

His-Purkinje conduction system pacing

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Summary

His bundle pacing is performed at our centre since 2017 and has been adopted in tertiary centres across Switzerland. It provides true physiological stimulation, thereby avoiding the detrimental effects of right ventricular pacing. However, relatively high incidences of lead revision and increases in capture thresholds have been reported. An alternative technique, practiced at our centre since 2020, is left bundle area pacing, which provides excellent electrical parameters. However, long-term data on lead performance and extractability are lacking. Furthermore, although these techniques are conceptually very attractive, there is a dire need for studies randomizing conduction system pacing with right ventricular / biventricular pacing, before they can be considered as becoming the gold standard.

Introduction

Traditional right ventricular apical pacing has been pursued for decades but results in dyssynchronous ventricular activation and can lead to impairment of left ventricular function. As the deleterious effects of long-term apical right ventricular pacing have become evident, alternative pacing sites such as the right ventricular septum or right ventricular outflow tract have been attempted, but this did not prevent pacing-induced cardiomyopathy [1].

To provide a more physiological activation of the ventricles, attention has shifted to conduction system pacing, comprising His bundle pacing (HBP) and, more recently, left bundle branch area pacing (LBBAP). By directly stimulating the specialised His-Purkinje network, this technique offers the ability to preserve physiological activation in patients with a narrow QRS complex, but it can also offer cardiac resynchronisation therapy by correcting underlying bundle branch block (BBB).

The main features of His bundle pacing and left bundle branch area pacing are compared in table 1.

His bundle pacing

The first experience of a pacing lead actively fixed on the His bundle was published in 2000 [2]. However, the initial technique was cumbersome and time-consuming and HBP was not readily adopted. Recently, the interest in and adoption of HBP has known an exponential growth, not only due to the advent of new implant tools specifically de-

signed to locate the His bundle, but also following a growing number of publications and the dissemination of information through social media in the cardiology community [3].

Implantation technique and success rates

After venous access is obtained, a lumenless lead (Medtronic SelectSecure 3830®) is steered towards the His bundle region, located between the right atrium and right ventricle immediately superior to the tricuspid valve in a right anterior oblique 30° view. A pre-shaped sheath (Medtronic SelectSite C315HIS®) is used to guide the lead placement. In rare cases when lead positioning is difficult, a deflectable delivery sheath is used (Medtronic SelectSite C304®). With the HBP lead connected to a device programmer or an electrophysiology recording system, the His bundle region is mapped in a unipolar configuration. If no His potential is visualised, pacemapping can be used to locate the target site. Once an adequate position is found, the lead is fixated by rotating it 6–10 times. The use of a 12-lead ECG during implantation is mandatory to assess His bundle capture and correction of an underlying BBB. A His bundle threshold <2 V/1 ms (or <2.5 V/0.5 ms) is acceptable, and improves with experience. Of note, sensing values are lower than those for right ventricular pacing, usually around 2–4 mV and may even be <1 mV. HBP with stylet-driven leads has also been described [4].

HBP can be challenging, especially in dilated hearts, as the target zone is relatively narrow. There is a reported learning curve of ± 40 cases [5].

Figure 1A shows a chest X-ray after implantation of an HBP lead and figure 1C shows an ECG during His bundle pacing.

HBP implant success rates range from 56 to 93%, depending on the definition used for successful His bundle capture and on the degree of conduction system disease present. Lower success rates are seen when HBP is used to correct a BBB [5, 6].

A concern with HBP is the rise in capture thresholds and necessity for lead revision, reported in up to 11% of patients [7]. This rise in HBP capture threshold may result in premature battery depletion and compromise patient safety. Furthermore, oversensing of atrial or His signals or undersensing of ventricular signals can be encountered. Oversensing may lead to inhibition of pacing, which may

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cause prolonged asystole in pacing dependent patients. Therefore, implantation of a right ventricular backup lead should be considered for backup pacing or to ensure proper

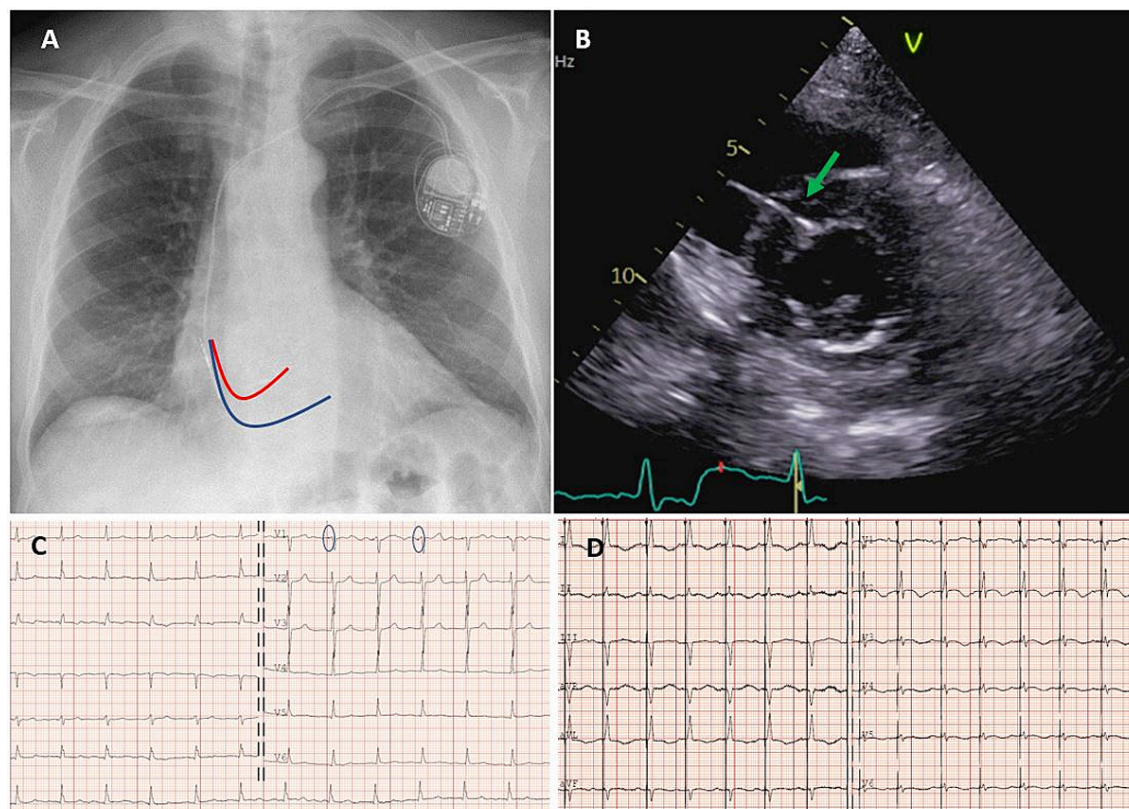
sensing in selected cases (e.g., pacing-dependent patients, infra-nodal block, suboptimal sensing, etc.). This results in higher costs, not only from the extra lead but also the

Table 1:

Comparison between His bundle pacing and left bundle branch area pacing.

	His bundle pacing	Left bundle branch area pacing
Anatomy	Narrow target area	Larger target area. May be challenging in patients with septal scar or hypertrophy
Confirmation of conduction tissue capture	Endpoints well defined	Successful conduction tissue capture may be more difficult to demonstrate
Capture threshold	May be high or increase over follow-up	Usually low and reported to be stable over time (but no long-term data available)
Sensing parameters	Lower amplitudes (electrically inert fibrous tissue)	Higher amplitudes (abundant surrounding myocardial tissue)
	– Risk of atrial and/or His oversensing	
	– Risk of ventricular undersensing	
Physiology	More synchronous ventricular activation due to full capture of conduction tissue (in case of narrow QRS)	Less synchronous ventricular activation due to capture of the left bundle branch ramification or myocardium only
	Limited to correction of proximal conduction block only	Higher success in proximal conduction block
	Risk if distal conduction block develops	Potential to correct more distal conduction block
Backup right ventricular lead	Indicated in selected cases if sensing issues or for patient safety (risk of threshold rise)	Not required (good sensing and low capture thresholds)
Atrioventricular node ablation	Risk of compromising His bundle pacing lead function	No risk of compromising left bundle pacing lead function due to distal position of the lead
Extraction	Feasibility has been demonstrated	Concern for long-term extractability (no data)
Complications	Atrial and His potential oversensing, ventricular undersensing	Septal perforation (acute and delayed)
	High (>6%) incidence of lead revision for elevated capture thresholds	Septal coronary artery lesion (rare)
	Lead dislodgement	Lead dislodgement

Figure 1: A. Chest radiography of a patient with a dual-chamber pacemaker. In red is shown a typical position of a His bundle pacing (HBP) lead, in blue is shown a typical position of a left bundle branch area pacing (LBBAP) lead. Note the more apical and distal position of the LBBAP lead compared to the HBP lead. The position of the LBBAP lead can be confused with a conventional right ventricular pacing lead in a high septal position, however as shown in figure 1B on a transthoracic echocardiography, short axis view, the LBBAP lead penetrates deep into the interventricular septum (green arrow). Figure 1C shows the ECG during HBP with bipolar stimulation (pacing artefact barely visible, blue circle). This can be easily confused with an intrinsic rhythm. Figure 1D shows the ECG during LBBAP. Note the narrow QRS (100ms) and memory T waves. With unipolar pacing, the pacing artefact is now clearly visible.



use of a different type of pulse generator (single vs dual chamber vs cardiac resynchronisation therapy (CRT) device). The backup lead also adds significant complexity to device programming [8].

His bundle pacing as an alternative to right ventricular pacing

Based on observational data, HBP has been reported to result in improvements in quality of life, 6-minute walk test, left ventricular ejection fraction (LVEF, mean difference 4.33%, range 0.85 to 7.81%), left ventricular dimensions (mean difference in left ventricular end-systolic volume -7.09 ml, range -11.27 to -2.91), heart failure hospitalisations and mortality in comparison with right ventricular pacing [9, 10].

In an observational study comparing 304 patients with HBP to 433 patients with right ventricular pacing, the primary outcome of death, heart failure hospitalisation and upgrade to biventricular pacing was significantly lower with HBP, in particular in the patient subgroup that required >20% RV pacing [11].

His bundle pacing as an alternative to biventricular pacing

The first report that pacing the distal part of the His bundle could correct a BBB was published in the 1970s [12]. In recent observational studies, it was found that permanent HBP for cardiac resynchronisation therapy (His-CRT) is feasible and safe and results in significant reductions in QRS duration and improvements in LVEF and functional class [13–16].

For patients with a right bundle branch block (RBBB) and heart failure, in whom the benefits of biventricular pacing (BVP) may be limited, HBP holds promise. In a study including 39 heart failure patients (LVEF <50%, New York Heart Association [NYHA] class II–IV) with RBBB, QRS correction, either complete by direct recruitment of the right bundle or by means of fusion, was successful in 95% with significant improvements in LVEF and NYHA functional class [17].

The His-Sync (His Bundle Pacing vs. Coronary Sinus Pacing for Cardiac Resynchronization Therapy) trial was the first pilot randomised controlled trial that assessed the feasibility and efficacy of corrective HBP as a first-line strategy for CRT. Forty-one patients were enrolled, of whom 21 were randomised to HBP and 20 to BVP. The study was limited by a relatively high crossover rate in both groups. The primary intention-to-treat analysis showed significant reductions in QRS duration with His-CRT compared with BVP-CRT, and a trend towards greater echocardiographic improvement in the His-CRT arm relative to the BVP-CRT arm [15]. Recent work has indicated that the success of corrective HBP depends on the location of the conduction block within the His–Purkinje system. Among patients with an LBBB pattern, those with conduction block within the proximal left conduction system can be corrected by HBP. However, those patients with LBBB pattern but more distal conduction disease, as in nonspecific intraventricular conduction disease, cannot be corrected by HBP [18]. In the latter population, right and left ventricular and His fusion pacing (HOT-CRT) may be promising [19].

To date, no large scale randomised controlled trials have been published and no long-term data on clinical and echocardiographic outcomes for HBP as an alternative to biventricular pacing are available. Biventricular pacing is a proven therapy and remains the gold standard for patients with heart failure with reduced ejection fraction and left bundle branch block. However, HBP can be considered a reasonable backup option in patients in whom traditional biventricular pacing either cannot be performed or has failed despite optimal lead placement and optimisation attempts.

Left bundle branch (area) pacing

Left bundle branch area pacing (LBBAP) has been introduced recently and is rapidly emerging as an alternative for failed or suboptimal HBP cases or even as a primary strategy for conduction system pacing. Left bundle branch pacing (LBBP) describes the direct stimulation of the left bundle branch. “Left bundle branch area”, “peri-left-bundle-branch” and “deep septal” pacing are used to refer to the general trans-interventricular septum approach to attempting LBBP but do not specify if conduction system capture is achieved. Confirmation of conduction system capture is more challenging than with HBP, but whether this is necessary for clinical outcome is a matter of debate [20]. In general, its wider target zone, lower and more stable thresholds, better sensing (no atrial or His oversensing and higher R-wave amplitude) make the concept of LBBAP more favourable over HBP for physiological pacing.

Implantation technique and success rates

The implantation technique for LBBAP was first reported by Huang et al. in 2017 [21]. With the use of a preshaped delivery sheath (Medtronic SelectSite C315HIS®), the same lumenless lead used for HBP is positioned 1.5–2cm distal to the His bundle towards the right ventricular apex, where a “W” paced QRS pattern in V1 is sometimes observed. The lead is advanced by several rapid rotations to penetrate the septum. Advancing the lead further into the septum towards the left bundle branch will provoke the emergence of a RBBB type pattern with a “Qr” pattern in V1. QRS morphology and lead impedance (decreasing values) should be checked periodically to evaluate when to stop further lead rotations to avoid septal perforation. A 12-lead ECG is mandatory, ideally with an electrophysiology recording system to measure R-wave peak times in V6. Left bundle branch (LBB) potentials are reported in 30–80% of the patients [22, 23]. Contrast injection through the sheath may help to confirm the intraseptal position of the lead.

In patients with septal hypertrophy and significant scarring, implantation can be difficult.

A chest X-ray, short-axis transthoracic echocardiography image and ECG after implantation of an LBB pacing lead are shown in figure 1A, B and D, respectively.

The success rate of LBBAP is reported to be high (>80%), but as for HBP there is a learning curve to be considered, and the procedure should be performed by physicians with expertise in standard device implantation [22–27].

A recently published study prospectively enrolled 632 pacemaker-eligible patients (CRT indication with LBBB in

14% of patients, atrioventricular block or “ablate and pace” strategy for permanent atrial fibrillation in 60% of patients and sick sinus syndrome in 26%) and reported a success rate of 97.8% [25].

In a large retrospective multicentre study including patients with an LVEF <50% and indications for CRT or pacing, permanent LBBAP was achieved in 85% (277 of 325 patients) [27]. In both studies, failure was mainly due to the inability to penetrate the septum because of fibrosis or hypertrophy.

Serious procedure-related complications associated with LBBAP, such as lead dislodgments, septal perforation, septal haematoma, septal coronary artery injury or left ventricular thrombus have been reported, but are rare [24–27].

In patients undergoing atrioventricular node ablation, LBBAP provides easier and safer ablation than with His bundle pacing, where capture thresholds may rise if the ablation site is close to the pacing lead [28].

The main concern with LBBAP is how feasible it will be to extract chronically implanted leads, as they are drilled deep into the interventricular septum.

Left bundle branch (area) pacing as an alternative to right ventricular pacing

The likelihood of LBBAP to correct distal conduction disease as compared with HBP is higher, since it bypasses the level of the block in a majority of the patients and the target region is wider, with fibres of the left bundle branch fanning on the left subendocardium. In patients with atrioventricular conduction disease, a 90% success rate was reported for LBBAP [22].

As the LBB pacing lead is surrounded by abundant myocardium, generally no significant sensing issues arise and thresholds are reported to be low and stable [25].

Left bundle branch (area) pacing as an alternative to biventricular pacing

In a prospective multicentre study involving 63 patients with non-ischaemic cardiomyopathy and LBBB, LBBAP had a success rate as high as 97% along with significant improvement in LVEF, and even normalisation of LVEF (LVEF >50%) in 75% of patients at 1 year [26].

In a large retrospective multicentre study published by Vijayaraman et al., LBBAP was attempted in 325 CRT-eligible patients (44% of patients had ischaemic cardiomyopathy, 39% LBBB, 17% RBBB, and 15% intraventricular conduction delay) and successfully implanted in 277 (85%). LBBAP resulted in significant reduction in QRS duration and significant improvement in LVEF, in both ischaemic and non-ischaemic patients and similarly in patients with LBBB and non-LBBB. The lead threshold was low (0.6 ± 0.3 V at 0.5 ms), and R-wave amplitudes were high (10.6 ± 6 mV at implantation) and remained stable during a mean follow-up of 6 ± 5 months. Clinical response (improvement in NYHA functional class by at least one class) was noted in 72% of patients.

Recently, mid-term data on LBBAP have been published, showing stable and high sensed R-wave amplitudes and low pacing thresholds during a mean follow-up of 18.6 ± 6.7 months, as well as significant reductions in QRS dura-

tion and improvement in LVEF and left ventricular end diastolic dimensions with LBBAP [25].

Key points

- HBP and LBBAP are increasingly being adopted as alternatives to current standard right ventricular and biventricular pacing techniques.
- HBP provides the most physiological ventricular activation, but there is concern about high capture thresholds and a high rate of lead revisions, which may be mitigated by a more liberal use of ventricular backup leads.
- LBBAP is a recently introduced pacing modality, which seems to provide excellent electrical parameters (without the requirement for backup ventricular pacing), but the long-term performance and lead extractability remains to be evaluated. It is currently a valuable alternative if HBP does not yield satisfactory results.
- Although there is a growing volume of observational data on these pacing modalities, there is a dire need for randomised studies to prove their safety and efficacy for them to be fully implemented in practice guidelines.

In the University Hospital of Geneva, based on current experience and published studies, indications for conduction system pacing include:

- Patients expected to be paced >20% of the time (nodal and infra-nodal atrioventricular block; slowly conducted atrial fibrillation, pacing-induced cardiomyopathy)
- As part of an ablate and pace strategy in rapidly conducted atrial fibrillation
- Failed coronary sinus lead implantation for patients with a CRT indication
- Non-responders to biventricular pacing
- In combination with left ventricular or biventricular pacing for His-optimised CRT (in patients with permanent atrial fibrillation in whom the HBP or LBBAP lead may be connected to the atrial port)

Theoretically, the indications between HBP and LBBAP should not differ.

Disclosure statement

HB has received institutional fellowship support/research grants or consultancy/speaker fees from Abbott, Biotronik, Boston Scientific, Medtronic and Microport. EB has reported that she has no conflicts relevant to the contents of this paper to disclose.

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