3D Fusion of LV Venous Anatomy on Fluoroscopy Venograms With Epicardial Surface on SPECT Myocardial Perfusion Images for Guiding CRT LV Lead Placement

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ABSTRACT

OBJECTIVES The aim of this study was to develop a 3-dimensional (3D) fusion tool kit to integrate left ventricular (LV) venous anatomy on fluoroscopy venograms with LV epicardial surface on single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) for guiding cardiac resynchronization therapy (CRT) LV lead placement.

BACKGROUND LV lead position is important for CRT response. For LV lead placement into viable regions with late activation, it is important to visualize both LV venous anatomy and myocardium.

METHODS Major LV veins were manually identified on fluoroscopic venograms and automatically reconstructed into a 3D anatomy. 3D LV epicardial surface was extracted from SPECT MPI. SPECT-vein fusion that consisted of geometric alignment, landmark-based registration, and vessel-surface overlay was developed to fuse the 3D venous anatomy with the epicardial surface. The accuracy of this tool was evaluated using computed tomography (CT) venograms. LV epicardial surfaces and veins were manually identified on the CT images and registered with the SPECT image by an independent operator. The locations of the fluoroscopic and CT veins on the SPECT epicardial surfaces were compared using absolute distances on SPECT short-axis slice and the 17-segment model.

RESULTS Ten CRT patients were enrolled. The distance between the corresponding fluoroscopic and CT veins on the short-axis epicardial surfaces was 4.6 ± 3.6 mm (range 0 to 16.9 mm). The presence of the corresponding fluoroscopic and CT veins in the 17-segment model agreed well with a kappa value of 0.87 (95% confidence interval: 0.82 to 0.93). The tool kit was used to guide LV lead placement in a catheter laboratory and showed clinical feasibility and benefit to the patient.

CONCLUSIONS A tool kit has been developed to reconstruct 3D LV venous anatomy from dual-view fluoroscopic venograms and to fuse it with LV epicardial surface on SPECT MPI. It is technically accurate for guiding LV lead placement by the 17-segment model and is feasible for clinical use in the catheterization laboratory. (J Am Coll Cardiol Img 2014;:–:–) © 2014 by the American College of Cardiology Foundation.

Left ventricular (LV) lead location is an essential factor for patient response to cardiac resynchronization therapy (CRT) (1). It is important that LV leads are placed away from scars and at or near the site of the latest activation (1,2). Friehling et al. (3) used single-photon emission computed...
tomography (SPECT) myocardial perfusion imaging (MPI) to identify the optimal LV lead positions. In that study, a concordant LV lead position was defined as the LV lead placed in the segment with myocardial viability and with or adjacent to the latest mechanical activation. That study showed that 96% of the patients, who had baseline mechanical dysynchrony, acceptable scar burden (<40%), and a concordant LV lead position, had favorable acute CRT response and long-term outcome (3). Other imaging modalities, such as cardiac magnetic resonance (CMR) (4) and echocardiography (5,6), were also used to attempt optimization of LV lead positions for potential improvement in CRT response. All of the mentioned imaging studies identified the optimal LV lead position on the myocardial wall, which is not visualized on x-ray fluoroscopy venograms during implantation. The LV lead positions recommended on the myocardial wall may not contain any suitable venous branches for LV lead placement. Furthermore, implanters may not accurately correspond the venous anatomy with the myocardial wall segmentation. Such inaccurate correspondence may result in suboptimal or inappropriate LV lead positions because changes of LV lead position by approximately 20 mm could impact CRT response (7). The TARGET (Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy) trial reported that LV leads were not optimally placed in 37% of the patients in the guided group, even if the implanters knew the target regions given by echocardiography before implantation (6). Consequently, the CRT response rate in the guided group was 70%, marginally better than that found in current practice. Therefore, visualization of LV myocardial wall and recommended LV lead positions by myocardial imaging techniques during implantation is critical for image-guided LV lead placement.

The objectives of this study were to develop a 3-dimensional (3D) fusion tool kit to integrate LV venous anatomy on fluoroscopy venograms with LV epicardial surface on SPECT MPI for image-guided LV lead placement and to evaluate its technical accuracy and clinical feasibility.

METHODS

PATIENT DATA. This study included 10 patients who underwent CRT because of standard indications. These patients had SPECT MPI before CRT, fluoroscopic venography during CRT, and computed tomography (CT) venography after CRT. The baseline characteristics of these patients are listed in Table 1.

The pre-CRT SPECT scan was performed approximately 30 min after injection of 20 to 30 mCi of Tc-99m sestamibi. SPECT images were acquired on a dual-headed camera (CardioMD, Philips Medical Systems, Milpitas, California) using a standard resting protocol. The acquisition parameters were 20% energy window around 140 KeV, 180° orbit, 32 steps with 25 s per step, 8-bin gating, and 64 projections per gate. The pixel size of images was 6.4 × 6.4 × 6.4 mm³. All patients underwent standard CRT implantation. During CRT implantation, retrograde fluoroscopy venograms, with in-plane pixel size of 0.3 × 0.3 mm² were obtained by placing a venogram balloon catheter in the coronary sinus. Dual-view fluoroscopic venograms were acquired from the left anterior oblique (LAO) 45° and anteroposterior (AP) orientations.

Contrast-enhanced CT venograms were acquired using a 64-slice CT scanner within 1 week after the CRT procedure. A standard protocol of CT angiography was modified to image the venous system. The imaging time was delayed by an additional 8 to 10 s beyond the arterial scan timing. The pixel size of the CT image was 0.38 × 0.38 × 0.38 mm³.

Figure 1 shows the major steps of this study. 3D LV venous anatomy was reconstructed from the fluoroscopic venograms. LV epicardial surface and landmarks were extracted from the SPECT images and then fused with the 3D LV venous anatomy. CT epicardial surface and venous anatomy were extracted from the CT venograms and registered to the SPECT epicardial surface. The locations of the fluoroscopic and CT veins on the SPECT epicardial surface were compared to evaluate the accuracy of the 3D fusion tool kit.

<table>
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<tr>
<th>Table 1 Pre-CRT Baseline Characteristics of Study Population (N = 10)</th>
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<td>Age, yrs</td>
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CRT = cardiac resynchronization therapy; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.
FLUOROSCOPIC IMAGE PROCESSING. Figure 2 demonstrates the processing steps to generate 3D LV venous anatomy from the dual-view fluoroscopic venograms.

The first step was to select an LAO frame and an AP frame from the dual-view fluoroscopic venograms, as shown in Figure 2A. The selected frames should contain clear venous anatomy and approximately correspond to the end-diastolic time point over the cardiac cycle.

A semiautomatic algorithm was used to extract the centerlines of the major veins. An interactive tool was developed for the operator to manually identify the major veins and pair them accordingly. The major

![Workflow Diagram of Fluoroscopic Image Processing](image)

**FIGURE 1** Major Steps of SPECT-Vein Fusion and Its Validation

Three-dimensional (3D) left ventricular (LV) venous anatomy was reconstructed from fluoroscopic venograms. LV epicardial surface and interventricular grooves were extracted from single-photon emission computed tomography (SPECT) images. The SPECT-vein fusion integrated 3D LV venous anatomy onto SPECT epicardial surface. CT epicardial surface and venous anatomy were extracted from the CT venograms and registered to the SPECT epicardial surface to evaluate the accuracy of the SPECT-vein fusion. MPI = myocardial perfusion imaging.
The veins include, but are not limited to, coronary sinus (CS), great cardiac vein (GCV), anterior vein (AV), left marginal vein (LMV), posterior vein (PV), and middle cardiac vein (MCV). The tracked venous branches should be clearly visible on the fluoroscopic images, as shown in Figure 2B.

The following step was to establish the topology of the venous anatomy. The tracked vessels were automatically connected to identify the bifurcations of the major veins. Because the LAO and AP fluoroscopic images were not acquired simultaneously, the isocenters of the 2 images could be different. Thus, a calibration algorithm on the basis of multiobjective optimization was used to calculate the locations of the isocenters using the system-provided geometric parameters and the identified bifurcations as shown in Figure 2C. The multiobjective function was the summation of 2 equally weighted components: the back-projection error (8) and the projection–back-projection mismatch error (9), illustrated as the red lines in Figure 3. A genetic algorithm, which simulates the natural selection process to find the globally optimal solution (9), was used to minimize the objective function to calibrate the isocenters.

The next step was to pair the points between the corresponding vessel segments on the LAO and AP images. For the segments between 2 bifurcations (green lines in Figure 2C), linear interpolation was used to pair the points within the segments. For the segments with an open ending (blue lines in Figure 2C), a dynamic programming technique was used to establish the point correspondence. The dynamic programming technique searched for all possible point correspondences and identified the optimal one, which minimized the total back-projection error (10).

Finally, 3D venous anatomy was reconstructed by backprojecting the matched point pairs with the calibrated fluoroscopic imaging parameters, as shown in Figure 2D.

SPECT IMAGE PROCESSING. Figure 4 shows the interface used to manually identify LV parameters and landmarks on the reconstructed SPECT image. Once the LV parameters and landmarks were identified, an automatic algorithm was used to construct the 3D epicardial surface. The algorithm searched in 3D for the maximal count circumferential profiles on the short-axis images (11,12), which represented the myocardial mass contour. Then a line profile of the myocardial wall along the myocardium’s radius of sampling was created for each sample of the myocardial mass contour. Gaussian functions were fit to the line profiles; 50% of the maximal counts of the fitted line profiles represented the epicardial surface (13).

3D FUSION OF SPECT EPICARDIAL SURFACE AND FLUOROSCOPIC VENOUS ANATOMY. The SPECT-vein fusion consisted of 3 steps: geometric alignment, landmark-based registration, and vessel-surface overlay. In geometric alignment, the geometric parameters in the images’ DICOM headers,
such as rotation centers and angles, and pixel sizes were used to align the 3D LV venous anatomy and SPECT epicardial surface into the same short-axis view. Then landmark-based registration was applied to improve alignment. It was a rigid registration on the basis of the landmarks illustrated in Figure 5A (14): 1) CS and GCV approximately course the atrioventricular groove, which was considered the same as the LV basal short-axis slice; and 2) AV and MCV approximately course the anterior and posterior interventricular grooves, respectively. The landmark-based registration method used a least-square-error algorithm, which minimized the total square error of the distances between the landmarks on the SPECT image and the corresponding vessels on the 3D venous anatomy. After the landmark-based registration, the vessels were overlaid onto the LV epicardial surface using a vessel-surface overlay algorithm (15), which wrapped each point of the vessel centerlines to the epicardial surface along the line profiles of the epicardial sampling, as shown in Figure 5B.

**EVALUATION OF THE SPECT-VEIN FUSION.** The accuracy of the SPECT-vein fusion was evaluated using the post-implant CT venograms. CT images were reconstructed by the standard filtered back-projection algorithm and then manually processed by experienced operators, who were blinded from the fluoroscopic images and the landmarks on the SPECT images. The manual processing included segmentation of the 3D epicardial surface from the CT images, identification of the major veins on the CT epicardial surface, and rigid registration of the CT and SPECT epicardial surfaces. The rigid transformation was also applied to the identified CT veins, so that they were closely aligned with the SPECT epicardial surface. The same vessel-surface overlay algorithm as in the SPECT-vein fusion was used to overlay the CT veins onto the SPECT epicardial surface, which then served as the reference standards to evaluate the accuracy of the 3D fusion tool kit.

Figure 6A shows the rendered CT LV volume with the LV veins in 1 patient example. The rendered CT LV volumetric image demonstrated the landmarks used in the SPECT-vein fusion: CS and GCV are well matched with the LV base, and AV and MCV are well matched with the interventricular grooves (black lines), respectively. Figure 6B shows that the fluoroscopic and CT veins are closely aligned on the SPECT epicardial surface and their distance is small compared with the segmental size of the American Heart Association (AHA) 17-segment model.

Two metrics were used to quantitatively assess the accuracy of the SPECT-vein fusion:

1. The distance-based mismatch error on the epicardial surface. It is the short-axis view point-to-point distance between the fluoroscopic and CT veins on the SPECT LV epicardial surface, as illustrated by
the red line in Figure 6B. If the fluoroscopic and CT vessel lengths were different, distances were only measured when both were present in the same short-axis slice. The thickness of the short-axis slice used in the evaluation was 1.33 mm, which is approximately the size of typical LV lead tips.

2. The segment-based kappa agreement rate using AHA 17-segment model. The 17 segments were rendered on the epicardial surface. Then the presence of the fluoroscopic and that of the CT veins in these segments were compared to calculate the kappa agreement rates for all veins and the individual veins, respectively.

**PROSPECTIVE CLINICAL STUDY.** A prospective clinical study with 1 patient, who had CRT implantation because of standard indications, was conducted in the Department of Cardiology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu, China. This patient (68-year-old man) had dilated cardiomyopathy with New York Heart Association functional class II, low LV ejection fraction (32%), and wide QRS duration (168 ms). This patient had pre-CRT SPECT MPI to identify the optimal LV lead position. The SPECT-vein fusion software was loaded on a laptop computer and used to guide LV lead placement during CRT in the catheterization
laboratory. Post-implant electrocardiograms (ECGs) were acquired at CRT device ON and OFF. The patient was followed up by echocardiography at approximately 1 month post-CRT.

RESULTS

ACCURACY OF THE SPECT-VEIN FUSION. Table 2 shows the distance-based mismatch errors between the fluoroscopic and CT veins. The distance-based mismatch errors between the fluoroscopic and CT veins were 4.3 ± 3.0 mm, 2.9 ± 2.9 mm, 3.1 ± 2.8 mm, and 7.3 ± 3.6 mm for AV, MCV, LMV, and PV, respectively. The overall distance-based mismatch error for the entire population was 4.6 ± 3.6 mm (minimum 0 mm; maximum 16.9 mm). The largest overall mismatch error for a single patient was 7.9 ± 3.1 mm (minimum 0.2 mm; maximum 13.1 mm).

Table 3 shows the segment-based mismatch errors between the fluoroscopic and CT veins on the SPECT epicardial surface. The kappa agreement rates were 0.88, 0.87, 0.91, and 0.84 for the AV, MCV, LMV and PV, respectively. The overall kappa agreement rate for all veins was 0.87 (95% confidence interval: 0.82 to 0.93). In all cases where the presence of the fluoroscopic and CT veins did not match in the same segments, they were located in the immediately adjacent segments.

Noteworthy, for the fusion accuracy of individual veins as shown in Tables 2 and 3, the fusion was least accurate for PV because: 1) AV and MCV were used as the landmarks, and so their fusion accuracy was higher; and 2) PV was usually longer in length and more distant from the landmarks than LMV. Nevertheless, it should not impact the clinical utility of the fusion tool kit. The longer the vessel, the closer its distal site is to the LV apex, which is suggested to be avoided for CRT LV lead placement (16).

PROCESSING TIME. All image processing ran on a personal computer with 3.40 GHz CPU, 8 GB memory, and Windows 7 operation system (Microsoft, Redmond, Washington). In fluoroscopy image processing, the reconstruction of 3D venous anatomy required
approximately 18 ± 8 s. In SPECT image processing, the construction of epicardial surface consumed 82 ± 20 s. The SPECT-vein fusion consumed 22 ± 10 s.

The interactive identification of the vein centerlines from fluoroscopic venograms was the time bottleneck because SPECT image processing can be done before implantation and the fusion step can be done automatically within 1 min. In this study, the time to interactively identify venous centerlines was approximately 5 min.

**PROSPECTIVE CLINICAL STUDY.** Figure 7 shows the prospective clinical study. Pre-implant SPECT was used to identify the optimal LV lead position, which was the mid anterior myocardial segment. As shown in Figure 7A, the middle segment of the anterior vein was close to the optimal segment, and therefore, it was targeted for LV lead placement. The post-implant fluoroscopy in Figure 7B shows that the LV lead was placed in the targeted position. The post-CRT ECG with the CRT device ON and OFF in Figure 7C showed that the QRS duration was significantly narrowed (from 168 to 140 ms) after the device was turned on.

It took approximately 6 min for the software to produce the 3D SPECT-vein fusion results. Most of the time was spent on the step to manually draw the LV veins on the fluoroscopic images.

This patient had been followed up with echocardiography at 1 month post-CRT. From baseline to the 1-month follow-up, his LV diastolic diameter decreased from 64 to 53 mm, and his LVEF increased from 32% to 57%. It clearly confirmed that the image-guided LV lead placement resulted in a superior response to CRT.

**DISCUSSION**

This is the first study to integrate 3D venous anatomy from fluoroscopic venograms with the SPECT epicardial surface for guiding CRT LV lead placement. The distance-based mismatch errors between the fluoroscopic and CT veins in the segments agreed well, with all kappa values greater than 0.80, as shown in Table 3. The clinical feasibility of the 3D fusion tool kit was confirmed by a prospective clinical study guiding LV lead placement during CRT in the catheter laboratory. In summary, this study showed that the 3D fusion tool kit was technically accurate and clinically effective to fuse fluoroscopic venous anatomy and SPECT epicardial surface for guiding CRT LV lead placement.

**EXISTING NAVIGATION STRATEGIES OF LV LEAD PLACEMENT.** The TARGET trial (6) used a 2-dimensional (2D) visual correspondence method, which aligned the venous anatomy from steep LAO fluoroscopic venograms with the short-axis parasternal echocardiographic view. As a result, two-thirds of the patients had LV leads placed in the recommended positions. The STARTER (Speckle Tracking Assisted Resynchronization Therapy for Electrode Region) trial (5) used a similar visual correspondence method: the anterior, lateral, and posterior segments assessed on the LAO fluoroscopy venograms were aligned with the corresponding segments on the echocardiographic images; in addition, the right anterior oblique venograms were used to assess the basal, middle, and apical segments. Consequently, the exact concordance between the recommended segments and LV lead positions was achieved in only 30% of the patients in the guided group, and the number increased to 85% of the

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<th>Table 3: Segment-Based Mismatch Errors Between the Fluoroscopic and CT Veins on the SPECT LV Epicardial Surface</th>
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<td>95% CI</td>
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CI = confidence interval; CT-N = total number of segments without CT veins; CT-Y = total number of segments with CT veins; Fluoro-N = total number of segments without fluoroscopic veins; Fluoro-Y = total number of segments with fluoroscopic veins; LV = left ventricle; other abbreviations as in Table 2.
patients when segments immediately adjacent to the recommended site were included. As the 2 trials showed, visual correspondence of the venous anatomy and myocardial segments was not accurate in many patients. Therefore, the registration of the 2 types of images is needed.

Ma et al. (17) used pre-procedural CMR imaging to assess venous anatomy, projected the 3D LV epicardial surface extracted from the CMR images onto the 2D intraoperative fluoroscopic venograms, and then manually registered them using multiple views of a catheter looped in the right atrium. A similar method based in cardiac CT is being validated in an ongoing clinical trial (18). All of these methods provide only 2D navigability and require anatomic imaging.

The methodology in this study unified LV venous anatomy onto the LV myocardial wall in 3D and thus allowed 3D navigation, such as translation, rotation, and scale, to conveniently identify the target venous branch and optimal site for LV lead placement. In addition, our tool kit used the landmarks identified on SPECT MPI for registration and did not require additional anatomic imaging. This is clinically important because it will reduce the radiation dosage and save operational costs and scanning time. In addition, the fusion technique is automatic; therefore, it has potentially less user variability than manual registration techniques.

CLINICAL APPLICABILITY. The availability and reliability of the landmarks is the most essential factor for the clinical applicability of the SPECT-vein fusion tool. Despite the large variations of LV venous anatomy in CRT patients, the anatomic correspondence used in the landmark-based registration of this tool constantly exists. In addition, the timing of fluoroscopic image acquisition may influence the visibility of the veins, especially the MCV, where the contrast agent enters later than other branches. Because the MCV was not considered for LV lead placement in the majority of patients, recordings of the fluoroscopic images were usually terminated when other veins were clearly visualized. Therefore, in 5 of 10 patients, only the upper portion of the MCV was clearly visible but not the entire branch. The fusion accuracy was slightly lower in these patients with short visible MCV than those with entire MCV (5.0 ± 3.3 mm vs. 4.3 ± 3.8 mm; kappa = 0.85 vs. 0.90), indicating that the more landmark points used in the landmark-based registration, the more accurate the fusion was.

The clinical applicability of the 3D fusion tool kit was confirmed in the prospective clinical study shown in Figure 7. During the procedure, the electrophysiologist frequently returned to our tool kit and referred to the results with 3D navigation. The tool kit took approximately 6 min to process the images and target the venous site for LV lead placement. It was
quite short compared with the time of the entire CRT procedure (approximately 2 h).

**STUDY LIMITATIONS.** The technical accuracy and clinical feasibility of the 3D fusion tool kit were tested in a relatively small sample size. A prospective validation in a larger population with a control or comparison group is needed to establish the clinical usefulness of this technique.

**CONCLUSIONS**

A tool kit has been developed to reconstruct 3D LV venous anatomy from dual-view fluoroscopic venograms and to fuse it with the LV epicardial surface on SPECT MPI. It is technically accurate for guiding LV lead placement by the AHA 17-segment model and is feasible for clinical use in the catheterization laboratory.

**REFERENCES**


**KEY WORDS** cardiac resynchronization therapy (CRT), heart failure (HF), image-guided implantation, SPECT