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Abstract. Recent studies show that the response rate to cardiac resynchronization therapy (CRT) could be improved if the left ventricle (LV) is paced at the site of the latest mechanical activation, but away from the myocardial scar. A prototype system for CRT lead placement guidance that combines LV functional information from ultrasound with live x-ray fluoroscopy was developed. Two mean anatomical models, each containing LV epi-, LV endo- and right ventricle endocardial surfaces, were computed from a database of 33 heart failure patients as a substitute for a patient-specific model. The sphericity index was used to divide the observed population into two groups. The distance between the mean and the patient-specific models was determined using a signed distance field metric (reported in mm). The average error values for LV epicardium were -0.4 ± 4.6 and for LV endocardium were -0.3 ± 4.4 . The validity of using average LV models for a CRT procedure was tested by simulating coronary vein selection in a group of 15 CRT candidates. The probability of selecting the same coronary branch, when basing the selection on the average model compared to a patient-specific model, was estimated to be $95.3 \pm 2.9\%$. This was found to be clinically acceptable. © 2015 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: [10.1117/1.JMI.2.2.025001](https://doi.org/10.1117/1.JMI.2.2.025001)]

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1 Introduction

Cardiac resynchronization therapy (CRT) is a good treatment to recover heart function and improve health for a number of selected patients with heart failure (HF), as described in Ref. 1. However, studies² show that only 70% of patients respond to this treatment. Several reasons have been suggested, including patient selection and suboptimal left ventricle (LV) lead placement. The current guidelines³ suggest that the LV lead is to be positioned at the lateral or posterolateral branch of the coronary sinus (CS).

As a more individualized approach, some authors^{4,5} have suggested that LV electrical activation patterns could determine optimal LV lead placement site during CRT implantation. Additionally, several other studies^{6–8} have proposed LV mechanical activation patterns as a surrogate for LV electrical activation patterns. In concordance with these findings, research papers^{9–11} have reported that there are individual variations of the optimal pacing site, and that resynchronization may be improved if the LV lead is placed at the site of the latest mechanical activation and away from the myocardial scar.

CRT implantation is performed under x-ray guidance. X-ray provides an excellent visualization of catheters and pacing leads, but fails to provide detailed functional and morphological information. Recent examples¹² have demonstrated that fusing

other modalities with x-ray fluoroscopy can be a useful tool for the CRT implantation procedure. Our approach combines ultrasound (U/S) parametric imaging, three-dimensional (3-D) cardiac geometry, and coronary venogram to generate a roadmap for lead implantation planning and guidance. Measurements of myocardial strain, obtained by speckle-tracking echocardiography, represent the magnitude and timing of myocardial deformation. Strain imaging provides information about delayed activation and may also reveal myocardial scar.

In this paper, we present a prototype system for CRT guidance that combines LV functional information from U/S with live x-ray fluoroscopy into a single multimodal image. The system supports targeted LV lead placement guided by ultrasound parametric imaging. In addition, we present a method to generate a mean cardiac anatomical model (LV and its corresponding RV). The mean model may be used in cases when a patient-specific model is not available. The accuracy of using a mean model as a surrogate for a patient-specific model has been assessed only in silico.

2 Methods

A system for echo-guided CRT LV lead placement was designed to support the following workflow steps shown in Fig. 1: pre-operative U/S imaging, preoperative LV function parameters extraction, preoperative color-coded parametric map construction, 3-D cardiac model to x-ray fluoroscopy registration,

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Fig. 1 Cardiac resynchronization therapy (CRT) left ventricle (LV) lead placement guidance workflow.

coronary venogram imaging, projecting color-coded LV anatomical model over live x-ray fluoroscopy, and comparing the heart's spatial and temporal activation patterns against coronary veins' viability. The resulting fusion of multimodal image information provides an intuitive combination of relevant information that can be used to assist interventionists in finding optimal LV lead placement sites.

2.1 Left Ventricular Echocardiographic Parametric Maps

Parametric mechanical activation maps can be computed using images from either three apical views acquired with a two-dimensional (2-D) probe or a real-time triplane (RT3P) acquisition. We used RT3P (see Fig. 2), where apical echo views were simultaneously acquired in three planes using GE Vivid E9 (GE Vingmed Ultrasound, Horten, Norway) and 4V probe. The view planes intersect each other at the LV long-axis (LAX), and are separated by 60 deg. Echo operators were asked to align one plane with the direction of the left ventricle outflow tract (LVOT). RT3P strain analysis of the LV midwall was done using the EchoPAC (GE Vingmed Ultrasound, Horten, Norway) workstation.

Strain analysis involves the tracking of natural acoustic tags (speckles) within myocardium over the cardiac cycle. Dots along the mid myocardial wall (schematically marked as blue and red vertices) and the change of their positions are used to visualize underlying speckle motion in Fig. 3(a). The spatial and temporal speckle information were used to individually compute longitudinal strain¹³ values along the contour of each RT3P view. The fact that all slices share a common point in the LV apex, are aligned along a common LAX, and are 60 deg

apart was used to create a texture map of the strain data. This texture map [Fig. 3(b)] represents a cylindrical coordinate system (aligned with LAX) with the base on top and the apex at the bottom. The texture map can be applied to any LV geometry with known LAX and LVOT.

The variation of the longitudinal strain during cardiac cycle can be used to detect the time point of maximal segment shortening. In our study, time from R-wave peak to max segment shortening (time-to-peak-strain) was used as the marker for latest mechanical activation. The segments without sufficient contractility (max amplitude of contraction lower than 4.5%, as suggested in Ref. 14) were marked as potentially ischemic.

Tri-plane U/S derived data were spatially interpolated to fit a rectangular grid structure (the texture map). Figure 3(b) shows a color-coded parametric map that maps the time-to-peak-strain values to a LV anatomical model. A colormap varying from blue (low values), over green, and yellow (medium values) to red (high values) was used in the mapping process. Ischemic regions were marked with gray color. The areas with red color (high time-to-peak-strain) can be considered as candidates for LV lead placement.

2.2 Mean Cardiac Anatomical Model

A 3-D anatomical model was used to perform both the manual registration and the echo parametric map visualization in the CRT workflow (Fig. 1). CT or MRI datasets could be used to define a patient-specific anatomical model. However, in common clinical practice, patients selected for CRT are not evaluated with a CT or MRI exam. For this reason, we developed a mean cardiac anatomical model as a substitute for a patient-specific model. Individual mean surfaces for LV epicardium, LV endocardium, and RV endocardium were generated.

The mean anatomical models were created from a database containing 33 anonymized MR scans of HF patients; 11 acquired at the Oslo University Hospital and 22 from the Sunnybrook¹⁵ Cardiac MR Database. No aberrant anatomies were reported for the observed population. The volumetric images were manually segmented using the ITK-SNAP¹⁶ application and the resulting meshes were exported. Only the frames acquired during cardiac diastole were selected for segmentation. For each patient, segmentations of LV epicardium, LV endocardium, and RV endocardium were performed. Landmark positions for LV and RV apices, centers of mitral and tricuspid valves, LVOT, and RVOT directions were estimated from observed datasets.

Each input model was first normalized. The LV LAX length was used as a normalization factor for both surfaces (LV and its corresponding RV). The LAX has a clear anatomical definition and can easily be quantified from a standard echo exam. Furthermore, all models were coregistered in a common coordinate frame. A set of LV derived anatomical pseudo-landmarks

Fig. 2 An example of tri-plane acquisition.

Fig. 3 Randomly selected patient: (a) LV and coronary vein (CV) meshes, (b) LV with CV centerline, (c) centerline projected onto LV.

were used to spatially align the input models and ensure their correct orientation. LV derived alignment transformation was also applied to its corresponding RV. It was assumed that the surfaces, LV and its corresponding RV, form a coupled system. The anatomical pseudolandmarks were defined to be located at the corners of the segments described by the 17-segment American Heart Association (AHA) model. The LV models were divided into three vertical levels (basal, mid, and apical) perpendicular to their corresponding LAX. It was assumed that the LVOT centerline (together with LAX) defines a plane that halves LV vertically along the antero-septal–posterior direction. The LVOT centerline was used as the reference direction to determine circumferential start and end points for each segment. Segments make either 60 deg (base and mid) or 90 deg (apical) sectors.

To compute an average anatomical model, we defined an implicit representation based on a signed distance field (SDF) for each model (separately for LV and its corresponding RV) in the dataset. A segmented model, presenting a closed boundary (either $\Omega_{LV_{ps}}$ or $\Omega_{RV_{ps}}$), was described as a set of vertices and faces. The 3-D discrete SDF was represented as a uniform voxel grid. For a given voxel with position $\vec{v} \in \mathbb{R}^3$, the signed distance value is defined with Eq. (1). More details on the SDF computation mechanics for triangular meshes can be found in the relevant literature.¹⁷ The SDF representations of all models were averaged and the zero distance isosurface (mean model) was extracted using the marching cubes¹⁸ algorithm. The resulting normalized mean anatomical model was up-scaled. The average value ($\bar{S}$) of normalization scales for all input models was computed. The inverse value of $\bar{S}$ was used as the up-scale factor for both the $\bar{LV}$ and the $\bar{RV}$ surfaces.

$$f(\vec{v}) = \begin{cases} -d(\vec{v}, \Omega) & \text{if } \vec{v} \text{ inside } \Omega \\ d(\vec{v}, \Omega) & \text{if } \vec{v} \text{ outside } \Omega \\ 0 & \text{if } \vec{v} \text{ on } \Omega \end{cases} \quad (1)$$

where $d(\vec{v}, \Omega) = \inf_{\vec{p} \in \Omega} \|\vec{v} - \vec{p}\|$.

2.3 Left Ventricular Shape Variability

The segmented cardiac models exhibited considerable shape variability. To capture this variability, the models were divided into two groups. The k -means clustering¹⁹ algorithm was applied with the LV sphericity index (SI) as a discriminative feature. The LV end-diastolic SI was defined as the LV volume (V_{lv}) divided by the volume of sphere whose diameter is equal to the length of the LV long axis (L_{lax}), as shown in Eq. (2):

$$SI = \frac{V_{lv}}{\frac{4}{3}\pi \left(\frac{L_{lax}}{2}\right)^3}. \quad (2)$$

2.4 Average Left Ventricular Anatomical Model Accuracy Assessment

We used the leave-one-out cross-validation technique to assess the accuracy of using an average LV model ($\bar{LV}$ for shorthand) as a substitute for a patient-specific model (LV_{ps} for shorthand). One model was left-out as test data and the other models from the same cluster were used to compute the $\bar{LV}$ (as described in Sec. 2.2). To determine test-to-mean shape distances, the $\bar{LV}$

Fig. 4 Randomly selected patient: (a) LV and CV meshes, (b) LV with CV centerline, (c) centerline projected onto LV.

Fig. 5 Example of CV viability labeled images for one dataset: (a) CV_{ps} -to- LV_{ps} mapping, (b) CV_{ps} -to- $\bar{LV}$ mapping.

and the test LV models were coregistered using the iterative closest point (ICP)²⁰ algorithm. The test meshes' SDF values were then sampled at the $\bar{LV}$ vertices. This way we measured the signed Euclidean distance from the $\bar{LV}$ vertices to the test mesh surface. The process was repeated for each LV surface.

Furthermore, we estimated the accuracy of the $\bar{LV}$ from a clinical perspective related to coronary branch selection. For this purpose, we used a set of 15 HF patients from the Lugano²¹ study. The volumetric images were acquired by CT examination. The Lugano²¹ dataset was provided with segmentations for both LV and coronary veins (CVs). An example is shown in Fig. 4(a). The Lugano²¹ segmentations were not used in the mean cardiac model computations.

A rectangular grid was used as a mediator to map CV viability onto a LV surface. For practical reasons and to appropriately balance the grid cell size (big enough to average over a sufficient number of speckles) against the size of 17-AHA segments, a grid size of 15×24 was considered as an adequate choice for our study. Each LV mesh (from Lugano²¹ dataset) was mapped to the rectangular grid. CV centerline points [see Fig. 4(b)] were computed through a process of skeletonization. The CV centerline vertices were mapped [see Fig. 4(c)] onto the same grid that was used for the corresponding LV_{ps} . The grid cells that contained CV centerlines were labeled as shown in Fig. 5(a). CV_{ps} -to- LV_{ps} mapping images were computed for all members of the Lugano²¹ dataset.

Furthermore, for each member of the Lugano²¹ dataset, the SI was calculated and a corresponding $\bar{LV}$ selected. The normalized $\bar{LV}$ was scaled to match the LAX length of the LV_{ps} . The ICP²⁰ method was used to perform 3D-3D $\bar{LV}$ to LV_{ps} registration. The patient-specific CV centerlines were projected onto the rectangular grid bound to $\bar{LV}$. The result was a CV_{ps} -to- $\bar{LV}$ mapping image, see Fig. 5(b). The process was performed for all Lugano²¹ patients generating 15 image pairs.

Each cell was labeled with a tag that identified the closest CV branch. The labeling process was performed for all grid cells in

both mappings (CV_{ps} -to- LV_{ps} and CV_{ps} -to- $\bar{LV}$). The probability that the same CV branch would be selected when the $\bar{LV}$ was used instead of LV_{ps} was defined as the ratio of identical tags to the total number of grid cells.

2.5 Image Fusion

The fusion system was developed as an extension to the GE EPVision (GE Healthcare, Buc, France) guidance system. The EPVision dynamically fuses 2-D x-ray images with 3-D cardiac models [Fig. 6(a)] and supports localization and positioning of guidewires and ablation catheters during electrophysiology procedures. The EPVision system was augmented with the capability to load a color-coded LV anatomical model, see Fig. 6(c).

Manual registration was performed using tools to translate the position of the 3-D model in reference to the x-ray acquisition system. The registration is rigid. The 3D-2D registration workflow assumes x-ray acquisition in two different angulations separated by at least 30 deg. The registration is to be manually adjusted in each of the views. In the case of biventricular pacing, it is common to have the RV lead positioned near the RV apex. The tip of the RV lead can be used as a fiducial marker to estimate the position of the RV apex. The $\bar{RV}$ model (together with its corresponding $\bar{LV}$) can then be translated to match the estimated apex location. Furthermore, during the CRT implantation procedure, angiograms of the CVs are performed. The CVs are characterized by their epicardial course that represents the outer boundaries of the ventricles. Therefore, image fusion of the mean anatomical model (both the $\bar{LV}$ and the $\bar{RV}$) needs to be restrained by the outline of the CVs [Fig. 6(b)] independently of whether these (or similar coronary anatomy) are actually present in the mean model. Furthermore, the main CV transverses the base of the left ventricle and can be used to provide an estimation of the atrio-ventricular plane position (and its direction) to further support the process of manual registration,

Fig. 6 (a) Three-dimensional (3-D) anatomical model to x-ray image overlay, (b) manual registration using venogram, (c) parametric ultrasound (U/S) map applied to a LV model.

Fig. 7 Normalized $\overline{LV}_{epi}$ and $\overline{LV}_{endo}$ meshes for (a) $SI_{lo} = 0.49$, and (b) $SI_{hi} = 0.81$.

Fig. 8 Normalized cardiac meshes and their initial orientation in respect to head-first-supine (HFS) (a) $SI_{lo} = 0.49$, and (b) $SI_{hi} = 0.81$.

Fig. 6(b). Once manually registered, the registration can be automatically maintained throughout the procedure, as long as the patient does not move.

Furthermore, whenever a patient-specific cardiac anatomy is not available, a mean cardiac model (as detailed in this paper) can be used as a substitute. The patient-specific LV SI value can be calculated to determine which one, from two available mean models, is to be used. The initial orientation of the mean cardiac model, with respect to the head-first-supine (HFS) frame, was extracted as a mean orientation of the observed population. The interventionist can further personalize the selected mean model by using a scale derived from a patient's echo exam (e.g., to match the patient's LV LAX length or LV volume).

3 Results

As described in Sec. 2.3, the segmented patient-specific models were clustered into two groups based on their LV SI. The first cluster consisted of 17 models with the center at $SI_{lo} = 0.49$, while the second cluster consisted of 16 models with the center at $SI_{hi} = 0.81$. The corresponding mean LV models are shown in Fig. 7. Complete meshes ($\overline{LV}_{epi}$, $\overline{LV}_{endo}$, and RV-endo-cardial surface), and their orientation relative to the HFS patient coordinate system, are shown in Fig. 8.

The accuracy assessment of using an $\overline{LV}$ model as a substitute for the LV_{ps} model was established using two types of metrics, SDF and CV selection probability metrics. Results for the SDF metric can be visualized using the mean cardiac surfaces. An example for the case of the $\overline{LV}$ is shown in Fig. 9. Overall signed distances errors, for both clusters and their corresponding mean models, are summarized in Table 1. Statistical values are expressed as mean $\pm$ SD mm. There was no significant discrepancy in distance error values between the clusters.

Coronary veins CV-to-LV labeled maps were used to measure how often the same CV would be selected for LV lead placement when a cell with the same grid coordinates was consulted in both CV_{ps} -to- $\overline{LV}$ and CV_{ps} -to- LV_{ps} . The results for the observed population of 15 CRT candidates are presented in Table 2. The results show that when using the $\overline{LV}$ instead of a patient-specific model, the same CV branch would have been selected, on average, with a correspondence of 95% of the cases.

4 Discussion

In this paper, we have presented a system for guidance of LV lead placement in CRT. The system provides a means to covisualize U/S derived parametric maps (computed as a preoperative step) in the context of intraoperative x-ray fluoroscopy. This fusion was designed to allow electrophysiologists to visually integrate information about LV mechanical activation patterns, CVs accessibility, and myocardium tissue viability when selecting an optimal LV lead placement spot. Hence, the system has the potential to become a tool to perform echo-guided LV lead placement (as proposed in studies^{9,10}) and to test both alternative parameter selections and their cutoff values. The system can also be adapted for other clinical applications where parametric U/S imaging and live x-ray fluoroscopy need to be combined (e.g., coronary arteries disease diagnostic and treatment).

To alleviate the need for a patient-specific anatomical model, we developed a method to compute an average anatomical

Fig. 9 Signed distance field (SDF) distance error visualization, for a randomly selected patient, in case of (a) $\overline{LV}_{endo}$, and (b) $\overline{LV}_{epi}$.

Table 1 $\overline{LV}_{epi}$ and $\overline{LV}_{endo}$ signed distance errors.

	$SI_{lo} = 0.49$	$SI_{hi} = 0.81$
Number of patients	17	16
$\overline{LV}_{epi}$ distance error (mm)	-0.3 ± 4.5	-0.4 ± 4.7
$\overline{LV}_{endo}$ distance error (mm)	-0.2 ± 4.4	-0.4 ± 4.5

model. In fact, two mean cardiac anatomical models were generated to compensate for variable degrees of dilatation in the observed population. The SI was used to divide the LV_{ps} (and its corresponding RV_{ps}) models into two groups. Mean models for LV epicardium, LV endocardium, and RV endocardium were computed for each group. The LV epicardial surface contains the CVs (vessels targeted for LV implantation) and is thus essential for both the registration and the data visualization. On the other hand, the border of the LV endocardium is used to detect and quantify some important LV functional and geometrical properties (apex, LAX length, SI, mass, volume, ejection fraction, and so on). In addition, the 17-segment AHA model is often used to present various LV functional parameters. For this reason, the mean model generation method uses an array of anatomical pseudolandmarks (as described in Sec. 2.2) to closely capture the shape and the orientation of the LV segments.

The mean model accuracy and usability were assessed in two ways. The SDF metric provided a general means to measure overall distance error between the $\overline{LV}$ and the LV_{ps} models. However, the intrinsic rotational symmetry of the LV shape could lead to a case where the distance errors values are acceptable, while the $\overline{LV}$ (compared to the LV_{ps} orientation) is incorrectly rotated. If the model is incorrectly rotated this could lead to selecting the wrong CV for LV lead placement. Thus, only in silico have we estimated the probability of selecting the appropriate CV branch when the $\overline{LV}$ was used instead of the LV_{ps} model. As described in Sec. 2.4, CVs were projected onto the mean and patient-specific models to produce the CV-to-LV labeled mappings. The mappings were analyzed to estimate the probability that the same branches would be selected. The method was applied to a group of 15 patients (all CRT candidates and no aberrant anatomies reported). The results (reported in Table 2) showed that the same CV branch would be selected, on average, with a correspondence of 95% of the cases when the $\overline{LV}$ model was used instead of the patient-specific models. The results were considered clinically acceptable. The presented method assumes that the background methods, ultrasound imaging, LV segmentation, strain analysis, and estimation of scar regions, are accurate. We have not studied the effect of any inaccuracies, but clinical relevance has already been established by many studies.^{22–28}

Table 2 Selecting same coronary vein (CV) branches when $\overline{LV}$ used instead of LV_{ps} models.

	CV selection match probability
mean $\pm$ SD (%)	95.3 ± 2.9
MIN (%)	88.0
MAX (%)	99.0

The presence of aberrant anatomies should be a contraindication for the use of the average cardiac model. In such cases, a patient-specific model (extracted from suitable volumetric data) should be used instead of the mean model.

The validation method was performed in silico and did not account for errors introduced by the manual registration in the process of image fusion. In our study, the 3D-3D registration by the ICP²⁰ algorithm was used in place of the manual registration step. This was done to align the 3-D models in a reproducible manner. The ICP²⁰ related registration error was included in the overall validation. On the other hand, the registration in the clinical environment assumes that the CVs are to be visualized by contrast injection under fluoroscopy and observed from multiple (at least two) angulations. Multiple fluoroscopy views are useful to obtain better spatial understanding and optimize the registration. Section 2.5 describes in some detail how the coronary venogram and the presence of other landmarks (catheters, RV apex, and so on) can be utilized at this point. From our experience, achieving a clinically relevant registration is possible within the time frame of 1 to 2 min. Some studies^{29,30} describe a similar registration approach for the ablation procedures where the Innova EPVision platform was used to secure 3-D left atrium surface to 2-D x-ray image registration and overlay.

The LV lead placement is often limited by the CVs anatomy. Therefore, small rotational errors in registering the average model may not directly impact the selection of the wrong vein. In the future, epicardial or endocardial LV lead placement could increase the freedom to target a specific site, and hence increase the demand for accuracy.

As a modality to guide the LV lead placement, studies^{9,10} used 2-D radial strain analysis of the mid LV short-axis images. Reference 31 reported that longitudinal strain analysis has lower intra- and interobserver variability and higher reproducibility when compared to radial strain analysis. For this reason, we used longitudinal strain to derive parametric maps. However, it is not our intent to propose specific parameters, but rather to provide the means for physicians to use and test various parameters that can be derived from U/S imaging. Moreover, our platform is able to analyze 4-D echo acquisitions in order to compute strain-related parameters.

The presented echo-guided CRT system allows for direct and intuitive combination of relevant information into a single multimodal image that may assist electrophysiologists to find optimal LV lead placement sites and improve outcomes of CRT implantation procedures. The accuracy of using the mean anatomical model was considered clinically acceptable. However, the findings need to be confirmed by clinical studies.

5 Conclusion

In this paper, we have presented a system for echo-guided LV lead placement in CRT where LV deformation imaging is combined with live x-ray fluoroscopy into a single multimodal image. Ultrasound parametric images, representing the heart's spatial and temporal activation patterns, are mapped onto a 3-D LV model.

To alleviate the need for a patient-specific 3-D model of the heart, we presented a method to compute an average cardiac anatomical model which includes both the LV and RV geometries. The results show acceptable mean surface distance errors between the average model and the patient-specific models.

The application accuracy related to selecting the CV branch closest to the latest activating region when using an average LV model was found to be comparable to using a patient-specific model.

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