Title: 'Pacing System Analyzers to guide Conduction System Pacing implantation procedures: A comparison study of intracardiac and surface signals with an Electrophysiological Recording System'

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Running title: 'Pacing System Analyzers to guide Conduction System Pacing implantation procedures'

Word account: 4843

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Conflicts of interest: This publication has received no external financial support. All the authors of this manuscript have declared that no competing interests exist.

ABSTRACT

Background: Left bundle branch area pacing (LBBAP) needs confirmation of left conduction system capture assessed by testing of different electrical parameters. Guidelines recommend the use of an electrophysiological recording-system (EP-RS) to guide conduction system pacing (CSP) procedures. However, some experienced centers perform LBBAP procedures without an EP-RS.

Objective: We aimed to assess whether LBBAP criteria can be measured using the signals provided by the pacing system analyzers (PSA) as a surrogate for the EP-RS to simplify and universalize the technique.

Methods: This was an observational, prospective, multicenter study assessing the current LBBAP criteria using the PSA compared to the EP-RS during CSP procedures.

Results: 108 consecutive patients were included. Baseline QRS duration was 130±29 vs 128±29msec in the EP-RS vs PSA (p=0.7). An initial "W" morphology in V1 was noted in 88% patients with the EP-RS vs 86% patients with the PSA (p=0.7) during unipolar pacing. The QRS duration (122±17 vs 123±19 msec, p=0.7), the R-wave peak time interval in V6 (80±13 vs 79±14 msec (p=0.9) and the V6-V1 inter-peak interval (39±16 vs 38±17 msec (p=0.7) were superimposable in the EP-RS compared to the PSA. Pearson coefficient for the last two criteria were 0.85 ($p<0.0001$) and 0.94 ($p<0.0001$), respectively. According to the current criteria, 91.5% of patients received a successful LBBAP implant using the EP-RS. Based on the PSA measurements, 96.6% of these patients accomplished LBBAP criteria.

Conclusions: Criteria for LBBAP can be assessed by PSAs with high accuracy. These results provide the basis for the usefulness of the PSA to guide LBBAP procedures.

KEYWORDS

Conduction system pacing; Left bundle branch area pacing; Electrophysiological recording system; Pacing system analyzer; Surface Electrocardiogram leads.

ABBREVIATIONS LIST

CSP: Conduction system pacing.

ECG: Electrocardiogram.

EGM: Electrogram.

EP-RS: Electrophysiological recording system.

LBBAP: Left bundle branch area pacing.

LBBP: Left bundle branch pacing.

PSA: Pacing system analyzer.

V6-RWPT: V6 R wave peak time.

V6-V1 IPT: V6-V1 inter-peak time.

INTRODUCTION

Conduction System Pacing (CSP) involves implantation of permanent pacing leads along different sites of the cardiac conduction system[1]. Nowadays, CSP is mostly performed by left bundle branch area pacing (LBBAP)[2,3], due to its advantages compared to His bundle pacing[4]. Several criteria have been described to assess the appropriate capture of the left bundle[5,6], including intracardiac electrograms (EGM), as well as different morphology and duration 12-lead electrocardiogram (ECG) criteria. Currently, LBBAP procedures are mainly performed in centers where an electrophysiology recording system (EP-RS) is available to assess the above-mentioned criteria. However, pacing system analyzers (PSA) are capable of displaying intracardiac EGMs and several ECG surface leads. The performance of the PSA to assess the accomplishment of LBBAP criteria compared to EP-RS has never been previously studied.

METHODS

All patients provided written informed consent before undergoing the implantation procedure. The study was approved by the Institutional Review Board (Ethics-Committee approval no. 2023 /10850/I and registered in Clinicaltrials.gov (ID) NCT06371846) and was compliant with the declaration of Helsinki as revised in 2013.

Study objectives, protocol and data collection

Our aim was to assess the LBBAP criteria using the signals from the PSA, compared to the gold standard EP-RS signals, during CSP implantation procedures.

This was an observational, prospective, multicentric study. From March/2023 to May/2024, consecutive patients undergoing a LBBAP implantation procedure were enrolled from eight different participating centers in Spain.

Baseline characteristics including demographics, pacing indication, baseline ECG characteristics and cardiac ultrasound parameters, were collected. From the implantation procedure, total and fluoroscopy time, acute thresholds, and baseline and final paced ECG parameters, including the stimulated QRS (S-QRS) morphology and duration, the V6 R wave peak time (V6-RWPT), the V6-V1 inter-peak time (V6-V1 IPT) and changes between selective and non-selective LBBP, were collected, among others. Complications occurring during the first 24 hours were all documented.

Recording of precordial leads and measurements with the PSA

The PSA leads were placed as explained:

Briefly, we modified the Mason-Likar electrode lead placement to record V1 and V6. In PSAs with bipolar configuration, we placed the reference electrode (right arm) of leads I and II on the back, and the exploring electrodes (left arm and left leg) adjacent to V1 and V6. In PSAs with unipolar configuration, we placed the additional unipolar electrode adjacent to V1 and moved down the exploring electrode of lead aVL (left arm) adjacent to V6.

The pacing artifact location and the corresponding voltage/time curve representation, as well as the marker channel, depend on each PSA software characteristics. To simplify the measurement process and to avoid differences between PSA manufacturers (Figure 1), we considered the beginning of all measurements at the initial deflection of the pacing

artifact on the surface ECG channels while unipolar stimulation at the lowest output capturing the ventricle (see 'Signals Optimization' in supplementary material).

Procedure preparation and implantation

All patients underwent a LBBAP implantation procedure as follows. Briefly, the 12-leads ECG and one channel with intracardiac EGMs were displayed in the EP-RS for measurements and criteria assessment. The bipolar +/- unipolar PSA ECG surface leads were placed as previously described. The duration and morphology characteristics of baseline QRS corresponding to V1-V6 in the PSA were compared to those with the EP-RS to confirm the correct position of the PSA electrodes.

Operators mainly used an anatomic approach, aiming for a "W" pattern in V1 during unipolar stimulation. A non-stylet active fixation 4F lead or a stylet-driven active fixation 6F lead was implanted using an appropriate dedicated CSP sheath. The pacing lead position was reassessed in posteroanterior, right anterior oblique and left anterior oblique projections. The pacing electrode was then screwed in guided by a moderate drop in the unipolar impedance, the achievement of a small q wave in the current of injury, and the conversion of the "W" in V1 into a qR or rSR pattern. LBBP criteria were then evaluated during unipolar pacing. Lastly, thresholds were obtained, both in unipolar and bipolar configuration. Bipolar EGMs on the EP-RS were filtered through a band-pass of 30-500Hz at a speed of 100mm/s and a gain of 0.1mV/cm. In the PSA, signals were optimized and displayed at a speed range between [50-100] mm/sec and at gain of 0.5-1 mm/mV. Intracardiac EGMs, paced QRS duration, measured from the QRS onset and from the stimulation artifact (S-QRS), QRS morphology, V6-RWPT, and V6-V1 IPT were obtained simultaneously at the operator's discretion in both systems. The EP-RS

signals were analyzed and measured by an expert electrophysiologist from the control room and served to guide the LBBAP lead implantation. The PSA signals were recorded and measured by a dedicated engineer in the operating room solely for the purpose of comparing them with the EP-RS signals at separate analysis. The electrophysiologist in the control room and the engineer in the operating room were blinded to each other (Supplemental Figure 1). After the implantation procedure, all these measurements were validated by two independent electrophysiologists of each participating center.

Definitions

Following recent step-by-step recommendations[8], LBBP was defined as conclusive in the presence of at least one of the following criteria:

1. QRS transition from non-selective LBBP to selective LBBP or non-selective LBBP to left ventricular septal pacing during pacing threshold.
2. V6-RWPT interval <75 msec in patients with narrow QRS or <80 msec in patients with left bundle branch block, interventricular conduction disturbances, right bundle branch block + fascicular block, wide escape rhythm, or asystole.
3. V6–V1 IPT >44 msec.
4. CS potential to V6-RWPT = stimulation artifact to V6-RWPT (±10 msec).

In addition, LBBP was defined as likely in the following situations:

1. V6-RWPT interval between 75-85 msec (native narrow QRS or isolated right bundle branch block) or V6RWPT between 80-100 msec in patients with left bundle branch block, interventricular conduction disturbances, right bundle branch block + fascicular block, wide escape rhythm, or asystole).
2. V6–V1 IPT between 33-44 msec.

3. QRS transition from CS potential (selective or non-selective) capture to myocardial only capture associated with V6-RWPT prolongation by 10-14ms.

Left ventricular septal pacing was defined by a S-QRS showing a typical terminal R wave in V1, and anatomical position of the lead in the interventricular septum documented by fluoroscopy, but not fulfilling the criteria previously described for LBBP. Deep septal pacing was defined by absence of terminal R-wave in V1, despite having an anatomical position of the lead deep in the interventricular septum.

Monitoring and discharge

Patients were discharged after an observation period of at least 24 hours and after the performance of a 12-lead ECG, an X-ray, and a device interrogation.

Statistical Analysis

Data were expressed as mean ± SD or number of cases and proportions according to the variable type (continuous or discrete). Normality was tested using the Shapiro-Wilk test. The T-test was used to assess continuous variables. The Z test was used to compare discrete variables. Pearson and Spearman correlation coefficients were employed as appropriate for measurements correlation analysis as well as Bland-Altman analysis for continuous variables. Indirect comparison of correlation coefficients was performed using the Fisher R to Z transformation. Statistical analysis was performed using STATA, version 15.1 for Windows (StataCorp LLC, College Station, TX).

RESULTS

Demographic characteristics

One hundred and eight patients were included. Baseline characteristics of the patients are shown in Table 1. Briefly, the mean age was 72±15 years, with clear predominance of the male sex, and presenting more than 50% of the population structural heart disease. Intraventricular conduction disorders were observed in most of the patients, and it should be noted that the main indication for cardiac pacing in more than half of the patients was the development of a high degree atrioventricular block.

Intraprocedural characteristics

Out of the total, 73% of patients received a dual chamber pacemaker and 23% received a single chamber pacemaker. In 4% of patients, the original indication was cardiac resynchronization therapy device, but a LBBAP procedure was decided after failure of coronary sinus cannulation. The percentage of the different PSA employed during the procedure was as follows: Abbott 40%, Medtronic 31%, Boston Scientific 15% and Biotronik 14%. Average skin-to-skin procedure time, LBBAP electrode implantation time, and fluoroscopy time were 80±23, 27±23, and 7.5±5 minutes, respectively. A steerable sheath was used in 8% of the patients and contrast injection was employed in 14% of the patients. A non-stylet active fixation 4F lead was implanted in 43% of the patients.

QRS measurements

At the beginning of the procedure, no significant differences (p=0.7) were observed in the baseline QRS duration when comparing the EP-RS (130±29msec) and the PSA (128±29msec) (Table 2).

A "W" morphology was observed during initial pacing in V1 in 88% vs 86% of patients using the EP-RS vs the PSA (p=0.7). A conduction system potential was documented during the procedure in 24.5% vs 21.2% of the patients with the EP-RS vs the PSA (p=0.56).

In patients accomplishing LBBP criteria (definitive or likely), a “qR” or “rSR” morphology in V1 was observed in 77% with the EP-RS compared to 75% with the PSA (p=0.77). Regarding specific criteria, the V6-RWPT was 80±13 vs 79±14 msec (p=0.9), and the V6-V1 IPT was 39±16 vs 38±17 msec (p=0.7), with the EP-RS vs the PSA, being the Pearson correlation coefficients for these two last measurements 0.85 (p<0.0001) and 0.94 (p<0.0001), respectively (Figure 2) (See Supplemental Table 1). An “rS” pattern in V6 during pacing was observed in 12 patients (11,3%). Eight of these patients were assigned to LVSP because they did not meet other specific LBBP criteria.

LBBP criteria (definitive or likely), LVSP criteria, and DSP criteria were fulfilled in 76.4%, 15.1% and 8.5% of patients respectively, assessed by EP-RS. When comparing LBBAP criteria based on EP-RS vs PSA measurements, we observed an excellent correlation (Spearman correlation coefficient of 0.97). QRS transition during stimulation was employed to confirm LBBAP in 18.6% of the patients (assessed by EP-RS), without differences between both systems. The V6-RWPT and the V6-V1 IPT were the most frequent criteria employed to confirm LBBAP capture (81.4% in the EP-RS vs 80.4% in the PSA), with a global correlation coefficient of 0.96 (p <0.0001) (Figure 3 and 4).

The S-QRS averaged 144±15 msec with the EP-RS, vs 143±17 msec with the PSA ($p=0.5$), with a Pearson correlation coefficient of 0.83 ($p<0.0001$); the QRS duration from the QRS onset averaged 122±17 msec with the EP-RS, vs 123±19 msec with the PSA ($p=0.7$), with Pearson correlation coefficient of 0.81 ($p<0.0001$). The Bland-Altman plot for the analysis of baseline QRS duration, V6-RWPT interval, V6-V1 IPT and paced-QRS duration rendered non-significant bias (Figure 5).

Analysis of each PSA separately showed significant correlation in most of the measurements as compared with the EP-RS (Supplemental Tables 2-5). Indirect comparisons of the correlations coefficients (with Fisher r to z transformation) between the different PSA did not render superiority of any specific system over the others (Supplemental Tables 6-6'). In addition, there was no superiority in the unipolar vs bipolar PSA configuration comparison (Supplemental Tables 7-9).

Considering the absence of previous data on acceptable differences between EP-RS and PSA measurements in the context of the present study, a post-hoc power calculation was performed, setting the EP-RS measurements as a reference, in order to detect 10msec or 10% differences, as appropriate (Supplemental Table 10).

Learning curve

Learning curves, addressed by quadratic regression for different variables, rendered a plateau after performing less than 30 procedures (Supplemental Figures 2-4). Absolute differences of less than 5 msec were observed in the measurements between both systems after performing the first 10 procedures. The reduction in the lead placement time was progressive, reaching times of less than 20 minutes after the first 20 cases.

DISCUSSION

The main finding of this study is the usefulness of the PSA as a simple and reliable alternative tool to guide CSP implantation procedures, which can accurately provide similar information compared to EP-RS (comparable intracardiac EGM, surface ECG leads, and time-calipers).

We propose a new technique to obtain V1 and V6 PSA leads, analogous to those displayed by the EP-RS, in a simple and standardized manner. No differences were observed in the measurements obtained by any individual PSA compared to each other or when comparing all PSAs with unipolar/bipolar configuration to the EP-RS. These results suggest that a standardized configuration could be used for all the PSAs (Supplementary material Figure 5).

Although current guidelines highly recommend the use of an EP-RS to guide CSP implantation procedures, not all the centers, even the most experienced, have an EP-RS available. This scenario should not be a major limitation to perform CSP procedures. In fact, a study from the Working Group of Pacing and Electrophysiology of the French Society of Cardiology[9] based on an online survey showed that the absence of an EP-RS available in the lab was perceived as a limitation only in 14% of respondents.

Recently, Wang M et al[10] have shown for the first time the effectiveness and feasibility of LBBAP performance combining a multi-lead surface ECG monitoring and the intracardiac EGMs from the PSA. In this regard, new portable devices capable of displaying a virtual 12-lead ECG and including time-calipers could be of interest for future research. However, these devices do not include intracardiac EGMs. Instead, we propose the PSA as a universal alternative method, which uses two surface ECG leads combined with the intracardiac EGMs.

Considering that most of the ECG criteria assessing LBBAP rely on QRS morphology and/or time intervals using V1 and V6 leads, this new approach could highly simplify the standard approach. Thus, this method is able even to display slight differences in the QRS, offering the possibility to observe progressive reduction in V6-RWPT and/or lengthening in V6-V1 IPT with stimulation during the lead rotations[11]. In fact, these two criteria were the most used to assess LBBAP in our study, in line with routine clinical practice[12,13], showing an excellent correlation between EP-RS and PSA. Other criteria (i.e. transition in the QRS morphology), were also observed in the same proportion with both methods and in a similar proportion to previous studies[14]. In contrast with our proposed approach, a12-leads ECG can further predict the final altitudinal position of the pacing-lead (i.e. pure left bundle vs left posterior or left anterior fascicles capture). However, a recent study concluded that, in patients with heart failure and complete left bundle branch block, LBBP on the trunk or a specific fascicle, can achieve similar favorable QRS complex narrowing, cardiac function improvement, and cardiac reverse remodeling[15].

Overall, we found a 96.4% concordance during the assessment of LBBAP criteria for the final lead location comparing both methods, suggesting that the use of the PSA is feasible and useful during CSP implantation procedures. This simplified approach could probably facilitate the performance of LBBAP implantation procedures in different scenarios (i.e: urgent pacemaker implantation procedures) and spread the technique to more centers (i.e. centers without an EP-RS available).

Finally, the learning curves show that only a few cases are needed in order to achieve similar measurements with the PSA compared to the EP-RS. In addition, the reduction in the lead placement time after the first 20 cases is similar to previous studies[16].

Although all the main investigators were highly experienced electrophysiologists and participant centers had a high volume of CSP procedures, from these results we can

conclude that this approach could be useful for centers without an EP-RS or with a low experience in CSP procedures.

Suggested Step-by-Step recommendations for simplified PSA approach:

- To check baseline V1 and V6 EP-RS leads vs PSA leads for quality control.
- To set the speed rate on the PSA at 25 or 50 mm/sec to identify the initial 'W' pattern (Figure 6 in supplementary material) or the paced right bundle branch morphology pattern. Thereafter a speed rate of 100 mm/sec will improve QRS measurements. Alternatively increase the gain.
- Visualization of CS potentials could be challenging specially during stimulation, due to differences in the filters and software of the PSA. It is recommended to take into account any pre-QRS intracardiac EGMs, independently of its frequency and/or voltage (see Figure 7 in Supplementary material).

LIMITATIONS

This was a non-randomized multicenter study. Although patients were consecutively enrolled, a selection bias cannot be ruled out. The sample size was not calculated before starting the study. However, a post-hoc analysis rendered high power to detect significant differences between the EP-RS/PSA measurements. The main investigator of each center was responsible for the final measurements reviewed, so an observer bias in the results cannot be excluded. The absence of significant differences between the different PSAs could be related to the small sample size. Studies with larger cohorts of patients would be needed. Because these two approaches have not been directly compared, a comparative

trial evaluating the efficacy and accuracy of using PSA signals alone versus EP-RS signals could provide insightful data.

CONCLUSIONS

These results suggest that a simplified PSA approach focusing on specific measurements could be feasible and useful for LBBAP procedures as compared to current approach with the EP-RS.

Acknowledgements

The authors would like to thank the Department of Medicine, Universitat Autònoma de Barcelona, for their support of PhD studies of Dr González-Matos. They also thank the patients who have made this work possible.

Data availability statement:

All relevant data are within the manuscript and its Supporting Information files.

REFERENCES

1.- Jastrzebski M, Dandamudi G, Burri H, Ellenbogen KA. Conduction system pacing: overview, definitions, and nomenclature. Eur Heart J Suppl. 2023 Nov 9;25(Suppl G):G4-G14. doi: 10.1093/eurheartjsupp/suad114. PMID: 37970514; PMCID: PMC10637837.

2.- Wu S, Sharma PS, Huang W. Novel left ventricular cardiac synchronization: left ventricular septal pacing or left bundle branch pacing? Europace. 2020 Dec 26;22(Suppl_2): ii10-ii18. doi: 10.1093/europace/euaa297. PMID: 33370804.

3.- González-Matos CE, Rodríguez-Queralto O, Záraket F, et al. Conduction System Stimulation to Avoid Left Ventricle Dysfunction. Circ Arrhythm Electrophysiol. 2024;17(2): e012473. doi: 10.1161/CIRCEP.123.012473. Epub 2024 Jan 29. PMID: 38284238.

4.- Yuan Z, Cheng L, Wu Y. Meta-Analysis Comparing Safety and Efficacy of Left Bundle Branch Area Pacing Versus His Bundle Pacing. Am J Cardiol. 2022 (1);164:64-72. doi: 10.1016/j.amjcard.2021.10.025. Epub 2021 Dec 7. PMID: 34887071.

5.- Briongos-Figuero S, Estévez-Paniagua Á, Sánchez-Hernández A, et al. Tailored electrocardiographic-based criteria for different pacing locations within the left bundle branch. Heart Rhythm. 2024 ;21(1):54-63. doi: 10.1016/j.hrthm.2023.09.015. Epub 2023 Sep 21. PMID: 37741525.

6.- Pujol-López M, Ferró E, Borràs R, et al. Stepwise application of ECG and electrogram-based criteria to ensure electrical resynchronization with left bundle branch pacing. Europace. 2023 2;25(6): euad128. doi: 10.1093/europace/euad128. PMID: 37294671; PMCID: PMC10254073.

8.- Burri H, Jastrzebski M, Cano Ó, et al. EHRA clinical consensus statement on conduction system pacing implantation: endorsed by the Asia Pacific Heart Rhythm

Society (APHRS), Canadian Heart Rhythm Society (CHRS), and Latin American Heart Rhythm Society (LAHRS). Europace. 2023;25(4):1208-1236. doi: 10.1093/europace/euad043. PMID: 37061848; PMCID: PMC10105878.

9.- Ollitrault P, Chaumont C, Font J, et al. Conduction system pacing in France in 2022: A snapshot survey from the Working Group of Pacing and Electrophysiology of the French Society of Cardiology. Arch Cardiovasc Dis. 2023;116(5):265-271. doi: 10.1016/j.acvd.2023.04.004. PMID: 37179224.

10.- Wang M, Sun Y, Shan Y, et al. The effectiveness and feasibility of using multi-lead ECG monitoring combined with a programmed intracavitary ECG to complete left bundle branch area pacing. Pacing Clin Electrophysiol. 2023;46(3):205-216. doi: 10.1111/pace.14676. Epub 2023 Mar 1. PMID: 36788130.

11.- Jastrzębski M, Kiełbasa G, Moskal P, et al. Transseptal Transition Patterns During Left Bundle Branch Area Lead Implantation. JACC Clin Electrophysiol. 2024 Sep 16:S2405-500X(24)00754-0. doi: 10.1016/j.jacep.2024.07.025. Epub ahead of print. PMID: 39387738.

12.- Vijayaraman P, Ponnusamy S, Cano Ó, et al. Left Bundle Branch Area Pacing for Cardiac Resynchronization Therapy: Results From the International LBBAP Collaborative Study Group. JACC Clin Electrophysiol. 2021 Feb;7(2):135-147. doi: 10.1016/j.jacep.2020.08.015. Epub 2020 Oct 28. PMID: 33602393.

13.- Keene D, Anselme F, Burri H, et al. Conduction system pacing, a European survey: insights from clinical practice. Europace. 2023;25(5):euad019. doi: 10.1093/europace/euad019. PMID: 36916199.

14.- Jastrzębski M, Kiełbasa G, Cano O, et al. Left bundle branch area pacing outcomes: the multicentre European MELOS study. Eur Heart J. 2022;43(40):4161-4173. doi: 10.1093/eurheartj/ehac445. PMID: 35979843; PMCID: PMC9584750.

15.- Liu W, Fulati Z, Tian F, et al. Relationship of different left bundle branch pacing sites and clinical outcomes in patients with heart failure. Heart Rhythm. 2024 Sep 2:S1547-5271(24)03285-5. doi: 10.1016/j.hrthm.2024.08.059. Epub ahead of print. PMID: 39233256.

16.- Cano Ó, Jover P, Ayala HD,et al. Left bundle branch pacing versus left ventricular septal pacing as a primary procedural endpoint during left bundle branch area pacing: Evaluation of two different implant strategies. J Cardiovasc Electrophysiol. 2024 Jan;35(1):120-129. doi: 10.1111/jce.16128. Epub 2023 Nov 14. PMID: 37962088.

FIGURES

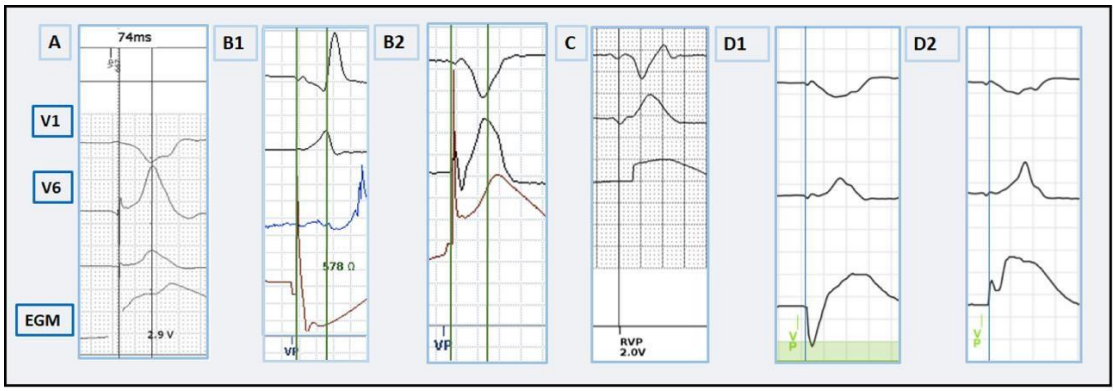


Figure 1- A to D.- Different ventricular EGMs, marker channels, and their relation with the surface ECG signals. The rationale of using the pacing artifact of the surface ECG is based on the different relationship between the initial pacing artifact of the intracardiac EGM channels compared to the surface ECG signals**. A.-** Biotronik PSA: the ventricular channel is usually oversaturated. **B1-2.-** Abbott PSA: in the marker channel, VP is observed before a small initial (negative or positive) deflection. This deflection corresponds to a blanking window in the ventricular channel so that stimulation can be delivered. **C.-** Boston Scientific PSA: the marker channel matches with the initial pacing artifact of the surface ECG, due to its software characteristics. However, the initial deflection of the pacing stimulus is always located after the onset of the QRS complex. **D1-2.-** Medtronic PSA: the ECG input signal and the EGM/Marker signal are coming from two unique input sources. These two sources are independently processed by two different processing units. An algorithm gradually adjusts the waveform alignment to achieve a more time aligned view of the two different sources. The degree of temporal alignment of the two inputs can differ based on a variety of factors inherent in the input systems. EGM: ventricular electrogram.

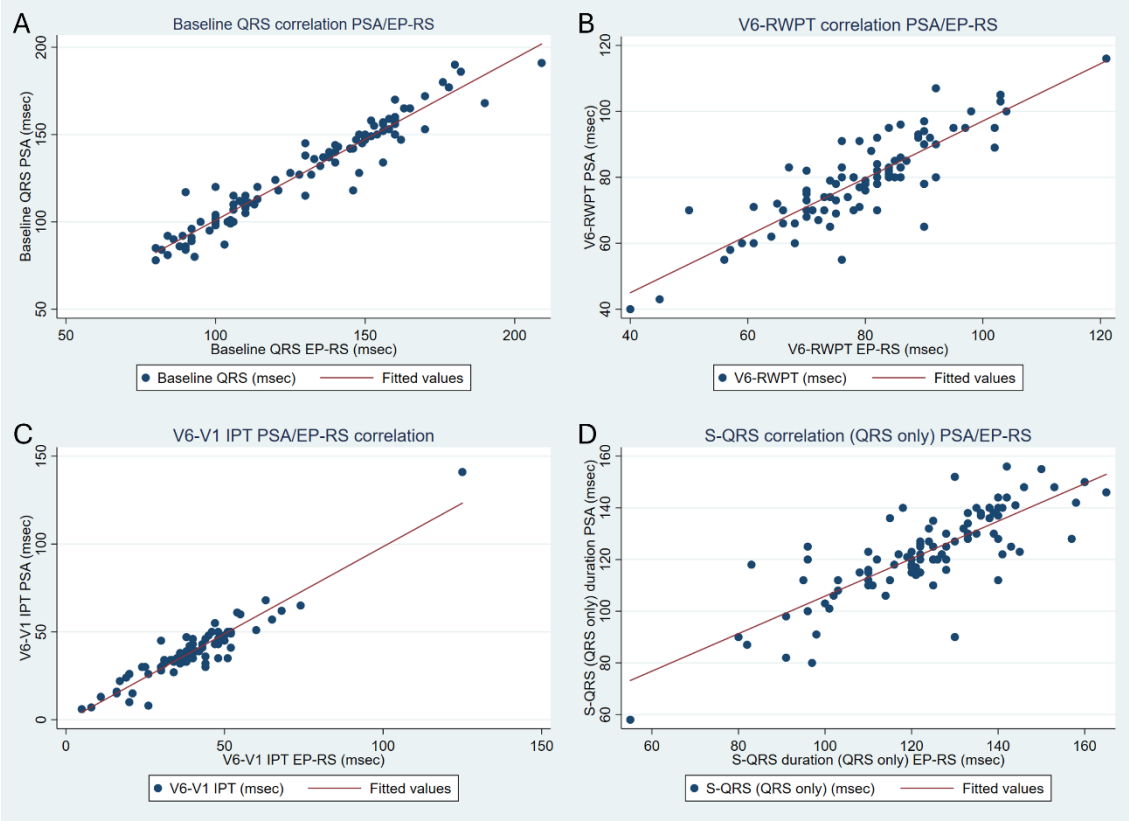


Figure 2. Pearson correlations coefficient analysis shows a strong correlation of measurements between the PSA and the EP-RS. **A.** Baseline QRS duration (msec). **B.** V6-RWPT (msec). **C.** V6-V1 IPT (msec). **D.** S-QRS (Only QRS) duration (msec). EP-RS: Electrophysiological recording system. PSA: Cardiac pacing analyzer. S-QRS: Paced QRS duration. V6-RWPT: V6 R-Wave peak time. V6-V1 IPT: V6-V1 inter-peak time.

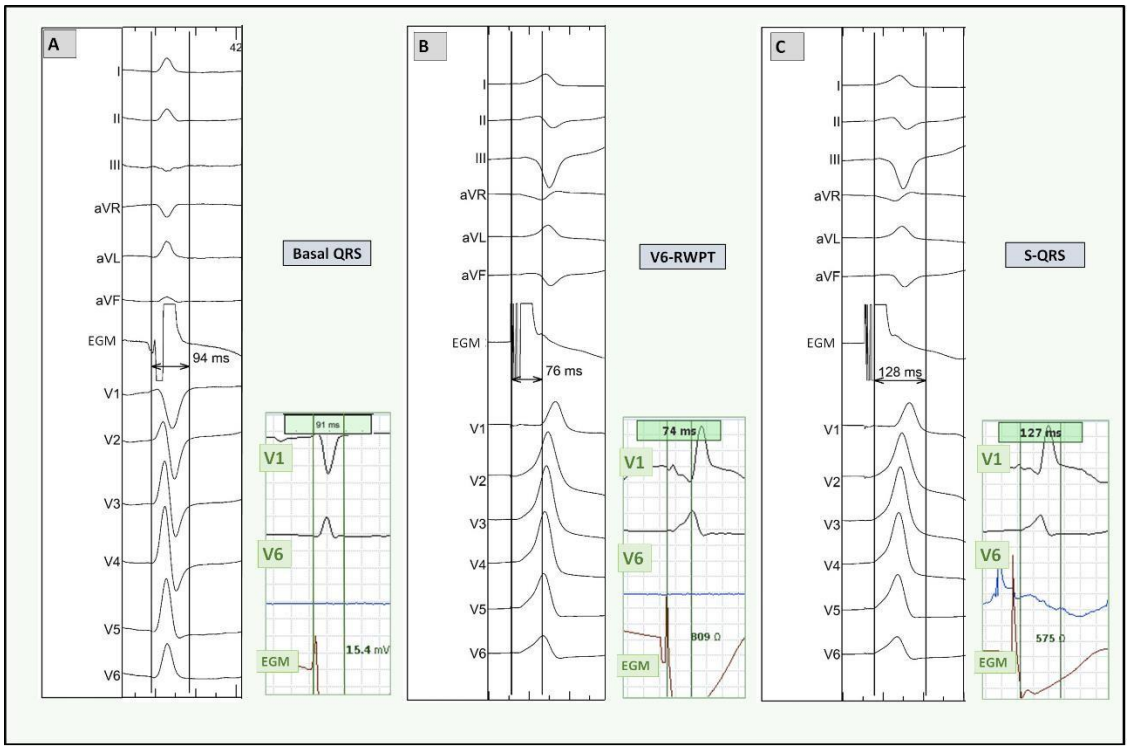


Figure 3. Comparison of EP-RS to PSA tracings during a LBBAP procedure in a patient with intact intraventricular conduction. Panel **A** shows baseline preprocedural tracings. To the left, and from top to bottom: Limb leads, distal unipolar intracardiac EGM, and precordial leads from the EP-RS. To the right, and from top to bottom, the corresponding PSA tracings of: V1, V6, and distal unipolar intracardiac EGM. QRS duration is displayed and is similar with both methods. Panel **B** shows final position S-QRS with V6-RWPT displayed and compared; and Panel **C** shows final position S-QRS with QRS duration displayed and compared.

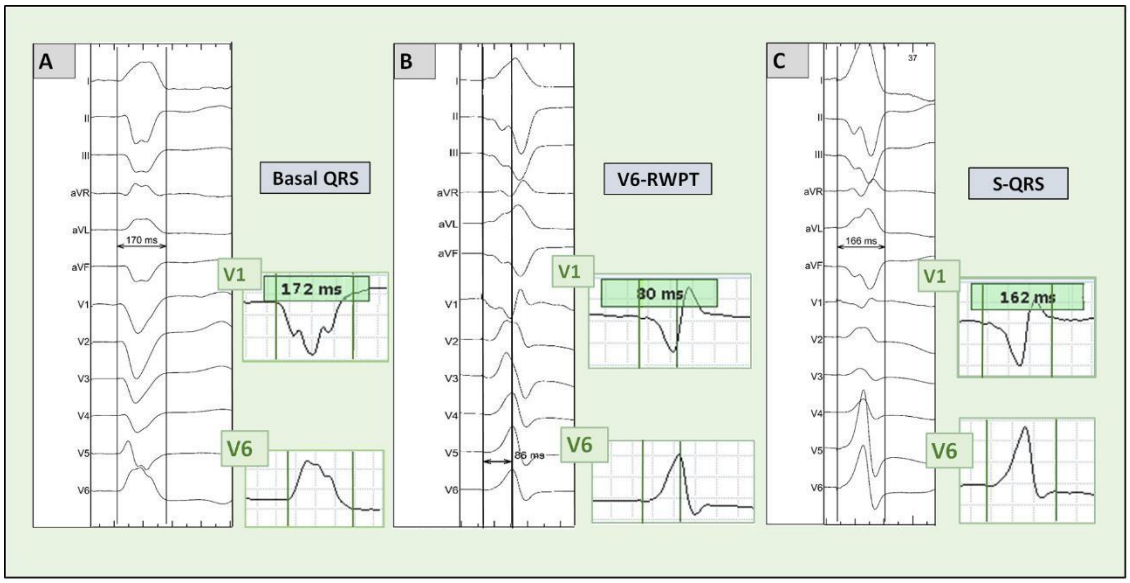
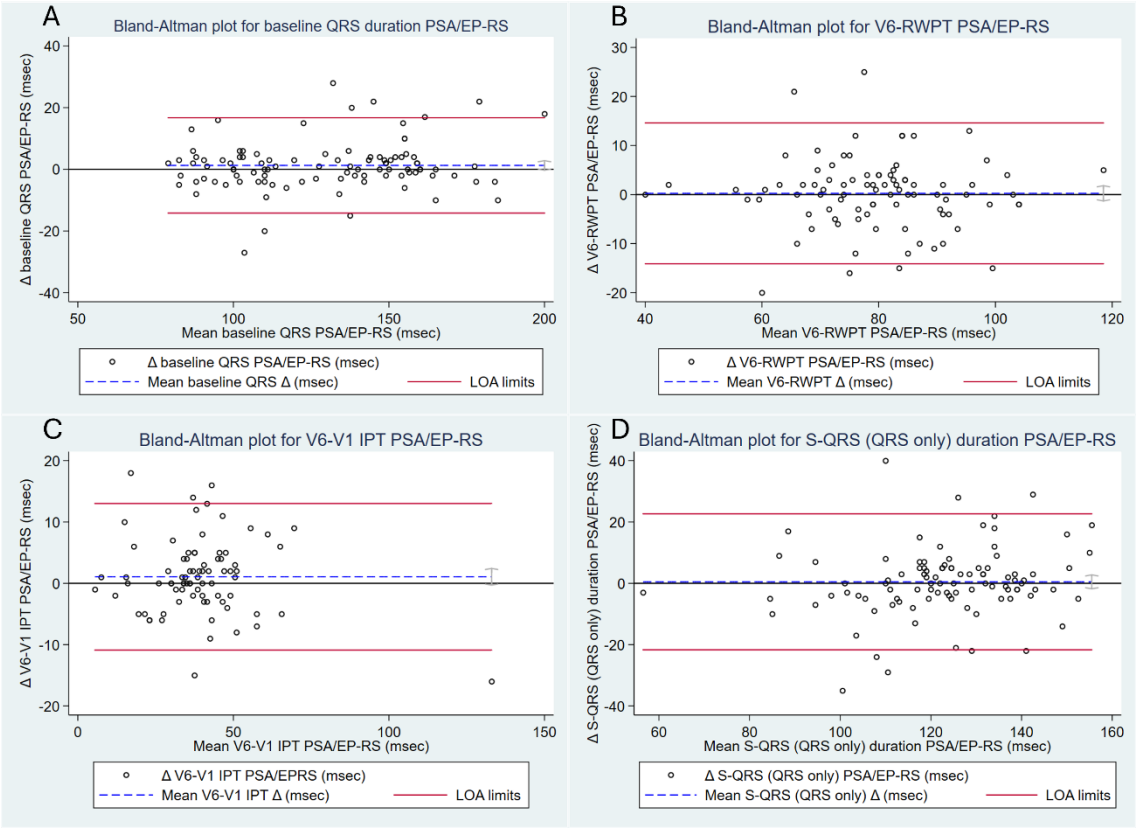


Figure 4. Comparison of EP-RS to PSA tracings during a LBBAP procedure in a patient with left bundle branch block, with emphasis on the PSA QRS morphologies and measurements. Panel **A** shows baseline QRS duration. Panel **B** shows V6-RWPT. Panel **C** shows final S-QRS duration.



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459 **Figure 5.** Bland-Altman plots showing non-significant differences between the PSA and
460 EP-RS measurements (Red line: 95% Limits of agreement. Blue dashed line: Mean bias.
461 Gray lines: 95% bias confidence interval). **A.** Baseline QRS duration (msec). **B.** V6-
462 RWPT (msec). **C.** V6-V1 IPT (msec). **D.** S-QRS (Only QRS) duration (msec). EP-RS:
463 Electrophysiological recording system. LOA: 95% Limits of agreement. PSA: Cardiac
464 pacing analyzer. S-QRS: Paced QRS duration. V6-RWPT: V6 R-Wave peak time. V6-
465 V1 IPT: V6-V1 inter-peak time.

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Table 1. Baseline patients' characteristics

Variable	Total group (n 108)
Age (Years ± SD)	72 ±15
Male sex (%)	73
Structural heart disease (%)	52
Ischemic	34
Dilated	29
Valvular	23
Others	14
QRS morphology (%)	
RBBB / LBBB	45 / 37
Non-specific	16
Normal QRS	2
Atrial fibrillation (%)	37
Paroxysmal	47
Permanent	53
LVEF (% ±SD)	53 ± 10
Procedure indication (%)	
High degree AV block	56
Sinus node disease	14
Atrial fibrillation (slow ventricular response or before AV node ablation)	11
Others	19

Atrioventricular. LBBB: Left bundle Branch block. RBBB: Right bundle Branch block. SD: Standard deviation. SHD: Structural heart disease.

Table 2. Comparison between EP-RS and PSA during the LBBAP procedure

Variable	EP-RS values	PSA values	Mean difference (95% CI)	P	Correlation coefficient	P	Mean bias (95% CI)	95% Limits of agreement
Intraprocedural measurements								
Baseline QRS (msec) ± SD	129.8 ± 29.4	128.3 ± 28.7	1.5 (-6.4 to 9.5)	0.70	0.96	<0.0001	1.26 (-0.3 to 2.8)	-14.2 to 16.7
Initial "W" in V1(%)	88	86.2		0.71	0.85	<0,0001		
CS Potential (%)	24.5	21.2		0.56	0.84	<0.0001		
Final qR/rSR V1 (%)*	77	75.3		0.77	0.92	<0.0001		
V6-RWPT (msec) ± SD	79.7 ± 13.5	79.5 ± 13.7	0.3 (-3.8 to 4.3)	0.90	0.85	<0.0001	0.3 (-1.3 to 1.8)	-14.1 to 14.6
V6-V1 IPT (msec) ± SD	39.4 ± 16.4	38.4 ± 17.4	1.1 (-4.3 to 6.4)	0.69	0.94	<0.0001	1.1 (-0.3 to 2.4)	-10.9 to 13.0
QRS duration (msec) ± SD	122.5 ± 17	123.4 ± 18.8	-1 (-6 to 4.1)	0.71	0.81	<0.0001	0.5 (-1,8 to 2.8)	-21.7 to 22.7
S-QRS (msec) ± SD	144.1 ± 15.1	142.8 ± 16.6	1.3 (-3.5 to 6.1)	0.58	0.83	<0.0001	1.7 (-0.3 to 3.8)	-16.3 to 19.8
Capture (%)								
LBBAP	91.5	92.4		0.80	0.94	<0.0001		
DSP	8.5	7.5						
LBBAP (%)								
Def LBBP	55.7	52.8		0.91	0.97	<0.0001		
Likely LBBP	20.8	26.4						
LVSP	15.1	13.2						

EP-RS: Electrophysiological recording system. CS: Conduction System. LBBAP: Left bundle branch area pacing. LBBP: Left bundle branch pacing. LVSP: left ventricular septal pacing. DSP: Deep septal pacing. Msec: milliseconds. PSA: Pacing system analyzer. SD: Standard deviation. S-QRS: Stimulated QRS duration. V6-RWPT: V6 R wave peak time. V6-V1 IPT: V6-V1 inter-peak time. Def: Definitive.

*In patients accomplishing LBBP criteria (definitive or likely).