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A new era of physiologic cardiac pacing

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Cardiac pacing aims to improve our patients' well-being by adapting heart rate to their physiological needs and may in some instances be lifesaving by avoiding asystole. However, it may also have adverse effects on acute and chronic cardiac pump function. Researchers have been striving to find alternative means of pacing the heart to mitigate these detrimental effects. Right ventricular septal pacing (as an alternative to apical pacing) has had mixed results.[1] Cardiac resynchronization therapy (CRT) by biventricular pacing (BVP) has proven to be a success story for treating selected patients with heart failure and there are some data showing that it also preserves ventricular function in patients requiring anti-bradycardia pacing with normal ejection fraction.[2] However, this therapy usually requires implantation of more complex systems and may be associated with issues such as elevated thresholds of the coronary sinus lead and phrenic nerve capture.

His bundle pacing (HBP) was first performed in the canine model by Scherlag *et al.*[3] in 1967 and in man in 1970 using temporary leads.[4] It was not until 2000 that permanent HBP using standard pacing leads was achieved in man.[5] This was a major milestone in physiological pacing but the technique was not widely adopted due to technical challenges. Furthermore, the main focus of research at that time was CRT, and the device industry's efforts were directed toward developing tools to facilitate implanting leads in coronary sinus tributaries. The advent of the Medtronic (Minnesota, MN, USA) 3830 lumenless 4.1F catheter-delivered lead introduced 20 years ago (initially intended for selective site pacing of the right atrium and ventricle) however opened up new perspectives for HBP and improved success rates compared to traditional stylet-driven leads.[6] Positioning and fixation of the 3830 lead on the His bundle region was further facilitated by the introduction of the 3D-shaped C315-His delivery catheter which served to markedly increase HBP adoption since 2017, along with the buzz on social media about the technique.[7]

Investigators in the Netherlands used an adapted version of the 3830 lead with a long helix positioned deep in the interventricular septum to pace the left ventricular septum. This proved to yield superior acute hemodynamics compared to right ventricular apical and septal pacing.[8] The concept evolved to left bundle branch area pacing (LBBAP) introduced by Huang *et al.*,[9] which provided excellent electrical parameters and which has since gained widespread adoption due to excellent electrical parameters (which is the Achilles' heel of HBP).

FDA approval for the 3830 lead was granted for HBP in 2018 and for LBBAP in 2022. CE-labelling for the 3830 lead and the C304-His catheter (a 3D-shaped deflectable catheter) were obtained for HBP in 2021 (MDR approval is pending for LBBAP). Stylet-driven leads are also used for HBP and LBBAP in clinical practice,[10,11] but currently no such leads have received regulatory approval for conduction system pacing (CSP). An overview of the currently approved CSP tools is provided in *Table 1*.

Recognition of CSP is progressively being established by international cardiac societies. HBP was introduced in the European Society of Cardiology (ESC) supra-ventricular arrhythmia guidelines in 2019[12] (for a 'pace and ablate' indication) and in the ESC pacing guidelines (*in lieu* of right ventricular anti-bradycardia pacing and in case of failed CRT implantation) in 2021.[13] Recently, the Heart Rhythm Society published a guideline on cardiac physiological pacing which includes indications for HBP and LBBAP along with BVP.[14] A European Heart Rhythm Association (EHRA) consensus document was recently published to standardize CSP implantation.[15]

In this supplementary issue of the journal, the authors overview CSP indications, implantation, and management. In addition, the role of CSP in treating heart failure patients with prolonged PR intervals and atrioventricular 'dromopathy' is discussed. A new treatment entity, also covered in this issue, is personalized accelerated physiological pacing which individualizes programming of lower pacing rate according to patient gender and height based on healthy individuals.[16] It promises to provide a new treatment strategy for heart failure patients with preserved ejection fraction, although more research is

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Table 1 Currently approved hardware for conduction system pacing (as of July 2023)

	FDA	CE-MDD	CE-MDR
Abbott			
Tendril STS 2088 lead Ultipace LPA 1231	To be submitted in 2023-LBBAP	—	To be submitted in 2024-LBBAP
Locator 3D catheter	—	—	To be submitted in 2023 for generic indications
Direct 3D	—	—	Generic indications
Biotronik			
Solia lead	IDE trial ongoing	—	In preparation
Selectra 3D catheter	IDE trial ongoing	—	Approved for HBP + LBBAP
Amvia pacemaker	IDE trial ongoing	—	Approved for LBBAP
Boston Scientific			
Ingevity + lead	—	—	—
SSPC catheters	—	—	—
Medtronic			
SelectSecure™ MRI SureScan™ Model 3830 Pacing Lead	Approved for HBP + LBBAP	Approved for HBP	Approved for HBP In preparation for LBBAP
C315 Delivery System, includes C315-HIS shape	Cleared for various lead implants; often used with HBP and LBBAP.	Approved for various lead implants; often used with HBP and LBBAP.	In preparation
SelectSite™ C304 Deflectable Catheter System, and SelectSite™ C304-HIS Deflectable Catheter System	Cleared for various lead implants; often used with HBP.	Approved for various lead implants; often used with HBP.	In preparation
Microport			
Pacing lead	—	—	In preparation
3D catheter	—	—	In preparation
Alizea/Borea/Celea pacemakers	—	—	In preparation

Boston Scientific did not provide any information beyond the fact that none of the hardware is currently approved. Readers should consult product technical manuals for update of approved or cleared indications.

CE-MDD, Conformité Européenne Medical Device Directive; FDA, Food and Drug Administration; HBP, His bundle pacing; IDE, investigational device exemption; LBBAP, left bundle branch area pacing; CE-MDR, Conformité Européenne Medical Device Regulation.

needed. As it may result in an increased percentage of ventricular pacing, CSP is well suited to be coupled with this pacing mode to avoid the untoward effect of ventricular pacing. The entity is also associated with increased rates of atrial pacing. Bachman's bundle pacing, which aims to mitigate interatrial dyssynchrony, may also be judicious for personalized accelerated physiological pacing as it may avoid atrial tachyarrhythmias associated with right atrial appendage pacing.[17] An overview of the implantation technique and the evidence in favour of Bachman's bundle pacing is revisited in this issue.

Over the past two decades, we have witnessed exciting developments in physiological pacing. By connecting to the patient's natural conduction system, these new modalities for pacing the heart avoid the detrimental effects of myocardial stimulation and may even correct underlying conduction disease. New frontiers are being explored, which promise to provide innovative solutions for the benefit of our patients.

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Data availability

No new data were generated or analysed in support of this research.

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