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His bundle combined with deep septal left bundle branch area pacing for atrial fibrillation prior to atrioventricular node ablation

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Abstract

Background: To mitigate the risk of dyssynchrony-induced cardiomyopathy, international guidelines advocate His bundle pacing (HBP) with a ventricular backup lead prior to atrioventricular node ablation in treatment-refractory atrial fibrillation and normal left ventricular ejection fraction. As a result of concerns with long-term pacing parameters associated with HBP, this case series reports an adopted strategy of HBP combined with deep septal left bundle branch area pacing (dsLBBAP) in this patient cohort, enabling intrapatient comparison of the two pacing methods.

Methods and Results: Eight patients aged 72 ± 10 years (left ventricular ejection fraction 53 ± 4%) underwent successful combined HBP and dsLBBAP implant prior to AV node ablation. Intrinsic QRS duration was 118 ± 46 ms. When compared to dsLBBAP, HBP had lower sensed ventricular amplitude (2.4 ± 1.1 vs. 15 ± 5.3 V, p = .001) and lower lead impedance (522 ± 57 vs. 814 ± 171ohms, p = .02), but shorter paced QRS duration (101 ± 20 vs. 119 ± 17 ms, p = .02). HBP pacing threshold was 1.0 ± 0.6 V at 1 ms pulse width, and dsLBBAP pacing threshold was 0.5 ± 0.2 V at 0.4 ms pulse width. Five patients underwent cardiac CT showing adequate dsLBBAP ventricular septal penetration (8.6 ± 1.3 mm depth, 2.4 ± 0.5 mm distance from left ventricular septal wall). No complications occurred during a mean follow-up duration of 121 ± 92 days.

Conclusions: Combined HBP and dsLBBAP pacing is a feasible approach as a pace and ablate strategy for atrial fibrillation refractory to medical therapy.

KEYWORDS
atrial fibrillation, AV node ablation, conduction system pacing, his bundle pacing, left bundle branch area pacing

1 | INTRODUCTION

Atrioventricular node ablation and permanent pacemaker implantation are an effective treatment strategies in patients with atrial fibrillation with symptoms refractory to both rhythm and rate control.[1] However, the implications of long-term ventricular pacing and increasing evidence of the deleterious effect of inter- and intraventricular dyssynchrony on ventricular function have stimulated interest in a conduction system pacing approach.[2] Although biventricular cardiac resynchronization therapy is beneficial in restoring electrical and mechanical synchrony in patients with prolonged QRS duration, its use is less established in the context of normal- or tachycardia-induced left ventricular systolic dysfunction. His bundle pacing (HBP) has been shown to recruit the intrinsic conduction system, resulting in near physiological paced QRS duration. Recent studies have demonstrated the feasibility and favorable short-term safety profiles.[3] Therefore, the latest international guidelines support HBP in patients undergoing AV node ablation in the absence of significant left ventricular systolic dysfunction.[1] However, concerns with late increases in pacing thresholds have limited its widespread adoption and guidelines even recommend consideration of an additional backup ventricular lead. Deep septal left bundle branch area pacing (dsLBBAP) by deploying a pacemaker lead deep into the interventricular septum has increasingly become an alternative conduction system pacing approach because of its high reported implant success rate, reduced fluoroscopy times, and stable lead parameters.[4] To exploit both these properties, our center adopted a strategy of HBP combined with dsLBBAP in patients with difficulties to manage atrial fibrillation prior to atrioventricular node ablation. The aim of this study is to report our experience with this approach, specifically commenting on radiological and pacing parameters of combined HBP and dsLBBAP placement in this patient cohort.

2 | METHODS

This was a retrospective observational study. Eight patients who had undergone both HBP and dsLBBAP lead implantation prior to AV node ablation between January 2020 and August 2021 were included in the study. This research has been granted ethical approval by the local Human Research and Ethics Committee (QA2021076).

2.1 | Device implant procedure

Our institution has previously reported procedural techniques for HBP.[5] In brief, all HBP procedures were performed via subclavian access using a 69 cm Medtronic SelectSecure 3830 pacing lead (Medtronic) and a preformed non-steerable sheath (Medtronic C315 His). His location was determined through the identification of a His bundle potential through the catheter/lead system via the Model 2090 Medtronic Pacemaker and ICD Programmer (Medtronic) and/or the Bard Labsystem Pro electrophysiology mapping system (Boston Scientific). Pace mapping and threshold testing were performed prior to HBP lead fixation. Pacing selectivity was determined by 12-lead electrocardiogram (ECG) according to standard definitions with selective capture of the His-Purkinje system (identical to native QRS) or non-selective capture of the His-Purkinje system with additional localized septal myocardial capture.[6] Successful HBP was defined as the identification of His bundle potential presence on the electrogram observed after lead fixation and demonstrable evidence of either non-selective or selective His capture. His-bundle pacing capture threshold (V at 1 ms pulse duration), impedance (ohms), and R wave amplitude (V) were determined at the time of implant.

DsLBBAP lead placement was carried out using identical equipment. The fluoroscopic location of the HBP lead was set as a marker. The dsLBBAP was positioned distal to the HBP site in the direction of the right ventricular apex in the RAO 30 view. The paced QRS morphology recorded a "w" shape with a notch at the nadir of the QRS in lead V1 at the initial site from the right ventricular septum before fixation. DsLBBAP was achieved by screwing the lead deep into the interventricular septum. Selective capture of the left bundle was targeted during dsLBBAP deployment, which was determined by the following criteria: (1) paced (pseudo) right bundle branch block (RBBB) QRS morphology with terminal r/R' in lead V1, (2) recording of a LBB potential during intrinsic rhythm (only in patients with normal ventricular activation), (3) constant left ventricular activation time (LVAT) during high and low pacing outputs, and (4) clear transition from non-selective to selective left bundle branch pacing (LBBP), or non-selective LBBP to myocardial only capture during decreasing pacing output. Selective LBBP was defined as a change in QRS morphology without a change in stim to LVAT time during decreasing the pacing output from non-selective LBBP combined with an isoelectric interval between pacing spike and the QRS complex (pacing spike distinct from the ventricular electrocardiogram). Non-selective LBBP was defined as a change in QRS morphology which occurred after increasing the pacing output from selective LBBP or myocardial capture only. DsLBBAP capture threshold (V at 0.4 ms pulse duration), impedance (ohms), and R wave amplitude (V) were determined at the time of implant. If lead impedance falls during lead deployment and the pacing threshold increases, then this is indicative of over-deployment into the left ventricular cavity. The lead is then retracted and redeployed at a different septal location.

Leads were inserted into a dual-chamber pacemaker generator. The His lead was inserted into the atrial port and the septal lead into the ventricular port. This was programmed in VVI mode until AV node ablation, after which DDD with the shortest AV delay enabling inhibition of the septal lead resulting in His only pacing or VVI (dsLBBAP) was programmed according to most narrow-paced QRS duration also taking into consideration pacing parameters, particularly thresholds. In patients with paroxysmal AF, an atrial lead was also implanted. Leads were inserted into a CRT-P generator with the His lead in the LV port. This was programmed by DDD initially. After AV node ablation, programming was set to pace His or dsLBBAP according to superior pacing parameters and shortest-paced QRS duration.

2.2 | AV node ablation

Indications for AV node ablation were as per international guidelines, which comprised symptomatic permanent AF with difficult rate control or symptomatic paroxysmal AF with failed, declined, or unsuitability for, catheter ablation. AV node ablation was performed at least 1 month after the device implant. Radiofrequency ablation was performed using an irrigated 4 mm-tip ablation catheter through a long sheath. If the right atrium was severely enlarged, a deflectable sheath (Agilis, Abbott Electrophysiology) was used. Ablation was initially targeted at the mid-septum superior to the coronary sinus ostium at a location showing a His potential on the mapping catheter. If unsuccessful, the ablation catheter was moved upwards toward the HBP lead tip.

2.3 | Outcome measures

Pacing parameters: HBP and dsLBBAP lead thresholds, impedance, and QRS duration at initial pacing check follow-up (within 2 months following implantation) were determined from medical records.

2.4 | ECG analysis

QRS duration in milliseconds was manually measured from 12-lead electrocardiographs at a sweep speed of 25 mm per second for intrinsic, HBP-paced, and dsLBBAP-paced rhythms following each procedure. ECG measurements were performed by two independent experienced cardiologists (MN/IT) who were blinded to pacing mode and patient data for each ECG recording. Intrinsic and paced QRS duration was defined by the longest QRS duration at 12 leads measured from the beginning of the Q wave to the end of the S wave. A Pearson's correlation coefficient was determined to assess the degree of agreement between the two readers of the ECG's. Figure 1 illustrates a patient example of ECG and intracardiac recordings.

2.5 | Imaging

Transthoracic echocardiography was performed prior to and after pacemaker implantation.

Given the relatively novel approach, the initial five patients underwent CT scans to evaluate lead position after the procedure. Measurements were taken using multiplanar reconstruction to assess the position of the HBP lead (in atrium or ventricle), and measurements were taken of the distance between the HBP penetration point and the level of the aortic annulus (see Figure 2A). The depth of penetration of the dsLBBAP lead into the muscular interventricular septum was also assessed. The depth measurement was taken perpendicular to the point of penetration (as shown in Figure 2B). Finally, the distance between the HBP and septal insertion point of the dsLBBAP leads was measured and defined as the paraseptal distance.

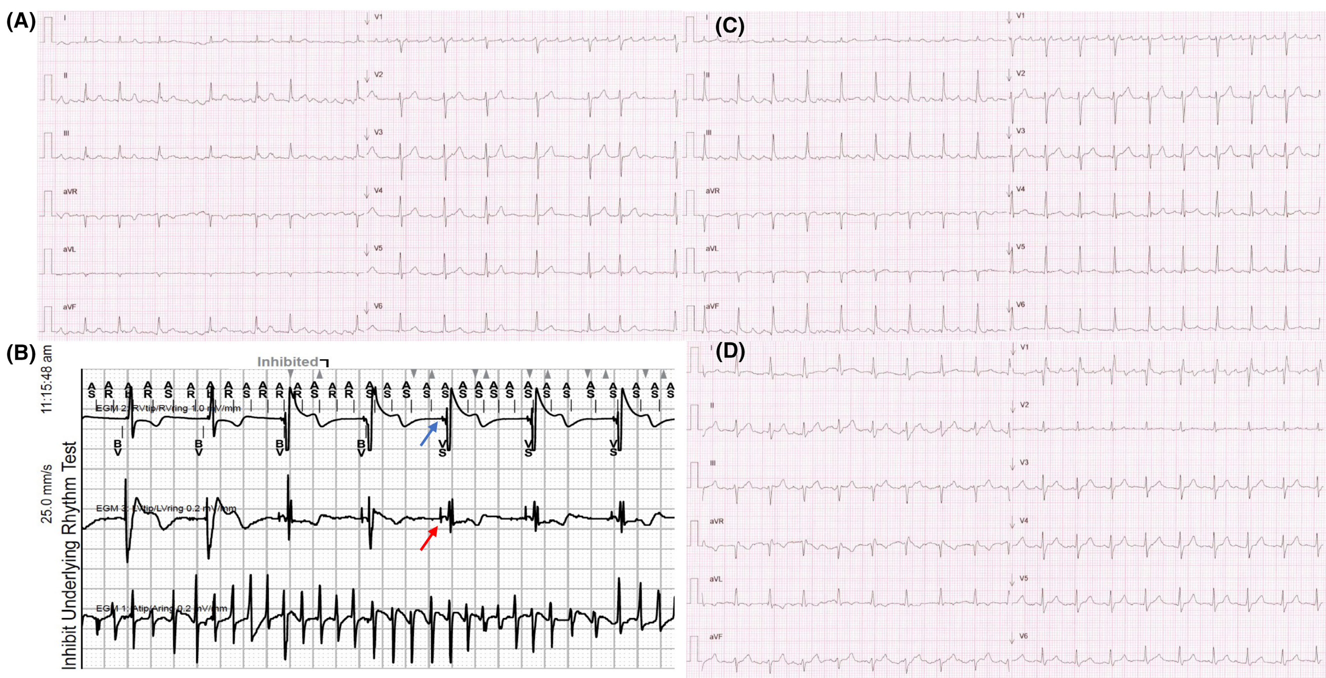

FIGURE 1 Example of electrocardiogram (ECG) and intracardiac recordings in the same patient who received combined His bundle pacing (HBP) and deep septal left bundle branch area pacing (dsLBBAP) pacing and connected to a biventricular CRT generator. (A) Intrinsic ECG showing atrial fibrillation with a ventricular rate of approximately 80 bpm. Intrinsic QRS duration 102 ms. (B) Intracardiac recordings were taken after AV node ablation (upper channel—dsLBBAP lead, middle channel—HBP lead, lower channel—atrial lead). Ventricular escape is seen upon cessation of pacing to reveal sensed ventricular electrograms after the 4th ventricular complex. Left bundle potential is seen immediately prior to the ventricular complex in the upper channel (blue arrow). His bundle potential is seen in the middle channel (red arrow). (C) Selective his pacing at VVI 110 0.5 V at 0.4 ms pulse width. Paced QRS duration 100 ms. (D) Left bundle pacing at VVI 110 0.5 V at 0.4 ms pulse width. Paced QRS duration 130 ms.

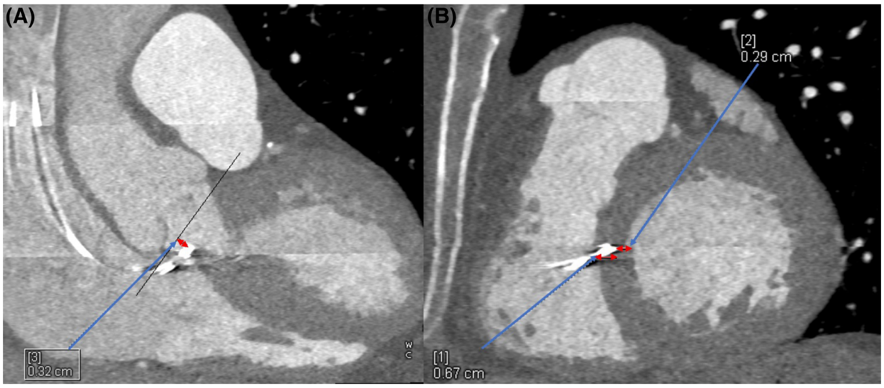

FIGURE 2 CT measurements of lead position using multiplanar reconstruction (measured distances denoted by red bilateral arrows). (A) Measurement of distance (mm) between His bundle pacing penetration point and level of aortic annulus—labeled [3]. (B) Measurement of depth of penetration of deep septal left bundle branch area pacing lead into muscular interventricular septum (mm)—labeled [1] and distance from the left ventricular septal wall (mm)—labeled [2].

TABLE 1 Patient characteristics

Patient	Age	Sex	Left ventricular ejection fraction (%)	LA diameter (cm)	AF category	Heart rate (bpm)	QRS duration (ms)	Anticoagulation	Prior AF catheter ablation	CRT generator
1	76	M	50	5.2	Permanent	106	92	Apixaban	No	No
2	73	F	51	4.9	Permanent	97	96	Apixaban	No	No
3	89	F	50	4.6	Paroxysmal	109	90	Apixaban	No	Yes
4	55	F	54	5.5	Paroxysmal	96	122	Dabigatran	Yes	Yes
5	73	M	50	4.3	Paroxysmal	69	106	Apixaban	Yes	Yes
6	77	F	52	4.8	Permanent	111	88	Apixaban	No	No
7	61	M	50	4.4	Permanent	102	218	Apixaban	Yes	No
8	75	M	63	3.5	Paroxysmal	86	102	Apixaban	No	Yes

2.6 | Statistical analysis

Statistical analysis was performed using SPSS statistical software (SPSS 26, IBM). Numerical indices are expressed as means and standard deviations unless otherwise stated. Student-paired t-test was used to compare lead parameters between His and dsLBBAP leads.

3 | RESULTS

Patient clinical characteristics are listed in Table 1. Mean age was 72 ± 10 years and 4 (50%) were male. The mean left ventricular ejection fraction was 53 ± 4%, and the mean left atrial diameter was 4.5 ± 0.6 cm. Intrinsic QRS duration was 118 ± 46 ms. There was a good correlation in QRS duration measurements between both observers ($r = 0.86$, $p < .01$).

3.1 | Pacing parameters

Pacing parameters for each lead are summarized in Table 2. Five out of the eight patients showed definitive evidence of LB capture during dsLBBAP lead deployment. All were included in the analysis to reflect real-world practice.

Figure 3 illustrates intrinsic, dsLBBAP, and HBP-paced QRS durations. There was no significant difference between intrinsic QRS and paced dsLBBAP QRS or paced His QRS durations.

3.2 | Anatomical considerations

In five patients CT imaging confirmed all HBP and dsLBBAP lead positions. His leads were deployed at the ventricular aspect of the A-V junction with the lead tip at a distance of 4.0 ± 1.4 mm from the aortic annulus. All dsLBBAP leads were deployed at the level of the interventricular septum with a septal penetration depth of 8.6 ± 1.3 mm and 2.4 ± 0.5 mm distance from the left septal wall. The paraseptal distance between His and dsLBBAP leads was 18.4 ± 2.7 mm.

3.3 | Follow-up

All pacemaker implants were successful. There were no incidences of septal perforation into the left ventricle during dsLBBAP lead deployment. All patients underwent successful AV node ablation after pacemaker implantation. The mean follow-up duration was 121±92 days. During the follow-up period, none of the patients required heart failure hospitalization. None of the study patients developed complications, including lead dislodgement, cardiac perforation, or tricuspid valve injury. No significant deterioration in pacing parameters was detected during follow-up device checks in all leads. On follow-up device checks, all patients effectively required 100% ventricular pacing. All patients paced from the HBP lead except the 1 case where dsLBBAP resulted in a shorter QRS duration compared to HBP (patient 4).

4 | DISCUSSION

In this patient series, implantation of a deep septal LBBAP lead provides backup ventricular pacing in addition to His bundle pacing in patients undergoing AV node ablation. Current dsLBBAP implantation techniques provide sufficient septal penetration to capture the left bundle conduction system. Furthermore, dsLBBAP pacing provides comparable electrical evidence of interventricular synchrony and superior sensing and pacing thresholds to HBP. To the best of our knowledge, there has been no prior study evaluating combined HBP and deep septal pacing in patients undergoing AV node ablation for the management of atrial fibrillation.

TABLE 2 Implant pacing parameters

	His ($n = 8$)	DsLBBAP ($n = 8$)
Sensed ventricular amplitude (V)	2.4 ±1.1	15±5.3*
Pacing threshold (V)[a]	1.0 ±0.6	0.5 ±0.2
Lead impedance (ohms)	522±57	814±171**
Paced QRS duration (ms)	101±20	119±17**

[a]His thresholds in V@1 ms, dsLBBAP thresholds in V@0.4 ms.
*$p = .001$; **$p = .02$.

4.1 | Adverse effects of interventricular dyssynchrony

International guidelines advocate a cardiac resynchronization pacing strategy in patients likely to receive high percentage pacing with reduced left ventricular systolic function.[1] However, evidence for the preferred pacing strategy is less clear in those with preserved left ventricular systolic function or tachycardia-induced left ventricular dysfunction undergoing atrioventricular node ablation. Emerging studies highlight the detrimental effects of chronic right ventricular pacing on previously normal left ventricular function.[7–10] The mechanism for such decline is not fully understood, but adverse cardiac remodeling is thought to be consequent to abnormal contractile function and elevated filling pressures produced by long-term electromechanical dyssynchrony.[2] Interestingly, large cohort studies report that paced QRS duration is an independent predictor in the development of dyssynchrony-induced left ventricular dysfunction.[8,10] One such study defined a cut-off paced QRS duration of greater or equal to 150 ms to be 95% sensitive to the development of heart failure.[11] Although biventricular pacing via the right ventricle and lateral coronary sinus has been consistently shown to reverse electrical dyssynchrony in heart failure patients, it significantly increases QRS duration in patients with narrow intrinsic QRS.[12] Numerous studies have shown that conduction system pacing either by HBP or more recently left bundle branch area pacing produces a short-paced QRS duration comparable to intrinsic QRS duration and can even reverse left bundle branch block.[13–15] However, only one study has compared combined HBP and left bundle branch pacing

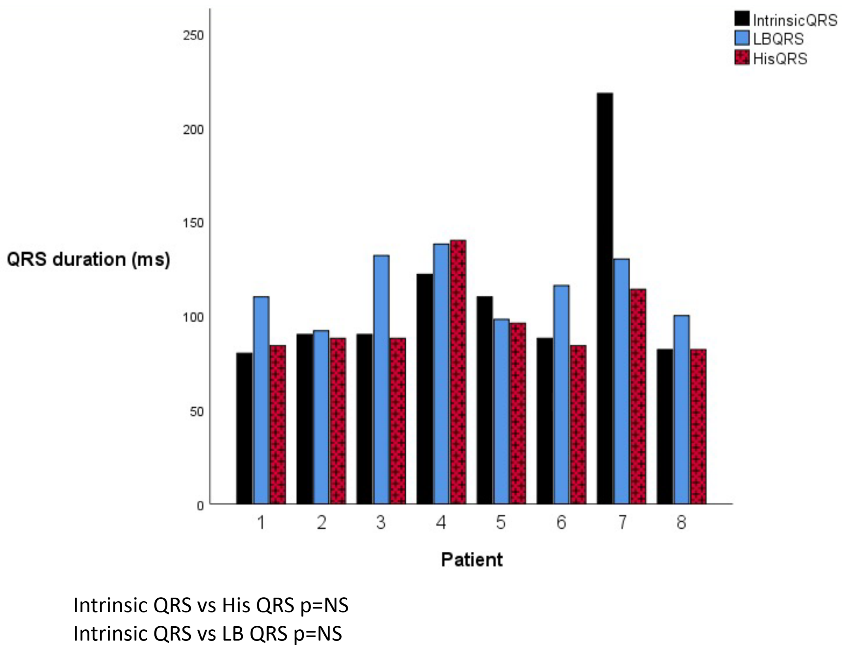

FIGURE 3 Comparison of intrinsic QRS duration, HBP QRS, and left bundle paced QRS durations across all patients.

within the same patient. This group studied 20 patients with permanent atrial fibrillation and slow atrioventricular conduction requiring permanent pacing.[16] They showed that although LBBAP produced a longer paced QRS duration compared to HBP, this difference was small (113.2 ± 14.5 ms vs. 104.5 ± 22.3 ms, respectively) with similar indices of mechanical synchrony performed with echocardiographic assessment. We report similar findings in our series, where HBP provided the shorter paced QRS duration when compared to dsLBBAP, but mean-paced QRS duration at both locations was still below 120 ms. Furthermore, one of the patients had a broad left bundle branch block at baseline. In this case, both HBP and dsLBBAP successfully restored electrical interventricular synchrony by significantly reducing the QRS duration during pacing.

4.2 | Clinical application of conduction system pacing in preserved left ventricular systolic function undergoing AV node ablation

The recently published APAF-CRT trial reported combined biventricular CRT and AV node ablation resulted in a 27% mortality benefit in patients with symptomatic AF when compared to rate control therapy alone.[17] However, approximately 40% of the patient population had an ejection fraction of less than 35%. Conduction system studies have produced more compelling data in patients requiring high percentage pacing with preserved ejection fraction. Abdelrahman showed in their retrospective series of 765 patients with a mean ejection fraction of 54% that HBP was superior to conventional right ventricular pacing in reducing a composite of all-cause mortality, heart failure hospitalization, and need for biventricular CRT upgrade.[18] HBP has also been shown to be a feasible pacing strategy in patients requiring pacing prior to AV node ablation.[3] Emerging studies are showing the superiority of HBP over conventional biventricular CRT in this patient group.[12] However, concerns with reduced sensing and late rises in ventricular pacing thresholds have resulted in international guidelines advocating the additional implant of a backup ventricular pacing lead in this group of patients.[1] Left bundle branch area pacing is also emerging as a feasible conduction system alternative in this patient group, but with the added benefit of superior sensing and pacing threshold parameters.[4] This study was able to perform an intra-patient comparison of two conduction system pacing strategies. We found that a combined HBP and dsLBBAP approach offers the advantageous paced QRS of HBP with the improved stability parameters of left bundle branch area pacing as a backup lead. However, while commonly used in this context, the Medtronic 3830 lead was not designed for dsLBBAP pacing and thus its use is off-label. The only other study to perform an intra-patient comparison of these two pacing modalities discussed the potential suboptimal implantation of a dsLBBAP lead using sheaths and leads designed for HBP.[16] While we agree that implant techniques and delivery equipment require ongoing refinement, detailed CT scans in five of our patients confirmed the correct anatomical lead deployment position and adequate penetration to capture the left bundle branch with current implant technology. A further important consideration of this combined approach in terms of patient selection is MRI compatibility. At the time of writing, the Medtronic 3830 lead has only been approved as 'MRI-safe' when plugged into a right ventricular port. Therefore insertion into either an atrial port or left ventricular port currently precludes the future use of MRI in this group of patients.

4.3 | Limitations

Interpretation of clinical outcomes is limited by this study being a small retrospective evaluation. Although paced QRS duration in high percentage ventricular pacing patients is a predictor of downstream heart failure, the reported rates of dyssynchrony-induced heart failure are only in the region of 15%–20%. We did not perform any objective measures comparing mechanical or specific electrophysiological differences between intrinsic, HBP, or dsLBBAP pacing. Furthermore, left bundle capture could not be demonstrated in all patients, and in these patients paced QRS complexes were likely a fusion of left bundle and left ventricular septal capture. Nonetheless, this reflects real-world practice in this developing pacing technique, and a recent study found LV septal pacing produced similar hemodynamic improvement and electrical resynchronization when compared to HBP and biventricular pacing.[19] Finally, conduction system pacing remains a relatively novel pacing technique, and long-term clinical outcome data including the safety of lead extraction is lacking.

4.4 | Future directions

This study has shown that HBP and dsLBBAP display comparable ECG markers of conduction system pacing. A further detailed study into the differences in ventricular activation and subsequent hemodynamic effects between pacing modalities would provide deeper insight into protective mechanisms against heart failure. Whether a single dsLBBAP implant approach alone offers sufficient protection against dyssynchrony-induced heart failure remains an important unanswered question. As the technique becomes more refined, the marginal superior pacing qualities of HBP over left bundle pacing may narrow further.

5 | CONCLUSION

This case series demonstrates that combined HBP and dsLBBAP pacing is a feasible approach as a pace and ablate strategy for atrial fibrillation refractory to medical therapy.

AUTHOR CONTRIBUTIONS

Michael C. Y. Nam: Concept/design, data analysis/interpretation, drafting the article, critical revision of the article, approval of article, statistics, and data collection. Patricia O'Sullivan: Data analysis/interpretation, drafting the article, and critical revision of the article.

Ivaylo Tonchev: Concept/design, data analysis/interpretation, and data collection. Benjamin M. Moore: Concept/design, data analysis/interpretation, and data collection. Troy Watts: Data analysis/interpretation, and data collection. Gareth Wynn: Concept/design, data collection, and critical revision of the article. Geoff Lee: Concept/design, data collection, and critical revision of the article. Subodh Joshi: Concept/design and critical revision of the article. Irene Stevenson: Concept/design, data collection, and critical revision of the article.

CONFLICT OF INTEREST

None to declare.

ETHICS APPROVAL

This research has been granted ethical approval by the local Human Research and Ethics Committee (QA2021076).

INFORMED CONSENT

Obtained from each participant.

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