Left ventricular lead placement in the latest activated region guided by coronary venous electroanatomic mapping

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Aim
Left ventricular (LV) lead placement in the latest activated region is an important determinant of response to cardiac resynchronization therapy (CRT). We investigated the feasibility of coronary venous electroanatomic mapping (EAM) to guide LV lead placement to the latest activated region.

Methods and results
Twenty-five consecutive CRT candidates with left bundle-branch block underwent intra-procedural coronary venous EAM using EnSite NavX. A guidewire was used to map the coronary veins during intrinsic activation, and to test for phrenic nerve stimulation (PNS). The latest activated region, defined as the region with an electrical delay ≥75% of total QRS duration, was located anterolaterally in 18 (basal, n = 10; mid, n = 8) and inferolaterally in 6 (basal, n = 3; mid, n = 3). In one patient, identification of the latest activated region was impeded by limited coronary venous anatomy. In patients with >1 target vein (n = 12), the anatomically targeted inferolateral vein was rarely the vein with maximal electrical delay (n = 3). A concordant LV lead position was achieved in 18 of 25 patients. In six patients, this was hampered by PNS (n = 4), lead instability (n = 1), and coronary vein stenosis (n = 1).

Conclusion
Coronary venous EAM can be used intraprocedurally to guide LV lead placement to the latest activated region free of PNS. This approach especially contributes to optimization of LV lead electrical delay in patients with multiple target veins. Conventional anatomical LV lead placement strategy does not target the vein with maximal electrical delay in many of these patients.

Keywords
Cardiac resynchronization therapy • Left ventricular lead placement • Electroanatomic mapping • Left ventricular electrical activation • Feasibility

Introduction
Cardiac resynchronization therapy (CRT) reduces morbidity and mortality and reverses left ventricular (LV) remodelling in heart failure patients with LV systolic impairment and electrical dyssynchrony.1–3 Despite the striking effectiveness of CRT, a substantial proportion of apparently eligible patients fail to benefit.1 Part of this reduced benefit has been attributed to a suboptimal LV lead position.4 There is increasing evidence to suggest that positioning of the LV lead in the region of latest electrical activation provides superior clinical outcome.5,6 The conventional LV lead placement strategy involves an anatomical approach, targeting a coronary venous branch situated on the posterolateral wall.7 This strategy is based on the contention that the posterolateral wall is typically the latest activated site of the ventricle in patients with left bundle-branch block (LBBB). However, studies have shown a considerable variability in the ventricular activation pattern in LBBB, resulting in inter-individual variability in the optimal pacing site.8–10 Therefore, a more patient-specific physiological approach focused on achieving maximal LV lead electrical delay may improve CRT response. Electroanatomic mapping (EAM) is typically used in the electrophysiology lab to guide diagnostic or ablation procedures of cardiac arrhythmias.
LV lead placement in the latest activated region guided by EAM

What’s new?
- We describe a novel method of coronary venous electroanatomic mapping that utilizes the EnSite NavX system in combination with a guidewire that allows mapping and pacing of the coronary veins.
- This technique can be used at the time of cardiac resynchronization therapy implantation to assess left ventricular (LV) electrical activation pattern and guide LV lead placement to the latest activated region.
- The technique also enables comprehensive identification of sites that are free of phrenic nerve stimulation.

Recently, the technique has also been applied during CRT implantation to determine the electrical activation pattern of the coronary venous system. \(^{11,12}\) Final LV lead position, however, depends on several factors such as cardiac venous anatomy, performance and stability of the lead, and the absence of phrenic nerve stimulation (PNS). The feasibility of coronary venous EAM to guide LV lead placement to the latest activated region during CRT implantation remains to be assessed. The aim of the present study was to assess the feasibility of positioning the LV lead in the latest activated region guided by coronary venous EAM in patients undergoing CRT implantation.

Methods

Population
From December 2012 to May 2013, consecutive patients referred for CRT device implantation, with LV ejection fraction (LVEF) < 35%, New York Heart Association (NYHA) functional class 2, 3, or ambulatory 4, and LBBB according to European Society of Cardiology (ESC) guidelines, \(^{13}\) were prospectively enrolled. The study complied with the Declaration of Helsinki. Our locally appointed ethics committee approved the study protocol and waived the need for informed consent.

Electroanatomic mapping and left ventricular lead placement
All patients underwent intra-procedural coronary venous three-dimensional (3D) EAM using EnSite NavX (St Jude Medical). Prior to LV lead placement, an occlusive coronary venogram was recorded under fluoroscopy in right anterior oblique (RAO) and left anterior oblique (LAO) view for optimal visualization of the coronary veins. Subsequently, a 0.014 inch guidewire (Vision Wire, Biotronik SE & Co.KG) was inserted into the coronary sinus and connected to EnSite NavX along with the surface electrocardiogram (ECG). This guidewire has complete polyethylene isolation except for 15 mm at the distal "J"-shaped tip and 30 mm at the proximal end permitting unipolar sensing and pacing. \(^{14}\) The guidewire was used to map all target veins located on the anterolateral or inferolateral LV wall as defined by the American Heart Association (AHA) 17-segment heart model. \(^{15}\) A 3D electrical activation map was constructed during intrinsic ventricular activation. Electrical delay was measured in milliseconds from QRS onset on the surface ECG to the peak negative slope on the unipolar intra-cardiac electrogram (EGM) and expressed as a percentage of total QRS duration. All measurements were generated in EnSite NavX at a screen speed of 400 mm/s. The latest activated region of the LV was defined as the region with an electrical delay comprising >75% of total QRS duration. This definition was chosen because epicardial mapping via the coronary veins is limited by coronary venous anatomy, which means that some areas cannot be mapped because they do not contain any veins. Therefore, the latest activated LV region can only be identified using coronary venous mapping by relating the electrical activation time of the anatomical region to its timepoint within the QRS complex. Candidate pacing sites were tested for PNS by 10 V unipolar pacing on the tip of the guidewire and regions with PNS or absence thereof were annotated on the EAM using EnSite NavX. After the mapping procedure, the LV lead was connected to EnSite NavX for real-time visualization and navigation of the lead to the latest activated region free of PNS in the created EAM. Standard bipolar leads of various vendors were used. Figure 1 shows an example of a coronary venous EAM together with the results of PNS testing and the final LV lead position. The latest activated region and final LV lead position were classified according to the AHA 17-segment heart model by detailed evaluation of pre-implantation venograms and post-implantation LV lead fluoroscopy images (Figure 2). The final LV lead position was described as concordant if the lead was located in the same myocardial segment as the latest activated region.

Statistical analysis
Continuous variables are expressed as mean ± SD. Categorical variables are expressed as observed number and percentage values. Continuous variables were compared using Mann–Whitney U test. Statistical significance was accepted at the 95% confidence interval (\(P < 0.05\)). Statistical analysis was performed using SPSS version 20.0 (SPSS Inc.) software.

Results

Patient characteristics
Twenty-five consecutive patients with LBBB referred for CRT device implantation were included in this study. The patient characteristics are described in Table 1.

Cardiac resynchronization therapy implantation
In 21 patients, a de novo CRT defibrillator was implanted. Two patients were upgraded from an implantable cardioverter-defibrillator to a CRT defibrillator and two patients received a CRT pacemaker. Left ventricular lead implantation was successful in all patients. There were no procedural complications.

Coronary venous electroanatomic mapping
In all patients, occlusive coronary venography revealed at least one target vein on the anterolateral or inferolateral LV wall. In 12 of 25 patients, two target veins were available. All target veins were successfully mapped. Three-dimensional electrical activation maps were generated from an average of 46 ± 28 unique anatomical points. Mapping time was 19 ± 6 min and fluoroscopy time during the entire procedure was 20 ± 6 min. Figure 3 shows the distribution of the latest activated regions in all patients. The latest activated region was located anterolaterally in 18 (basal, \(n = 10\); mid, \(n = 8\)) and inferolaterally in 6 (basal, \(n = 3\); mid, \(n = 3\)). In one patient (No. 7), identification of the latest activated region was impeded by limited coronary venous anatomy.
Left ventricular lead placement

Figure 4 shows the distribution of the final LV lead position in all patients. The LV lead was positioned anterolaterally in 16 (basal, \( n = 9 \); mid, \( n = 7 \)) and inferolaterally in 9 (basal, \( n = 4 \); mid, \( n = 5 \)). The final LV lead position was concordant with the latest activated region in 18 of 25 patients. In six patients, concordant LV lead placement was hampered by PNS (\( n = 4 \), one of them depicted in Figure 5), lead instability (\( n = 1 \)), and coronary vein stenosis (\( n = 1 \)). In the patient in whom the latest activated region could not be identified (No. 7), the LV lead was positioned at the site where maximal electrical delay was measured with coronary venous EAM. An overview of the latest activated regions and final LV lead positions of all patients together with the corresponding electrical delays at these sites is provided in Table 2. In patients with a concordant LV lead position, electrical delay was \( 132 \pm 15 \) ms (85 ± 6% of QRS duration) at the latest activated region and \( 128 \pm 13 \) ms (83 ± 5% of QRS duration) at the final lead position (\( P = 0.17 \)). In patients with a discordant LV lead position, electrical delay was \( 125 \pm 10 \) ms (84 ± 3% of QRS duration) at the latest activated region and \( 94 \pm 15 \) ms (63 ± 7% of QRS duration) at the final lead position (\( P = 0.002 \)). Left ventricular lead electrical delay was significantly longer in patients with a concordant compared with patients with a discordant LV lead position (\( P < 0.001 \)).

In 9 of 12 patients with two available target veins (Nos. 1, 11, 12, 13, 14, 15, 18, 23, and 24), the latest activated region was located in a
different vein than the anatomically targeted inferolateral vein (Table 2). In these patients, maximal electrical delay was $89 \pm 14$ ms (58 \pm 6\% of QRS duration) in the anatomically targeted vein vs. $133 \pm 15$ ms (87 \pm 5\% of QRS duration) at the latest activated region ($P < 0.001$). The LV lead was positioned in the latest activated region in seven of nine patients (Nos. 1, 11, 12, 14, 15, 23, and 24). In these patients, maximal electrical delay was $89 \pm 16$ ms (57 \pm 7\% of QRS duration) in the anatomically targeted vein vs. $131 \pm 14$ ms.

Figure 2  Angiographic classification of the latest activated region and final LV lead position. (A) The AHA standardized 17-segment heart model, adapted from Cerqueira et al.\textsuperscript{15} (B) Coronary venogram in RAO. This view, representative of the long axis of the heart, was used to classify the latest activated region and final LV lead position into basal, mid-ventricular, and apical segments. (C) Coronary venogram in LAO. This view, comparable with the short axis of the heart, was used to divide the LV wall into four equal parts; anterior, anterolateral, inferolateral, and inferior. AIV, anterior inter-ventricular vein; ALV, anterolateral vein; IIV, inferior inter-ventricular vein; ILV, inferolateral vein.

Table 1  Patient characteristics ($n = 25$)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>$72 \pm 6$</td>
</tr>
<tr>
<td>Male gender ($n, %$)</td>
<td>14 (56)</td>
</tr>
<tr>
<td>Ischaemic heart disease ($n, %$)</td>
<td>8 (32)</td>
</tr>
<tr>
<td>NYHA functional class ($n, %$)</td>
<td>II 11 (44)</td>
</tr>
<tr>
<td></td>
<td>III 14 (56)</td>
</tr>
<tr>
<td>Echocardiography characteristics</td>
<td></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>$27 \pm 5$</td>
</tr>
<tr>
<td>LV end-diastolic diameter (mm)</td>
<td>$59 \pm 4$</td>
</tr>
<tr>
<td>LV end-systolic diameter (mm)</td>
<td>$55 \pm 5$</td>
</tr>
<tr>
<td>LV end-diastolic volume (mL)</td>
<td>$146 \pm 30$</td>
</tr>
<tr>
<td>LV end-systolic volume (mL)</td>
<td>$107 \pm 24$</td>
</tr>
<tr>
<td>ECG characteristics</td>
<td></td>
</tr>
<tr>
<td>LBBB ($n, %$)</td>
<td>25 (100)</td>
</tr>
<tr>
<td>QRS duration (ms)</td>
<td>$154 \pm 15$</td>
</tr>
<tr>
<td>Intrinsic rhythm ($n, %$)</td>
<td></td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>22 (88)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Treatment ($n, %$)</td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td>17 (68)</td>
</tr>
<tr>
<td>ACE-i/ARB</td>
<td>24 (96)</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>22 (88)</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>15 (60)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>3 (12)</td>
</tr>
</tbody>
</table>

ACE-i, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Figure 3  Distribution of the latest activated region. Each circled number represents a patient. Numbers refer to the order of inclusion. The latest activated region was mainly located on the anterolateral LV wall. In one patient (No. 7), the latest activated region could not be identified by coronary venous EAM due to limited coronary venous anatomy. A, anterior; AL, anterolateral; AS, anteroseptal; I, inferior; IL, inferolateral; IS, inferoseptal; L, lateral; S, septal.
(85 ± 4% of QRS duration) at the final LV lead position (P = 0.001).
In the other two patients (Nos. 13 and 18), coronary vein stenosis and
PNS hampered concordant LV lead placement. Figure 6 illustrates the
additional value of mapping-guided LV lead placement as compared
with the conventional anatomical LV lead placement approach. In
this example, the coronary venous EAM of Patient No. 24 is shown
where a pure anatomical approach would have resulted in a subopti-
mal LV lead position in the inferolateral vein with a maximal electrical
delay of only 90 ms. However, additional mapping of the small
anterolateral vein resulted in a potentially far better LV lead position
with an electrical delay close to 140 ms.

Discussion
Pacing at the latest activated region of the LV appears to improve the
outcome of CRT. The present study demonstrates that coronary
venous EAM using EnSite NavX in combination with a mapping guide-
wire can be used intraoperatively to guide LV lead placement to the
region of latest electrical activation. In addition, the potential of this
mapping approach to facilitate comprehensive identification of
regions free of PNS is demonstrated.

Targeted left ventricular lead placement at
the latest activated left ventricular region
Several studies have investigated the relationship between pacing in
the region of latest activation and the response to CRT. Studies on
mechanical activation suggest superior CRT outcome when the LV
lead position coincides with the region of latest mechanical contrac-
tion compared with discordant positions.16–22 Two recent

Figure 4 Distribution of the final LV lead position. Each circled
number represents a patient. Numbers refer to the order of inclu-
sion and correspond with the numbers in Figure 3. A, anterior; AL,
anterolateral; AS, anteroseptal; I, inferior; IL, inferolateral; IS, infer-
oseptal; L, lateral; S, septal.

Figure 5 (A) Coronary venous 3D electrical activation map
during intrinsic ventricular activation of a patient in whom PNS ham-
pered placement of the LV lead in the latest activated region.
Mapping of the anterolateral and inferolateral vein revealed the
latest activated region at the mid-anterolateral LV wall. Unfortu-
nately, this was also a region with PNS. The LV lead was eventually
placed as close as possible to the latest activated region and pacing
was performed at the ring of the LV lead, which in contrast to the tip
still offered some space between ventricular capture and PNS. (B)
Corresponding coronary venogram. (C) X-ray of final LV lead place-
ment. Red dot, PNS; Green dot, no PNS; R, LV lead ring; T, LV lead
tip; AIV, anterior inter-ventricular vein; ALV, anterolateral vein; IIV,
inferior inter-ventricular vein; ILV, inferolateral vein; RV, right ventricular.

prospective single-centre trials randomized a total of 407 patients
to speckle-tracking echocardiography-guided LV lead placement tar-
getting the site of latest mechanical activation or to standard unguided
LV lead placement. In both trials, patients with a LV lead position con-
cordant with the site of latest activation had a higher echocardi-
ographic response rate, more clinical responders, and a reduced risk
of mortality and heart failure hospitalization.23,24 Studies focusing
on the electrical activation pattern have demonstrated that a
greater delay in time from onset of the QRS complex to the local
sensed LV lead EGM (Q-LV) is also associated with a greater likeli-
hood of benefit from CRT.25,26 Recently, Zanon et al. measured
the Q-LV interval of various pacing sites within patients, and evalu-
ated the haemodynamic effect of pacing at the different sites by inva-
sive measurement of LVdP/dtmax. Pacing the LV at the latest activated
site resulted in greatest haemodynamic improvement.6 The choice
between targeting the region of latest electrical or latest mechanical
activation is still a matter of debate and definitive randomized trials
that support the use of either approach to reliably select an
optimal LV pacing site are lacking. Accordingly, current ESC
guidelines have assigned a class 2b indication to targeted LV lead placement at the latest activated LV segment. A slightly stronger recommendation (class 2a) has been assigned to avoiding an apical LV lead position despite conflicting results in the literature. Therefore, larger prospective studies are required to settle the issue of whether pacing the latest activated LV region provides the best outcome of CRT.

While the position of the LV lead with respect to the site of latest activation is a factor that can influence CRT response, several studies have shown that the proximity of the LV lead to an area with myocardial scar is an important factor as well. Assessment of scar tissue should therefore be considered before CRT, especially in the population with ischaemic heart disease. Integrating information obtained from scar imaging with measurements of electrical and mechanical delay may further optimize LV lead positioning and the clinical response rate.

Table 2 Overview of the latest activated regions, final LV lead positions, and empirical target veins of all patients together with the corresponding electrical delays

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>No. of target veins</th>
<th>Latest activated region</th>
<th>Electrical delay (ms)</th>
<th>Final LV lead position</th>
<th>Electrical delay (ms)</th>
<th>Reason for discordance</th>
<th>Empirical target vein for LV lead</th>
<th>Maximal electrical delay (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>B-AL</td>
<td>139 (93%)</td>
<td>B-AL</td>
<td>131 (87%)</td>
<td>–</td>
<td>IL vein</td>
<td>90 (60%)</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>B-AL</td>
<td>136 (86%)</td>
<td>B-AL</td>
<td>126 (80%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>M-IL</td>
<td>122 (79%)</td>
<td>M-IL</td>
<td>122 (79%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>M-AL</td>
<td>131 (84%)</td>
<td>M-AL</td>
<td>128 (82%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>B-IL</td>
<td>131 (85%)</td>
<td>B-IL</td>
<td>128 (83%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>M-AL</td>
<td>110 (85%)</td>
<td>M-IL</td>
<td>72 (56%)</td>
<td>PNS</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>Not identified</td>
<td>–</td>
<td>M-IL</td>
<td>103 (63%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>M-AL</td>
<td>126 (87%)</td>
<td>M-AL</td>
<td>126 (87%)</td>
<td>–</td>
<td>AL vein</td>
<td>–</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>B-AL</td>
<td>137 (84%)</td>
<td>M-AL</td>
<td>103 (63%)</td>
<td>Lead instability</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>10</td>
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<td>156 (96%)</td>
<td>B-AL</td>
<td>149 (92%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>11</td>
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<td>B-AL</td>
<td>130 (85%)</td>
<td>B-AL</td>
<td>128 (83%)</td>
<td>IL vein</td>
<td>70 (45%)</td>
<td>–</td>
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<tr>
<td>12</td>
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<td>B-AL</td>
<td>119 (91%)</td>
<td>B-AL</td>
<td>119 (91%)</td>
<td>IL vein</td>
<td>72 (55%)</td>
<td>–</td>
</tr>
<tr>
<td>13</td>
<td>2</td>
<td>M-AL</td>
<td>124 (86%)</td>
<td>B-IL</td>
<td>94 (65%)</td>
<td>Coronary vein stenosis</td>
<td>IL vein</td>
<td>94 (65%)</td>
</tr>
<tr>
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<td>B-AL</td>
<td>138 (86%)</td>
<td>–</td>
<td>IL vein</td>
<td>106 (66%)</td>
</tr>
<tr>
<td>15</td>
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<td>M-AL</td>
<td>116 (91%)</td>
<td>M-AL</td>
<td>111 (87%)</td>
<td>–</td>
<td>IL vein</td>
<td>80 (63%)</td>
</tr>
<tr>
<td>16</td>
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<td>M-IL</td>
<td>131 (78%)</td>
<td>M-IL</td>
<td>131 (78%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>17</td>
<td>1</td>
<td>M-AL</td>
<td>111 (76%)</td>
<td>M-AL</td>
<td>111 (78%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>18</td>
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<td>118 (79%)</td>
<td>M-IL</td>
<td>94 (63%)</td>
<td>PNS</td>
<td>IL vein</td>
<td>94 (63%)</td>
</tr>
<tr>
<td>19</td>
<td>2</td>
<td>M-IL</td>
<td>130 (83%)</td>
<td>B-AL</td>
<td>116 (74%)</td>
<td>PNS</td>
<td>IL vein</td>
<td>–</td>
</tr>
<tr>
<td>20</td>
<td>1</td>
<td>B-AL</td>
<td>128 (83%)</td>
<td>B-AL</td>
<td>127 (82%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>21</td>
<td>1</td>
<td>B-IL</td>
<td>143 (80%)</td>
<td>B-IL</td>
<td>141 (79%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>22</td>
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<td>B-AL</td>
<td>128 (85%)</td>
<td>M-AL</td>
<td>87 (57%)</td>
<td>PNS</td>
<td>–</td>
<td>–</td>
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<tr>
<td>23</td>
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<td>160 (84%)</td>
<td>M-AL</td>
<td>155 (81%)</td>
<td>–</td>
<td>IL vein</td>
<td>113 (59%)</td>
</tr>
<tr>
<td>24</td>
<td>2</td>
<td>B-AL</td>
<td>140 (83%)</td>
<td>B-AL</td>
<td>133 (79%)</td>
<td>–</td>
<td>IL vein</td>
<td>90 (54%)</td>
</tr>
<tr>
<td>25</td>
<td>2</td>
<td>B-IL</td>
<td>103 (80%)</td>
<td>B-IL</td>
<td>101 (78%)</td>
<td>–</td>
<td>IL vein</td>
<td>–</td>
</tr>
</tbody>
</table>

Patient numbers correspond with the numbers provided in Figures 3 and 4. Electrical delay is reported in milliseconds (percentage of total QRS duration). In Patient No. 6, the anterolateral vein anastomosed with the inferior inter-ventricular vein, which made it possible to position the LV lead inferolaterally (via the anastomosis) despite the patient having only one target vein on the anterolateral LV wall. In Patient No. 7, identification of the latest activated region was impeded by limited coronary venous anatomy. Patient No. 8 had two target veins on the anterolateral wall. For patients with two target veins, the second column from the right reports the target vein for the LV lead if the conventional anatomical lead placement approach would be used. The right-most column provides the maximal electrical delay measured within that vein. B, basal; M, mid; AL, anterolateral; IL, inferolateral; PNS, phrenic nerve stimulation.

Feasibility of coronary venous electroanatomic mapping to guide left ventricular lead placement to the latest activated region

Our observation that the location of the latest activated region varies between patients agrees with previous EAM studies in patients with heart failure and LBBB, and emphasizes the need for a patient-tailored approach to optimize LV lead positioning. The present study demonstrates that coronary venous EAM using EnSite NavX in combination with a mapping guidewire is a feasible method to tailor LV lead placement to the individual patient at the time of implantation. Using this approach, we were able to position the LV lead in the latest activated region in >70% of our patients. Conventional LV lead placement strategy involves an anatomical approach, targeting a coronary vein situated on the posterolateral wall.
Approximately half the patients in our study cohort had more than one target vein available on the lateral LV free wall. In most of these patients, the empirically targeted posterolateral vein was not the vein with maximal electrical delay, which is consistent with the findings of a previous study that also used coronary venous EAM to assess LV epicardial activation. In the present study, coronary venous EAM resulted in targeting of an alternative vein in many of these patients, significantly increasing LV lead electrical delay from an average of 57–85% of total QRS duration. In addition, in patients with a single target vein, coronary venous EAM enabled targeting of the vein segment with maximal electrical delay. These results demonstrate the additional value of coronary venous EAM-guided LV lead placement as compared with the conventional anatomical LV lead placement approach for optimization of LV lead electrical delay.

Unfortunately, concordant LV lead placement was still hampered in one-quarter of patients due to PNS, lead instability, and unfavourable coronary venous anatomy. The use of additional technologies...
may increase the success rate of targeted LV lead placement on the basis of electrical delay. Venous angioplasty, for example, may have benefited one of our patients in whom coronary venous stenosis hampered LV lead placement in the latest activated region. In addition, the use of new lead technologies, such as active-fixation leads and multipolar leads, could overcome the problem of lead instability and avoid PNS, which hindered concordant LV lead positioning in several other patients in our study. When confronted with PNS, also alternative pacing strategies such as thoracoscopic epicardial or LV endocardial pacing may be considered to stimulate the site of optimal electrical delay.

Our mapping approach was easy to implement intraprocedurally using a commercially available EAM system in combination with a guidewire that allows mapping and pacing of the coronary veins, making the approach applicable in any catheter laboratory that has access to the relevant instruments. In addition, the same wire used to guide the LV lead was also used to map the coronary veins, which obviated the need for inserting additional electrophysiology mapping catheters during implantation. Echocardiography and other imaging modalities have also been proposed as methods to assess the LV activation pattern and guide LV lead placement, but these techniques are challenging to apply in the catheter laboratory and often require a separate pre-operative assessment.

In current clinical practice, most implanters that tend to target LV lead placement to a region with significant electrical delay do not perform full EAM in favour of a simpler approach where electrical mapping of the anatomically targeted region is performed using the LV lead to test if electrical delay is sufficiently late. However, using this approach the latest activated region may be missed because other potential LV pacing sites are generally not tested when electrical delay at the empirically targeted LV region is considered late enough. Previous reports suggest that a Q-LV > 95 ms or > 50% of total QRS duration is sufficient to increase the odds of a favourable response. However, further increase of the Q-LV to > 120 ms has been shown to considerably improve these odds, suggesting that implanters should aim to optimize LV lead electrical delay to maximize the chance of a positive CRT outcome. Besides, with simple electrical mapping, measurements are generally performed after final LV lead implantation. If the measured electrical delay is judged unsatisfactory, the implanter may have to relocate the LV lead to an alternative target vein, thus extending procedure and fluoroscopy time. Compared with simple electrical mapping using the LV lead, our 3D EAM approach has important advantages that can significantly contribute to LV lead placement optimization. The EnSite NavX system can be used to create an anatomical geometry of the coronary veins while electrical delay and PNS are assessed for any anatomical region accessible with the mapping guidewire. The small and flexible mapping guidewire allows for more detailed data collection by easy and quick mapping of multiple coronary veins and multiple points per vein, which provides information on electrical activation timing and PNS of all potential LV pacing sites. Thus, all information about coronary venous anatomy, LV electrical activation, and PNS can be readily obtained prior to LV lead placement. The LV lead can then be targeted to the latest activated region free of PNS in a single approach, thus reducing placement attempts at unsuitable sites. Targeted LV lead placement is further facilitated by real-time visualization and navigation of the lead in the NavX-created EAM.

Avoiding phrenic nerve stimulation
Phrenic nerve stimulation accounts for failure to deliver proper CRT or urgent need for LV lead relocation in a substantial number of patients. Studies addressing the issue have reported PNS at implantation in 7.6–37% of patients, resulting in failure to pace the target site in 10–14%. PNS at follow-up has been reported in 11–33% of patients, requiring LV lead replacement in a substantial proportion of patients and eventual turn-off of CRT in some. In the present study, PNS was assessed by systematic pacing of the coronary veins with the tip of the mapping guidewire. The usefulness of this approach for detecting PNS has previously been demonstrated by de Cock et al. In addition, the EAM system used in our study allowed comprehensive annotation of PNS-free areas on the created coronary venous geometry, consequently providing 3D visualization of the anatomical location of these areas with respect to the target LV pacing site and the position of the LV lead tip. Subsequently, real-time navigation of the LV lead in the geometry allowed targeting of a PNS-free zone with optimal electrical delay. This approach proved to be effective to avoid PNS at medium-term follow-up (4 ± 1 months) in all study patients.

Limitations
The sample size of this study was relatively small. However, the study was performed on consecutive patients and the study population resembled the typical population of patients with LBBB and heart failure referred for CRT implantation. Only standard bipolar LV leads were used. The use of new lead technologies, such as multipolar leads and active-fixation leads, may increase the success rate of targeted LV lead placement at the latest activated LV region by improving lead stability and avoiding PNS. Unfortunately, most device vendors did not have multipolar LV leads available at the time the current study was conducted. Cardiac magnetic resonance imaging was not performed in this study. Therefore, we could not assess the distribution and extent of scar and its potential effect on electrical activation. Also, the mapping method used in the current study did not allow for reliable differentiation between scar and healthy myocardium. Thus, the position of the LV lead with respect to regions of myocardial scar was not taken into account during LV lead placement. The current study demonstrates a feasible method to guide LV lead placement to the region of latest electrical activation. However, the clinical value of this lead placement strategy was not proven by acute haemodynamic measurements or long-term echocardiographic or clinical follow-up. Subsequent larger and long-term follow-up studies are therefore required to evaluate the impact of coronary venous mapping-guided LV lead placement on CRT outcome.

Conclusion
Coronary venous EAM using EnSite NavX in combination with a mapping guidewire can be used at the time of CRT implantation to guide LV lead placement to the latest activated region free of PNS. This approach especially contributes to optimization of LV lead electrical delay in patients with multiple target veins. The conventional anatomical LV lead placement strategy does not target the vein...
with maximal electrical delay in many of these patients. The clinical value of coronary venous mapping-guided LV lead placement needs prospective evaluation.

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References


Images in Electrophysiology

Bilateral confined pulmonary vein fibrillation

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Confined pulmonary vein (PV) fibrillation is a rare finding, which suggests that fibrillation can sustain in the isolated tissue independently. A 76-year-old woman underwent second catheter ablation procedure for recurrent atrial fibrillation (AF). The starting rhythm was AF. During ipsilateral right PV re-isolation, sinus rhythm was restored despite sustained fibrillation inside (panel A). Following the re-isolation of right PVs, confined PV fibrillation was also observed in isolated left superior PV (panel B). To the best of our knowledge, this is the first case presenting simultaneous confined bilateral PV fibrillation. The case highlighted the strong association with the mechanism of sustaining AF and bilateral PVs.

Conflict of interest: none declared.

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