# Use of acoustic cardiography to assess left ventricular electromechanical synchronization during left bundle branch pacing



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**BACKGROUND** Left bundle branch pacing (LBBP) is a physiological pacing that captures the main left bundle or its proximal branch. Electromechanical activation time (EMAT) is an acoustic cardiographic metric that provides a simple method for evaluating left ventricular (LV) synchrony. Prolonged EMAT reflects impaired LV electromechanical coupling.

**OBJECTIVE** The purpose of this study was to explore whether EMAT can confirm that LBBP produces more satisfactory LV electromechanical synchronization than conventional right ventricular pacing modalities.

**METHODS** Patients with standard pacing indications and narrow QRS duration were recruited for this study. Unipolar pacing under 3 different modalities—right ventricular apical pacing (RVAP), right ventricular high septal pacing (RVHSP), and LBBP—were successively performed in each patient. Pacing parameters, echocardiographic characteristics, and acoustic cardiographic parameters at different pacing modalities and during normal rhythm were collected.

**RESULTS** A total of 55 patients were enrolled, and all had successful LBBP. Left ventricular activation time (LVAT) was significantly

# Introduction

High-percentage right ventricular pacing (RVP) is known to induce ventricular remodeling and subsequent pacinginduced cardiomyopathy (PICM), manifested as atrial arrhythmias, cardiac dilatation, and recurrent heart failure hospitalization due to dyssynchronous electromechanical activation of the left ventricle (LV).<sup>1,2</sup> In recent years, permanent His-bundle pacing (HBP) has been considered the most physiological form of conduction system pacing, leading to significant QRS duration narrowing and LV functional preservation in patients with depressed left ventricular ejection fraction (LVEF).<sup>3,4</sup> However, the application of HBP has associated with EMAT, with LVAT vs EMAT correlation coefficient of 0.665 (P <.001). LVAT during LBBP was shorter than that during RVHSP (51.93 ± 2.732 ms vs 85.59 ± 2.240 ms; P <.001). EMAT of LBBP was significantly lower than either RVAP or RVHSP (95.44 ± 1.794 ms vs 143.32 ± 2.376 ms, and 132.22 ± 1.872 ms; both P <.001) but was similar to that of intrinsic rhythm (95.37 ± 2.271 ms; P = .862).

**CONCLUSION** We found EMAT significantly prolonged in RVHSP and RVAP but not in the LBBP mode. This finding indicates superior electromechanical synchronization in patients having LBBP. EMAT measurement could be an additional method for identifying the ideal pacing position.

**KEYWORDS** Electromechanical synchronization; Left bundle branch pacing; Right ventricular pacing; Acoustic cardiography; Electromechanical activation time

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been limited because of the challenges in lead delivery, high pacing thresholds, low R-wave amplitudes, and poten-tial distal conduction block.<sup>5–7</sup> Left bundle branch pacing (LBBP), first demonstrated in 2017,<sup>8</sup> has been suggested as an effective alternative to correct PICM and infranodal atrioventricular block<sup>9</sup> because it achieves a higher success rate of implantation than HBP and has a low and stable pacing capture threshold, high R-wave amplitude, and short stimulus to left ventricular activation time (Sti-LVAT),<sup>10–12</sup> which represents the depolarization period of the LV walls. Therefore, short Sti-LVAT indicates rapid LV electric activation during LBBP. However, Sti-LVAT, an electrocardiographic (ECG) parameter, remains inadequate in evaluating the mechanical synchrony of a pacing modality. Because ventricular remodeling caused by pacing is triggered by regional myocardial stain via the holistic electromechanical feedback mechanism.<sup>13</sup> a simple and reliable indicator that reflects acute changes of both electrical and mechanical stimuli is of significance in clinical practice.

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## **KEY FINDINGS**

- Electromechanical activation time (EMAT) is an acoustic cardiographic parameter.
- Prolonged EMAT indicates dyssynchronous electromechanical coupling and consequent regional delay in the activation of left ventricular walls.
- Left bundle branch pacing provided a more rapid electrical-mechanical response in terms of short EMAT whereas prolonged EMAT characterized right ventricular apical pacing and right ventricular high septal pacing, implying an impaired mechanical response.
- Acoustic cardiography might be a helpful addition when identifying the ideal pacing position.

Acoustic cardiography is a novel technique that facilitates simultaneous analysis of the heart sound signals and their timing relationships with the corresponding ECG to objectively characterize myocardial contractility. Electromechanical activation time (EMAT) is an acoustic cardiographic parameter that measures the interval between the onset of QRS and the closure of the mitral valve, which essentially reflects the function of the myocyte's latent period from the onset of LV membrane depolarization to the beginning of LV contraction in the excitation-contraction process.<sup>14</sup> Hence, EMAT corresponds to the average time of LV activation. Prolonged EMAT indicates dyssynchronous electromechanical coupling and consequent regional delay in activation of the LV walls.<sup>15,16</sup> In multiple studies, EMAT has demonstrated a strong correlation with both LVEF and LV contractility (dP/dt<sub>max</sub>), providing a composite index of cardiac performance that is effective in identifying hemodynamic abnormalities associated with LV systolic dysfunction.<sup>17–20</sup>

With this background and rationale, we adopted EMAT as an independent indicator of integrated LV electromechanical activation in the present study, hypothesizing its direct implications for the mechanism underlying both deleterious and beneficial remodeling with different pacing sites. In addition, although previous case-controlled studies suggested superior synchrony for LBBP over RVP,<sup>21–23</sup> few direct withinpatient analyses have been conducted to compare the variable responses between different pacing modalities, which may be relevant to the potential selection bias that occurred in some observational cohort studies. Thus, the present study was undertaken to provide a comparative intrapatient analysis of electromechanical synchronization to better clarify the effectiveness of LBBP vs RVP.

# Methods Subjects

This prospective study was conducted between July 2021 and October 2022 at Shanghai Tong Ren Hospital, affiliated with Shanghai Jiao Tong University School of Medicine. Consecutive patients >18 years of age who were diagnosed with sick sinus syndrome or atrioventricular block, QRS duration <130 ms, and standard ventricular pacing indications were enrolled in the study. The research reported herein adhered to the Helsinki Declaration guidelines, and all patients signed written informed clinical consent. Acquisition, analysis, and review of the data were approved by the local Institutional Review Board.

#### Implantation procedure

During the procedure, unipolar pacing at different sites, including LBBP, right ventricular high septal pacing (RVHSP), and right ventricular apical pacing (RVAP) were successively performed in each patient. In brief, a SelectSecure lead (Model 3830, Medtronic, Minneapolis, MN) was directed via a fixed curve sheath (C315 His, Medtronic) 1–1.5 cm below the His bundle along an axial line between the distal HBP site and right ventricular (RV) apex in the right side of the septum. The lead was then gradually advanced into the septum by clockwise rotations, with close monitoring of pacing impedance, paced ECG morphology, and capture thresholds. During lead maneuvering, the terminal R wave in lead  $V_1$  and an increase in unipolar pacing impedance were observed. Thereafter, low and high output were performed to confirm the capture of the left conduction system. Left conduction system capture was confirmed based on the following criteria<sup>24,25</sup>: (1) paced QRS of right bundle branch block (RBBB) configuration in lead V1; (2) abrupt shortening of Sti-LVAT with increasing output or remaining abbreviated and constant at high and low outputs or demonstration of output-dependent transition of nonselective LBBP and selective LBBP at near-threshold outputs; and/or (3) recording of left bundle branch (LBB) potentials during escape rhythm or premature beats. Patients who meet the first and at least one of the latter 2 criteria can be confirmed to have LBB capture. Finally, we recorded LBB potentials as previously reported and fixed the 3830 lead using unipolar tip pacing as the final pacing modality (Figure 1A). RVHSP was achieved by programmed unipolar pacing via the ring electrode of the 3830 lead (Figure 1B). A temporary pacing electrode was placed at the RV apex for RVAP (Figure 1C).

#### ECG measurements

Intracardiac electrograms along with 12-lead body surface ECGs (LABSYSTEM<sup>™</sup> Pro EP Recording System, Boston Scientific, Marlborough, MA) were continuously recorded during the entire procedure. Ventricular pacing parameters were programmed to unipolar pacing with an output of 3 V/0.4 ms. Pacing rate was set 10 bpm higher than the intrinsic rate to ensure total pacing capture. The following parameters, including intrinsic QRS duration (QRSd), paced QRSd, intrinsic LVAT, and Sti-LVAT at different pacing sites, were measured in each patient. Intrinsic QRSd was measured from the first to the last sharp vector of the QRS complex. Paced QRSd was measured from the onset of the pacing spike to the end of the last deflection of the QRS complex under



**Figure 1** Schematic representation of His–Purkinje conduction system and target positions of different pacing sites. **A:** Left bundle branch pacing (LBBP) under unipolar pacing from the tip electrode of 3830 lead. **B:** Right ventricular high septal pacing (RVHSP) achieved by unipolar pacing from the ring electrode of the 3830 lead. **C:** Temporary right apical ventricular pacing (RVAP).

unipolar pacing. Intrinsic LVAT was measured from the beginning of the QRS complex to the peak of the R wave in lead  $V_5-V_6$ . Sti-LVAT was measured from the pacing stimulus to the peak of the R wave in leads  $V_5-V_6$ . Three continuous QRS complexes of each state were measured and the averaged values reported.

### Synchronized ECG and heart sound measurement

Acoustic cardiographic parameters were obtained using the SynPatch (Wenxin Tech Inc., Fuzhou, Fujian, China), a wearable patch equipped with a dual sensor that acquires a single-lead ECG and heart sound data simultaneously. Using a Bluetooth connection, the patch can be paired with and controlled by a customized application on a smartphone or tablet. The data acquired by the patch are sent to the application and then auto-uploaded to a cloud-based analysis system for algorithmic interpretation and archiving. The result can be returned and displayed in the application.

In this study, we primarily focused on the specific variable EMAT, generated by the SynPatch. EMAT was measured in milliseconds by the algorithm as the interval from the beginning of electrical activation of LV (Q-wave onset) to the point of maximum intensity of the first heart sound (S1). S1 occurs when the mitral or tricuspid valves are closed. Higher pressure on the left side of the heart results in a louder sound of the closure of the mitral valve than that of the tricuspid valve. Therefore, the closure of the mitral valve acts as the main component of the first heart sound. Figure 2 shows an example of time–frequency analysis of synchronized phonocardiogram and ECG by the SynPatch. The 2-dimensional

and 3-dimensional scalogram views (Figures 2A and 2B) are visual representations of heart sound signals, which are used by the algorithm for the detection of heart sounds, murmurs, and the intensity of these components.

SynPatch was placed at the  $V_5$  position of each patient, continuously recording synchronized single-lead ECG and heart sound data throughout the implantation, and a 2-minute recording was obtained during each pacing modality and sinus rhythm. Pacing parameters and ECG characteristics including paced QRS duration and Sti-LVAT of the same time interval were collected for further analysis.

### Statistical analysis

SPSS 26.0 software (IBM, Armonk, NY) was used to perform statistical analysis. Continuous variables are given as mean  $\pm$  SD. Categorical variables are given as frequency (percentage). We applied the Student *t* test and Mann-Whitney test for continuous variables and the  $\chi^2$  analysis for categorical variables to compare the differences among 3 pacing modalities (LBBP, RVHSP, RVAP) and intrinsic rhythm. Pearson correlation analysis and linear regression were used to test the correlation derived between EMAT and LVAT. Two-tailed *P* <.05 was considered significant.

## Results

A total of 55 subjects were recruited for this study. Baseline characteristics and clinical variables are summarized in Table 1. Mean age was  $76.55 \pm 1.066$  years (range 54–93 years), and 25 (45.5%) of the subjects were men. Permeant LBBP, temporary RVAP, and RVHSP were successfully



**Figure 2** Waveform and scalogram views of synchronized electrocardiogram (ECG) and phonocardiogram (PCG) recording of a subject. A: Threedimensional scalogram view of the heart-sound recording. B: Two-dimensional scalogram view of the heart-sound recording. C: Waveform of PCG signal. D: Waveform of ECG signal. EMAT = electromechanical activation time.

achieved in all 55 patients (100%) without procedure-related complications. LBB potential was recorded in 47 cases (85.5%).

From Pearson correlation analysis, EMAT demonstrated a notable positive relationship with LVAT (r = 0.665; *P* <.001) (Figure 3), that is, the faster the LV depolarization (short LVAT), the shorter the EMAT, and vice versa.

Table 2 and Figure 4 show ECG and acoustic cardiographic parameters under 3 different pacing modalities and intrinsic rhythm. Whereas paced QRS duration in general (LBBP: 109.19 ± 2.837 ms; RVHSP 158.35 ± 3.276 ms; RVAP 182.12 ± 4.341 ms) was longer than that of intrinsic rhythm (99.20 ± 2.482 ms), LBBP demonstrated significantly narrower QRSd compared to RVHSP and RVAP (both P <.001) (Table 2 and Figure 4A). Moreover, LBBP (51.93 ± 2.732 ms) also showed the shortest Sti-LVAT among all 3 pacing modalities (RVHSP 85.59 ± 2.240 ms; RVAP 108.25 ± 6.222 ms; P <.001) (Table 2 and Figure 4B).

With regard to acoustic cardiographic parameter, EMAT showed a significant drop during LBBP (95.44  $\pm$  1.794 ms) compared with that during RVAP and RVHSP (143.32  $\pm$  2.376 ms and 132.22  $\pm$  1.872 ms; both *P* <.001) (Table 2 and Figure 4C) but was not significantly different from that of intrinsic rhythm (95.37  $\pm$  2.271 ms; *P* =

.862). Examples of the acoustic cardiographic parameter during different pacing modalities are shown in Figure 5.

The pacing parameters of RVAP, LBBP, and RVHSP are given in Table 2 and Figure 6. A relatively higher threshold was demonstrated during RVAP ( $0.92 \pm 0.038$  V) compared

**Table 1** Baseline patient characteristics (N = 55)

$76.55 \pm 1.066$
25 (45.5)
39 (70.9)
99.2 $\pm$ 2.482
22 (40.0)
13 (23.6)
8 (14.5)
19 (34.5)
$59.04 \pm 1.218$
1 (1.8)
49 (89.1)
2 (3.6)
3 (5.5)

Values are given as mean  $\pm$  SD or n (%).

AVB = atrioventricular block; CRT-D = cardiac resynchronization therapy-defibrillator; CRT-P = cardiac resynchronization therapy-pacemaker; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; SSS = sick sinus syndrome.



**Figure 3** Linear correlation between left ventricular activation time (LVAT) and electromechanical activation time (EMAT).

with that during LBBP ( $0.75 \pm 0.028$  V; P < .001) but was significantly lower than that during RVHSP ( $1.78 \pm 0.102$ V; P < .001). Mean R-wave amplitude during RVAP ( $11.75 \pm 1.445$  mV) and RVHSP ( $10.44 \pm 0.505$  mV; P = .853) were similar, which was relatively lower than that during LBBP ( $12.98 \pm 0.473$  mV; P < .001). Hence, LBBP achieved the highest R-wave amplitude and the lowest threshold among all 3 pacing modalities demonstrated in the present study. With regard to impedance, mean impedance of RVAP ( $715.53 \pm 13.276 \Omega$ ) was lower than that of LBBP ( $783.49 \pm 23.153 \Omega$ ; P = .002) but was significantly higher than that of RVHSP ( $427.33 \pm 4.737 \Omega$ ; P < .001).

## Discussion

Electromechanical synchronization refers to the organized electrical depolarization of the heart followed by synchronous myocardial fiber shortening. Altered electromechanical activation from pacing is a critical marker for PICM and subsequent morbidity and mortality. RV pacing alters the natural sequence of cardiac electrical activation and elicits persistent changes of myocardial electrophysiological properties manifested electrocardiographically as significant and persistent wide QRS duration and T-wave changes that eventually lead to deleterious mechanical remodeling due to heterogeneous strain.<sup>13</sup> Previous studies further suggested that the underlying mechanisms of PICM, on an ionic basis, likely are associated with intracellular Ca<sup>2+</sup> accumulation at the lateactivated LV sites, causing apoptosis and subsequent LV dysfunction.<sup>26–28</sup> Pacing through the conduction system, on preserves the contrary, the native synchronized electromechanical coupling in the ventricles, preventing the overload of intracellular Ca<sup>2+</sup> and hence PICM. The present study evaluated the acute responses to different pacing sites on QRSd, LVAT, and EMAT. We performed comparative analysis among LBBP, temporary RVAP, RVHSP, and intrinsic rhythm within each patient. The major findings of this study are to demonstrate that LBBP maintained the most satisfactory LV electrical and mechanical synchrony compared to other pacing modalities and that EMAT could be an additional indicator that helps to determine the ideal pacing position during implantation.

### **Electrical synchronization**

QRSd has been a practical indicator for evaluating ventricular electrical synchrony, with short QRSd normally

**Table 2** Electrocardiographic characteristics, acoustic cardiographic parameters, and pacing parameters under intrinsic rhythm and different pacing modalities, and pacing parameters under different pacing modalities

	Pacing mod	acing modalities			P value					
Parameters	Intrinsic	LBBP	RVHSP	RVAP	Intrinsic vs LBBP	Intrinsic vs RVHSP	Intrinsic vs RVAP	LBBP vs RVHSP	LBBP vs RVAP	RVHSP vs RVAP
QRS duration (ms)	99.20 ± 2.482	109.19 ± 2.827	158.35 ± 2.276	182.12 ± 4 241	.027	<.001	<.001	<.001	<.001	<.001
LVAT (ms)	30.15 ± 1.637	51.93 ± 2 732	85.59 ± 2.240	4.541 108.25 ± 6.222	<.001	<.001	<.001	<.001	<.001	.002
EMAT (ms)	95.37 ± 2.271	95.44 ± 1 794	132.22 ± 1 872	143.32 ± 2 376	.862	<.001	<.001	<.001	<.001	<.001
Impedance (Ω)	_	783.49 ±	427.33 ± 4737	715.53 ±	_	—	_	<.001	.002	<.001
Threshold (V)	_	0.75 ±	1.78 ±	0.92 ±	_	—	_	<.001	<.001	<.001
R-wave amplitude (mv)	_	12.98 ± 0.473	10.44 ± 0.505	11.75 ± 1.445	_	_	_	<.001	<.001	.853

EMAT = electromechanical activation time; LBBP = left bundle branch pacing; LVAT = left ventricular activation time; RVAP = right ventricular apical pacing; RVHSP = right ventricular high septal pacing.



**Figure 4** Electrocardiographic characteristics (QRS duration, left ventricular activation time [LVAT]) and cardiac acoustic biomarker (electromechanical activation time [EMAT]) under different pacing sites and natural rhythm. **A:** QRS duration. **B:** LVAT. **C:** EMAT. LBBP = left bundle branch pacing; RVAP = right ventricular apical pacing; RVHSP = right ventricular high septal pacing.

representing rapid electrical activation of the ventricles. In contrast, wide QRSd represents ventricular desynchronization that is associated with the development of heart failure.<sup>29</sup> During LBBP, electrical conduction is initiated from the LBB followed by activation propagation along the native LBB–Purkinje system to the whole ventricles. In RVAP and RV septal pacing, paced activation propagates through the myocardial cell-to-cell mechanism to the whole ventricles, leading to dyssynchronous ventricular contraction and ventricular dysfunction. However, QRSd in LBBP was slightly prolonged compared with normal inherent rhythm. This prolonged QRSd in LBBP was mainly because of pacing-induced RBBB morphology, not dyssynchronous LV activation.

Sti-LVAT indicates the depolarization duration of the LV wall. A shorter Sti-LVAT may represent a rapid propagation of LV activation leading to synchronous LV contraction. Thus, Sti-LVAT has been used as a parameter to determine the capture of LBB according to electrophysiological mapping. However, QRSd often fails to provide diagnostic utility for confirming LBB capture because the delayed RV activation during LBBP can cause a prolonged QRSd even though there is a rapid activation propagation in LV via the LBB system. The findings of our study are consistent with previous reports demonstrating preservation of electrical synchrony the during LBBP.<sup>21,30,31</sup>

#### Electromechanical synchronization

Echocardiography is the most commonly adopted method to assess LV synchrony and cardiac resynchronization therapy response. Liang et al<sup>32</sup> used transthoracic echocardiographic examinations to assess acute cardiac resynchronization in heart failure patients who had undergone LBBP implantation and found that LBBP elicited greater improvement in intraventricular synchrony compared with conventional biventricular pacing. However, conducting echocardiographic examinations during implantation can be technically challenging and time-consuming and can be associated with hygienic concerns, potentially posing unnecessary risks to patients. With these considerations in mind, we adopted acoustic cardiography for evaluating LV electromechanical effects by different pacing modalities. Defined as the time from regional electrical activation to the onset of ventricular mechanical contraction, EMAT represents the electricalmechanical coupling and synchrony in the ventricles. Assessing EMAT seems to provide an accurate, simpler, and safer methodology for evaluating LV synchrony. Using the technology of SynPatch to facilitate the simultaneous detection and analysis of ECG and heart sound data, minimal time, effort, and technical skill are required to obtain acoustic cardiographic parameters, which overcome the limitations of conventional echocardiology.

Our study demonstrated that EMAT notably prolonged with RVAP and RVHSP but remained abbreviated with



**Figure 5** Twelve-lead electrocardiogram (ECG), synchronized single-lead ECG, phonocardiogram (PCG), and fluoroscopic images of 2 cases at different pacing modalities. **A–I:** Case 1. Twelve-lead ECG recorded at intrinsic rhythm (**A**), LBBP with LBB potential (**B**), RVHSP (**C**), and RVAP (**D**); corresponding synchronized single-lead ECG and PCG data recorded at intrinsic rhythm (**E**), LBBP (**F**), RVHSP (**G**), and RVAP (**H**); and fluoroscopic image at LAO 45° of LBBP (**I**). **J–R:** Case 2. Twelve-lead ECG recorded at intrinsic rhythm (**J**), LBBP with LBB potential (**K**), RVHSP (**L**), and RVAP (**M**); corresponding synchronized single-lead ECG and PCG data recorded at intrinsic rhythm (**J**), LBBP (**O**), RVHSP (**C**), and RVAP (**M**); corresponding synchronized single-lead ECG and PCG data recorded at intrinsic rhythm (**N**), LBBP (**O**), RVHSP (**P**), and RVAP (**Q**); and fluoroscopic image at LAO 45° of LBBP (**R**). LAO = left anterior oblique; Sti-LVAT = stimulus to left ventricular activation time. QRSd = QRS duration; RV = right ventricle; other abbreviations as in Figure 4.

LBBP, suggesting that RV pacing delayed LV electromechanical coupling and caused ventricular dyssynchrony, whereas LBBP preserved near-normal ventricular synchrony and electrical-mechanical response to the pacing. Linear regression analysis in the present study also confirmed the strong association between EMAT and Sti-LVAT, both representing the degree of ventricular synchrony.

As an early exploration of alternative RV pacing sites, RV septal pacing has a controversial role in terms of clinical benefits. In the present study, we found RVHSP, a novel pacing strategy from the ring electrode of the LBBP lead, showed an

overall favorable performance over RVAP in QRSd, Sti-LVAT, and EMAT. These findings indicate RVHSP could be a better pacing site than the RV apex. Moreover, RVHSP presented in our study demonstrated clear capture of the septum by the ring electrode of the 3830 lead screwed in the septum, which could be more deeply captured compared to that of conventional RV septal pacing. Thus, RVHSP could result in better synchrony than conventional RVSP. In future studies, a dual-cathode pacing strategy that activates both LBB and RV septum could be designed to explore whether pacing-induced RBBB could be corrected to achieve more synchronous activation than LBBP.



Figure 6 Pacing parameters under different pacing modalities. A: Impedance. B: Threshold. C: R-wave amplitude. Abbreviations as in Figure 4.

## Correlation between EMAT and LV systolic function

The mechanism underlying EMAT represents the process of electromechanical coupling, with short EMAT signifying a fast electrical activation for initiation of mechanical contraction in the LV and hence a better ventricular synchrony. EMAT initially was considered a hemodynamic parameter for its strong association with the maximal rise in LV pressure over time (dP/dt<sub>max</sub>), demonstrated previously in several studies.<sup>18,33,34</sup> EMAT is similar to LV dP/dt as it measures the time required for closure of the mitral valve, which also reflects the rate of LV pressure development. Reduced LV contractility was signified by a low dP/dt<sub>max</sub> and quantitatively related to prolonged EMAT (ie, a longer time interval for mechanical contraction development). Prolonged EMAT at lower dP/dt in patients with LV systolic dysfunction may represent the extended duration needed for the LV to generate active force for shortening when myocardial contractility is impaired, representing mechanical dyssynchrony.

Accordingly, noninvasive measurement of EMAT may be used as a convenient methodologic alternative to invasive assessment of dP/dt in evaluating acute hemodynamic responses during pacemaker implantation and help to select the optimal pacing site. It also can serve as a convenient tool of large-scale screening for undiagnosed LV systolic dysfunction as well as provide follow-up monitoring for interventions designed to improve LV function. A future study is required to validate the correlation between dP/dt<sub>max</sub> and acoustic parameters derived by SynPatch to determine ventricular hemodynamic responses.

# **Study limitations**

The present study was conducted in a single center on a relatively small number of subjects. HBP was not included in the comparative analysis of different pacing sites because the length and complexity of the procedure might increase the risk of complications. Additional follow-up randomized-controlled studies of LBBP compared with other pacing strategies are needed to evaluate the long-term clinical outcomes of electromechanical synchrony.

### Conclusion

The present study for the first time assessed ventricular electrical synchrony and electrical-mechanical response during different pacing modalities (LBBP, RVHSP, RVAP) in an intrapatient comparison. Our study demonstrates that LBBP elicited narrower QRSd and shorter Sti-LVAT, achieving accelerated cardiac electrical activation compared with RVAP and RVHSP. Moreover, LBBP provided a more rapid electrical-mechanical response in terms of short EMAT whereas prolonged EMAT characterized RVAP and RVHSP, implying an impaired mechanical response. The measures of electrical and mechanical synchrony during LBBP were significantly superior over conventional RVP strategies. EMAT measurement is safe and convenient and thus could be an additional method to help identify the ideal pacing position.

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**Ethics Statement:** The research reported herein adhered to the Helsinki Declaration guidelines. Acquisition, analysis, and review of the data were approved by the local Institutional Review Board.

# **Data Availability**

The relevant data are available through the corresponding author on request.

## References

- Rosenqvist M, Isaaz K, Botvinick EH, et al. Relative importance of activation sequence compared to atrioventricular synchrony in left ventricular function. Am J Cardiol 1991;67:148–156.
- Kiehl EL, Makki T, Kumar R, et al. Incidence and predictors of right ventricular pacing-induced cardiomyopathy in patients with complete atrioventricular block and preserved left ventricular systolic function. Heart Rhythm 2016; 13:2272–2278.
- Shan P, Su L, Zhou X, et al. Beneficial effects of upgrading to His bundle pacing in chronically paced patients with left ventricular ejection fraction <50. Heart Rhythm 2018;15:405–412.
- Deshmukh P, Casavant DA, Romanyshyn M, Anderson K. Permanent, direct Hisbundle pacing: a novel approach to cardiac pacing in patients with normal His-Purkinje activation. Circulation 2000;101:869–877.
- Abdelrahman M, Subzposh FA, Beer D, et al. Clinical outcomes of His bundle pacing compared to right ventricular pacing. J Am Coll Cardiol 2018;71:2319–2330.
- Vijayaraman P, Naperkowski A, Ellenbogen KA, Dandamudi G. Electrophysiologic insights into site of atrioventricular block: lessons from permanent His bundle pacing. JACC Clin Electrophysiol 2015;1:571–581.
- Zanon F, Abdelrahman M, Marcantoni L, et al. Long term performance and safety of His bundle pacing: a multicenter experience. J Cardiovasc Electrophysiol 2019;30:1594–1601.
- Huang W, Su L, Wu S, et al. A novel pacing strategy with low and stable output: pacing the left bundle branch immediately beyond the conduction block. Can J Cardiol 2017;33:1736.e1–1736.e3.
- Wu S, Su L, Wang S, Vijayaraman P, Ellenbogen KA, Huang W. Peri-left bundle branch pacing in a patient with right ventricular pacing-induced cardiomyopathy and atrioventricular infra-Hisian block. Europace 2019;21:1038.
- Li X, Li H, Ma W, et al. Permanent left bundle branch area pacing for atrioventricular block: Feasibility, safety, and acute effect. Heart Rhythm 2019;16:1766–1773.
- Su L, Wang S, Wu S, et al. Long-term safety and feasibility of left bundle branch pacing in a large single-center study. Circ Arrhythm Electrophysiol 2021; 14:e009261.
- Huang W, Wu S, Vijayaraman P, et al. Cardiac resynchronization therapy in patients with nonischemic cardiomyopathy using left bundle branch pacing. JACC Clin Electrophysiol 2020;6:849–858.

- Jeyaraj D, Wilson LD, Zhong J, et al. Mechanoelectrical feedback as novel mechanism of cardiac electrical remodeling. Circulation 2007;115:3145–3155.
- Cordeiro JM, Greene L, Heilmann C, Antzelevitch D, Antzelevitch C. Transmural heterogeneity of calcium activity and mechanical function in the canine left ventricle. Am J Physiol Heart Circ Physiol 2004;286:H1471–H1479.
- Caso P, D'Andrea A, Martiniello AR, et al. Myocardial systolic activation delay in patients with left bundle branch block and either normal or impaired left ventricular function. Echocardiography 2006;23:14–23.
- Constantino J, Hu Y, Trayanova NA. A computational approach to understanding the cardiac electromechanical activation sequence in the normal and failing heart, with translation to the clinical practice of CRT. Prog Biophys Mol Biol 2012; 110:372–379.
- Li XC, Liu XH, Liu LB, Li SM, Wang YQ, Mead RH. Evaluation of left ventricular systolic function using synchronized analysis of heart sounds and the electrocardiogram. Heart Rhythm 2020;17(5 Pt B):876–880.
- Roos M, Toggweiler S, Zuber M, Jamshidi P, Erne P. Acoustic cardiographic parameters and their relationship to invasive hemodynamic measurements in patients with left ventricular systolic dysfunction. Congest Heart Fail 2006; 12(Suppl 1):19–24.
- Zuber M, Kipfer P, Attenhofer Jost C. Systolic dysfunction: correlation of acoustic cardiography with Doppler echocardiography. Congest Heart Fail 2006; 12(Suppl 1):14–18.
- Huang J, Zhang W, Pan C, et al. Mobile cardiac acoustic monitoring system to evaluate left ventricular systolic function in pacemaker patients. J Clin Med 2022;11:3862.
- Hou X, Qian Z, Wang Y, et al. Feasibility and cardiac synchrony of permanent left bundle branch pacing through the interventricular septum. Europace 2019; 21:1694–1702.
- Cai B, Huang X, Li L, et al. Evaluation of cardiac synchrony in left bundle branch pacing: insights from echocardiographic research. J Cardiovasc Electrophysiol 2020;31:560–569.
- Jastrzębski M, Kiełbasa G, Cano O, et al. Left bundle branch area pacing outcomes: the multicentre European MELOS study. Eur Heart J 2022;43:4161–4173.
- Chen X, Wu S, Su L, Su Y, Huang W. The characteristics of the electrocardiogram and the intracardiac electrogram in left bundle branch pacing. J Cardiovasc Electrophysiol 2019;30:1096–1101.
- Huang W, Chen X, Su L, Wu S, Xia X, Vijayaraman P. A beginner's guide to permanent left bundle branch pacing. Heart Rhythm 2019;16:1791–1796.
- Jeyaraj D, Wan X, Ficker E, et al. Ionic bases for electrical remodeling of the canine cardiac ventricle. Am J Physiol Heart Circ Physiol 2013;305:H410–H419.
- Chan YH, Tsai WC, Ko JS, et al. Small-conductance calcium-activated potassium current is activated during hypokalemia and masks short-term cardiac memory induced by ventricular pacing. Circulation 2015;132:1377–1386.
- Orrenius S, Zhivotovsky B, Nicotera P. Regulation of cell death: the calciumapoptosis link. Nat Rev Mol Cell Biol 2003;4:552–565.
- Sandhu R, Bahler RC. Prevalence of QRS prolongation in a community hospital cohort of patients with heart failure and its relation to left ventricular systolic dysfunction. Am J Cardiol 2004;93:244–246.
- Vijayaraman P, Panikkath R, Mascarenhas V, Bauch TD. Left bundle branch pacing utilizing three dimensional mapping. J Cardiovasc Electrophysiol 2019; 30:3050–3056.
- Chen K, Li Y, Dai Y, et al. Comparison of electrocardiogram characteristics and pacing parameters between left bundle branch pacing and right ventricular pacing in patients receiving pacemaker therapy. Europace 2019;21:673–680.
- 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:e011181.
- Roos M, Toggweiler S, Jamshidi P, et al. Noninvasive detection of left ventricular systolic dysfunction by acoustic cardiography in cardiac failure patients. J Card Fail 2008;14:310–319.
- Efstratiadis S, Michaels AD. Computerized acoustic cardiographic electromechanical activation time correlates with invasive and echocardiographic parameters of left ventricular contractility. J Card Fail 2008;14:577–582.