Permanent His-bundle pacing for cardiac resynchronization therapy: Initial feasibility study in lieu of left ventricular lead

Olujimi A. Ajijola, MD, PhD,* Gaurav A. Upadhyay, MD, FHRS,† Carlos Macias, MD,* Kalyanam Shivkumar, MD, PhD, FHRS,* Roderick Tung, MD, FHRS†

From the *UCLA Cardiac Arrhythmia Center, David Geffen School of Medicine at UCLA, Los Angeles, California, and †The University of Chicago Medicine, Center for Arrhythmia Care, Pritzker School of Medicine, Chicago, Illinois.

BACKGROUND Permanent His-bundle pacing (HBP) has the potential to physiologically normalize wide QRS duration in patients with bundle branch block and cardiomyopathy.

OBJECTIVE The purpose of this study was to assess the feasibility of incorporating a His-bundle lead for cardiac resynchronization therapy (CRT) in lieu of a coronary sinus lead.

METHODS Patients with an indication for CRT (n = 21) underwent attempted implantation of an HBP placed into the left ventricular (LV) lead port. Intracardiac intervals, QRS duration, New York Heart Association functional class, ejection fraction (EF), echocardiography, and lead characteristics were measured at baseline and at follow-up.

RESULTS Of the 21 patients in whom implantation was attempted, HBP was successfully implanted in 16 (age 62 ± 18 years, 4 females, EF 25 ± 8). A significant reduction in mean QRS was observed, with narrowing from 180 ± 23 ms to 129 ± 13 ms (P <.0001). During the follow-up period, median New York Heart Association functional class improved from III to II (P <.001), and mean LV EF and left ventricular internal dimension in diastole (LVIDd) improved from 27% ± 10% to 41% ± 13% (P <.001) and from 5.4 ± 0.4 cm to 4.5 ± 0.3 cm (P <.001), respectively. At median 12-month follow-up, no dislodgments were observed, and only one patient lost nonselective capture that resolved with increased pacing output.

CONCLUSION Permanent HBP is feasible for patients with an indication for CRT using the LV port in lieu of a coronary sinus lead. In this initial experience, narrowing of QRS duration was achieved in 76% of patients with bundle branch block, and improvements in clinical and echocardiographic measures were observed with HBP. Future prospective comparative studies with HBP to achieve CRT are justifiable.

KEYWORDS Cardiac resynchronization; His bundle; Pacing; Bundle branch block; Heart failure

Introduction

Direct stimulation of the His bundle has been proposed to represent the most physiologic mode of ventricular pacing.1 The safety and efficacy of His-bundle pacing (HBP) have been demonstrated in patients with sick sinus syndrome and complete heart block.2–5 Normalization of bundle branch block has been demonstrated from pacing at the distal His bundle. Although several case reports have reported successful cardiac resynchronization therapy (CRT) achieved with HBP,6–8 incorporation of a permanent HBP into an implantable cardioverter–defibrillator system in lieu of a left ventricular (LV) lead has been reported in only a few small series to date.9–11 We performed an initial pilot study to assess the feasibility of implanting an HBP for CRT using the LV port in patients with cardiomyopathy and wide QRS.

Methods

Patient selection

Patients who had indications for CRT (bundle branch block with QRS >120 ms, New York Heart Association [NYHA] functional class II–IV, ejection fraction [EF] <35%) over a
2-year period (2014–2016) at 2 academic centers were included, and data were retrospectively analyzed. One patient with EF <50% with anticipated pacing burden >40% was included. Patients in this feasibility pilot study were given the option of standard resynchronization via a coronary sinus lead or permanent HBP. Two patients underwent implantation of a His lead after an unsuccessful attempt at coronary sinus lead placement. The remaining patients chose to undergo an initial attempt at placement of a His-bundle lead, in which a standard coronary sinus lead would be placed if nonselective or selective His-bundle capture with >20% QRS narrowing could not be achieved. Patients provided informed consent and demonstrated an understanding of HBP as a nonstandard approach to achieve physiologic pacing, counterbalanced by an up to 30% nonresponse rate with a standard LV lead. Data analysis was approved by the institutional review board at both centers.

**Implantation technique**

In the initial patients (n = 12), the His-bundle electrogram was mapped with fluoroscopic guidance of a diagnostic quadripolar catheter (CRD-2, St. Jude Medical, St. Paul, MN) placed from the femoral approach to map a discrete His-bundle electrogram. The remaining patients underwent implantation without the aid of a diagnostic catheter to local His-bundle electrogram. Two patients underwent implantation of a His lead after an unsuccessful attempt at coronary sinus lead placement. The remaining patients chose to undergo an initial attempt at placement of a His-bundle lead, in which a standard coronary sinus lead would be placed if nonselective or selective His-bundle capture with >20% QRS narrowing could not be achieved. Patients provided informed consent and demonstrated an understanding of HBP as a nonstandard approach to achieve physiologic pacing, counterbalanced by an up to 30% nonresponse rate with a standard LV lead. Data analysis was approved by the institutional review board at both centers.

Figure 1  Two examples of acute current of injury on the local His bundle electrogram indicative of adequate lead fixation through the pace–sense analyzer. Injury signal is indicated by the arrows.

fixation, high-output bipolar pacing at 10 mA at 1 ms was performed to assess for His capture. Fixation was performed by rotating the lead typically 4–10 turns, with the delivery sheath advanced up to the proximal electrode for guide support. Acute injury current in the local His and/or ventricular electrogram was assessed (Figure 1), and thresholds were analyzed as previously described.

The lead position was accepted if His recruitment (selective or nonselective capture) with QRS narrowing was obtained at <5.0 V at 1 ms. Selective His-bundle capture was defined as an isoelectric segment (S–QRS) after the pacing stimulus equal or shorter than the HV interval with rapid-onset QRS activation. Nonselective His-bundle capture was defined as a pseudo-delta wave after the pacing stimulus and an S–QRS interval less than the HV interval. QRS narrowing was present when the paced QRS was less than the native QRS. If His capture did not result in >20% narrowing of the QRS, an LV lead was placed in the coronary sinus. An atrial lead was placed in a standard manner using a curved stylet in the right atrial appendage. The generator was attached to the leads and secured, and the incision site closed. Prophylactic intravenous antibiotics (Vancomycin or Ancef) were administered intraprocedurally. At the physician’s discretion, the device was programmed to maximize HBP, with maximum LV pre-excitation to prevent fusion (–60 to –80 LV–RV offset). In cases of selective His-bundle capture, AV delay was shortened to account for the HV interval or the stimulus-to-QRS time to minimize the risk for fusion with intrinsic rhythm. To minimize current drain, the RV pacing threshold was acutely programmed at threshold.

**Clinical follow-up**

Patients were seen for routine clinical follow-up at standard time periods (1 month, 3 months, 6 months, and 12 months). Functional status was assessed by NYHA classification. Device thresholds were checked and adjusted as needed to maximize battery longevity. Echocardiography were performed as clinically indicated for follow-up.

**Statistical analysis**

Continuous variables are given as mean ± SD or median. Paired comparisons were made using a Student 𝑡 test if the
data were normally distributed, and with the Wilcoxon signed-rank test for nonparametric data. Paired categorical data (NYHA functional class) were compared using the Wilcoxon test. \( P < 0.05 \) was considered significant.

**Results**

Between 2014 and 2016, permanent HBP for CRT was attempted in 21 patients at 2 centers. In 16 of these 21 patients, nonselective His-bundle capture was achieved with QRS narrowing in 15 patients and selective His-bundle capture was observed in 1 patient (Figures 2 and 3). In the patient with selective His capture, an isoelectric S–QRS and rapid-onset QRS activation but shortened S–QRS relative to HV interval was observed (Figure 4). In 5 patients in whom His capture and/or >20% QRS narrowing could not be obtained despite multiple attempts and positions around the His-bundle region, an LV lead was placed into the coronary sinus (Figure 5). Among the 16 patients with successful His recruitment with QRS narrowing, 12 had left bundle branch block (LBBB) and 4 had right bundle branch block (RBBB) pattern with mean QRS duration of 181 ± 23 ms. The paced QRS duration was 129 ± 13 ms, representing a narrowing of QRS duration by 30%.

Mean age in the successfully implanted patients was 62 ± 18 years (75% male). Thirty-eight percent had ischemic cardiomyopathy, with mean baseline LV EF across the cohort of 25% ± 8%, and 25% with NYHA functional class IV status. One patient had permanent atrial fibrillation, and two had a prosthetic aortic valve (Figure 6). Characteristics of patients with and those without His capture are given in Table 1.

There was no difference in HV intervals between those who achieved nonselective capture and those who could not (65 ± 10 vs 67 ± 11; \( P = .1 \)). However, baseline QRS was wider in those with successful nonselective His capture compared to those who failed to narrow the QRS (180 ± 23 ms vs 150 ± 22 ms). Acute thresholds for His capture were 1.9 ± 1.2 V @ 0.6 ± 0.2 ms and remained stable at follow-up (1.4 ± 0.8 V). Mean lead impedance at implant was 566 ± 137 \( \Omega \) and remained stable at follow-up (476 ± 106 \( \Omega \)). Mean implant time was 188 ± 57 minutes.

**Clinical follow-up**

Median follow-up in the study was 12 months (range 2–19 months). No dislodgments were observed. One patient lost nonselective His capture 1 month after implant with a parahisian response due to a threshold increase to 3.5 V, which was restored with increased programmed output of 5 mV. Of the 16 patients implanted with permanent HBP, 11 demonstrated clinical improvement and 3 (nonischemic cardiomyopathy, \( n = 2 \)) showed “hyperresponse” with EF >50%. All 5 patients who did not respond or died early during follow-up, however, also had nonischemic cardiomyopathy etiology. In patients with complete follow-up, mean LV EF improved from 27% ± 10% to 41% ± 13% (\( P < .001 \)) (Figure 7). NYHA functional class improved from III to II (\( P < .001 \)), and left ventricular internal dimension in diastole (LVIDd) improved from 5.4 ± 0.4 cm to 4.5 ± 0.3 cm (\( P < .001 \)). At the time of implant, 1 patient (92-year-old man treated with CRT-P) was on home oxygen that was discontinued after institution of nonselective HBP. He was still alive at the time of manuscript preparation.

Four deaths occurred during follow-up (3 His bundle, 1 LV lead). The patient who had standard CRT via LV lead died of pneumonia and respiratory failure. In the His-bundle group, the causes of death were progression of eosinophilic myocarditis, pulseless electrical activity after

**Figure 2** Chest radiographic image showing His lead placement with CRT-D system in a patient with nonischemic cardiomyopathy in whom nonselective His-bundle capture achieved QRS narrowing from 172 to 125 ms. CRT = cardiac resynchronization therapy; HB = His bundle; ICD = implantable cardioverter–defibrillator; RA = right atrium.
appropriate ventricular fibrillation shock, and progression of heart failure in the chronic debilitated state (intensive care unit >3 months). All occurred within 2 months of implantation. One patient with a previous transcatheter aortic valve replacement developed an *Enterococcus faecalis* bacteremia and underwent device extraction.

**Discussion**

The major findings of the present study are as follows:

1. Electrical resynchronization via HBP was achieved in 76% of patients presenting with bundle branch block who had an indication for CRT.
2. Incorporation and programming of an HBP lead into the LV port in a standard CRT-D or CRT-P system is feasible.
3. Fifteen of 16 patients with QRS narrowing demonstrated nonselective His capture, with 1 case of selective His capture.
4. Favorable echocardiographic indices with improvement in EF, reduction in LV size, and improvement in NYHA functional class were observed in this cohort of patients with nonselective HBP.

Normalization of bundle branch block pattern was first reported by Narula et al in the 1970s, in which stimulation of the distal, but not proximal, His resulted in QRS narrowing. This finding fueled the theory of longitudinal dissociation within the His bundle and was confirmed one year later in a small series of six patients by El-Sherif et al. However, longitudinal dissociation of the His bundle may exist only in pathologic disease states. It is notable that we did not observe split His local electrograms in any patient in this cohort.

HBP captures the normal conduction system and results in more physiologic activation of the heart. The first published series of permanent HBP was presented in 2000 by Deshmukh et al in a patient cohort with chronic atrial fibrillation and cardiomyopathy. Favorable improvements in EF (11%) were observed, although all patients had narrow QRS (<120 ms), and the majority of patients underwent AV nodal ablation. Although the feasibility of permanent HBP...
was demonstrated in the largest published series to date in patients with narrow QRS by Sharma et al., only 2 studies reported HBP in lieu of LV lead. Su et al. first demonstrated the feasibility of His-bundle incorporation in CRT-D with optimized thresholds using an HB tip to RV coil configuration in a series of 16 patients for permanent CRT-D, but they did not emphasize clinical and echocardiographic outcomes. Barba-Pichardo et al. reported a series of 16 patients with indication for CRT and failed coronary sinus LV lead implant. Although 81% of this nonconsecutive cohort could achieve normalization of wide QRS, only 9 patients underwent successful permanent implantation for resynchronization (QRS duration 166 to 97 ms). All patients experienced an improvement in EF (29% to 36%; P < .05), reduction in left ventricular end-diastolic dimension (LVEDD) (66 to 60 mm; P < .01), and improvement from NYHA functional class III to II at follow-up of 31 ± 21 months. Despite small increases in threshold observed (3.09 to 3.7; P < .05) at follow-up, no capture loss of dislodgment was observed. Our results are consistent with these findings, and, to

Figure 4  Selective His-bundle capture with QRS narrowing and an isoelectric segment (44 ms) between pacing stimulus and QRS, which is shorter than the intrinsic HV interval (76 ms). LBBB = left bundle branch block.

Figure 5  Two patients with incomplete narrowing of QRS during attempted His-bundle pacing. A nonselective response (top) narrows the QRS <20%, and an isoelectric segment precedes a similar wide QRS left bundle branch block pattern (bottom). Both patients underwent placement of a left ventricular lead via the coronary sinus.
the best of our knowledge, the current study is the largest multicenter series examining permanent HBP with the intention of achieving CRT in patients with bundle branch block. The long-term stability and durability of results require further longitudinal follow-up and cannot be discerned from the present study.

The achievement of physiologic pacing has several potential advantages over an epicardial LV lead. Optimal LV lead placement may be limited by venous anatomy and proximity to phrenic nerve. LV epicardial stimulation has been shown to have neutral to modest effects in patients with apical lead positions and wall-motion abnormality, ischemic cardiomyopathy, and non-LBBB QRS morphologies. In this study, patients with LBBB and those with RBBB achieved narrowing with HBP, although patients with nonspecific intraventricular conduction delay were not studied. Importantly, biventricular stimulation has been shown to result in persistent dyssynchronous contraction of the heart. In addition, with nonphysiologic reversal of epicardial to endocardial LV activation wavefront, concerns of proarrhythmia, although rare, have been substantiated.

The definitions of selective and nonselective His-bundle capture that have been proposed for narrow QRS patients, for whom selective and “pure” His capture requires a post-pacing isoelectric segment equal to the HV interval, may not apply to patients with wide QRS. We observed only one patient who met the criteria for selective His capture, with S–QRS interval shorter than native HV intervals. It is likely that at higher outputs, capture more distal in the conduction system is possible or overcomes the local tissue safety factor sufficiently to allow capture of previously latent diseased His–Purkinje tissue. Both scenarios may account for isoelectric intervals that are shorter than the HV interval. Barba-Pichardo reported “pure” His capture in 3 of 9 patients, although stimulus-to-QRS intervals were shorter than expected HV intervals in both examples provided. The nomenclature of physiologic pacing may also require further refinement as the cumulative experience increases with specific attention to mechanisms.

Lustgarten et al were the first to demonstrate the feasibility of permanent HBP as a first-line approach, using a crossover study design. In an innovative prospective crossover study that featured a Y-adaptive connection that enabled both pacing modalities, they showed equivalence in favorable clinical and echocardiographic outcomes between LV lead and HBP in 21 of 29 patients. The present data complement and extend the findings that patients receiving a His-bundle lead in lieu of a standard LV lead demonstrate electrical synchronization and echocardiographic improvement with stand-alone permanent HBP. Lustgarten et al demonstrated that 72% of patients had QRS narrowing, and cases of both selective and nonselective HBP capture advanced the LV activation time. Of 10 patients studied, only 2 were reported to exhibit selective His-bundle capture with narrowing of QRS, although the illustration provided also does not exhibit an isoelectric interval equal an expected HV interval.

This initial feasibility study suggests that nonselective His capture may be sufficient for CRT, as the majority of patients studied demonstrated improvements in EF, LV diameter, and NYHA functional class. The extent of myocardium activated in cases of nonselective capture during the pseudo-delta interval is not known. Further studies are needed to assess the exact mechanisms by which “pure” His capture and QRS narrowing are achieved and whether there is differential benefit between selective and nonselective capture. We believe that the present data add to the existing body of single-center experiences by suggesting a role for HBP in CRT patients. Because of the reported nonresponse rate of 30%–40% with an LV lead, clinical equipoise exists to compare HBP with standard LV lead prospectively in a multicenter pilot study design (His Bundle Pacing Versus Coronary Sinus Pacing for Cardiac Resynchronization Therapy [His-SYNC], ClinicalTrials.gov Identifier: NCT02700425).
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Etiology</th>
<th>Baseline EF (%)</th>
<th>NYHA</th>
<th>CRT type</th>
<th>QRS pattern</th>
<th>Baseline QRS (ms)</th>
<th>HV interval (ms)</th>
<th>Paced QRS (ms)</th>
<th>Implant His threshold (V)</th>
<th>Pulse width (ms)</th>
<th>Lead impedance</th>
<th>Follow-up EF (%)</th>
<th>NYHA functional class</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>74</td>
<td>F</td>
<td>NICM</td>
<td>15</td>
<td>III</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>170</td>
<td>67</td>
<td>123</td>
<td>2.00</td>
<td>0.6</td>
<td>513</td>
<td>55</td>
<td>I</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>M</td>
<td>NICM</td>
<td>33</td>
<td>III</td>
<td>CRT-D</td>
<td>RBBB</td>
<td>174</td>
<td>45</td>
<td>145</td>
<td>1.30</td>
<td>0.5</td>
<td>576</td>
<td>dc</td>
<td>II</td>
<td>dc</td>
</tr>
<tr>
<td>3</td>
<td>81</td>
<td>M</td>
<td>NICM</td>
<td>33</td>
<td>III</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>172</td>
<td>65</td>
<td>125</td>
<td>5.00</td>
<td>0.5</td>
<td>513</td>
<td>45</td>
<td>I</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>51</td>
<td>F</td>
<td>NICM</td>
<td>23</td>
<td>III</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>192</td>
<td>63</td>
<td>136</td>
<td>1.25</td>
<td>0.5</td>
<td>589</td>
<td>23</td>
<td>III</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>55</td>
<td>M</td>
<td>NICM</td>
<td>33</td>
<td>III</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>200</td>
<td>74</td>
<td>112</td>
<td>3.00</td>
<td>0.8</td>
<td>442</td>
<td>40</td>
<td>II</td>
<td>16</td>
</tr>
<tr>
<td>6</td>
<td>92</td>
<td>M</td>
<td>NICM</td>
<td>28</td>
<td>IV</td>
<td>CRT-P</td>
<td>LBBB</td>
<td>232</td>
<td>n/a</td>
<td>140</td>
<td>0.75</td>
<td>0.4</td>
<td>791</td>
<td>35</td>
<td>II</td>
<td>19</td>
</tr>
<tr>
<td>7</td>
<td>73</td>
<td>M</td>
<td>NICM</td>
<td>14</td>
<td>III</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>213</td>
<td>76</td>
<td>160</td>
<td>0.50</td>
<td>0.5</td>
<td>544</td>
<td>n/a</td>
<td>III</td>
<td>n/a</td>
</tr>
<tr>
<td>8</td>
<td>64</td>
<td>M</td>
<td>NICM</td>
<td>45</td>
<td>III</td>
<td>CRT-P</td>
<td>LBBB</td>
<td>159</td>
<td>76</td>
<td>125</td>
<td>3.50</td>
<td>0.5</td>
<td>560</td>
<td>55</td>
<td>I</td>
<td>17</td>
</tr>
<tr>
<td>9</td>
<td>67</td>
<td>M</td>
<td>NICM</td>
<td>28</td>
<td>III</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>163</td>
<td>n/a</td>
<td>120</td>
<td>0.75</td>
<td>0.5</td>
<td>550</td>
<td>60</td>
<td>II</td>
<td>12</td>
</tr>
<tr>
<td>10</td>
<td>43</td>
<td>M</td>
<td>NICM</td>
<td>16</td>
<td>III</td>
<td>CRT-D</td>
<td>RBBB</td>
<td>172</td>
<td>65</td>
<td>138</td>
<td>2.00</td>
<td>0.5</td>
<td>640</td>
<td>25</td>
<td>n/a</td>
<td>6</td>
</tr>
<tr>
<td>11</td>
<td>58</td>
<td>M</td>
<td>NICM</td>
<td>23</td>
<td>III</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>164</td>
<td>n/a</td>
<td>128</td>
<td>1.00</td>
<td>0.4</td>
<td>931</td>
<td>n/a</td>
<td>I</td>
<td>n/a</td>
</tr>
<tr>
<td>12</td>
<td>64</td>
<td>M</td>
<td>NICM</td>
<td>28</td>
<td>II</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>174</td>
<td>59</td>
<td>130</td>
<td>1.00</td>
<td>0.5</td>
<td>460</td>
<td>42</td>
<td>II</td>
<td>4</td>
</tr>
<tr>
<td>13</td>
<td>69</td>
<td>M</td>
<td>NICM</td>
<td>74</td>
<td>III</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>198</td>
<td>74</td>
<td>121</td>
<td>2.00</td>
<td>1.0</td>
<td>513</td>
<td>28</td>
<td>I</td>
<td>7</td>
</tr>
<tr>
<td>14</td>
<td>39</td>
<td>F</td>
<td>NICM</td>
<td>20</td>
<td>IV</td>
<td>CRT-D</td>
<td>RBBB</td>
<td>195</td>
<td>48</td>
<td>125</td>
<td>2.25</td>
<td>1.0</td>
<td>418</td>
<td>dc</td>
<td>n/a</td>
<td>dc</td>
</tr>
<tr>
<td>15</td>
<td>81</td>
<td>M</td>
<td>ICM</td>
<td>27</td>
<td>III</td>
<td>CRT-D</td>
<td>RBBB</td>
<td>140</td>
<td>CHB</td>
<td>120</td>
<td>1.10</td>
<td>0.5</td>
<td>463</td>
<td>n/a</td>
<td>II</td>
<td>3</td>
</tr>
<tr>
<td>16</td>
<td>68</td>
<td>F</td>
<td>NICM</td>
<td>16</td>
<td>IV</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>168</td>
<td>71</td>
<td>114</td>
<td>2.80</td>
<td>1.0</td>
<td>440</td>
<td>dc</td>
<td>IV</td>
<td>dc</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete QRS narrowing treated with standard LV lead</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>54</td>
<td>M</td>
<td>NICM</td>
<td>23</td>
<td>III</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>172</td>
<td>73</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>M</td>
<td>ICM</td>
<td>26</td>
<td>III</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>142</td>
<td>48</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>67</td>
<td>M</td>
<td>ICM</td>
<td>28</td>
<td>II</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>130</td>
<td>65</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>74</td>
<td>F</td>
<td>NICM</td>
<td>25</td>
<td>III</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>175</td>
<td>71</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td>F</td>
<td>ICM</td>
<td>28</td>
<td>II</td>
<td>CRT-D</td>
<td>LBBB</td>
<td>133</td>
<td>76</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CRT = cardiac resynchronization therapy; dc = deceased; EF = ejection fraction; ICM = ischemic cardiomyopathy; LBBB = left bundle branch block; LV = left ventricle; n/a = not available; NICM = nonischemic cardiomyopathy; NYHA = New York Heart Association; RBBB = right bundle branch block.
Study limitations

The present initial feasibility study is a small cohort by design, and the generalizability to all patients meeting CRT criteria is limited. The inclusion of patients in this cohort were nonconsecutive, which may introduce inclusion bias because not all patients meeting CRT criteria at both institutions during the study time period were approached equally by all operators. Implantation at a His-bundle location is operator dependent, which likely impacts the extent to which selective His-bundle capture can be achieved, and a learning curve is present. Because of the nature of tertiary referral centers and the observational design of this feasibility cohort, clinical follow-up was nonuniform, and 3 patients were lost to follow-up. Furthermore, the recognition and definition of subtle changes in morphology between nonselective His capture and parahisian capture may affect the exact determination of pacing thresholds. In theory, there may be 4 distinct pacing thresholds from a permanent His bundle lead: (1) parahisian myocardial capture, (2) nonselective capture, (3) selective capture without normalization, and (4) selective capture with QRS normalization. Due to the retrospective nature of this study analysis, we only reported the nonselective His capture threshold, which was retrievable in every patient. Optimal AV and VV intervals cannot be discerned from the present data.

The proposed nomenclature for His-bundle capture to differentiate “nonselective” and “selective” capture was applied to patients with narrow QRS morphology. Although we chose to use these definitions to classify our cases that exhibited nonselective capture, it is possible that selective His-bundle capture can occur with shorter S–QRS than recorded HV intervals in patients with bundle branch block.21 Higher-output pacing may capture distal to the recorded local electrogram. However, it also is possible that myocardial recruitment can occur within the isoelectric segment without a critical mass to comprise a pseudo-delta wave.

Additional mechanistic investigation to assess septal myocardial recruitment during HBP, such as that performed by Lustgarten et al,11 is necessary to understand the nature and frequency of selective His-bundle capture and whether S–QRS relative to the intrinsic HV interval criteria needs to be revised in patients with bundle branch block. The inclusion of local ventricular electrogram capture on the His lead may be the most specific criterion to distinguish selective from nonselective His capture compared to surface ECG appearance after the pacing stimulus. In this study, we did not systematically print out the His lead electrogram from the analyzer during pacing; therefore, these data could not be retrieved. Finally, HV interval measurements may be influenced by the size and configuration of the recording electrode, particularly differences between the diagnostic catheter and fixed pacing lead.

Conclusion

Permanent HBP is feasible for patients with an indication for CRT using the LV port in lieu of a coronary sinus lead. In this initial experience, QRS duration narrowing was achieved in 76% of patients with bundle branch block, and improvements in clinical and echocardiographic measures were observed with His-bundle capture. Future prospective comparative studies with HBP to achieve CRT are justifiable.
Acknowledgment
The authors thank Weijian Huang, MD, PhD, for sharing his experience with His-bundle pacing.

Appendix
Supplementary data
Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.hrthm.2017.04.003.

References