A n important clinical role of cardiac resynchronization therapy (CRT) in the treatment of systolic heart failure has emerged over the past decade. Clinical trials have consistently demonstrated improvements in quality of life (QOL), functional status, and exercise capacity among symptomatic patients with reduced left ventricular (LV) systolic function and significant intraventricular conduction delay; benefits that have translated into reduced heart failure hospitalizations, cardiac morbidity and mortality (MUSTIC SR, MIRACLE, CONTAK-CD, MIRACLE ICD CARE-HF).1–5

Clinical Perspective on p 1047

One dominant mechanism of benefit from CRT is reverse remodeling of the left ventricle, a manifestation that seems to evolve during the first 6 months of therapy and can have sustained effect.6 Unfortunately, not all patients experience this, with as much as 30% to 40% of patients being classified as nonresponders by remodeling criteria.7–9 Reasons for this failure to respond are multifactorial but include a lack of baseline mechanical dyssynchrony,10 suboptimal geographic placement of the LV lead,11–14 and the presence of transmural scar within the LV pacing region.15–17

Detailed studies evaluating characteristics of the LV pacing region, inclusive of mechanical delay and myocardial scar, have shown significant associations with CRT response rates.16–18 In particular, an inverse relationship has been noted between LV lead placement to regions of transmural scar and the occurrence of LV remodeling.16 Mounting evidence now
supports that a similar influence of transmural scar exists for the right ventricular (RV) pacing site, its presence also being associated with reduced rates of CRT response.\textsuperscript{20,21} The latter is of potential importance as its prevalence is significantly higher for RV lead targets than for LV targets.\textsuperscript{22}

In recognition of these findings, a new paradigm of image-guided CRT has recently been proposed, whereby imaging markers of myocardial health are used to recommend lead placement to preferred targets. To date, this concept has been evaluated for the delivery of LV leads to dysynchronous but viable (nonscarred) segments using the echocardiographic surrogate marker of radial strain.\textsuperscript{23} In the current study, we explored the clinical feasibility of performing dual (LV and RV) CRT lead navigation to optimal targets using an interactive 3-dimensional (3D) surface-rendered model, derived from routine cardiac magnetic resonance (CMR) imaging. Procedural success was determined by a blinded segmental scoring of LV and RV lead tip location from a postprocedural 3D cardiac-gated computed tomography (CT) with measures of LV remodeling assessed by serial transthoracic echocardiography.

**Methods**

**Study Population**

Thirty-two consecutive patients referred for CRT between May 2011 and February 2013 at the London Health Sciences Center met study eligibility and consented to study participation. Inclusion criteria were age ≥18 years, LV ejection fraction (EF) ≤35%, QRS duration ≥120 ms, New York Heart Association (NYHA) class ≥II, and maximal tolerated medical therapy for ≥6 weeks. Exclusion criteria were myocardial infarction or revascularization procedure ≥3 months, mal tolerated medical therapy for ≥6 weeks. Exclusion criteria were myocardial infarction or revascularization procedure ≤3 months, standard contraindications to MRI (MRI), a glomerular filtration rate ≤30 mL/min/1.73 m² or a preexisting pacemaker or implantable cardiac defibrillator system. Patients were classified according to cardiomyopathy etiology. Ischemic cardiomyopathy was defined as those with prior myocardial infarction (admission for chest pain with cardiac marker elevation and development of new Q waves on ECG) or an intracoronary angiogram with obstructive coronary artery disease (≥1 coronary artery with ≥70% stenosis). Patients not meeting these criteria were classified as having a dilated cardiomyopathy.

**Study Protocol**

All patients underwent a standardized study protocol inclusive of baseline clinical evaluation, late gadolinium enhancement (LGE) CMR with 3D model generation, preprocedural and serial postprocedural echocardiography, and a postprocedural cardiac-gated CT, the latter used to accurately establish final LV and RV lead tip location relative to respective target segments.

All clinical evaluations were performed by an experienced research nurse and included a 12-lead ECG, NYHA class determination, 6-minute walk test\textsuperscript{24} and a QOL assessment using the Minnesota Living With Heart Failure questionnaire.\textsuperscript{25} LGE-CMR and cardiac CT studies were blindly analyzed using a 16-segment cardiac model,\textsuperscript{26} with standardized anatomic markers (RV insertion site) used to provide a consistent segmental assignment. Model-prescribed target segments (based on CMR data), and final targeted segments (based on cardiac CT data) were recorded using the same AHA 16-segment bull’s-eye map. Detailed components of imaging procedures are provided below.

The study protocol was approved by Western University’s ethics review board, and all patients provided informed consent.

**LGE-CMR Protocol and Image Analysis**

LGE-CMR was performed using a 3.0-Tesla scanner (Trio or Verio, Siemens Medical Solutions, Germany) equipped with a 32-channel cardiac coil. Retrospectively gated, breath-held cine imaging was performed in serial short-axis planes from the atriocardiac annulus to apex in addition to 2-, 3-, and 4-chamber views. Typical pulse sequence parameters were as follows: slice thickness 6 mm, gap 2 mm, echo time 1.8 ms, flip angle 50, matrix 256x213, temporal resolution 30 to 35 ms, and iPAT = 2. Ten to 15 minutes after intravenous administration of 0.2 mmol/kg gadolinium chelate (Gadovist, Bayer Inc., Canada), LGE imaging was performed using a standard inversion-recovery gradient pulse sequence in matched slice orientations. The inversion time was manually adjusted to provide optimal nulling of the normal myocardium, as previously described.\textsuperscript{27} Typical pulse sequence parameters were as follows: slice thickness=6 mm, gap=2 mm, temporal resolution=800 ms, echo time=3.9 ms, flip angle=20°, matrix 256x205, iPAT = 2.

All CMR images were analyzed using commercially available visualization and analysis software (CVI42, Circle Cardiovascular Imaging, Calgary, Canada). Short-axis cine images were analyzed to obtain segmental measures of time to maximal wall thickening using semiautomated endocardial and epicardial contour tracking throughout the cardiac cycle (all phases). The time to maximal radial wall thickness was determined for each myocardial segment, as previously described.\textsuperscript{28}

A blinded investigator visually scored all myocardial segments for any myocardial scar, defined as unequivocal signal enhancement within the myocardium not because of image artifact. Quantitative assessment of myocardial scar was performed by trained core laboratory personnel using a signal threshold–based analysis and reported in volume percentage for each myocardial segment (segmental percentage scar), as well as for the whole LV (total percentage scar). A Signal Threshold versus Reference Myocardium approach was used, as previously described,\textsuperscript{29,30} where a signal threshold of ≥2SD above the mean signal of normal myocardium was used to define scar. Careful attention was paid to avoid tissue-blood and tissue-fat interfaces and to select only homogeneous regions of signal-nulled tissue within the reference tissue region.

**Three-Dimensional Navigation Model Generation**

Segmental values of percentage myocardial scar and time to maximal wall thickening were transferred to locally developed software designed to generate a color-coded, surface-rendered 3D cardiac model, as shown in Figure 1. A patient-averaged cardiac model (ie, atlas) was generated with segmentation of both the LV and the RV chambers; this model then divided into 16 American Heart Association (AHA) segments. Each candidate LV pacing target (4 basal and 4 mid) was presented using a red color scale and RV sites in a blue color scale. A range from white (not recommended) to 100% opacity (recommended) was used to represent rank. Predefined ranking was established based on prior published data.\textsuperscript{31} This algorithm ensured that: (1) the LV lead was directed to the segment with (i) lowest scar burden, (ii) greatest mechanical delay, and (iii) greatest geographic distance from the prescribed RV lead tip location; and (2) the RV lead tip was directed to the segment with lowest scar burden. The algorithm used an iterative mathematical formula starting with the RV lead assignment, and then sequentially removing the LV lead targets with lowest rank. Each 3D model was displayed to the implanting electrophysiologist throughout device implantation, with projections matched to procedural fluoroscopic views, as shown in Figures 1 and 2.

**Echocardiography Imaging Protocol and Image Analysis**

Standard 2D echocardiography was performed at baseline, 3 months, and 6 months using a 3.5-MHz transducer (SS-1, Philips, Bothell, WA) on commercially available equipment (iE33, Philips, Eindhoven, Netherlands). Digitally captured images were stored for off-line analysis using the Xcelera software suite version 3.1 (Philips, Eindhoven, Netherlands). All imaging was performed at end-expiration. The LV end-diastolic volume and LV end-systolic volume (ESV) were determined using the biplane method of discs method (modified Simpson technique)\textsuperscript{32} by an experienced, blinded echocardiographer.
CRT Device Implantation

CRT device systems were installed according to standard clinical practice with exception of the described lead implantation strategy. All patients received a left-sided device system with a subcutaneous generator pocket in the prepectoral fascia. After securing axillary or subclavian vein access, the right heart leads were implanted first. The active fixation right atrial lead was placed in a stable appendage or high lateral wall site that yielded adequate sensing and pacing capture. Both RV and LV leads were implanted with focused effort to match the final lead tip locations to prescribed geographic targets, as shown by the navigational model. This was accomplished by simultaneous visualization of fluoroscopic balloon occlusive coronary venography and 3D models in matched spatial orientation. The electrophysiologist was instructed to first place the RV lead in the target septal segment, if necessary using a separate active fixation lead (if stability or defibrillation efficacy was felt to be of concern). Of note, the study protocol provided choice to the implanting physician to deliver a pace defibrillation lead to nonapical targets or to deliver a separate pacing lead to the target. It was felt by the implanting physicians at the enrolling site that routine defibrillation testing would be required using the latter approach, which was not desired, and therefore a separate RV pace lead was delivered for all nonapical RV targets. For apical RV targets, the lead was fluoroscopically guided to the apex in the PA projection and confirmed by right anterior oblique 15° and left anterior oblique 30° to 40° views. For CRT defibrillator systems where the RV target site was nonapical, a separate RV implantable cardioverter-defibrillator lead was typically placed at the RV apex with a bipolar pace-sense lead introduced to the target location.

After cannulation of the coronary sinus and performance of occlusive venograms, a coronary vein branch that best approximated the target LV cardiac segment was identified. Venograms were obtained in PA, RAO 15°, and LAO 30° to 40° with approximately 10° of caudal angulation. A bipolar LV lead was advanced to the most stable location within this segment where LV stimulation parameters were considered clinically acceptable. If this was not achieved, the implantor was directed to the next ranked LV segment. Following this, the implantor was allowed to proceed to a non-navigated approach. The choice of LV lead and accessories used to deliver the lead was at the discretion of the implantor. Once all leads were anchored, the generator was connected and inserted in the pocket and the wound closed. Total procedural time (skin to skin) and fluoroscopy times were recorded.

Postimplant chest x-rays were obtained to confirm lead stability and exclude complications. Pre-discharge device programming was at the discretion of the responsible physician but, in general, sensed and paced AV delay were set to 110 and 150 ms, respectively, and RV-LV pacing timing was left at nominal values (~4 ms).

Cardiac CT Imaging Protocol and Image Analysis

Cardiac CT imaging was performed at the 1-month follow-up device interrogation visit using a 64-slice CT scanner (LightSpeed VCT, GE Medical Systems) using standard acquisition protocols. As part of an expanded study protocol (although not required for lead localization), contrast enhancement was used with 80 to 100 mL of iodinated contrast agent (Visipaque [iodixanol], Amersham Health, Princeton, NJ) administered. Typical imaging parameters were as follows: slice thickness 0.625 mm, tube voltage 120 kV, and tube current 550 mA, followed by a 40 mL saline flush. Image reconstruction was performed using retrospective ECG gating to obtain the optimal phase for lead visualization with overlapping 0.75-mm cross-sectional images reconstructed at 0.5 mm and image matrix of 512×512 pixels.

Segmental assignment of LV and RV lead tip location was performed by a blinded interpreter using 3D multiplanar reconstruction (OsiriX, version 3.7.1), as previously described. To minimize artifact related to the CRT lead system, we reconstructed images using a 2.5-mm slice thickness and displayed this data set using 3D multiplanar reconstruction, averaging signal of 4 consecutive slices (MIP thickness 10 mm). The tips of the LV and RV lead were separately localized on axial images and orthogonal short- and long-axis projections generated. A radial grid was manually overlaid on the short-axis

![Image](https://via.placeholder.com/150)
Primary Outcome: Procedural Success

Based on cardiac CT analysis, the RV lead was delivered to the target or immediately adjacent segment in 30 of 31 patients (97%). A nonapical RV pacing target was prescribed by the navigational model in 8 patients (26%), 7 having their RV lead delivered to a target or adjacent segment. LV leads were prescribed to typical locations (basal or mid posterolateral wall segment—AHA segments 5 and 11) in 10 patients (32%), an anterolateral wall segment (segments 6 and 12) in 12 patients (39%), and an anterior or inferior wall segment (segments 1, 4, 7, and 10) in 9 patients (29%). Model-prescribed LV lead targets were found to differ between those with typical left bundle branch block and those without. Among those with left bundle branch block, the optimal LV pacing site was typically prescribed as a posterolateral (43%) or anterolateral (39%) wall segment. In contrast, those without left bundle branch block pattern had atypical locations prescribed as follows: anterior wall (46%), anterolateral wall (27%), inferior wall (18%), and posterolateral wall (9%). Irrespective of prescription location, the LV lead was successfully navigated to the target or immediately adjacent segment.

Table 1. Non-MRI Baseline Patient Characteristics, Presented for the Total Population (n=31)

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>65±8</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>23 (72)</td>
</tr>
<tr>
<td>Ischemic etiology, n (%)</td>
<td>14 (44)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>16 (50)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>14 (44)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>9 (28)</td>
</tr>
<tr>
<td>Prior revascularization, n (%)</td>
<td>11 (34)</td>
</tr>
<tr>
<td>Baseline QOL score</td>
<td>50±24</td>
</tr>
<tr>
<td>Baseline NYHA, n (%)</td>
<td></td>
</tr>
<tr>
<td>Class II</td>
<td>13 (41)</td>
</tr>
<tr>
<td>Class III–IV</td>
<td>19 (59)</td>
</tr>
<tr>
<td>GFR, ml/min/1.73 m²</td>
<td>74±17</td>
</tr>
</tbody>
</table>

ECG parameters

<table>
<thead>
<tr>
<th>Heart rate, bpm</th>
<th>66±11</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS duration, ms</td>
<td>161±16</td>
</tr>
<tr>
<td>LBBB, n (%)</td>
<td>22 (69)</td>
</tr>
<tr>
<td>RBBB, n (%)</td>
<td>5 (16)</td>
</tr>
<tr>
<td>Nonspecific delay, n (%)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td>3 (9)</td>
</tr>
</tbody>
</table>

Medications

| ACE inhibitor or ARB, n (%) | 30 (97) |
| Spironolactone, n (%)      | 17 (55) |
| Beta-blocker, n (%)        | 30 (97) |
| Diuretic, n (%)            | 26 (84) |

Continuous variables expressed as mean±SD, categorical variables as total (%). ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; GFR, glomerular filtration rate; LBBB, left bundle branch block; NYHA, New York Heart Association; QOL, quality of life (Minnesota Living with Heart Failure); and RBBB, right bundle branch block.
Table 2. Baseline Cardiac MRI and Echocardiographic Imaging

<table>
<thead>
<tr>
<th>Cardiovascular MRI variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV indexed to BSA, mL/m²</td>
<td>141±36</td>
</tr>
<tr>
<td>LVEVS indexed to BSA, mL/m²</td>
<td>105±33</td>
</tr>
<tr>
<td>LVEF</td>
<td>26±8</td>
</tr>
<tr>
<td>LV mass indexed to BSA, g/m²</td>
<td>105±26</td>
</tr>
<tr>
<td>RVEDV indexed to BSA, mL/m²</td>
<td>66±18</td>
</tr>
<tr>
<td>RVESV indexed to BSA, mL/m²</td>
<td>35±17</td>
</tr>
<tr>
<td>RVEF</td>
<td>47±14</td>
</tr>
<tr>
<td>Total scar volume (≥5SD), g</td>
<td>26±25</td>
</tr>
<tr>
<td>Total percentage scar (≥5SD) (% LV mass)</td>
<td>13.7±14.7</td>
</tr>
</tbody>
</table>

Table 3. Comparison of Baseline and 6 mo Echocardiographic and Clinical Response Criteria for Study Population (n=31)

<table>
<thead>
<tr>
<th>Echocardiography</th>
<th>Baseline</th>
<th>6 mo</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV indexed to BSA</td>
<td>140.8±36.3</td>
<td>100±30</td>
<td>0.002</td>
</tr>
<tr>
<td>LVEVS indexed to BSA</td>
<td>105.2±32.8</td>
<td>71±27</td>
<td>0.013</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>25.9±7.8</td>
<td>31±8</td>
<td>0.040</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>Values</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-min hall walk, m</td>
<td>358±114</td>
<td>381±129</td>
</tr>
<tr>
<td>QOL score</td>
<td>49±23</td>
<td>34±26</td>
</tr>
</tbody>
</table>

Values expressed as mean±SD. BSA indicates body surface area; EDV, end-diastolic volume; ESV, end-systolic volume; EF, ejection fraction; LV, left ventricular; RV, right ventricular; SD, standard deviation; SPWD, septal to posterior wall delay; and V-V delay, interventricular delay.

the prescribed segment or its immediately adjacent segment in 30 of 31 patients (97%).

In one patient where the RV lead was scored as remote to the target, the lead had been placed directly adjacent to the prescribed segment (apical), however, was on the free wall. As this did not comply with our prespecified 16-segmental model, it was categorized as remote.

Secondary Outcomes: Procedural End Points

Patients received a mean of 3±1 leads during device implantation. In total, there were 8 nonapical RV lead positions prescribed. In 6 of these cases, an RV pace-sense lead was used in addition to the high voltage lead as it was considered sufficiently basal as to potentially compromise defibrillation. Two patients did not receive atrial leads because of chronic persistent atrial fibrillation.

Total mean procedural and fluoroscopy time was 154±43 and 27±15 minutes, respectively. One patient required a second procedure because of a drop in sensing on the RV lead, which was identified at the first follow-up device interrogation. This lead had been prescribed to a typical apical position and was successfully moved to an adjacent apical position. No other procedural complications were encountered throughout the study.

Secondary Outcomes: Clinical End Points

At 6-month follow-up, patients appreciated an overall improvement in LV volumes compared with baseline, both with respect to LV end-diastolic volume indexed to BSA (100±30 versus 141±36 mL/m², P=0.002) and LVEVS indexed to BSA (71±27 versus 105±33 mL/m², P=0.013; Table 3). Twenty-three patients (74%) net predefined echocardiographic remodeling criteria for standard response (LVEVS reduction ≥15%), whereas 18 patients (58%) met predefined criteria for super-response (LVEVS reduction ≥30%). Patients also showed a significant improvement in LVEF at 6 months versus baseline (31±8 versus 26±8%, P=0.04).

Significant benefit was found in secondary clinical end points at 6 months with both an improvement in mean 6-minute hall walk (358±114 versus 381±129 m, P=0.002) and the Minnesota Living with Heart Failure Quality of Life Score (49±23 versus 34±26, P=0.029; Table 3). Eighteen patients (58%) met the prespecified criteria for significant improvement in QOL score, 15 patients (48%) meeting criteria for the 6-minute hall walk.

Comparison With Historical Controls

While exploratory, we performed a post hoc evaluation of CRT response rates in the current cohort versus those in our previously published observational cohort study. The latter enrolled an identical referral population and evaluated outcomes following standard CRT (nonguided) implantation. This cohort was similar in age, LVEF, and all other relevant baseline characteristics. The current cohort showed higher 6-month response rates versus the historic cohort for both standard (≥15% LVESV reduction) and super-response (≥30% LVESV reduction) criteria with a relative increase of 6% (74% versus 70%) and 53% (58% versus 38%), respectively. Procedural times and device-related complications were similar; the historic cohort having a mean total procedure time of 139±36 min (P=0.99) and mean total fluoroscopy time of 25±14 min (P=0.78) compared with the current cohort. Early device-related complications were similar at 8% (2 lead dislodgements, 2 infections, 1 perforation leading to tamponade) compared with 3% in the current cohort.

Discussion

This study is the first to explore the clinical feasibility of dual CRT lead navigation to optimal myocardial targets in patients with heart failure. We used a 3D navigational model, matched to intraprocedural fluoroscopic views as a practical and intuitive approach to procedural guidance, one that resulted in high procedural success, acceptable procedural times, and low procedural complications.

A paradigm of image-guided CRT seems justified on the basis of a strong inverse association between pacing site scar burden and response to CRT. This association has been identified for both LV and RV lead pacing regions, while
mechanisms of response interference may be distinct, a compelling argument for scar avoidance at both sites exists. Elevated interest in LV lead navigation suggests broader recognition of scar as an important determinant of CRT response; however, studies to date remain focused on the isolated modification of the LV lead position. While important sentinel studies, an incremental consideration of RV pacing site characteristics and optimal LV lead placement relative to this RV pacing site may provide the most ideal solution to image-guided CRT.

Recently published studies support that a greater response to CRT may be achieved through the targeted delivery of LV leads to dysynchronous segments free of transmural scar. In the TARGET trial, echocardiographic speckle tracking with radial strain estimation (used as a surrogate marker for regional scar) was used to guide LV lead placement and yielded a 15% improvement in CRT response by standard LV remodeling criteria. Similarly, a feasibility study by Bakos et al recently used a combination of echocardiographic speckle tracking and CMR to guide placement of the LV lead to prescribed targets. Similar to the current study, procedural success was defined as lead delivery to the prescribed or immediately adjacent segment and was achieved in 95% of patients. Neither of these studies evaluated or prescribed targets for the RV lead. The concept of using an intraprocedural model to guide lead delivery was recently described by Shetty et al. CMR was similarly exploited to identify optimal segmental targets for the LV lead based on both scar and mechanical dysynchrony measures. Their approach was to incorporate this model into a vendor-based architecture to provide image fusion with live fluoroscopy. Using this sophisticated approach, they identified procedural success of 75% with respect to LV lead delivery to the prescribed segment, noting a higher rate of echocardiographic response among such patients.

Compared with prior studies, our approach used a spatially matched 3D navigational model presented adjacent to intraprocedural fluoroscopy and provided for navigation of both LV and RV pacing leads. The use of adjacent visualization rather than image fusion provides both advantages and potential disadvantages. Two clear advantages are the elimination of dependence on vendor-based software integration and the removal of inherent technical challenges associated with image fusion and motion correction. Although removal of the latter may be perceived as a disadvantage, image fusion of organs with both intrinsic (cardiac) and extrinsic (respiratory) motion poses substantial generic and patient-specific challenges. The introduction of a complex architecture to manage these substantive barriers may not be necessary in the context of a desired clinical end point; in this case, the delivery of a lead to a segmentally defined region. In this study, the adjacent visualization approach appeared to provide sufficient spatial information to achieve this goal while maintaining an easily translatable architecture.

The concept of navigating both the RV lead and the LV lead to nonscarred myocardial segments is novel and is based on the consistent recognition that RV pacing site scar is similarly associated with a reduced response to CRT. The most recently published study by Wong et al showed that transmural scar was 3 times more prevalent in the RV versus LV pacing region, being seen in one-third of CRT patients. This study found that the delivery of both pacing leads to nonscarred regions resulted in an 82% response rate versus 55% if the RV pacing site was scarred, 25% if the LV site was scarred, and 0% if both were scarred. While focused on basal RV septal lead placement, a small cohort study by Duckett et al suggested that targeted placement of the RV lead to nonscarred basal septal segments was associated with greater response to CRT. This finding was in contrast to patients paced from a transmurally scarred RV apical segment who experienced a 36% absolute reduction in clinical response. These findings support that the prescribed placement of RV leads away from transmural scar may be of clinical benefit. Although contrasting results from post hoc analysis of the REVERSE study suggested no benefit from nonapical RV lead placement, this study was not designed to assess targeted RV lead delivery to nonscarred myocardium among those with apical scar.

Finally, one important consideration for the navigation of CRT leads to prescribed geographic sites is its potential impact on procedural times, fluoroscopy usage, and early device-related complications. In this study, we observed a mean use of 3±1 leads, mean total procedural time of 154±43 min, and mean total fluoroscopy time of 27±15 min and identified 1 patient (3%) to have an early device-related complication (drop in R wave sensing requiring revision).

**Study Limitations**

As a single-center feasibility study, the current analysis cannot evaluate the clinical impact of dual-lead navigation in response to CRT. Such outcomes are more appropriately evaluated within a randomized control trial study, which has now been initiated. Although our study design provided choice to the implanting physician to deliver a single pace defibrillation lead to nonapical RV targets or to add a separate RV pace lead to the target, our implanting physicians reliably chose the latter. As stated previously, the reason was to avoid the need for routine defibrillation testing, which was not routine practice at the enrolling site. Accordingly, future studies must address the efficacy of the former approach, which would eliminate requirement for additional lead delivery.

**Conclusions**

This study demonstrates clinical feasibility of performing dual (LV and RV) CRT lead navigation to optimal myocardial targets using a 3D navigational model. The described approach is practical, is easily translated into clinical practice, and was associated with high procedural success, acceptable procedural times, and a low rate of early procedural complications. A higher than historical rate of super-response to CRT was also observed. The clinical impact of this novel image-guided paradigm for CRT lead delivery is currently being explored within a multicenter randomized clinical trial.

**Acknowledgments**

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Disclosures

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Cardiac resynchronization therapy (CRT) improves quality of life and reduces morbidity and mortality among select populations. However, 30% to 40% of individual patients may not derive benefit, a finding that has been associated with lead delivery to scarred or otherwise unfavorable pacing sites. In this pilot clinical study, we explored the clinical feasibility of navigating both left ventricular and right ventricular leads to optimal pacing targets using an interactive 3-dimensional model. This model incorporated previously validated predictors of response to CRT, including scar distribution, mechanical activation, and interlead distance, all derived from a single cardiac magnetic resonance study. Among 31 patients enrolled, left ventricular and right ventricular leads were guided to modeled targets with high procedural accuracy. Furthermore, a robust improvement in left ventricular remodeling was achieved at 6 months compared with a historic CRT patient cohort. The use of navigational models to guide delivery of CRT leads represents a logical intersection between an expanding knowledge of how myocardial disease influences CRT, a desire to improve clinical response rates, and recent advances in image processing. The latter enables the standardized selection and intuitive representation of procedural targets that can be achieved with high success. Although the clinical deployment of patient-specific CRT can be conceived through a range of methodologies, this pilot study suggests that the simple and practical provision of a spatially matched 3-dimensional model may be sufficient to achieve this goal. Accordingly, a larger scale, multicenter validation for this paradigm is feasible and should examine the impact on relevant clinical outcomes.
Model-Based Navigation of Left and Right Ventricular Leads to Optimal Targets for Cardiac Resynchronization Therapy: A Single-Center Feasibility Study

Zachary Laksman, Raymond Yee, John Stirrat, Lorne J. Gula, Allan C. Skanes, Peter Leong-Sit, Jamie Manlucu, David McCarty, Yosra Turkistani, David Scholl, Martin Rajchl, Aashish Goela, Ali Islam, R. Terry Thompson, Maria Drangova and James A. White

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