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Conduction system pacing: overview, definitions, and nomenclature

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Pacing from the right ventricle is associated with an increased risk of development of congestive heart failure, increases in total and cardiac mortality, and a worsened quality of life. Conduction system pacing has become increasingly realized as an alternative to right ventricular apical pacing. Conduction system pacing from the His bundle and left bundle branch area has been shown to provide physiologic activation of the ventricle and may be an alternative to coronary sinus pacing. Conduction system pacing has been studied as an alternative for both bradycardia pacing and for heart failure pacing. In this review, we summarize the clinical results of conduction system pacing under a variety of different clinical settings. The anatomic targets of conduction system pacing are illustrated, and electrocardiographic correlates of pacing from different sites in the conduction system are defined. Ultimately, clinical trials comparing conduction system pacing with standard right ventricular apical pacing and cardiac resynchronization therapy pacing will help define its benefit and risks compared with existing techniques.

Introduction

Chronic ventricular pacing modalities continue to evolve in clinical practice. Although initially designed as a life-saving measure, new indications for ventricular pacing have been studied to try to improve morbidity and mortality over time. However, the detrimental effects of chronic right ventricular pacing (RVP) have also been realized through large, randomized studies.[1,2] Patients with frequent RVP are at a significant risk of developing pacing-induced cardiomyopathy and subsequent heart failure (HF) symptoms.[3,4] Other right ventricular (RV) pacing locations such as the septum and outflow tract have been studied to try to mitigate these unintended consequences, but results have been equivocal at best.[5]

Biventricular pacing (BiVP) through the coronary sinus has shown significant benefits in carefully selected populations with left bundle branch block (LBBB) and HF symptoms with improvement in both morbidity and mortality.[6,7] However, BiVP in other clinical cohorts has not shown the same degree of benefit.[8,9] Despite development in lead technologies and delivery mechanisms, approximately one-third of the patients fail to derive clinical benefit from BiVP.

Conduction system pacing (CSP) has recently become a popular modality to try to obviate the detrimental effects of RVP and overcome some of the shortcomings of BiVP (inability to place a coronary sinus lead, diaphragmatic stimulation, suboptimal target veins, incomplete resynchronization, etc.). Conduction system pacing can be achieved at all levels of the conduction system axis. His bundle pacing (HBP) has been described as a possible pacing modality to correct underlying LBBB in the 1970s.[10,11] However, it was not until 20 years later

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that the first clinical study was published showing the feasibility in clinical practice.[12] Patients with HF and permanent AF with reduced left ventricular (LV) systolic function underwent successful atrio-ventricular (AV) nodal ablation and HBP. Over the next decade, several centres around the world published their data showing the safety, feasibility, and benefits of HBP.[13-17] His bundle pacing also presents some unique challenges. The His bundle (HB) is encased in fibrous skeleton, and specific leads and tools are often required to pace this region. Pacing at the atrioventricular annulus/basal septum can result in sensing issues (poor R waves, atrial over-sensing) and increases in pacing thresholds over time.[18]

Pacing of the LV septum via a trans-septal route as an alternative pacing site for more physiological ventricular activation was first described in 2002[19] and further explored by investigators in the Netherlands.[20-22] Pacing of the proximal left bundle branch (LBB) using the ventricular trans-septal route was first described in 2017 to overcome some of these challenges.[23] Left bundle branch area pacing (LBBAP) has been gaining significant popularity across the world.[24,25] Pacing deep within the interventricular septum can directly engage the left conduction system and result in normal LV activation times, thereby preserving LV synchrony. Several large single-centre and multi-centre observational studies showed favourable procedural and clinical outcomes of LBBAP both in bradycardia and HF indications.[26-28]

Patient cohorts that can derive particular benefit with conduction system pacing

Frequent right ventricular pacing

As described earlier, frequent RVP (>20%) has been shown to cause pacing-induced cardiomyopathy and increased HF hospitalizations.[3,4] In one study, there was close to a 50% reduction in HF hospitalizations in patients who underwent HBP compared with RVP.[3] In another study, LBBAP demonstrated a hazard ratio of 0.32 in significantly reducing the composite endpoint of HF or all-cause mortality compared with RVP.[29] Conduction system pacing seems ideally suited to reduce the risk of pacing-induced cardiomyopathy and subsequent HF compared with traditional RVP. It should be noted that there are limited data showing that BiVP is superior to RVP in patients with preserved LV systolic function.[30] Other RV pacing locations such as the septum and outflow tract have shown equivocal results at best.[8,9] His bundle pacing was also shown to improve the quality of life, and patients preferred this pacing modality compared with no pacing in a randomized trial consisting of patients with PR intervals >200 ms, QRS ≤ 140 ms, or right bundle branch block (RBBB) and reduced ejection fraction (EF).[31]

Ablate and pace strategies

Patients with symptomatic long-standing persistent atrial fibrillation and poorly controlled heart rates can benefit from an ‘ablate and pace’ strategy with RVP, which improves symptoms but does not have any effect on EF.[32,33] This strategy has been shown to reduce HF.[34] In this cohort, CSP can preserve intrinsic ventricular activation and preserve intra-ventricular synchrony, thereby reducing the risk of pacing-induced cardiomyopathy. Cardiac resynchronization therapy (CRT) has been shown to have a role in patients with permanent AF and HF with adequate pharmacologic rate control. In the ALTERNATIVE-AF randomized cross-over study,[35] HBP was associated with greater improvement in LV EF compared with BiVP in patients with reduced LV EF (≤40%) and adequate rate control.

Patients with left bundle branch block, failed cardiac resynchronization therapy, or non-responders

Two small, randomized trials have compared HBP with BiVP in patients with HF and reduced EF. The His-SYNC trial was a small pilot study that did not show any statistical difference between the two groups in terms of electrocardiographic or echocardiographic parameters.[36] On-treatment analysis demonstrated superior electrical resynchronization and a trend towards higher echocardiographic response in the HBP group.[37] In the His-Alternative trial, HBP provided similar clinical and physical improvement compared with BiVP.[38] However, pacing thresholds were higher in this group.

In a large multi-centre observational study that included patients with EF <35%, the primary outcome (composite endpoint of time to death or HF hospitalization) was significantly reduced with LBBAP compared with BiVP (20.8 vs. 28.0%).[39] Also, a recent meta-analysis of all studies comparing CSP vs. BiVP demonstrated a significant reduction in all-cause mortality and HF hospitalizations compared with CSP.[40]

Finally, CSP may be a good alternative to BiVP in patients where traditional CRT is either not feasible or results in a suboptimal response. Both HBP and LBBAP have shown significant improvement with electrical resynchronization, NYHA class, and LV EF.[41]

Based on the current data as outlined above, the 2021 ESC pacing guidelines[42] and the 2023 HRS/APHRS/LAHRS (Heart Rhythm Society/Asia Pacific Heart Rhythm Society/Latin American Heart Rhythm Society) guidelines[43] on cardiac physiologic pacing for the avoidance and mitigation of HF have endorsed CSP with either 2a or 2b recommendations in various pacing categories. Other populations that could potentially benefit from CSP include patients with HF and RBBB, patients with AV nodal disease (first-degree heart block) with HF symptoms, and patients with intra-ventricular conduction delay (IVCD). The clinical response rates to either CSP or BiVP may be suboptimal in patients with IVCD. Combining CSP with BiVP could potentially offer better ventricular resynchronization as both the conduction system and the myocardium are activated.[44] An international collaborative study demonstrated that this approach is safe and feasible and provides greater electrical resynchronization compared with BiVP alone.[45] Randomized trials will be needed in this particular cohort to show long-term clinical benefits.

Anatomy of the conduction system and its relevance to conduction system pacing

It is important to understand the anatomy of atrioventricular conduction system to guide implantation as well as appreciate the types of capture which may be

obtained with CSP. Implantation technique is covered in detail elsewhere in a recent European Heart Rhythm Association (EHRA) consensus document,[46] as well as in another article of this supplemental issue.[47]

His bundle and right bundle branch

The compact atrioventricular node (AVN) lies in the triangle of Koch, which is delimited anteriorly by the septal tricuspid leaflet, posteriorly by the tendon of Todaro, and at its base by the coronary sinus ostium (*Figure 1*). The membranous septum forms the apex of the triangle. The floor of the triangle of Koch is made up by atrial myocardium, separated from the underlying crest of the muscular inter-ventricular septum by fibro-adipose tissue occupying the inferior pyramidal space (which represents the ingress of epicardial tissues from the inferior atrioventricular groove).

In an elegant autopsy study of 41 patients, Cabrera *et al.*[49] described variable anatomy of the atrioventricular conduction axis. In a quarter of the patients, the compact AVN lay inferiorly within the triangle of Koch. In the remaining patients, it lay at the apex of the triangle in the atrioventricular portion of the membranous septum. When taking the site of penetration into the insulating tissues of the central fibrous body as representing the transition from the compact node to the bundle of His, the authors also found variations in anatomy. The site of penetration was found within the triangle of Koch in 54% of patients, whereas penetration was at the commissure of the septal and anterior leaflets of the tricuspid valve in 32% of patients. In the remaining 15% of patients, the site of penetration was within the ventricular membranous septum. In the same report, the authors studied 60 patients to delineate the tricuspid valve by contrast injection, while measuring the amplitude of the His signal. The greatest amplitude was found on the atrial aspect of the tricuspid valve in about half of the patients and at the level of the valve insertion or in the ventricle in the other half.[49] The His bundle may therefore be paced from the atrial aspect of the tricuspid valve in many patients. This explains why atrial tissue may be captured by the His lead.[50] As the tricuspid valve is inserted more apically than the mitral valve, the triangle of Koch is a structure, which overlies the muscular crest of the inter-ventricular septum. A lead screwed in this region may therefore be in contact with atrial myocardium, the His bundle, as well as ventricular myocardium and capture these three tissues (*Figure 2*). Non-selective HBP (i.e. with ventricular myocardial capture) with leads positioned in the atrium has been demonstrated by computed tomography (CT) scans.[51] A lead, which is placed in a region with atrial myocardium, may be prone to P-wave oversensing,[52,53] which may lead to inhibition of pacing and asystole in a pacemaker-dependent patient.

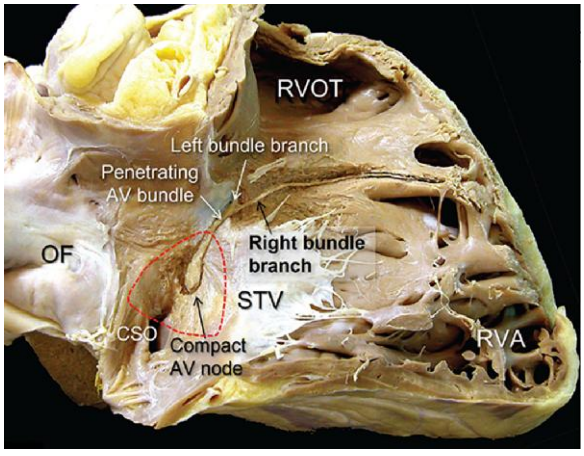

Figure 1 Dissection of the conduction system visualized from the right-sided chambers. The triangle of Koch is depicted by the red dotted triangle. Reproduced, with permission, from Cabrera *et al.*[48] AV, atrioventricular; CSO, coronary sinus ostium; OF, fossa ovalis; RVA, right ventricular apex; RVOT, right ventricular outflow tract; STV, septal leaflet of the tricuspid valve.

The bundle of His is ~1.8 cm long in an adult heart and is primarily located deep within the insulating tissue of the central fibrous body.[49,54] The central fibrous body adjoins the membranous septum and is a continuity between the aortic and mitral valves that extend rightwards to link with the septal tricuspid leaflet hinge line. The tendon of Todaro inserts into it at the apex of the Koch triangle (*Figure 1*). The His bundle emerges from the central fibrous body at the interventricular septal crest, most often on the left side,[55] and then immediately branches into the left and right bundles in most normal hearts. Therefore, in the majority of cases, it is the penetrating bundle of His which is being paced. This explains why it is important to feel torque build-up when screwing the lead, for it to be properly fixated in the central fibrous body.

In the report by Cabrera *et al.*[49] the membranous septum is located between the right atrium and the LV and lacks an inter-ventricular component in 59% of the hearts. In these cases, there is a rapid take-off of the fascicles of the LBB at the level of the hinge of the septal leaflet of the tricuspid valve. In a minority of hearts, the His bundle has a non-branching portion as it emerges from the central fibrous body and runs a variable course on the ventricular septum before dividing into LBB and right bundle branch (RBB). Kawashima and Sasaki[56] performed autopsies in 105 elderly patients and found 3 distinct courses of the His bundle with respect to the membranous septum. In 47% of cases, the His bundle runs just below the inferior border of the membranous septum under a thin layer of myocardium; in 32%, it runs at a distance below the membranous septum within the myocardium; and in 21%, it is 'naked' and runs just below the endocardium (but is surrounded by a fibrous sheath). This last instance explains why His capture may be selective, even on the ventricular aspect of the tricuspid valve.[51] In the IMAGE-HBP study,[51] it was shown that almost 80% of HBP leads were positioned on the ventricular aspect of the tricuspid valve, on average at 5–10 mm from the tricuspid valve plane. These findings seem at odds with the anatomical description of the length and course of the His bundle by Cabrera *et al.*,[49] and it is possible that some of these patients were in fact being paced in the proximal RBB or that the non-branching component of the HB is more often identified in clinical practice than in the referenced anatomical study.

The commissure between the anterior and septal leaflets of the tricuspid valve is adjacent to the membranous septum,[57] at proximity to the His bundle. In a case series of five patients with HBP leads located in the ventricle, three-dimensional echocardiography revealed that the

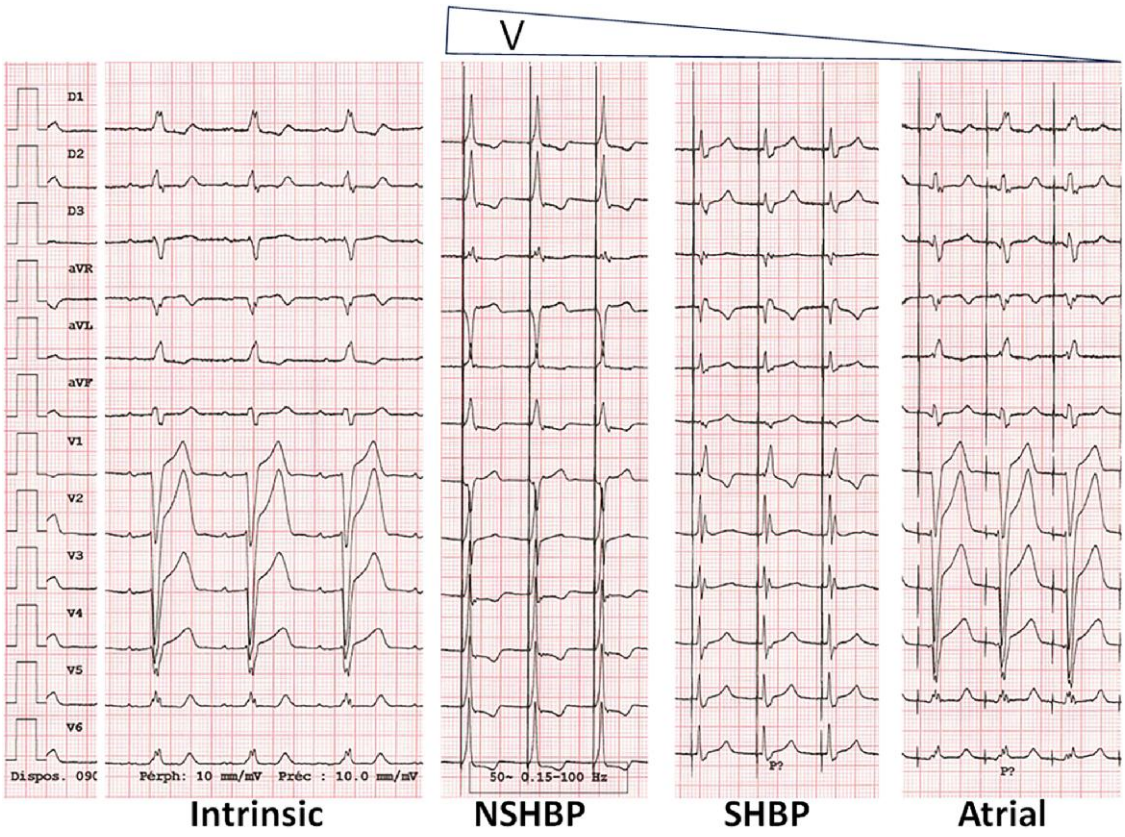

Figure 2 Illustration of His, ventricular, and atrial tissue capture by the His bundle lead. Intrinsic rhythm: sinus rhythm with preserved atrioventricular conduction and left bundle branch block. During the threshold test with decrementing pacing output (V), various transitions were noted. NSHBP, non-selective His bundle pacing with capture of the His bundle + local myocardium; SHBP, selective His bundle pacing with correction of left bundle branch block and QRS displaying a right bundle branch block pattern (due to selective capture of conduction fibres destined for the left ventricle. Atrial: lowering of pacing output resulted in capture of the right atrium only, with 1:1 atrioventricular conduction.

leads crossed the tricuspid valve in this commissure, without any impingement on the leaflets,[58] explaining why HBP does not increase tricuspid regurgitation. Although the His bundle is very close to the aortic root, being located just below the non-coronary and right coronary cusps, there have not been any cases reported of damage to the aortic root by HBP.

The RBB is a thin cord-like structure, which most often splits off from the His bundle at an angle from the left aspect of the muscular inter-ventricular septal crest and takes a short intramuscular course within the septum before it emerges in the sub-endocardium of the RV, where it continues superficially in the sub-endocardium of the septomarginal trabeculation.[59] In 5/32 hearts, Massing and James[55] found that the His bundle courses on the right side of the crest of the inter-ventricular septum. In these cases, the RBB formed a direct continuity with the His bundle. Pacing of the *proximal* RBB has recently been described[60,61] and was found in 19% of cases where HBP was originally intended.[61]

Left bundle branch and fascicles

The LBB immediately takes a sub-endocardial course on the left septum, most often immediately after the His bundle has reached the crest of the muscular ventricular septum.[48] In contrast to the RBB, the LBB has a very variable anatomy. It usually fans out into three main fascicles (the anterior, septal, and inferior/posterior fascicles). The anterior fascicle is the thinnest and the inferior fascicle the thickest (and therefore the easiest to target for LBBAP). Unlike HBP, where the target zone for effective pacing is very small, that of LBBAP is wide. Based upon results of the MELOS (Multicentre European Left Bundle Branch Area Pacing Outcomes Study) registry,[26] only 9% of patients were actually paced at the level of the LBB. Almost 70% of patients were paced at the fascicular level, usually at the septal and inferior fascicles. The septum is usually thinner and easier to penetrate at this level than more proximally. The fascicles are surrounded by a fibrous insulating sheath and require the lead to be in close proximity to achieve conduction system capture. Indeed, it has been shown by the IMAGE-LBBP study that the lead tip is most often sub-endocardial and on average only 2 mm from the LV blood pool.[62] However, fascicular potentials were sometimes recorded on the leads even at distances >4 mm from the blood pool, which raises the question of whether there are conduction system fibres which penetrate the inter-ventricular septum. Even though this has never been demonstrated, it is acknowledged that terminal fibres may be under-recognized by histological analysis owing to its destructive nature and by micro-CT due to loss of fibrous sheaths.[60]

The landing zone of the LBBAP lead may be on the right-sided septum at proximity to the RBB, resulting in transient or permanent RBB block[46] Pacing lead damage to septal perforators of the coronary arteries and veins has been reported, with acute myocardial ischaemia (possibly due to spasm), septal haematoma, as well as coronary fistulas.[26,46]

Overview conduction system pacing capture

The conduction system of the heart can be captured selectively (s-), i.e. without direct activation of the adjacent myocardium or non-selectively (ns-) when local myocardium is depolarized simultaneously with the His-Purkinje fibres. Selective capture is diagnosed when after the pacing spike there is an isoelectric interval before QRS in all 12 electrocardiogram (ECG) leads. This latency period corresponds with conduction within His-Purkinje fibres and might be very short with distal CSP and more prolonged with proximal CSP or in cases with diseased, slowly conducting His-Purkinje fibres. Lack of direct depolarization of the local myocardium reflects itself in endocardial tracing as a non-captured discrete local potential—because the local activation is not simultaneous with the pacing stimulus.

Clinical significance of selective vs. non-selective capture is not well delineated. Direct engagement of the myocardium during non-selective capture represents the non-physiological component of CSP. In some clinical scenarios, non-selective capture might be preferred over selective capture (in progressive conduction system disease, high conduction system capture threshold, or as a form of compensation for the delay in activation via the conduction system). Considering the selective vs. non-selective dilemma, it should be noted that non-selectivity is not a binary phenomenon. The degree of non-selectivity varies substantially from barely noticeable pseudo-delta wave to a dominant activation wavefront resulting in QRS not much different from pure myocardial paced QRS. This is because the degree of non-selectivity depends on the interplay of two latency periods: the latency in His-Purkinje fibres and the latency in the adjacent working myocardium, as well as its mass.

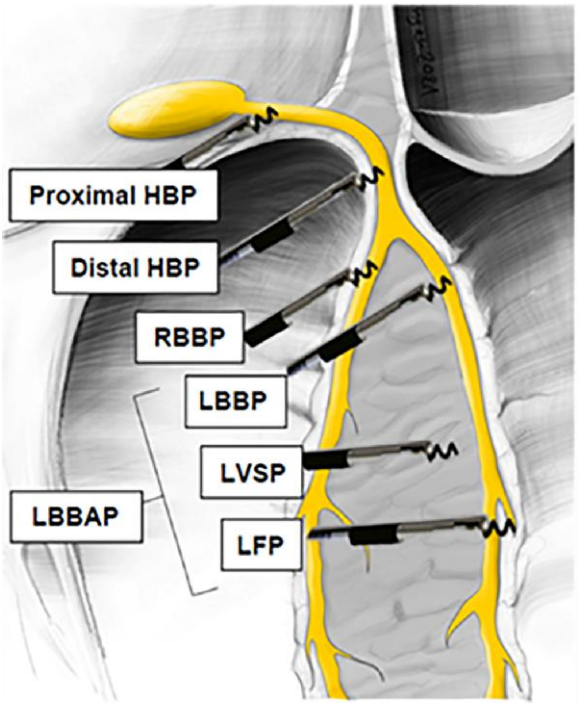

Figure 3 Outline of capture types obtainable at various levels of the conduction system. HBP, His bundle pacing; LBBAP, left bundle branch area pacing; LBPP, left bundle branch pacing; LFP, left fascicular pacing; LVSP, left ventricular septal pacing; RBBP, right bundle branch pacing; LAFP, left anterior fascicle pacing; LPFP, left posterior fascicle pacing; LSFP, left septal fascicle pacing. Modified with permission from Burri *et al.*[46]

Capture can be obtained at various levels of the conduction system axis—as illustrated by *Figure 2*. Each of these sites offers some relative advantages and disadvantages. Little is known about the differences in long-term clinical outcomes between these pacing modalities. The choice of one CSP type over the other depends on the physician preference/skills, clinical indications, and anatomical challenges. Definitions, nomenclature, and brief overview of various CSP capture types are provided in *Figure 3*.

His bundle pacing

His bundle pacing is the most physiological CSP option. His bundle pacing is identified when the pacing lead is positioned in the HB region either on atrial or ventricular side, and the criteria for HBP are met. These criteria rest on indicating that the direct activation of the HB during pacing is present (*Table 1*). His bundle pacing is characterized by narrow paced QRS, either nearly identical as native QRS (s-HBP) or slightly broader due to initial pseudo-delta wave (ns-HBP) but with a smooth subsequent activation without mid-QRS slur, notch, or plateau.[63] The hallmark of HBP is physiologically paced V6 R-wave peak time (V6RWPT)—which serves as electrocardiographic surrogate of local activation of the lateral wall of the LV.[63]

In the vast majority of HBP cases, the HB potential is recorded, and this confirms anatomical position of the pacing lead (His-ventricular interval $\geq$35 ms) and can also serve to confirm capture of the HB. If the HB is captured, then the interval from the pacing spike to the peak of the V6RWPT is the same ($\pm$10 ms) as the interval from HB potential to the V6RWPT (paced V6RWPT = native V6RWPT) because the activation pathway from HB to the lateral wall of the LV is identical (*Figure 4*).[64] In cases of LBBB or prolonged His-Ventricle (HV) interval, paced V6RWPT should be shorter than native V6RWPT, indicating that correction of conduction disturbances was obtained with HBP.

Limitations of the HBP (high capture threshold, long-term threshold rise, poor sensing) hopefully would be addressed by better implantation tools, matured implantation technique, proper patient selection (suitable anatomy, narrow QRS), and by more stringent success criteria at implant (not accepting borderline/high acute threshold, and unstable lead position).

Right bundle branch pacing

Right bundle branch pacing (RBBP) is defined as a direct capture of the right-sided conduction system distal to

Table 1 Criteria for conduction system capture

Criterion	Comments	SN (%)	SP (%)
HBP			
Absence of notch/slur/plateau in any of the leads: I, V4-V6	Does not exclude capture with underlying non-corrected LBBB/IVCD	67-83	92.5-96.3
Paced V_6RWPT <105 ms	Paced V_6RWPT measured from the pacing stimulus	64.9-70.4	~100
ΔV_6RWPT < 12 ms (paced V_6RWPT-native V_6RWPT)	Native V_6RWPT measured from HB potential. Not applicable in LBBB	100	99.1
QRS transition during threshold test	Non-invasive diagnostic gold standard	95	100
QRS transition during programmed stimulation or burst pacing	Alternative method to threshold test to obtain QRS transition	100	100
RBBP			
QRS transition and any of the below:			
ΔV_6RWPT > 10 ms (paced V_6RWPT-native V_6RWPT)	Onset of ventricular activation is due to retrograde conduction to the HB/LBB	87.2	95.3
Double transition in QRS morphology during threshold test	Excluding double transition due to BBB correction	—	—
Selective paced QRS morphology ≠ intrinsic QRS morphology	Selective paced QRS indicative of some delay in LV activation	—	—
Potential-QRS onset interval <35 ms	The shorter the interval, the higher the specificity	—	—
LBBP/LFP			
ΔV_6RWPT ≤ 10 ms	Paced V_6RWPT-native V_6RWPT	88.2	95.4
Paced V_6RWPT ≤75 ms		53	~100
Paced V_6RWPT ≤83 ms		84.7	96.3
QRS transition during threshold test		26.4-75.4	100
QRS transition during programmed stimulation		62.1	100
QRS transition during lead deployment		—	—
V6-V1 ≥ 44 ms		39	~100
LVSP			
Terminal r/R wave in V1		~90	—
Lead tip in the left sub-endocardial area	Lead depth >1 cm within septum probably can be used as less specific surrogate	—	—
ΔV_6RWPT ≥ 10 ms (paced V_6RWPT-LBBP V_6RWPT)	Applicable when LBBP paced V_6RWPT can serve as reference	>90	>90
LBBAP			
Any of the above LVSP or LBBP/LFP criteria		~90	—

HBP, His bundle pacing; LBBP, left bundle branch pacing; LBBAP left bundle branch area pacing; LFP, left fascicular pacing; LBBB, left bundle branch block; V_6RWPT, V_6 R-wave peak time; RBBP, right bundle branch pacing; —, no data.

the HB. Right bundle branch pacing is characterized by a short potential to ventricular electrogram interval (usually in the range 20-34 ms), pacing lead in the sub-endocardial area on the right side of the inter-ventricular septum and fulfilled criteria for conduction system capture (*Table 1*).[61] Proximal RBBP can be obtained inadvertently when HB is targeted and can easily be mistaken as HBP, although these two types of right-sided CSP can be differentiated (*Table 1*). Right bundle branch pacing paced QRS is nearly always non-selective, broader with more prominent pseudo-delta wave. Paced RBBP V6RWPT is also longer—reflecting slight delay in LV activation in comparison with HBP. When the pacing site is close to the HB bifurcation, both types of capture (HBP and RBBP) can be seen at different outputs resulting in a double transition pattern. Capture of very distal RBB is unlikely to have any clinical benefit, judging by its minor effect on the surface ECG and might easily be mistaken with RV septal pacing.[60] The diagnostic hallmark of RBBP is a mismatch between the paced and native V6RWPT (stimulus to V6RWPT is ≥10 ms longer than the potential to V6RWPT). Although RBBP is less physiological than other CSP options, it can potentially address some of the drawbacks of HBP and left bundle branch pacing (LBBP) and might be preferable in selected patients. Right bundle branch pacing does not require invasive ventricular trans-septal access to the conduction system (in contrast to LBBP), while ample myocardium around the RBB ensures good sensing and 'backup' myocardial capture (*Figure 5*).

Left bundle branch pacing

Left bundle branch pacing is defined as a capture of the pre-divisional LBB with simultaneous activation of all of its fascicles. Since the main LBB is a sizable structure, LBB potential should be present at the capture site, with potential to QRS interval in the range of 25-34 ms. Diagnosis of LBBP rests on the anatomical position of the pacing lead and the criteria for left conduction system

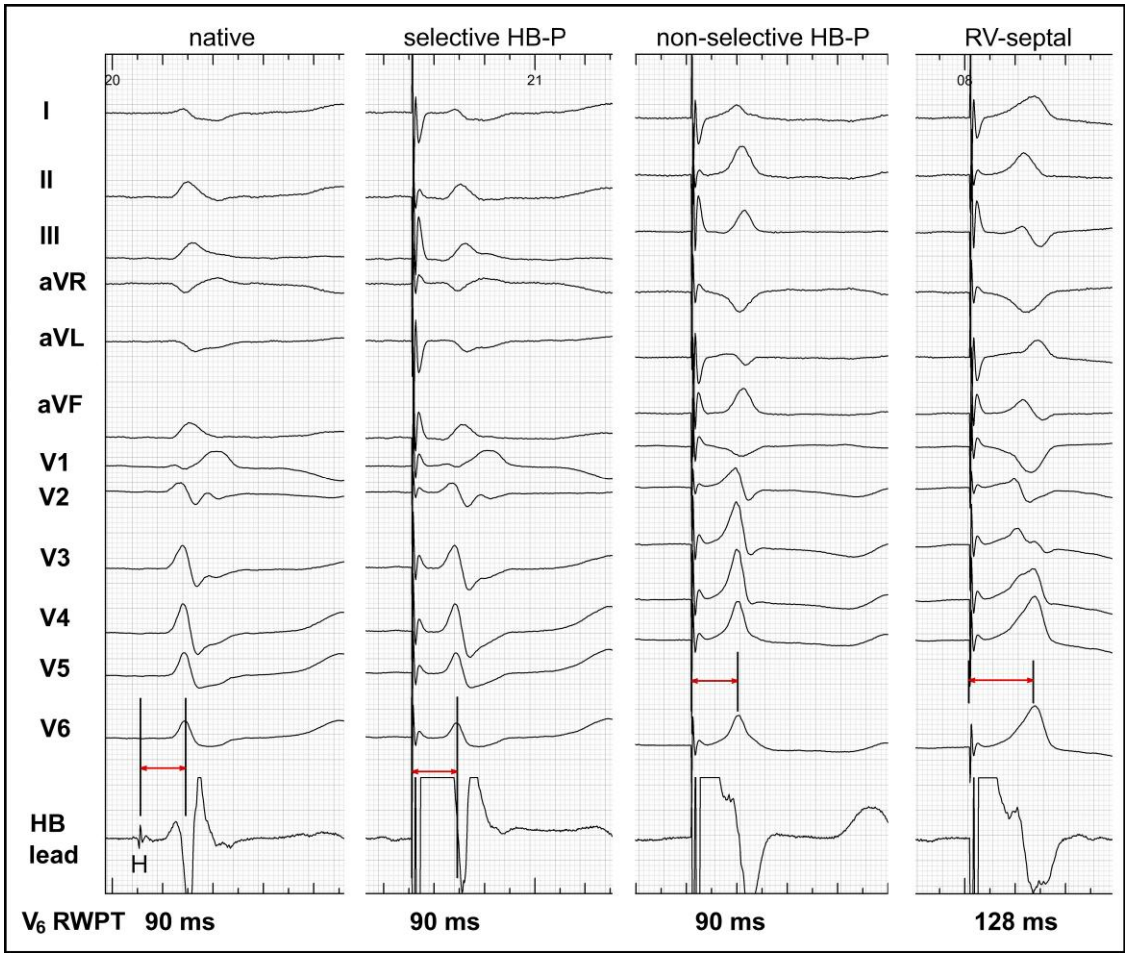

Figure 4 V_6 R-wave peak time reflects activation time of the lateral wall of the left ventricle. It remains constant during native conduction and both selective and non-selective His bundle pacing. Loss of His bundle capture, that is right ventricular septal-only capture, results in prolongation of paced V_6 R-wave peak time by 38 ms (from 90 to 128 ms). Reproduced with permission from Jastrzebski *et al.*[64]

capture (*Table 1*). Left bundle branch pacing paced QRS is characterized by fast activation of the LV reflected by physiological values of V6RWPT.[65] Since LBBP at the working pacing output is obligatory non-selective and the potential to QRS period is relatively long, the direct depolarization of the basal septal myocardium is substantial. Left bundle branch pacing should be differentiated from distal HBP with RBB block. This can be accomplished based on anatomical position of the pacing lead if distal HB is marked or by documenting transitional paced QRS complex morphologies during progression through the septum (phenomenon absent during HBP). In some cases, this differentiation is challenging and might be impossible when the lead is placed at the HB bifurcation. Left bundle branch pacing advantages over HBP include lower pacing thresholds, better ventricular sensing, and the ability to reliably recruit more patients with conduction system disease.

Left fascicular pacing

Left fascicular pacing (LFP) is defined as pacing of the left Purkinje network created by the inter-connected fascicles of the main LBB (*Figure 6*).[26] Left fascicular pacing is characterized by short potential to QRS interval (1–25 ms) or absence of Purkinje potential. The terminal Purkinje fibres generate small potential that might not be recordable from the distance that the virtual pacing electrode allows. During LFP, criteria for left conduction system capture must be fulfilled (*Table 1*)—these are based on QRS transition during dynamic manoeuvres and on paced QRS metrics as for LBBP. Paced QRS has minimal or no noticeable pseudo-delta wave and often superior QRS axis. Transition to left ventricular septal pacing (LVSP) is usually subtle as the Purkinje to myocardium junction is close, facilitating fast retrograde invasion. Left fascicular pacing is obtained when the pacing lead is on the left side of the interventricular septum, usually more mid-septal and inferior than during LBBP. Although in cases of early branching or ribbon fan-like LBB, capture of one of the fascicles rather than the main LBB can be obtained already at quite proximal/basal sites. Left fascicular pacing area seems to offer several advantages as the pacing lead is far away from the tricuspid valve, the fibrous sub-annular region where lead helix entanglement can be a problem, and larger coronary

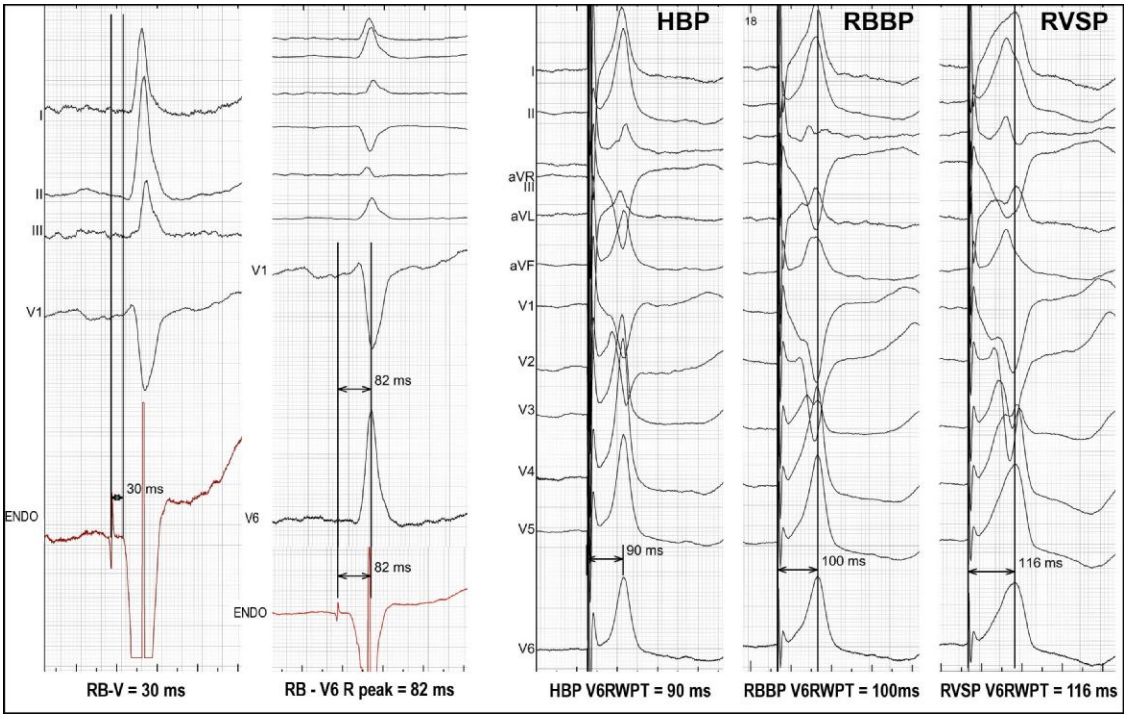

Figure 5 QRS and V_6 R-wave peak time difference between different His bundle area capture types. Patient with right bundle branch pacing, right bundle branch to ventricle interval of 30 ms, and potential to V_6 R-wave peak time of 82 ms. Two QRS transitions with small (<20 ms) increments of V_6 R-wave peak time were present. At high output, His bundle pacing was obtained with paced V_6 R-wave peak time of 90 ms, similar to native potential to V_6 R-wave peak time of 82 ms (±10 ms). At working output, right bundle branch pacing was observed, resulting in V_6 R-wave peak time increase by 10 ms. At low output, loss of right bundle branch capture was observed resulting in right ventricular septal pacing and further increase of V_6 R-wave peak time by 16 ms. Reproduced with permission from Jastrzebski *et al.*[61]

arteries. Moreover, LFP area is broader and more easily accessed and targeted than the proximal LBBP site. MELOS found LFP the most commonly obtained site of LBBAP capture type in real-world clinical practice.

Left ventricular septal pacing and left bundle branch area pacing

Left ventricular septal pacing (LVSP) is defined as a capture of the septal myocardium close to the left sub-endocardial area, albeit without direct activation of the left conduction system. During LVSP, the left conduction system is probably promptly activated (with variable delay of 5–35 ms) via retrograde invasion. Acute LVSP studies suggest very favourable LV activation and function despite lack of direct activation of the conduction system.[20,66] However, lack of prompt conduction system engagement might result in delayed activation of the lateral wall of the LV and suboptimal outcomes, especially in patients with HF[67]—this needs to be further addressed in clinical trials. It is likely that LVSP shows greater heterogeneity than other CSP pacing options. Depending on where the septum is penetrated, the obtained QRS and LV activation might vary substantially. Left ventricular septal pacing is usually a diagnosis of exclusion—made when there is terminal r/R wave in lead V1 but the criteria for left CSP are not fulfilled.[46] However, diagnosis of LVSP based on these criteria is neither 100% sensitive nor 100% specific. This is because it is possible to obtain LVSP/LBBAP without terminal r/R wave in lead V1,[68] while in other cases, r/R in V1 might appear already at deep septal pacing lead positions.[69] or even when pace mapping the right septal surface.[60] Therefore, diagnosis of LVSP based on the above does not fully exclude possibility of deep septal pacing or conduction system capture. Only in cases when LBBP/LFP capture was obtained but was subsequently lost, the diagnosis of LVSP can be made with high certainty because the LBBP/LFP paced QRS can be then used as the diagnostic reference. Left ventricular septal pacing paced QRS compared with LFP/LBBP is characterized by several features reflecting some deviation from physiology: usually more prominent pseudo-delta wave and/or broader QRS, evident repolarization abnormalities in leads I and V5–V6, and V6RWPT longer by 10–25 ms. The term LBBAP is used to address the common clinical scenario when differentiation among LVSP, LBBP, and LFP is uncertain or was not properly performed.

His bundle optimized/left bundle branch optimized-cardiac resynchronization therapy

His bundle optimized-CRT and left bundle branch optimized-CRT are denominations used to describe hybrid pacing options: sequential pacing of LV myocardium with cardiac vein lead and CSP using HBP or LBBAP, respectively.[67,70,71]

These pacing modalities are used when HBP or LBBAP alone does not result in adequate normalization of the LV activation. This might be reflected by broad paced

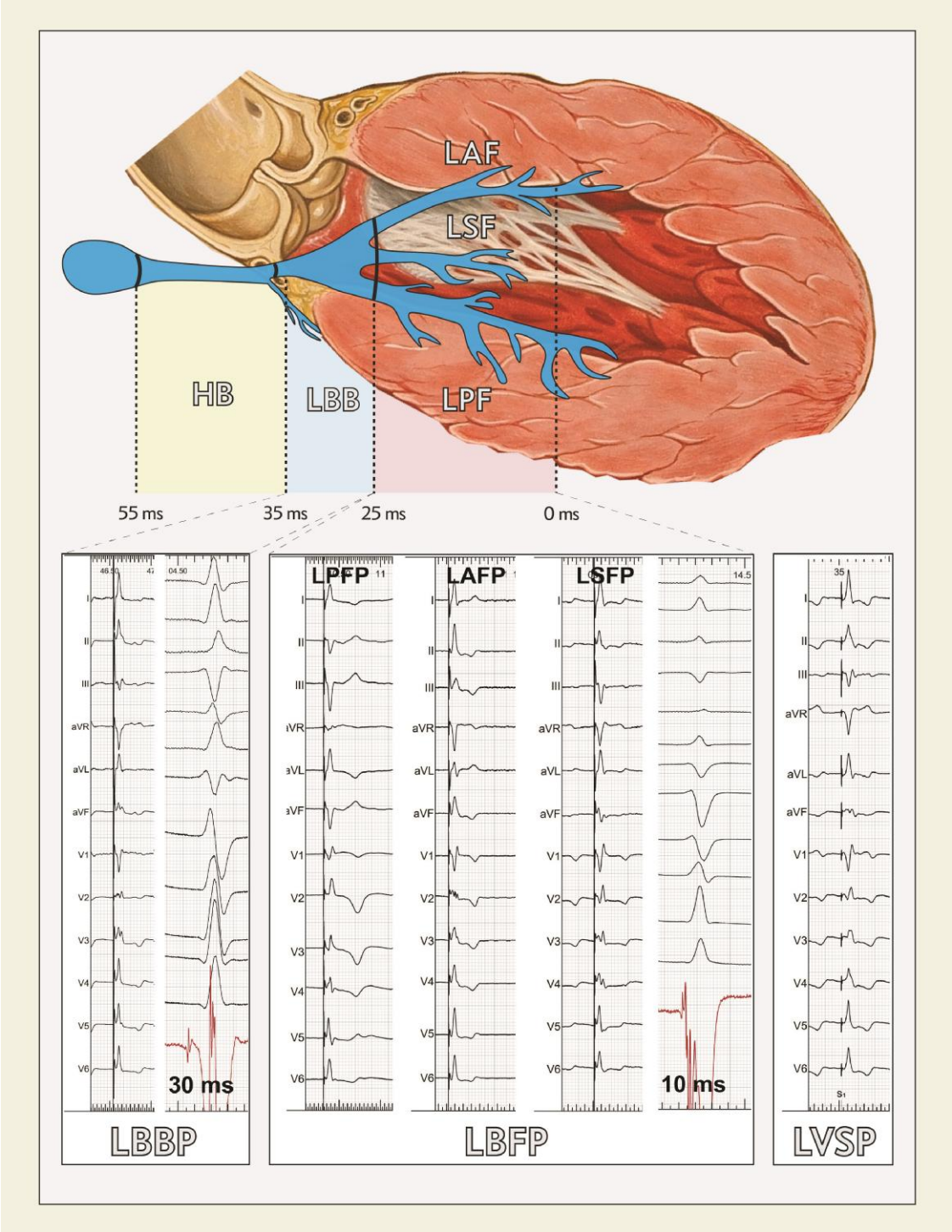

Figure 6 Examples of paced electrocardiogram patterns and endocardial electrograms during left bundle branch area pacing. Left bundle branch pacing characterized by left bundle branch potential to QRS interval of 34–25 ms and lead tip position ~1.5 cm from the His bundle. Left fascicular pacing—characterized by potential to QRS of 0–24 ms and lead tip position ~1.5–4.5 cm from His bundle. Left bundle fascicular pacing includes: left posterior fascicle pacing, left anterior fascicle pacing, left septal fascicle pacing. Left ventricular septal pacing: diagnosed when left bundle branch capture criteria are not met, any distance from His bundle. Heart drawing based on work by Patrick J. Lynch and C. Carl Jaffe, MD/CC-BY 2.5, https://commons.m.wikimedia.org/wiki/File:Heart_anterior_view_coronal_section.jpg, reproduced with permission from Jastrzebski *et al.*[26]

QRS, V6RWPT over the physiological values (>90 ms for LBBAP and >110 ms for HBP), paced QRS notch/slur, or lack favourable acute haemodynamic response to HBP/LBBAP pacing alone.

Conclusions

This review focuses on clinical aspects of the anatomy and electrocardiography of CSP. There are several

randomized trials underway that will help us better understand the benefits of CSP over both RVP and BiVP in patients with high right ventricular apex pacing burden, conductions system disease, and cardiomyopathy. The electrocardiography of pacing the conduction system and the ventricular myocardium alone and together typically require measurements of peak R wave but also transitions during pacing to really confirm the conduction system capture. The highly variable anatomy of the conduction system explains the complexity of the ECG patterns seen with CSP.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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