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BCS Editorial

Conduction System Pacing: The future of pacing?

Akriti Naraen MBChB

Cardiology Registrar

Liverpool Heart and Chest Hospital, Thomas Drive, L14 3PE

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Take Home Messages

- Conduction system pacing, (His-bundle and left bundle area pacing) is an emerging alternative method of pacing that is gaining prominence for superiority demonstrated in observational data when compared to conventional pacing.
- The level of block in the conduction system needs to be considered before lead implant in order to ensure lead placement is distal to the level of block.
- Technical challenges such as a higher capture threshold, less accessible anatomy and no dedicated device autoregulation algorithms remain an obstacle.
- Conduction system pacing is most commonly considered in biventricular pacing with a failed left ventricular lead implant, and as a primary implant in patient undergoing concomitant AV node ablation, patients with heart failure and biventricular pacing indications and in AV block.

Introduction

Conduction system pacing (CSP) is a novel method of cardiac pacing that uses the heart's own conduction system to enable efficient, physiological ventricular activation (1,2).

Right ventricular pacing (RVP) and biventricular pacing (BVP) are the known conventional pacing methods. In RVP, by the nature of lead placement, inter-ventricular dysynchrony is introduced. In patients with left bundle branch block (LBBB) and severe left ventricular dysfunction, dysynchrony is particularly deleterious, and so a left ventricular lead is added in an endeavour to overcome this dysynchrony (3–5).

Conduction system pacing, through careful placement of the lead in the His-bundle or the left bundle area (LBA), provides an alternative to overcome inter-ventricular dysynchrony through physiological activation (5,6).

Techniques

His-bundle pacing was first described in 2000 when leads were successfully implanted in the His-bundle in 12 patients undergoing atrio-ventricular node ablation and pacemaker insertion (7). It is a technically challenging procedure with complex criteria to establish capture of the conduction system (8). Over the last twelve years, sheaths, leads and techniques have been developed to faciliate these challenging implants. We are now seeing promising outcomes reported in observational studies. Initial work concentrated on pacing from the His-bundle, however techniques have evolved to now include left bundle area pacing (**Figure 1**).

About the author

Akriti Naraen graduated from the University of Liverpool Medical School in 2014 and is currently training as a Cardiology registrar in Mersey Deanery. She has an interest in Cardiac Devices and Inherited Cardiac Conditions, with several presentations and publications in these areas. She has a keen interest in teaching and research and has completed a Post-graduate certification in Health Research with the University of Oxford as well a second Post-graduate certification in Medical Education with the University of Lancaster.

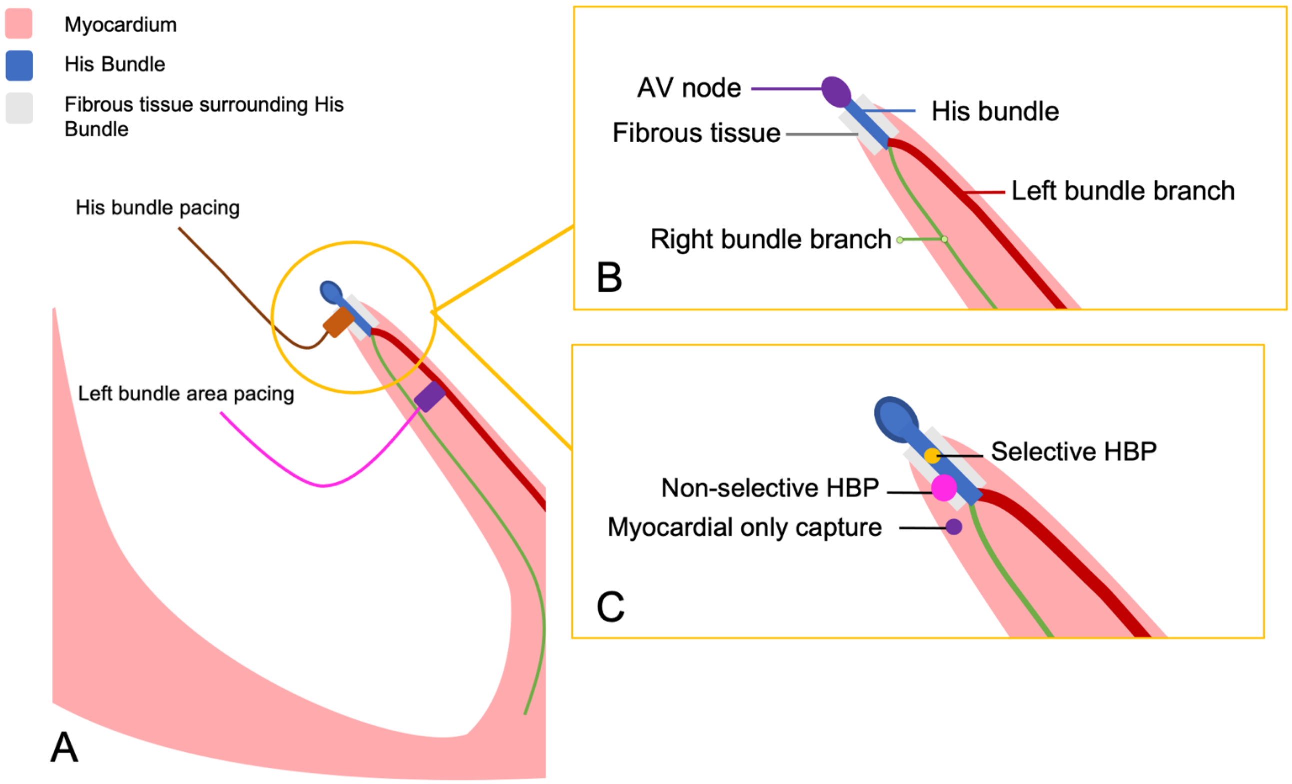

Figure 1.
A: Conduction system pacing sites.
B: Anatomy of the conduction system.
C: Capture sites; Selective HBP captures the His-bundle alone. Non-selective HBP captures the His-bundle and the myocardium. Myocardium only capture, captures the myocardium alone.

AV =Atrio-ventricular; HBP = His-bundle pacing.
(This image was produced by Akriti Naraen)

Both these methods aim to place a lead distal to the level of block in the conduction system, promoting rapid conduction through the specialised His-Purkinje fibres. This not only restores inter-ventricular synchrony but also improves efficiency of electrical conduction compared to the slow myocardial activation seen in both RVP and BVP. This is reflected with a narrow QRS complex with a similar morphology to the intrinsic QRS (**Figure 2**) (1,8).

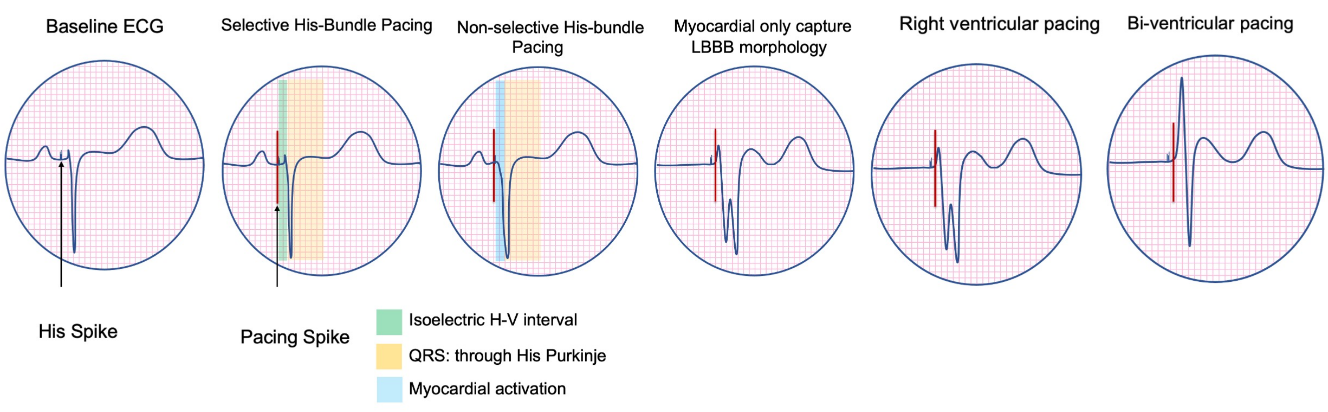

Figure 2: *ECGs with a His-bundle lead in comparison to conventionally paced ECGs*

LBBB = Left bundle branch block.
(This image was produced by Akriti Naraen)

Evidence

1. Observational data

Observational data has demonstrated improved left ventricular ejection fraction (LVEF), heart failure outcomes and mortality rates with His-bundle pacing (HBP) compared with RV pacing in those with atrioventricular nodal block (5,9,10). Improvement in symptoms, heart failure related hospitalisation, LVEF and mortality was also seen in CSP when compared to BVP across different patient populations (6,11,12). Similar improvements in LVEF were seen in patients undergoing AV node ablation and HBP (13). These findings are summarised in **Table 1**.

2. Randomised control trials

The conclusions from observational studies have formed the foundations for multi-centre randomised control trials such as His-SYNC (14), LBBP-RESYNC (15), LEVEL-AT (16) and PROTECT-HF (17). LEVEL-AT showed non-inferiority of CSP to BVP. And although His-SYNC, a pilot randomised trial, did not show a significant improvement in LVEF or reduction in QRS duration, LBBP-RESYNCH did show better LVEF in LBA pacing compared to BVP. However, in view of the small population, an overestimated effect size should be considered. Additionally, a high cross-over rate in His-SYNC invalidated the intention-to-treat analysis of the efficacy of HBP compared to BVP (14–16).

3. Meta-analyses

Several meta-analyses have reviewed the extensive observational and limited randomised data. These reviews confirm that CSP has superiority in preserving LV function compared to RVP in AV block (18,19). Improved LV function and NYHA class outcomes in CSP were seen when compared to BVP as a primary intervention and in device upgrade to cardiac resynchronisation therapy (CRT) (20,21).

4. Guidelines

The European Society of Cardiology (ESC) and American College of Cardiology (ACC) have recognised these consistent promising outcomes with inclusion of CSP in their guidelines.

Notably ESC recommends the use of CSP in failed LV implants and in those with an anticipated high RV pacing burden, where ACC recommends CSP in the latter indication alone (22,23).

5. Ongoing trials

PROTECT-HF is a large multicentre randomised trial that is underway. The study aims to recruit 2600 patients (with a median four-year follow-up) to assess CSP against RV pacing in bradycardia indications (17).

Limitations

Although CSP outcomes are encouraging, there remains challenges in delivering conduction system pacing universally. Firstly, there is the technical aspect of the procedure with an associated learning curve; the area for His-capture is small, usually needing electrophysiological expertise with specialist electrophysiology equipment to establish His-capture as per the agreed yet complex criteria of selective and non-selective capture (8). RV pacing, however, is usually delivered by general cardiologists in non-tertiary settings. Furthermore, the His-bundle is wrapped in a fibrous tissue (**Figure 1**) that can be difficult to penetrate and lead to high capture thresholds, which quickly deplete battery life, requiring multiple generator changes with their associated risks (1).

Additionally, LBA pacing does not have defined capture characteristics leading to ambiguous and inconsistent practice in lead placement (35).

Additional training is required for cardiologists, cardiac physiologists and the wider catheter lab team due to higher overall complexity of CSP, not only at the time of implant but during follow-up and in device programming. Devices do not have CSP-directed algorithms and therefore are unable to identify problems, or preserve battery life with auto-adjustments as in conventional pacing (36). Finally, there is limited experience in extracting CSP leads embedded deep in the septum (37).

Work is underway to overcome some of these challenges to enable widespread adoption of conduction system pacing outside of tertiary centres. In particular addressing the complexities in standardising the procedure and establishing capture.

The benefits and challenges of CSP are summarised in **Table 2** (1,8,22,35-39).

Table 1 (continued on page 5). Data on conduction system pacing in comparison to BVP

Study	Inclusion criteria	Year	Patient cohort	Study Design	Number of patients	Follow-up (months)	Outcomes
Vijayaraman *et al.* (11)	EF ≤ 35% Class I- II indication for CRT	2022	CSP (87 HBP, 171 LBAP) v BVP	Two-centre Retrospective Observational	477	12	Primary outcome of HFH + mortality (28.3% vs 38.4%; HR 1.52; 95% CI 1.082-2.087; p = 0.013) Improved EF in CSP (39.7% ± 13% vs 33.1% ± 12%; p < 0.001)
Chen *et al.* (12)	EF ≤ 35% LBBB	2022	LBAP v BVP	Multicentre Prospective Observational	100	12	Improved absolute EF at 1 year in CSP (49.10 ± 10.43% vs. 43.62 ± 11.33%, p = 0.021)
Vijayaraman *et al.* (24)	EF < 50% CRT or ventricular pacing indication	2021	LBAP v BVP	Multicentre Retrospective Observational	325	12	Improved EF in CSP (33 ± 10% to 44 ± 11%, p < 0.01)
Huang *et al.* (25)	Non-ischemic CM EF ≤ 50% LBBB CRT or ventricular pacing indication	2020	LBAP in pacing indication or failed BVP	Multicentre Prospective Observational	63	12	Improved EF in CSP (33 ± 8% vs. 55 ± 10%; p < 0.001) NYHA improved in CSP: 2.8 ± 0.6 at baseline to 1.4 ± 0.6 at 1 year
Wu *et al.* (6)	EV ≤ 40% LBBB CRT indication	2020	LABP v HBP v BVP	Multicentre Prospective Case control Observational	137	12	Comparable EF improvement LABP V HBP. (+23.9% vs +24%, p = 0.977) Improved EF compared to BVP Improved NYHA in CSP
Deshmukh *et al.* (26)	EF ≤ 35% LBBB NYHA 2-4	2020	HBP + LV lead in BVP indications	Single centre Retrospective Observational	21	30	Improved EF in CSP (27.6 ± 6.4% to 41.1 ± 12.5, at 25 mean months, p = 0.001) Improved NYHA in CSP: 3.1 ± 0.5 to 2.1 ± 0.8, at mean 32 months, p < 0.001).
Upadhyay *et al.* (14)	Conventional CRT indication: LBBB + EF ≤35% EF ≤ 35% + RVP > 40% AF + 100% RVP + EF ≤ 35%	2019	HBP v BVP	Multicentre Prospective Crossover RCT	41	12	No significant difference in EF (p = 0.33). High crossover rates. Trend toward high echo response in HBP (p = 0.078)
Huang *et al.* (27)	LBBB NYHA 2-4 Indication for CRT or pacing	2019	HBP in LBBB with CRT or pacing indications	Single centre Prospective Observational	74	37	Improved EF in CSP (32.4±8.9% to 55.9±10.7%, p < 0.001) Improved NYHA in CSP:2.73±0.58 to 1.03±0.18 (p < 0.001
Vijayaraman *et al.* (28)	Bradycardiac pacing indication Failed LV lead	2019	LBAP in pacing indication or failed BVP	Single centre Prospective Observational	100	3	High success of CSP (93%)
Vijayaraman *et al.* (29)	EF ≤ 35% LBBB	2019	HBP + LV lead in BVP indications	Multicentre Retrospective Observational	27	12	Improved EF (24±7% to 38±10%, p < 0.0001), NYHA improved: 3.3 to 2.04

Table 1 (continued). Data on conduction system pacing in comparison to BVP

Study	Inclusion criteria	Year	Patient cohort	Study Design	Number of patients	Follow-up (months)	Outcomes
Sharma *et al.* (30)	NYHA 2-4 EF ≤ 50%	2018	HBP in failed BVP or alternative to BVP	Multicentre Prospective Observational	106	14	Improved EF 30% ± 10% to 43% ± 13%, p = 0.0001) Improved NYHA: 2.8 ± 0.5 to 1.8 ± 0.6 p = 0.0001
Sharma *et al.* (31)	NYHA 2-4 EF ≤ 50% RBBB	2018	HBP in failed BVP in RBBB	Multicentre Retrospective Observational	39	15	Improved EF (31±10% to 39±13%, p = 0.004) Improved NYHA: 2.8±0.6 to 2±0.7, p = 0.0001)
Ajijola *et al.* (32)	NYHA 2-4 EF < 35% BBB	2017	HBP in BVP indications	Single centre Prospective Observational	21	12	Improved EF (27% ± 10% to 41% ± 13%, p < 0.001) NYHA: 3 to 2, p < 0.01
Lustgarten *et al.* (33)	CRT indication QRS >120ms	2015	HBP v BVP	Multicentre Prospective Crossover RCT	29	6	Improved NYHA
Barba-Pinchardo *et al.* (34)	Failed LV lead LBBB NYHA 3 despite medical management	2013	HBP in failed BVP	Single centre Prospective Observational	16	31	Improved NYHA

BVP = Biventricular pacing; CRT = Cardiac resynchronisation therapy; CSP = Conduction system pacing; EF = Ejection fraction; HBP = His-bundle pacing; LBAP = left bundle area pacing; LBBB = left bundle branch block; LV = Left ventricle(ular); NYHA = New York Heart classification; RBBB = Right bundle branch block; RCT = Randomised control trial

Conclusion

Conduction system pacing is a capable alternative to conventional pacing with very encouraging data from observational studies and small randomised control trials. Large scale trials are on-going to establish these findings. Although, there are challenges to widespread uptake, work is underway to overcome them. Conduction system pacing, the future of pacing? It may well be.

Table 2. Benefits and challenges of conduction system pacing(1,8,22,35–39)

Benefits of conduction system pacing	Challenges of conduction system pacing
• Synchronised ventricular contraction with intrinsic activation patterns to overcome dysynchrony of left bundle branch block • Improvement in ejection fraction when compared to conventional pacing • Reduces likelihood of right ventricular pacing induced cardiomyopathy when compared to biventricular pacing • Haemodynamic improvement in patients with heart failure seen by a rise in blood pressure when compared to biventricular pacing • Alternative implant site for failed left ventricular lead implantation • Contrast not required for implant	• An understanding of level of block is needed prior to implant to guide appropriate site selection, eg. Infranodal block would require pacing distal to the site of the block • Technically challenging with increased lead displacement and associated learning curve resulting in long procedure and fluoroscopy times. Often limited to specialist centres with specialised electrophysiology equipment and expert teams • Need for “back-up” RV pacing lead in high degree AV block and AV node ablation • Difficulty in identifying capture of the His-bundle and lack of defined capture characteristics of left bundle area pacing • High thresholds resulting in more readily depleted battery life, in turn requiring more frequent battery changes • Challenging and complex device programming, especially with the lack of dedicated conduction system algorithms for the devices

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