## Foreword

## Septal and Conduction System Pacing

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Specific conduction system pacing is a recent development in efforts to restore normal electrical conduction in the heart by means of artificial pacing.<sup>1</sup> It can be achieved by specific His or left bundle branch (LBB) pacing and, possibly, by non-specific high right ventricular (RV) septal pacing. There are several clinical situations in which conduction pacing is clearly indicated.

Abnormal conduction-induced cardiomyopathy refers to left ventricular (LV) systolic dysfunction caused by high-burden, apical right ventricular pacing, LBB block (LBBB) or pre-excitation.<sup>2-5</sup>

The deleterious effects of RV apical pacing in particular are now well established, and RV septal pacing, by means of intraventricular synchrony and LV function, is beneficial.<sup>6,7</sup> There is an increased risk of pacing-induced heart failure (HF), particularly during the first 30 and 180 days after implantation; randomised comparisons that showed septal had no benefit over apical pacing were limited by a relatively short-term follow-up and uncertainty about the precise position of the septal pacing lead.<sup>5,8–10</sup>

Mechanical dyssynchrony – nonsynchronous contraction of the wall segments of the left ventricle (intraventricular) or between the left and right ventricles (interventricular) – impairs systolic function and ventricular filling, increases wall stress and worsens mitral regurgitation. It is most readily identified by the presence of QRS widening and LBBB configuration on the electrocardiogram, or intraventricular conduction delay and a QRS duration of ≥150 ms even in the absence of LBBB.<sup>11</sup>

Biventricular pacing by atrial-synchronised pacing of the RV and the LV via the coronary sinus to the basal or midventricular LV region accomplishes reverse remodelling of the LV, and had been considered the gold standard for cardiac resynchronisation therapy (CRT) in patients with heart failure.<sup>12</sup>

CRT may even eliminate the need for an ICD in patients with LV systolic dysfunction, especially in patients with non-ischaemic cardiomyopathy.<sup>13–18</sup> However, approximately 30%–35% of patients are nonresponders in whom CRT fails to result in benefit despite appropriate indications for this therapy.<sup>19,20</sup>

Specific His bundle pacing offers comparable or better results than biventricular pacing by means of cardiac resynchronisation.<sup>21–23</sup> In the LBBP-RESYNC randomised controlled trial, LBB pacing-CRT was demonstrated to result in greater improvement in LV ejection fraction (LVEF) than biventricular pacing-CRT in HF patients with nonischaemic cardiomyopathy and LBBB.<sup>24,25</sup>

In patients with AF in whom drug or pulmonary vein ablation therapy has failed or who have signs of tachycardiopathy, atrioventricular (AV) nodal catheter ablation or modification followed by ventricular or biventricular pacing may be necessary.<sup>26</sup> Biventricular pacing if LVEF  $\leq$ 35% is superior to apical RV pacing in these patients, as it is for those who need permanent pacing for AV block where LVEF <50%.7.<sup>27–29</sup> However, in a systematic review for the 2018 American College of Cardiology/American Heart Association/Heart Rhythm Society guideline on bradycardia, among patients with LVEF >35%, LVEF was preserved or increased with either biventricular or His-bundle pacing compared with right ventricular pacing, but improvements in patient-centred clinical outcomes appeared to be limited primarily to those with chronic AF with rapid ventricular response rates who had undergone AV node ablation.<sup>30</sup>

LBB pacing has also improved LVEF, with a higher implant success rate and fewer late lead-related complications than His bundle pacing in patients with AF and HF after AV junction ablation.<sup>31</sup>

Biventricular pacing, therefore, is an attractive option in many clinical situations. However, it is a cumbersome procedure, and the potential for LV lead-related complications as well as an increased QT interval should be also considered.<sup>32</sup>

Specific conduction system pacing is emerging as a new option, potentially associated with improved clinical outcomes and fewer complications.

Potential problems with His-bundle pacing are higher pacing thresholds, lower R-wave amplitudes and the potential to develop distal conduction block. The potential need for a backup ventricular lead has been raised.<sup>33</sup>

LBB pacing has emerged as an alternative method for delivering physiological pacing to achieve electrical synchrony of the left ventricle,

especially in patients with infranodal AV block and LBBB.<sup>34,35</sup> Selective LBB pacing is indicated by a discrete electrogram in the LBBP lead and either an M or rsR' and wide R' with a notch in lead V1, and a discrete component between stimulus and ventricle activation in paced electrogram.<sup>35,36</sup> Non-selective LBB pacing has a narrower right bundle branch block morphology than selective LBBB pacing (as opposed to selective and non-selective Hisbundle pacing) and without the discrete pattern.

Theoretically, LBB pacing leads to a more synchronous activation of the left ventricle than non-selective septal pacing due to capture of the specialised conduction system. However, the procedure may be cumbersome, and septal perforation should be considered when pacing parameters are suboptimal and treated by reimplantation.<sup>37</sup>

High RV septal pacing is also theoretically beneficial, at least in patients with no previous anteroseptal MI. Preliminary animal and human studies have indicated that both selective LBBB and non-selective septal pacing strategies seem to maintain electrical and mechanical activation of the left ventricle to a near physiologic level.<sup>38</sup> Should this prove to be true in clinical studies, a new era for a simplified approach, with straightforward septal pacing of the RV, either with a lead or through a directly implanted pacemaker, will emerge.

The approach may not achieve the precise conduction system excitation offered by specific His or LBBB pacing, but it is considerably easier to perform and avoids complications that are inherent to specific pacing modes.<sup>39</sup> We are certainly entering a new era of cardiac pacing.  $\Box$ 

- Burri H, Jastrzebski M, Cano Ó, et al. EHRA clinical consensus statement on conduction system pacing implantation: executive summary. Endorsed by the Asia-Pacific Heart Rhythm Society (APHRS), Canadian Heart Rhythm Society (CHRS) and Latin-American Heart Rhythm Society (LAHRS). *Europace* 2023;25:1237–48. https://doi. org/10.1093/europace/euad044; PMID: 37061850.
- Ponnusamy SS, Vijayaraman P. Left bundle branch blockinduced cardiomyopathy: insights from left bundle branch pacing. JACC Clin Electrophysiol 2021;7:1155–65. https://doi. org/10.1016/j.jacep.2021.02.004; PMID: 33812829.
- Dai C, Guo P, Li W, et al. The effect of ventricular preexcitation on ventricular wall motion and left ventricular systolic function. *Europace* 2018;20:1175–81. https://doi. org/10.1093/europace/eux242; PMID: 29016834.
- Merchant FM, Mittal S. Pacing induced cardiomyopathy. J Cardiovasc Electrophysiol 2020;31:286–92. https://doi. org/10.1111/jce.14277; PMID: 31724791.
- Huizar J, Kaszala K, Tan A, et al. Abnormal conductioninduced cardiomyopathy. J Am Coll Cardiol 2023;81:1192– 200. https://doi.org/10.1016/j.jacc.2023.01.040; PMID: 36948737.
- Shimony A, Eisenberg MJ, Filion KB, Amit G. Beneficial effects of right ventricular non-apical vs apical pacing: a systematic review and meta-analysis of randomizedcontrolled trials. *Europace* 2012;14:81–91. https://doi. org/10.1093/europace/eur240; PMID: 21798880.
- Weizong W, Zhongsu W, Yujiao Z, et al. Effects of right ventricular nonapical pacing on cardiac function: a metaanalysis of randomized controlled trials. *Pacing Clin Electrophysiol* 2013;36:1032–51. https://doi.org/10.1111/ pace.12112; PMID: 23438131.
- Tayal B, Fruelund P, Sogaard P, et al. Incidence of heart failure after pacemaker implantation: a nationwide Danish registry-based follow-up study. *Eur Heart J* 2019;40:3641–8. https://doi.org/10.1093/eurheartj/ehz584; PMID: 31504437.
- Janousek J, van Geldorp IE, Krupickova S, et al. Permanent cardiac pacing in children: choosing the optimal pacing site: a multicenter study. *Circulation* 2013;127:613–23. https://doi. org/10.1161/CIRCULATIONAHA.112.115428; PMID: 23275383.
- Kaye GC, Linker NJ, Marwick TH, et al. Effect of right ventricular pacing lead site on left ventricular function in patients with high-grade atrioventricular block: results of the Protect-Pace study. *Eur Heart J* 2015;36:856–62. https://doi. org/10.1093/eurhearti/ehu304; PMID: 25189602.
- Friedman DJ, Al-Khatib SM, Dalgaard F, et al. Cardiac resynchronization therapy improves outcomes in patients with intraventricular conduction delay but not right bundle branch block: a patient-level meta-analysis of randomized controlled trials. *Circulation* 2023;147:812–23. https://doi. org/10.1161/CIRCULATIONAHA.122.062124; PMID: 36700426.
- Cleland JG, Abraham WT, Linde C, et al. An individual patient meta-analysis of five randomized trials assessing the effects of cardiac resynchronization therapy on morbidity and mortality in patients with symptomatic heart failure. *Eur Heart J* 2013;34:3547–56. https://doi.org/10.1093/eurhearti/ eht290; PMID: 23900696.
- Lam SK, Owen A. Combined resynchronisation and implantable defibrillator therapy in left ventricular dysfunction: Bayesian network meta-analysis of randomised controlled trials. *BMJ* 2007;335:925. https://doi.org/10.1136/ bmj.39343.511389.BE; PMID: 17932160.

- McAlister FA, Ezekowitz J, Hooton N, et al. Cardiac resynchronization therapy for patients with left ventricular systolic dysfunction: a systematic review. *JAMA* 2007;297:2502–14. https://doi.org/10.1001/ jama.297.22.2502; PMID: 17565085.
- Al-Khatib SM, Friedman P, Ellenbogen KA. Defibrillators: selecting the right device for the right patient. *Circulation* 2016;134:1390–404. https://doi.org/10.1161/ CIRCULATIONAHA.116.021889; PMID: 27799257.
- Marijon E, Leclercq C, Narayanan K, et al. Causes-of-death analysis of patients with cardiac resynchronization therapy: an analysis of the CeRtiTuDe cohort study. *Eur Heart J* 2015;36:2767–76. https://doi.org/10.1093/eurheartj/ehv455; PMID: 26330420.
- Packer M. What causes sudden death in patients with chronic heart failure and a reduced ejection fraction? *Eur Heart J* 2020;41:1757–63. https://doi.org/10.1093/eurheartj/ ehz553; PMID: 31390006.
- Patel D, Kumar A, Black-Maier E, et al. Cardiac resynchronization therapy (CRT) with or without defibrillation in patients with non-ischemic cardiomyopathy: a systematic review and meta-analysis. *Circ Arrhythm Electrophysiol* 2021;14:e008991. https://doi.org/10.1161/CIRCEP.120.008991; PMID: 33999647.
- Prinzen FW, Vernooy K, Auricchio A. Cardiac resynchronization therapy: state-of-the-art of current applications, guidelines, ongoing trials, and areas of controversy. *Circulation* 2013;128:2407–18. https://doi. org/10.1161/CIRCULATIONAHA.112.000112; PMID: 24276876
- Leyva F, Nisam S, Auricchio A. 20 years of cardiac resynchronization therapy. J Am Coll Cardiol 2014;64:1047–58. https://doi.org/10.1016/j.jacc.2014.06.1178; PMID: 25190241.
- Arnold AD, Whinnett ZI, Vijayaraman P. His–Purkinje conduction system pacing: state of the art in 2020. Arrhythm Electrophysiol Rev 2020;9:136–45. https://doi.org/10.15420/ aer.2020.14; PMID: 33240509.
- Vinther M, Risum N, Svendsen JH, et al. A randomized trial of His pacing versus biventricular pacing in symptomatic HF patients with left bundle branch block (His-alternative). JACC Clin Electrophysiol 2021;7:1422–32. https://doi.org/10.1016/j. jacep.2021.04.003; PMID: 34167929.
- Huang W, Wang S, Su L, et al. His-bundle pacing vs biventricular pacing following atrioventricular nodal ablation in patients with atrial fibrillation and reduced ejection fraction: a multicenter, randomized, crossover study – the ALTERNATIVE-AF trial. *Heart Rhythm* 2022;19:1948–55. https://doi.org/10.1016/j.hrthm.2022.07.009; PMID: 35843465.
- Wang Y, Zhu H, Hou X, et al. Randomized trial of left bundle branch vs biventricular pacing for cardiac resynchronization therapy. J Am Coll Cardiol 2022;80:1205–16. https://doi. org/10.1016/j.jacc.2022.07.019; PMID: 36137670.
- Liang Y, Wang J, Gong X, et al. Left bundle branch pacing versus biventricular pacing for acute cardiac resynchronization in patients with heart failure. *Circ Arrhythm Electrophysiol* 2022;15:e01181. https://doi.org/10.1161/ CIRCEP122.011181.
- Brignole M, Pentimalli F, Palmisano P, et al. AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: the APAF-CRT mortality trial. *Eur Heart J* 2021;42:4731–9. https://doi. org/10.1093/eurtheartj/ehab569; PMID: 34453840.

- Brignole M, Botto G, Mont L, et al. Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial. *Eur Heart J* 2011;32:2420–9. https://doi.org/10.1093/eurheartj/ ehr/162; PMID: 21606084.
- Curtis AB, Worley SJ, Adamson PB, et al. Biventricular pacing for atrioventricular block and systolic dysfunction. N Engl J Med 2013;368:1585–93. https://doi.org/10.1056/ NEJMoa1210356; PMID: 23614585.
- Chan JY, Fang F, Zhang Q, et al. Biventricular pacing is superior to right ventricular pacing in bradycardia patients with preserved systolic function: 2-year results of the PACE trial. *Eur Heart J* 2011;32:2533–40. https://doi.org/10.1093/ eurhearti/ehr336; PMID: 21875860.
- 30. Slotwiner DJ, Raitt MH, Del-Carpio Munoz F, et al. Impact of physiologic pacing versus right ventricular pacing among patients with left ventricular ejection fraction greater than 35%: a systematic review for the 2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2019;74:988– 1008. https://doi.org/10.1016/j.jacc.2018.10.045; PMID: 30412708.
- Cai M, Wu S, Wang S, et al. Left bundle branch pacing postatrioventricular junction ablation for atrial fibrillation: propensity score matching with His bundle pacing. *Circ Arrhythm Electrophysiol* 2022;15:e010926. https://doi. org/10.1161/CIRCEP122.010926. PMID: 36166683.
- Viskin S, Chorin E, Schwartz AL, et al. Arrhythmogenic effects of cardiac memory. *Circulation* 2022;146:1170–81. https://doi.org/10.1161/CIRCULATIONAHA.122.061259; PMID: 36214133.
- Glikson M, Nielsen JC, Kronborg MB, et al. 2021 ESC guidelines on cardiac pacing and cardiac resynchronization therapy. *Eur Heart J* 2021;42:3427–520. https://doi. org/10.1093/eurhearti/ehab364; PMID: 34455430.
- Jastrzebski M, Kielbasa G, Cano O, et al. Left bundle branch area pacing outcomes: the multicentre European MELOS study. *Eur Heart J* 2022;43:4161–73. https://doi.org/10.1093/ eurheartj/ehac445; PMID: 35979843.
- Hua W, Gu M, Niu H, Gold MR. Advances of implantation techniques for conduction system pacing. JACC Clin Electrophysiol 2022;8:1587–98. https://doi.org/10.1016/j. jacep.2022.09.022; PMID: 36543514.
- Jastrzebski M, Kielbasa G, Curila K, et al. Physiology-based electrocardiographic criteria for left bundle branch capture. *Heart Rhythm* 2021;18:935–43. https://doi.org/10.1016/j. hrthm.2021.02.021: PMID: 33677102.
- Ponnusamy SS, Basil W, Vijayaraman P. Electrophysiological characteristics of septal perforation during left bundle branch pacing. *Heart Rhythm* 2022;19:728–34. https://doi.org/10.1016/j. hrthm.2022.01.018; PMID: 35066178.
- Rijks J, Luermans J, Heckman L, et al. Physiology of left ventricular septal pacing and left bundle branch pacing. *Card Electrophysiol Clin* 2022;14:181–9. https://doi. org/10.1016/j.ccep.2021.12.010.
- Knops RE, Reddy VY, Ip JE, et al. A dual-chamber leadless pacemaker. N Engl J Med 2023;388:2360–70. https://doi. org/10.1056/NEJMoa2300080; PMID: 37212442.