Left bundle branch pacing for symptomatic bradycardia: Implant success rate, safety, and pacing characteristics

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BACKGROUND In patients with or without left bundle branch block, left bundle branch pacing (LBBP) can produce near normalization of QRS duration (QRSd). This has recently emerged as an alternative technique to His bundle pacing.

OBJECTIVES The purpose of this study was to characterize a novel approach for LBBP in patients with bradycardia indications for pacing and to assess implant success rate and midterm safety.

METHODS Patients with bradycardia indications for pacing underwent LBBP by a trans-ventricular-septal method in the basal ventricular septum. Procedural success, pacing parameters, and complications were assessed at implantation and at 3 months follow-up.

RESULTS This prospective study evaluated 87 patients (sinus node dysfunction 67.8%; atrioventricular conduction disease 32.2%) undergoing pacemaker implantation. LBBP implantation succeeded in 80.5% (70/87) of patients and the remaining 17 patients received right ventricular septal pacing. The procedure time of LBBP implantation was 18.0 ± 8.8 minutes with a fluoroscopic exposure time of 3.9 ± 2.7 minutes. LBBP produced narrower electrocardiographic QRSd than did right ventricular septal pacing (113.2 ± 9.9 ms vs 144.4 ± 12.8 ms; P < .001). There were no major implantation-related complications. The pacing threshold was low (0.76 ± 0.22 V at implantation and 0.71 ± 0.23 V at 3 months), with no loss of capture or lead dislodgment observed.

CONCLUSION This study demonstrates that in patients with standard bradycardia pacing indications, LBBP results in QRSd < 120 ms in most patients and can be performed successfully and safely in the majority of patients.

KEYWORDS Bradycardia; Left bundle branch pacing; Pacemaker; Physiological pacing; Success rate

Introduction
Cardiac pacing is the only effective therapy for patients with symptomatic bradycardia in the absence of reversible causes. Traditional right ventricular apical pacing (RVAP) has been widely used for ~ 50 years. However, RVAP can lead to ventricular electrical and mechanical asynchrony in patients who need frequent pacing. As a consequence of such effects, RVAP is associated with an increased risk of heart failure, mitral valve dysfunction, and atrial fibrillation.1–3 Pacing at alternative right ventricular sites, such as the septum or outflow tract, has not been shown to be superior to RVAP.3–5 Accordingly, there has been increased interest in physiological pacing techniques. His bundle pacing (HBP) is the most commonly used approach,6,7 with multiple studies demonstrating feasibility and clinical benefits.8–11 However, HBP also has some limitations, including high and unstable pacing threshold, low R-wave amplitude, damage to the His bundle during implantation, and potential limitations in long-term performance.5,12 To help address these issues, techniques for pacing the left bundle branch in patients with left bundle branch block (LBBB) were developed.13,14 We recently reported the first clinical implementation of left bundle branch pacing (LBBP) achieved by a trans-ventricular-septal approach in patients with bradycardia, which demonstrated a low and stable pacing threshold and large R-wave amplitude and shorter paced QRS duration (QRSd) compared to RV septal and apical
pacing.14 The aim of the present study was to assess success rate, safety, pacing characteristics, and midterm outcomes of LBBP.

Methods
Patient selection
From October 2017 to October 2018, patients who had symptomatic bradycardia with an indication for pacemaker implantation according to 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy underwent LBBP attempts at Beijing Fuwai Hospital after informed written consent was obtained. Patients were excluded if they underwent cardiac resynchronization therapy or implantable cardioverter-defibrillator implantation. This study was approved by the hospital institutional review board.

Lead implantation
An intracardiac electrogram (EGM) from the lead tip and a 12-lead surface electrocardiogram (ECG) were simultaneously recorded on a multichannel Bard recorder (Bard Electrophysiology Lab System, MA).

LBBP was achieved by the trans-ventricular-septal method in the basal ventricular septum (Supplemental PowerPoint Presentation) and performed by using the Select-Secure pacing lead (model 3830 69 cm, Medtronic Inc., Minneapolis, MN) delivered through a fixed curve sheath (C315 HIS, Medtronic Inc., Minneapolis, MN). During implantation, the tip electrode of the lead was used for unipolar pacing and recording. There were 2 methods of LBBP lead implantation. The first technique used the His bundle region as an anatomical marker. Briefly, the delivery sheath with the lead tip just beyond the distal part of the sheath in the right anterior oblique (RAO) 30° projection was first inserted into the His bundle region where the His bundle potential was recorded. The His bundle region was referred as a marker, and the sheath with the lead was further advanced toward the ventricular septum. Once the lead touched the right side of the septum and the paced QRS morphology showed ECG LBBB morphology during pacing with an output of 5 V/0.5 ms, the lead was pointed toward the left side of the septum and screwed in place. During the lead advancement procedure, paced QRS morphology and pacing impedance were closely monitored. Once the paced QRS morphology showed right bundle branch delay (RBBD; usually QR or rSR in ECG lead V1/2) or near-normal QRS complex, the lead advancement was stopped. In the second technique, the sheath was directly inserted into the right ventricle and the pacing lead was advanced through the sheath such that only the distal part was beyond the tip of the sheath. Subsequently, the sheath and the lead touched the right side of the septum and pacing with an output of 2.0 V/0.5 ms was applied. Once the paced ECG QRS morphology presented as LBBB morphology frequently with a notch (also called “W” waveform) at the nadir of the QRS waveform in ECG lead V5, the lead was fixed at this position with 4–5 clockwise rotations. A high-quality fluoroscopic radiograph confirmed the tip of the lead toward the septum in the left anterior oblique (LAO) 30° projection. Then the lead was screwed toward the left side of the septum in the RAO 30° projection. Once the paced QRS morphology became RBBD or near-normal QRS complex, the lead advancement was stopped. The depth of the lead inside the ventricular septum could be estimated by fluoroscopic imaging with contrast injection (Supplemental Video 1). If an acceptable LBBP could not be achieved after attempts at 3 locations, the lead was placed in the right ventricular septum.

As shown in Figure 1, in some special cases, especially in patients with bundle branch block, 2 sets of 3830 lead and C315 HIS delivery sheath were used to find an optimal pacing site. The first lead was placed in the His bundle region as an anatomical marker, and the second lead was then positioned in the left bundle branch region. Once LBBP was acceptable, the first lead was then moved to the right atrium.

Definitions
The criteria for LBBP were as defined previously14: (1) a left bundle branch potential could be recorded; (2) the interval from pacing to ECG QRS onset was significantly shorter than the interval of His pacing to ECG QRS onset reported previously; (3) the 12-lead ECG showed the pattern of RBBD during LBBP or correction of LBBB if the patient had ECG LBBB; and (4) a fast left ventricular (LV) peak activation time in ECG lead V5/6 was observed.

Selective LBBP is defined as follows:
1. There is an isoelectric interval between pacing spike and ECG QRS complex.
2. The pacing spike–QRS interval is almost identical with the left bundle potential–QRS interval.
3. A local ventricular EGM is present as a discrete component.

Nonselective LBBP is defined by the following criteria:
1. There is no isoelectric interval between pacing spike and ECG QRS complex.
2. The local ventricular EGM shows direct capture of local tissue by the pacing stimulus.

Examples of selective and nonselective LBBP are shown in Figures 2 and 3.

Device programming
Ventricular safety pacing and auto capture management were activated. Atrioventricular (AV) delay programming should be individualized, taking into consideration AV conduction times and the presence of heart block. The automatic AV search function was routinely turned on in patients with sick sinus syndrome and intermittent AV block.

Data collection and follow-up
Demographic data and medical history were collected at enrollment. Pacing electrical parameters (pacing threshold, lead impedance, and R-wave amplitude), ECG and
intracardiac EGM pattern, QRSd, LV peak activation time, the pacing spike-QRS interval, the amplitude of the left bundle branch potential, the interval from the left bundle branch potential to the beginning of ECG QRS complex, fluoroscopy exposure time, and imaging data were recorded during implantation. Patients were followed at predischarge and 3 months. Pacing electrical parameters were recorded at outpatient visit. Complications such as significant increases in pacing threshold, loss of capture, and lead dislodgement were tracked during follow-up visits.

**Statistical analysis**

The mean and standard deviation were used as the descriptive statistics for continuous variables and the number and percentage as descriptive statistics for categorical variables. Differences between 2 groups were compared using the Student $t$ test for continuous variables. The paired $t$ test was used to compare the differences between 2 means within the same group. An analysis of variance test was performed for multiple comparisons among ≥3 conditions, and post hoc tests with least-significant difference were performed for the variables that showed a statistically significant difference. A 2-sided $P$ value of $<$ .05 was considered statistically significant. All statistical analyses were performed using SPSS Statistics version 22.0 (Chicago, IL, USA).

**Results**

Between October 2017 and October 2018, a total of 87 patients with bradycardia underwent LBBP attempts. Indications for pacemaker implantation were sinus node dysfunction in 67.8% (59/87) of patients and AV conduction disease in 32.2% (28/87) of patients. The LV ejection fraction was 62.9% ± 5.6%. The baseline patient characteristics are summarized in Table 1.

**Implantation results**

LBBP was successful in 80.5% (70/87) of patients, and the remaining 17 patients received right ventricular septal pacing (RVSP). For LBBP, a single-chamber pacemaker was implanted in 2.9% (2/70) of patients and a dual-chamber pacemaker in 97.1% (68/70) of patients. The mean procedure time of LBBP implantation was 18.0 ± 8.8 minutes with a fluoroscopic exposure time of 3.9 ± 2.7 minutes. The cause of unsuccessful LBBP implantation was the failure of the lead tip to advance successfully to the left side of the septum. In these
instances, the lead tip remained on the right side of the septum or was in the middle of the septum but could not reach the left side of the septum. Possible causes of these failures may be related to the direction that the tip advanced with deployment, lead design limitation, or local hypertrophied myocardium.

**ECG characteristics**
There was a typical transition of ECG morphology during the lead implantation for LBBP. During the process of deploying the pacing lead from the right to the left side of the septum, the paced ECG morphology changed from LBBB to RBBD with a gradual change in the notch morphology in lead V1 (Figure 4).

The mean QRSd was 105.5 ± 22.2 ms, and the paced QRSd was 113.2 ± 9.9 ms ($P < .05$). During the implantation procedure, the paced QRSd during LBBP was significantly shorter than during pacing at the right side of the septum (113.2 ± 9.9 ms vs 139.5 ± 12.8 ms; $P < .001$).

Moreover, QRSd was <120 ms in 80% (56/70) of patients with LBBP and no patient with RVSP (0%) ($P < .001$). The LV peak activation time was 79.7 ± 8.5 ms during LBBP, which is shorter than during pacing at the right side of the septum (103.3 ± 11.4 ms; $P < .001$). A left bundle branch potential was recorded in 66% (46/70) of patients, with a mean amplitude of 0.17 ± 0.16 mV. LBB potential injury current was observed in 78% (36/46) of patients.

The interval from the left bundle branch potential to the onset of the QRS on the surface ECG was 25.6 ± 4.7 ms. There was a trend toward shorter paced QRSd in patients with recorded left bundle branch potential during intrinsic rhythm compared with patients without left bundle branch potential (110.7 ± 9.0 ms vs 116.2 ± 11.0 ms; $P = .069$).

During selective LBBP, the pacing-QRS interval was 28.0 ± 5.0 ms, which was similar to the left bundle potential–QRS interval (25.6 ± 4.7 ms). During nonselective LBBP, there was no delay in the onset of the QRS with no isoelectric interval.

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**Figure 2** Twelve-lead electrocardiogram and electrogram during left bundle branch (LBB) pacing in a patient with sinus node dysfunction. A: The LBB potential during intrinsic rhythm (red asterisk). B: Selective LBB pacing with a discrete local ventricular electrogram (black arrows) at the LBB pacing threshold (0.2 V/0.5 ms). C: Nonselective LBB pacing with local myocardial fusion (red circle) during pacing at 0.5 V/0.5 ms; there is no discrete local ventricular electrogram.
Pacing electrical parameters and complications
All patients completed predischarge follow-up, and 47 patients reached 3 months postimplantation and completed 3 months follow-up. Pacing threshold, R-wave amplitude, and lead impedance at implantation, predischarge, and after 3 months are summarized in Table 2. During follow-up, the pacing threshold remained low while the R-wave amplitude increased and pacing impedance decreased over the follow-up time.

During the implantation procedure, there were no major implantation-related complications. One patient who was receiving dual antiplatelet therapy developed a pocket hematoma. In 11 patients, right bundle branch block developed during the implantation procedure that resolved in all subjects before hospital discharge. No patient showed loss of capture nor lead dislodgment during follow-up.

Discussion
The present study describes implantation and 3-month follow-up of a novel approach for LV pacing to achieve more physiological ventricular activation compared to RVSP. The main findings of this study are that a high success rate of LBBP (80.5%) can be achieved with stable and low pacing thresholds over midterm follow-up. Moreover, there

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>63.8 ± 11.4</td>
</tr>
<tr>
<td>Men</td>
<td>31 (35.6)</td>
</tr>
<tr>
<td>Sinus node dysfunction</td>
<td>59 (67.8)</td>
</tr>
<tr>
<td>AV conduction disease</td>
<td>28 (32.2)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>22 (25.3)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18 (20.7)</td>
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<tr>
<td>Hypertension</td>
<td>50 (57.5)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>20 (22.7)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>62.9 ± 5.6</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>47.8 ± 5.1</td>
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<tr>
<td>Dual-chamber pacemaker implanted</td>
<td>84 (96.6)</td>
</tr>
<tr>
<td>Single-chamber pacemaker implanted</td>
<td>3 (3.4)</td>
</tr>
<tr>
<td>QRSd (ms)</td>
<td>106.8 ± 23.3</td>
</tr>
<tr>
<td>Normal QRS complex, LBBB, RBBB</td>
<td>76 (87.4), 6 (6.9), 5 (5.7)</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD for continuous variables and as n (%) for categorial variables.

AV = atrioventricular; LBBB = left bundle branch block; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; QRSd = QRS duration; RBBB = right bundle branch block.
were no serious complications resulting from this procedure. Of note, previous studies have shown successful LBBP, but the success rate and more long-term pacing stability from a large consecutive series have not been reported.\textsuperscript{13,14}

The QRSd on the surface ECG is a surrogate of ventricular activation time. It is interesting that the mean QRSd was <120 ms despite selective LBBP, which would be expected to produce complete right bundle branch block. This finding may be due to retrograde activation of the right bundle with pacing or connections between the main right and left bundles.\textsuperscript{15,16} Further studies are needed to help sort out the mechanism of relatively short paced QRSds with this technique. Mafi-Rad et al\textsuperscript{17} investigated LV septal pacing by a transvenous approach through the interventricular septum and found that QRSd was shorter during LV septal pacing (144 ± 20 ms) than during RVAP (172 ± 33 ms). Since the pacing lead in Mafi-Rad’s study might not be at or near the left bundle branch, QRSd (144 ± 20 ms) in that study seems much longer than that during LBBP (113 ± 10 ms) in our study.

The success rate of LBBP in this series is similar to what has been reported with early attempts at HBP.\textsuperscript{18} Further studies are needed to understand both the learning curve of this technique as well as the limitations of successful LBB capture. Possible explanations for failure to achieve LBB capture include the following: (1) the inability of the lead to penetrate sufficiently deep in the septum to reach the left bundle; (2) the sheath being malpositioned such that the lead is not advanced perpendicular to the ventricular septum (Supplemental Figure S1); (3) the failure of the lead tip to be deployed to the left side of the septum because of lead design limitation or local hypertrophied myocardium. During lead deployment, the flexibility of the delivery sheath, especially the distal part, might decrease by repeated procedural maneuvers, such that the lead tip could not be advanced through the sheath. This is also the possible reason for failure of achieving LBB capture. It is common to reposition pacing leads during RVAP and RVSP. However, LBBP is achieved by the trans-ventricular-septal method in the basal ventricular septum, so multiple repositioning attempts could cause damage to myocardial tissue and even possible perforation. Thus, we limited the number of LBBP attempts as a precaution, which may have decreased the success rate.

In 2000, Deshmukh et al\textsuperscript{19} conducted the pioneering investigation of permanent HBP by using a traditional pacing lead in a small number of patients with heart failure and achieved a success rate of 66%. The development of site-selective implantation tools, including the 3830 pacing lead.

Table 2 Electrical parameters

<table>
<thead>
<tr>
<th>Visit</th>
<th>Pacing threshold (V)</th>
<th>R-wave amplitude (mV)</th>
<th>Impedance (Ω)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At implantation (n = 70)</td>
<td>0.76 ± 0.22</td>
<td>11.99 ± 5.36</td>
<td>700.14 ± 134.87</td>
</tr>
<tr>
<td>Predischarge (n = 70)</td>
<td>0.51 ± 0.10*</td>
<td>16.16 ± 6.48*</td>
<td>501.01 ± 96.88*</td>
</tr>
<tr>
<td>3-mo follow-up (n = 47)</td>
<td>0.71 ± 0.23*</td>
<td>16.90 ± 6.78*</td>
<td>472.40 ± 91.41*</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD.

*P < .001 at implantation vs predischarge and 3-mo follow-up.

\textsuperscript{1}P < .001 predischarge vs 3-mo follow-up.
and the C315 HIS delivery sheath, made HBP more feasible.\textsuperscript{20} Vijayaraman et al\textsuperscript{21} reported the success rate of 95\% in 42 patients with atrial fibrillation undergoing AV node ablation in an experienced center. To date, the success rate of HBP has been reported to vary from 56\% to 95\%,\textsuperscript{22–26} which is similar to the success rate of 80.5\% with LBBP in the present study. With the improvement of implantation tools and techniques for standardized LBBP implantation, we expect an increase in success rate. The mean duration of fluoroscopy for HBP had ranged from 8 to 23 minutes.\textsuperscript{8,22,27} LBBP was performed with significantly short fluoroscopic exposure time (3.9 ± 2.7 minutes) in the present study, which may be another benefit of this approach.

Our previous study had demonstrated shorter QRSd with LBBP than with either RVSP or RVAP, suggesting that LBBP produces better ventricular electrical synchronization.\textsuperscript{14} Similar results were shown in the present study using a different method to perform LBBP. Monitoring the paced ECG while deploying the lead was helpful to guide lead placement. During implantation, the ECG transition was continuously monitored and checked with every 2–3 turns of the lead helix. A notch (“W” waveform) in lead V\textsubscript{1} gradually shifted and finally disappeared when the tip was advanced from the right to the left side of the septum. This observation can be used as a safety check to determine where the pacing lead is in the septum and when the advancement of the pacing lead should be stopped. In contrast, no change in ECG morphology with advancement of the lead suggests that the lead was not advanced into the left side of the septum or this position was not suitable for LBBP. In this scenario, the lead should be repositioned.

In the present study, we demonstrate evidence for both selective and nonselective capture of the LBB. Given the immediate proximity of the muscular septum and nonpenetrating portion of the left bundle, nonselective capture would be expected intuitively to be the more probable pattern. However, selective capture can be observed, especially at low output and/or pulse width. An example of the latter is seen in Figure 3, where selective capture occurs at a pulse width of 0.06 ms. The clinical implications of these findings are not currently known and will require further study.

As LBBP is achieved by the trans-ventricular-septal method, ventricular septum perforation can occur. However, because the diameter of the current lead is 1.4 mm, no serious ventricular septal defect is expected even if perforation occurs. Nevertheless, it is important to monitor the transition of the paced QRS morphology, lead impedance, and pacing threshold. A low capture threshold and high pacing impedance suggested that the pacing lead remained in the septum while a sudden decrease in lead impedance and loss of capture indicated the tip of the lead entering the left ventricle. The thickness of the ventricular septum is normally 6–11 mm. The helix electrode length of the lead is 1.8 mm, and the space from the ring electrode to the helix is 9 mm. The onset of the ring electrode capture at an output of 5 V\textsubscript{0}0.5 ms suggests that the tip of the lead is likely at or near the left side of the ventricular septum. Any further advancement of the lead should be conducted carefully. It is noteworthy that no implant complications were noted when taking these precautions.

There are several advantages of LBBP over HBP. First, high pacing threshold and threshold increase over time are relatively frequent with HBP, likely because of the anatomical characteristics of the His bundle, inadequate fixation, local fibrosis, tricuspid valve motion, and pathological progression in the His bundle region. The HBP capture threshold shows a clinically significant increase over time in ~10\% patients.\textsuperscript{28} LBBP is achieved by the trans-ventricular-septal method, and the pacing lead is positioned in the basal ventricular septum. The left bundle branch usually spreads below the membranous septum with well-defined dimensions, and there is less fibrosis wrapped than the His bundle.\textsuperscript{29} Thus, it is not surprising that a lower pacing threshold was noted. Second, because the pacing lead tip of LBBP bypasses the vulnerable region of the His bundle, the pacing threshold is stable. Third, since the pacing tip is fixed at or near the left bundle branch with nearby myocardial tissue and the myocardium can be captured at the pacing output, there is no need to implant a backup lead in case of loss of capture. Finally, the R-wave amplitude recorded at the site of LBBP is high, which is important for appropriate sensing and capture management by a pacemaker. HBP mimics native conduction since both fascicles are activated antegradely; however, LBBP maintains antegrade activation of the left fascicular system and often generates a near-normal QRS complex, possibly because of retrograde or trans-ventricular-septal activation of the RBB.

Limitations

This study should be interpreted in light of certain methodological limitations. First, the sample size was relatively small as a single-center study. More data are needed to confirm our findings. Selective LBBP may not be clearly observed at implantation because the far-field recording by the pacing lead is used and may not show the discrete EGM for selective LBBP. Second, more long-term follow-up is needed to assess the stability of pacing in this region of the heart. Finally, the role of LBBP needs to be explored for other pacing indications such as cardiac resynchronization therapy.

Conclusion

Using the technique described in this article, we were able to safely and successfully perform LBBP in 80.5\% of patients in a consecutive series. The accurate location for LBBP can be targeted during implantation given the characteristic changes in paced QRS morphology during lead deployment. The low pacing output and high R-wave amplitude during LBBP favor long-term pacing management and device longevity. LBBP produces a narrow QRSd and short LV peak activation time, suggesting synchronized ventricular activation. LBBP may be an ideal option for patients in need of ventricular pacing once long-term safety and clinical benefits are confirmed.
References