thickness calculation use the myocardium surface to generate the normal vectors whose inner part between epicardium and endocardium defines the 3D wall thickness. In this study, we observed that the distance between the corresponding points (ie, with the same $[\theta, \varphi]$) on both endocardium and epicardium surfaces can be directly used as the wall thickness, because their surface distances are already minimized in the surface registration step. In addition, the underlying equal area parameterization implies the correspondence relationships between any pair points on these two surfaces are reasonable and effective. Based on the wall thickness computational model, the LV wall motion series were generated by computing the wall thickness for each surface location at each time phase.

In our experiments, each sampling mesh on one surface has 32×32 nodes and each node has a wall thickness value. The wall motion series we created includes wall thickness values for each surface node at each time phase during a heart cycle, from end-diastolic phase to next end-diastolic one. Because we are only interested in the LV wall motion, we ignore the points appearing on the top of reconstructed surfaces. Even if only one point of the wall motion series appears on the top of its surface, the whole motion series is discarded. Then we obtained n wall motion series, where n varies from 80 to 100 in different experiments. The corresponding points of these n series are uniformly distributed on the LV surfaces.

Finally, a set of motion series is used to present the LV wall contraction. Given a pair of (θ, φ) , $WT(\theta, \varphi) = \{WT_1(\theta, \varphi), WT_2(\theta, \varphi), \dots, WT_n(\theta, \varphi)\}$ denotes its corre-

sponding wall motion series; $WT_i(\theta, \varphi)$ defines the wall thickness value in time phase i corresponding to the parameterized point (θ, φ) on the epicardium and we have $n = 17$ for our MRI data. These wall motion series can characterize local contraction behaviors of the LV wall and have a potential to capture the contraction abnormality of a failing heart.

Similarity Measurement

After the steps outlined, a set of motion series (we use LV motion series to include radial motion series and wall motion series) are used to present the LV wall contraction. To compare the LV motion series between different locations, we use a distance function to represent the similarities between them. It is important to pick an appropriate distance function. In this case, we observe that the Euclidean distance is not sensitive enough, and that a better choice is to use the Pearson correlation coefficient.

Given two LV motion series $x = \{x_1, x_2, \dots, x_n\}$ and $y = \{y_1, y_2, \dots, y_n\}$, we employed the following formula to measure the distance or dissimilarity between them:

$$d_{\text{corr}}(\mathbf{x}, \mathbf{y}) = 1 - r(\mathbf{x}, \mathbf{y}) \\ = 1 - \frac{1}{n} \sum_{i=1}^n \left(\frac{x_i - x_{\text{mean}}}{\sigma_x} \right) \left(\frac{y_i - y_{\text{mean}}}{\sigma_y} \right),$$

where

$$\sigma_g = \sqrt{\sum_{i=1}^n \frac{(g_i - g_{\text{mean}})^2}{n}},$$

$r(\mathbf{x}, \mathbf{y})$ is the Pearson correlation coefficient of two LV motion series, g_{mean} is the mean of LV motion series, and σ_g is the standard deviation of g . In our definition, g_{mean} is used to remove the shift difference. Similarly, σ is used to normalize the LV motion series when we calculate the similarity score between them. Because the Pearson correlation coefficient is sensitive to direction of change (increasing or decreasing), it is reasonable to use it to measure the similarity between LV motion series. The Pearson correlation coefficient is always between -1 and 1 , and we normalized distance function as $d_{\text{corr}}/2$ (the result will change from 0 to 1) in our experiments.

Hierarchical Agglomerative Clustering

By combining or clustering similar LV motion series, we can identify groups of LV motion series that are the main trend of LV contraction and dilation for different

Algorithm 1

The Hierarchical Agglomerative Clustering Algorithm

1. Assign each left ventricular motion series to a separate cluster.
2. Evaluate all pair-wise distances between clusters and store them into a distance matrix.
3. Repeat.
4. Find the clusters with the closest distance.
5. Merge those two clusters into one cluster.
6. Compute the distances between the new groups and the remaining groups to obtain a reduced distance matrix.
7. Continue until all of the left ventricular motion series are clustered into a single group.

locations in the 3D space. To group similar LV motion series together, we employed a hierarchical agglomerative clustering approach (16), which is a bottom-up clustering method in which clusters can have subclusters. The Algorithm shows the sketch of our approach.

For any set of n objects, hierarchical agglomerative clustering starts with every single object in a single cluster (see Algorithm lines 1–2). Then, in each successive iteration (lines 3–7), it merges the closest pair of clusters by satisfying their proximity information criteria, until all of the data are in one cluster. In our case, the objects are the LV motion series of sampled points on epicardium, and the proximity criteria was defined by the distance described in between pairs of LV motion series. In addition, the distance between two clusters (line 6) is defined as the average of distances between all pairs of LV motion series, in which each pair is made up of LV motion series from each group. Thus the distance matrix can be updated using the following formula:

$$d(R, P + Q) = \frac{n_P}{n_P + n_Q} d(R, P) + \frac{n_Q}{n_P + n_Q} d(R, Q),$$

where P and Q are merged into one new cluster, and n_P and n_Q are the numbers of LV motion series in group P and Q , respectively.

The hierarchical clustering process usually stops after performing $n-1$ iterations in Step 3, and results in a dendrogram, or a hierarchical tree. A dendrogram is a binary tree (Fig 3) in which each data point corresponds to a leaf node, and distance from the root to a subtree indicates the similarity of subtrees—highly similar nodes or subtrees have joining points that are farther from the root.

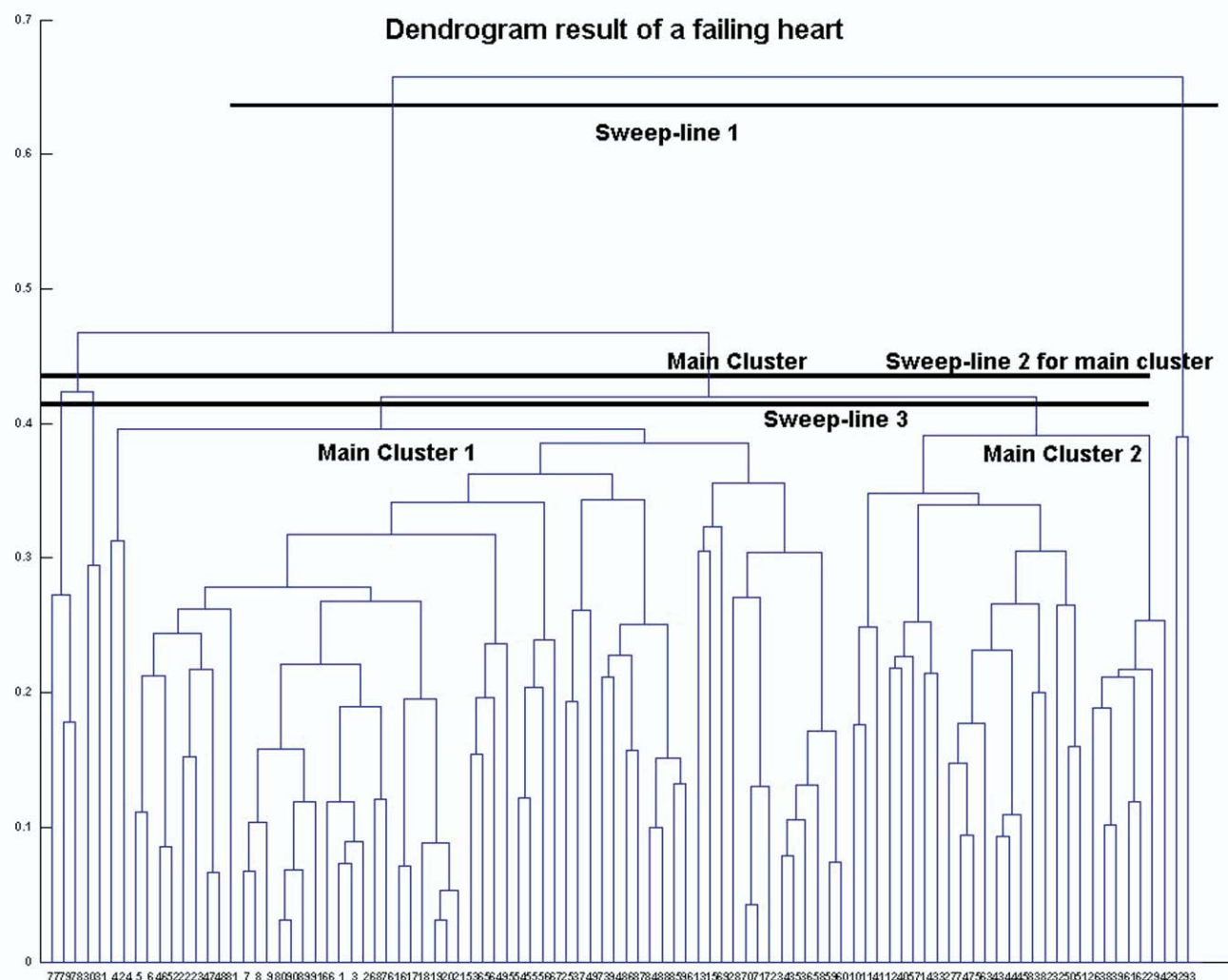


Figure 3. Dendrogram result of a failing heart. The x-axis label represents the number of wall motion series. The y-axis label corresponds to the distance between clusters. The dendrogram is cut into clusters by the “sweep line 3.”

Sweep Line Method

Our primary purpose for building a cluster hierarchy was to structure and present LV motion series at different levels of abstraction. Using a dendrogram, researchers and technicians can easily see the dissimilarity between sub-clusters that represent certain parts on the epicardium.

We move the horizontal sweep line from top to bottom in the dendrogram result (for example, “sweep line 1” in Fig 3) to get the abnormal clusters (small clusters) that have a large dissimilarity to the main cluster. Note that the pacemaker system uses electrical impulses to adjust the starting time of the contraction at these sites whose contraction characteristics are considerably different from other sites. Thus hierarchical clustering results can help

us to find these location candidates for installing the pacing leads.

Pacing Site Prefiltering

Cross-correlation.—For two LV motion series, we already can calculate the similarity between them. But to set the electrical impulses in a pacemaker system, a technician still needs to know the time delay value between the pacing position and a common position. Hence we use a cross-correlation method to acquire such a value between the LV motion series. For two LV motion series $x = \{x_1, x_2, \dots, x_n\}$ and $y = \{y_1, y_2, \dots, y_n\}$, the correlation function of two radial motion series is defined as:

$$cc_{xy}(t) = \mathbf{x} \circ \mathbf{y} = \sum_{m=1}^n x(m)y(m+t),$$

where “ $\circ$ ” is the correlation operator, and $t = 0, 1, \dots, n - 1$. If $t = t_0$ satisfies $cc_{xy}(t_0) = \max(cc_{xy}(t))$ for $t (0, n - 1)$, then the radial motion series x shifts t_0 to get the maximum correlation with the radial motion series y . Thus t_0 is the time shift (or delay). The time period between two neighboring phases can be calculated using the heartbeat velocity. Thus the time delay can be calculated as follows:

$$\text{timing delay} = t_0 \times \frac{\text{a heartbeat period}}{\text{the number of phases}}.$$

Pacing sites selection.—As mentioned previously, in CRT, the electrical pulse should be delivered at the sites with asynchronous contraction and time delay. The dendrogram resulting from the hierarchical clustering procedure described previously can provide valuable information to help identify these sites. In the implantation, a physician still needs to test the lead to see whether a candidate location is suitable for pacing, because the pacing lead cannot be placed into some regions of LV (such condition normally is created by epicardial scar or unacceptable phrenic nerve stimulation). Based on the dendrogram result, we provide the location candidates for implanting and they are rated by the distances from the main cluster, which is described in the following section.

We introduced a filtering step on the pacing site candidates list, because a few of them do not have contraction time delay to the normal activation. After picking up the site candidates, there is a single big cluster in the dendrogram, called the main cluster (see Fig 3 for a marked sample main cluster). The LV motion series (average motion series) of the main cluster is regarded as the normal ventricular motion variation of the LV; for example, the square-line in Fig 4 and Fig 5. Using the contraction time delay between pacing site candidates and main cluster, we filter out the site candidates without contraction delay.

RESULTS AND DISCUSSION

We implemented our pacing site prediction framework using Matlab 6.5, and both LV motion descriptors (radial motion series and wall motion series) are included in the framework. To show the effectiveness of our models, we use cardiac MRI data from 20 patients in our experi-

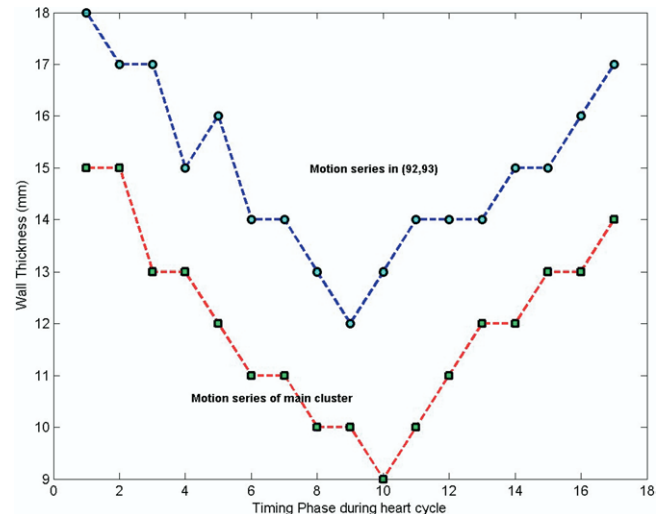


Figure 4. There is no obvious timing delay between the average wall motion series of the main cluster (square-curve) and the motion series of region {92, 93} (circle-curve).

ments, in which half have heart failure problems. All experiments are performed separately on each model based system, so that we can compare the performance of the two models. These experiments are conducted on a PC with a 2.40 GHz CPU and 768 MB main memory. Note that the patients are diagnosed by specialized physicians, and that these diagnostic results are used to validate our results in the experiments.

For convenience, we allocated a number to each LV motion series. From apex to basis of the LV, 1–96 are used to mark the points of LV motion series level by level. Therefore, the points represented by consecutive numbers are in the neighbor locations on the surface, the points with small numbers should be close to the apex, and the points with large numbers should be close to the basis of the LV.

Figure 3 shows the result of hierarchical clustering after application of the wall motion series model in a patient with heart failure. The dendrogram consists of a main cluster and several other small ones. The locations corresponding to the motion series in those small clusters are selected as the candidate pacing sites. Note that a single small cluster may include multiple regions on the LV, because the different regions may have similar motion behaviors. In Fig 3, {92, 93} (close to the basis of LV) is the top priority option for resynchronization therapy; the next pacing candidates that should be considered are {77, 78, 79} and {30, 31}.

Because the distance function we used cannot discriminate the time delay between wall motion series, the prefil-

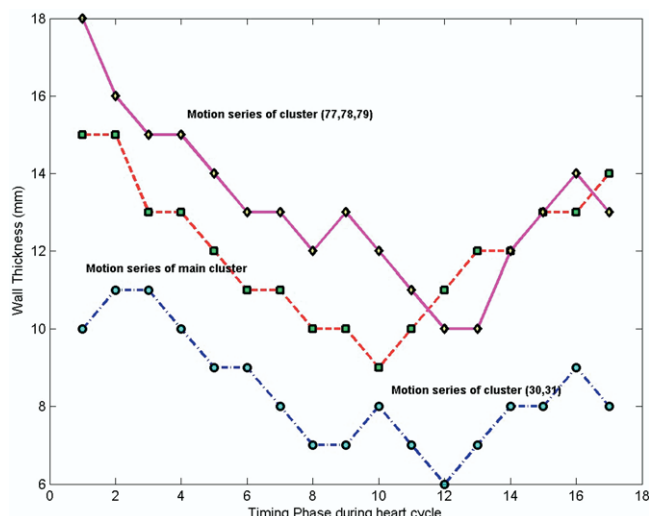


Figure 5. There is a contraction timing delay between the main cluster regions {77, 78, 79} (diamond-curve) and {30, 31} (circle-curve).

tering step should be executed here. Figures 4 and 5 show the pacing sites filtering step. In Fig 4, the curve with square tags is the average motion series of the main cluster in Fig 3 and the curve with circle tags is the average motion series of region {92, 93}. Because there is no time delay between the main cluster and this region, it is filtered out, although their average wall motion series is very different from that of the main cluster. Regions {77, 78, 79} and {30, 31} still remain in the candidate list, because obvious time delays are observed in Fig 5.

After the filtering step, our results can be used for the implantation of the electrodes. As mentioned previously, the pacing lead cannot be placed into some particular regions of the LV. The physician will test the pacing lead on candidate pacing sites according to the suggested site ordering until they find a suitable region for fixing the tip of pacing lead. If the list is empty and a suitable site is not found, the operator will continue and select a lower value sweep line in the dendrogram; for example, the “sweep line 2” and “sweep line 3” in Fig 3. Because the candidates list includes locations with notable asynchronous contraction and time delay, delivering the electrical pulses at these candidate sites will potentially provide optimal resynchronization. These sites are potentially good candidates to implant the pacemaker for a more efficient CRT. Furthermore, in some clinical cases, physicians may want to use multiple sites in left ventricular pacing for cardiac resynchronization, and they can select additional locations from the candidate list.

We have tested our methods on the MRI data of both normal and failing hearts. The dendrogram results of the normal hearts are very different from the failing ones. In the normal heart dendrogram (Fig 6), if the value of sweep line is selected as ≥ 0.3 (the distance between clusters), we obtain only one single main cluster without any other small clusters. This matches our intuition, because the wall motion of a normal heart tends to be synchronous and so the motion difference on different surface locations is very small. Thus our analysis may be useful in identifying patients requiring a helping diagnosis.

After obtaining 20 dendrograms for all subjects (10 normals and 10 abnormals) for each single case, we move the sweep line from top to bottom until the result contains exactly two clusters. The column pair 1 and 4 (in each pair of column, the blue column shows the experimental results on radial motion series model; the purple column shows the experimental results on wall motion series model) in Fig 7 summarize the final values of these sweep lines, sorted in two groups—one group holds low value (their average value is shown by column pair 4), and the other one holds high value (their average value is shown by column pair 1). The clinical diagnosis indicates that all low-value cases correspond to normal hearts and all high-value ones correspond to failing hearts. Note that there is a big gap between these columns, which means that such hierarchical clustering results can actually separate subjects with heart failure from normal subjects. This observation is helpful for heart failure diagnosis and prognosis. The value 0.4–0.6 seems to be a good threshold for the sweep line to distinguish failing hearts from normal hearts in our data.

In the heart failure data set, we continue to move the sweep line to extract all small clusters (this sweep line may separate the main cluster into two or more main clusters). “Sweep line 3” in Fig 3 is such an example, and in this case we have five clusters: {92, 93}, {77, 78, 79}, {30, 31}, main cluster 1, and main cluster 2. The column pair 3 in Fig 7 shows the average number of clusters retrieved from these 10 abnormal subjects. The column pair 2 in Fig 7 shows the average cutoff value of the sweep line to find the main cluster. Obviously the values of radial motion series in column pair 2 and 3 are larger than the values of wall motion series because the radial motion series describe less spatial motion information than wall motion series. Thus there are outliers in the clustering results of experiments on radial motion series model-based system. The wall motion series is a better model in

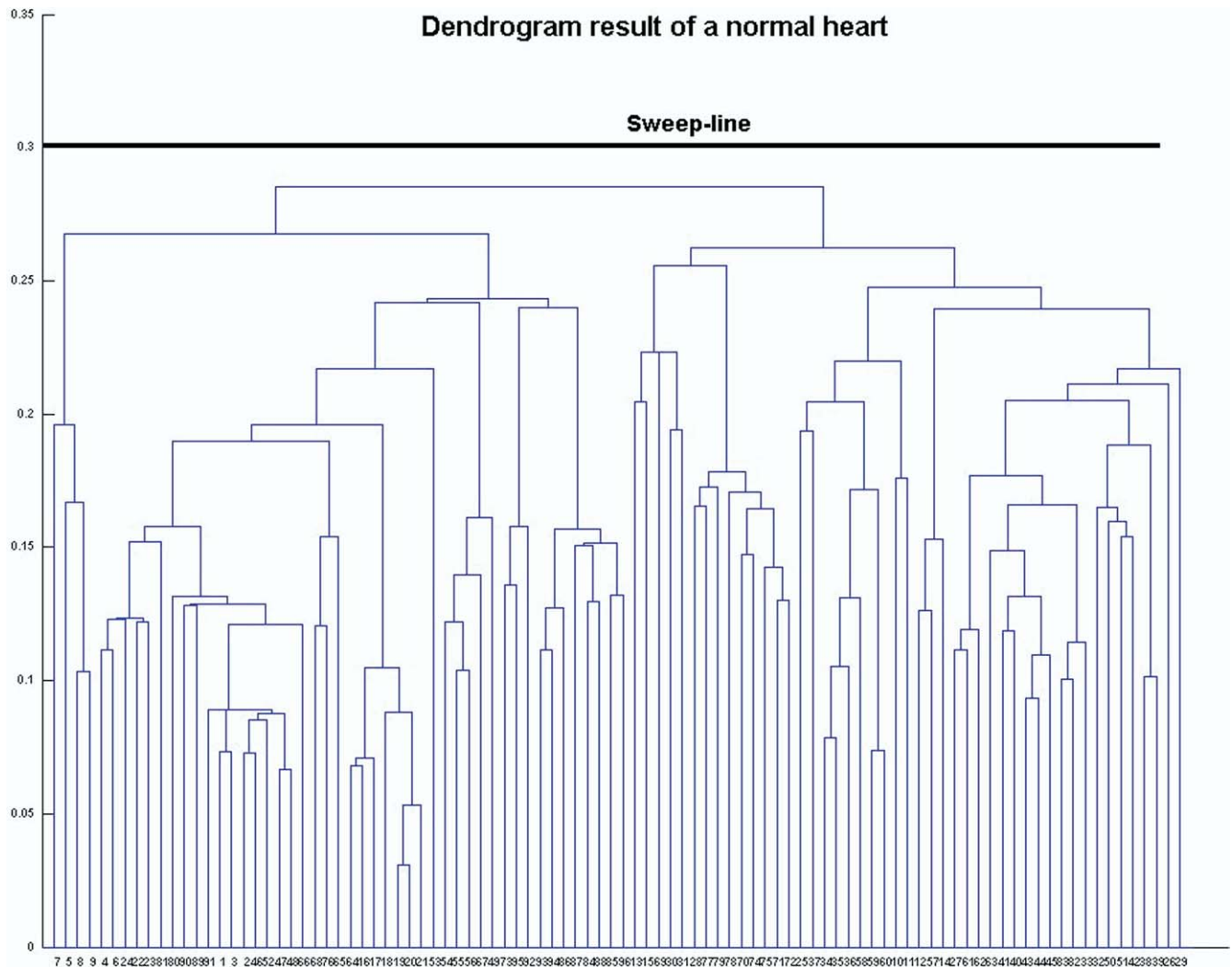


Figure 6. Dendrogram result of a normal heart. The x-axis label represents the number of wall motion series. The y-axis label corresponds to the distance between clusters.

pacing sites selection and heart failure symptom discrimination.

CONCLUSION

In this work, we have proposed a new system to help researchers and physicians select the candidate pacing sites that exhibit the maximum electromechanical delay. These candidate pacing sites have the potential to be treated for maximizing left ventricular ejection fraction and thus can provide helpful guidance for CRT in heart failure treatment (11). The core techniques in our system are based on the spatio-temporal analysis of cardiac wall motion patterns. In the analysis, except for the previous

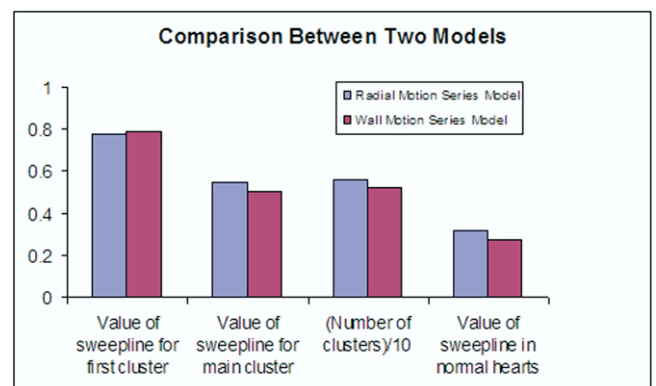


Figure 7. The average cutoff value of the sweep line. The y-axis label is the sweep line value. In each pair of columns, the blue column shows the experimental results obtained with the radial motion series model, and the purple column shows the experimental results obtained with the wall motion series model.

radial motion series model, we also present a new wall motion series model that combines the SPHARM surface modeling technique and a fast method for alignment of corresponding surfaces to characterize the LV wall motion and model ventricular contraction and dilation over a heartbeat cycle. A hierarchical approach is employed to cluster the LV motion series and to identify candidate pacing sites. As a result, our system can automatically generate the candidate site list to help electrophysiologists and specialists localize the pacing sites (with maximum delay).

Blinded analysis of clinical MRI data illustrates the ability of our spatio-temporal modeling techniques to efficiently compare wall motion dyssynchrony and compute contraction time delay between each pair points on the LV surface, and also demonstrates that our approach can correctly distinguish failing hearts from normal ones.²⁹

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