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Exploratory Use of Intraprocedural Transesophageal Echocardiography to Guide Implantation of the Leadless Pacemaker

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Running Title: Intraprocedural TEE: leadless pacemakers

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Abstract:

Background: Fluoroscopy is the standard tool for transvenous implantation of traditional and leadless pacemakers (LP). LP are used to avoid complications of conventional pacemakers, but there is still a 6.5% risk of major complications. Mid-Right Ventricular (RV) septal device implantation is suggested to decrease risk, but helpful cardiac landmarks cannot be visualized under fluoroscopy. Transesophageal Echocardiography (TEE) is an alternative intra-procedural imaging method.

Objective: We aim to explore the spatial relationship of the LP to cardiac landmarks via TEE, their correlations with electrocardiographic (ECG) parameters and outline an intraprocedural method to confirm mid RV non-apical lead positioning.

Methods: We enrolled 56 patients undergoing implantation of LP with TEE guidance. Device position was evaluated by fluoroscopy, ECG and TEE. Distances between the device and cardiac landmarks were measured by TEE and analyzed with ECG parameters with and without RV pacing.

Results: Mid-RV septal positioning was achieved in all patients. TEE trans-gastric (0-40/90-130°) view was the optimal view to visualize device position. The mean TV-LP distance was 4.9 +/- 0.9 cm, the mean PV-LP distance was 4.2 +/- 1 cm and the calculated RV apex-LP distance was 2.9 +/- 1 cm. The mean LP paced QRS width was 160.8 +/- 28 ms, increased from 117.2 +/- 34 ms at baseline. LP RV pacing resulted in LBBB pattern on ECG and 37.8% QRS widening by (43.5 +/- 29 ms).

Conclusion: TEE may guide LP implantation in the non-apical mid-RV position. Further studies are required to establish whether this reduces implant complications when compared with conventional fluoroscopy.
KEYWORDS
Pacemaker; Leadless, TEE, Non-fluoroscopy imaging, Septal pacing, intraprocedural imaging.

Abbreviations
RV = Right ventricle
TEE = Transesophageal echocardiogram
ECG = Electrocardiogram
PV = Pulmonic valve
TV = Tricuspid valve
LP = Leadless pacemaker
LVEF = Left ventricular ejection fraction
IVS = Intraventricular septum
Introduction

Fluoroscopy is the standard imaging modality used during permanent pacemaker implantation, including the FDA approved leadless pacemaker. The leadless pacemaker (LP) established itself as a device to avoid complications common to conventional pacemakers in the evolving world of electrophysiology. By omitting the need for transvenous leads and subcutaneous pocket creation, a LP avoids several complications. Nevertheless, in early experiences there was still a 6.5% risk of serious device-related complications including cardiac perforation, tamponade, elevated pacing thresholds, and dislodgement. (1) In 2020, leadless pacemaker was approved for the treatment of patients with AV block making nearly 50% of all pacemaker patients eligible candidates for this leadless system which will translate to a larger number of patients with leadless devices in our aging population.

This LP system utilizes four self-expanding nitinol tines to anchor onto the right ventricular (RV) myocardium before 2022. To obtain optimal pacing thresholds at implantation, device repositioning and redeployment may be required. It is recommended that at least two tines are engaged in tissue to hold the device securely; this can be done fluoroscopically by utilizing orthogonal views, IV contrast and a ‘tug’ test in addition to ensuring electrical measurements are within recommended values (pacing threshold of less than 1.0 V at 0.24 ms, pacing impedance 400–1500 V, and R-wave amplitude greater than 5 mV). However, no specific RV positioning had been recommended. (2)

The major complication of apical implantation is RV perforation. There are reports to suggest that mid septal implantation may decrease the risk of such serious complications. (3, 4) More patients had the LP implanted in a septal location in the Post Approval Registry (PAR) compared to those in the investigational device exemption (IDE) study (52% vs 33%). (5-7) Little guidance is currently available regarding alternative intra-procedural imaging besides conventional fluoroscopy. In the traditional pacemaker systems, generic fluoroscopic RV septal implantation criteria have proven to be unreliable with RV leads placed in the free wall despite being thought to be
positioned in the septum via fluoroscopy.\textsuperscript{(8-10)} For this reason, the definition of septal implantation in the literature may not be entirely accurate, and a broader term of ‘RV non-apical pacing’ has been suggested.\textsuperscript{(11)} This raises major concerns about the safety and efficacy of relying solely on fluoroscopic criteria for lead positioning. Helpful anatomic landmarks for implantation such as the tricuspid valve (TV) and pulmonary valve (PV) cannot be visualized fluoroscopically. The objective of this study is to establish the spatial relationship of the LP to cardiac landmarks via TEE, their correlations with ECG parameters, and outline a reproducible intraprocedural method to confirm the mid RV septal lead positioning.

\textbf{Methods and Materials}

This study is a single-center observational retrospective electronic medical record review of patients who underwent LP implantation in the electrophysiology lab of University of California Davis Medical Center (UCDH) from February 2019 to February 2022. The study was approved by the institutional review board (IRB) at UCDH and adhered to the Helsinki declaration in human research as revised in 2013.

The inclusion criteria were all adult patients undergoing intraprocedural TEE guided LP implantation between February 2019 and February 2022. All LP implantation guided by only fluoroscopy were excluded. All were Micra (Medtronic) devices. All implantations were performed under Philips FD 10-10 Fluoroscopic system. The Siemens SC2000 system was used for TEE. The GE Cardiolab Recording system was used for standard
12-lead ECG monitoring during implantation. All intraprocedural ECG data were processed with Cardiolab data station (General Electric GE) and all TEE imaging data were processed with Syngo Dynamic system (Siemens).

The procedures were performed in fasting state following standard protocol utilizing informed consent and under general anesthesia. (13) The position and stability of the LP were confirmed fluoroscopically during the procedure by utilizing orthogonal views (Figure 1), IV contrast and a ‘tug’ test in all patients. All TEEs were performed through a standard TEE protocol (Appendix I) at UCDH by one echo board-certified cardiologist as the second proceduralist. Post-operative PA/lateral x-rays were taken for all patients before discharge (Figure 2F). 12-lead ECG data was obtained for every patient prior to and after pacing. Using multichannel ECGs, all 12-leads were lined up in a time synchronized manner, the QRS width was measured from the earliest deflection point of any chest or limb lead to the latest deflection point of any chest or limb lead. This will give the highest and most consistent values of the QRS duration. This is more accurate than those obtained by conventional measurements of any individual chest or limb lead.(18)

The primary outcomes of interest were the TV-LP distance, PV-LP distance, and the RV Apex-LP distance (in cm), post LP pacing QRS width (in ms) and the change in paced QRS width (in percentage). Secondary outcomes included all immediate intraprocedural complications. Adopting identical criteria as in the Micra IDE study, major complications were defined as system and procedure related events resulting in death, permanent loss of device function, hospitalization, prolonged hospitalization by 48 hours, or system revision (7).

The following data was extracted: date of procedure, indication, patient’s age, gender, LVEF (prior to pacing) and co-morbidities. The QRS complex width pre and post LP pacing were recorded by the same operator on Cardiolab data station (figure 1C). The TEEs were individually reviewed by the same operator and the following measurements
were obtained: TV-LP distance and PV-LP distance was measured in the trans-gastric 0-40/90-130-degree views. The measurements were obtained from the tip of the LP to the delineated cardiac landmarks (center of coaptation of the PV in diastole (figure 2A) and the TV in systole (figure 2B)). The intraventricular septum (IVS) length was measured in the mid gastric 4 chamber 0–20-degree view at end diastole from the TV septal leaflet insertion to the RV apex (figure 2E). The RV apex-LP distance was calculated by subtraction (IVS – ½(TV-LP + PV-LP)) (figure 2D).

All measurements and numerical data were expressed as mean+/−SD for continuous variables and categorical variables were summarized as frequency and percentage. The t-test was used to compare continuous variables accounting for pairing as needed (e.g., for pre vs. post data within a same patient or for two independent groups), and the correlation between variables was studied using Pearson correlation coefficient; these parametric methods may be well justified as the data are reasonably symmetric. SAS version 9.4 was used for data analyses.

Results

Patient population

A total of 56 patients with procedural TEEs were included for this study. Demographics, clinical and procedural characteristics are described in Table 1. The average age of patients was 74.1 +/- 12 years and 64% of the participants were male. The average LVEF was 53.6 +/- 9%. The average IVS length was 7.5 +/- 1.2 cm. The baseline characteristics and medical treatments of the 56 consecutive patients who received a LP system are summarized in Table 1.

EKG changes
The average QRS width was 117.2 ± 34 ms at baseline and the average QRS width post LP-pacing was 160.8 ± 28ms. LP pacing resulted in mean QRS widening by 43.5 +/- 29 ms (43.9 +/- 33% (p < 0.01). The correlation between the baseline and post LP-pacing QRS width was 0.57 (p < 0.01). This suggested the wider the QRS at baseline, the wider the QRS post LP pacing. The correlation between the baseline QRS width and the IVS length was 0.41 (p < 0.01). The correlation between the post LP-pacing QRS width and the IVS length was 0.25 (p = 0.06). This suggested the wider the QRS at baseline as well as post pacing, the longer the IVS as depicted in table 2.

**TEE measurements**

The average TV-LP distance was 4.9 +/- 0.9 cm, the average PV-LP distance was 4.2 +/- 1 cm. The average distance of RV Apex-LP was 2.9 +/- 1 cm. The correlation between the baseline QRS width and the TV-LP was 0.31 (p = 0.02), and the correlation between the post LP-pacing QRS width and the TV-LP was 0.28 (p = 0.04). The correlation between the baseline QRS width and the LP-PV was 0.32 (p = 0.02), and the correlation between the post LP-pacing QRS width and the PV-LP was 0.48 (p < 0.01). The correlation between the baseline QRS width and the RV Apex-LP was 0.17 (p = 0.21) and the correlation between the post LP-pacing QRS width and the RV Apex-LP was 0.07 (p = 0.61). The correlation between the IVS and the RV Apex-LP was 0.72 (p < 0.01).

**Follow-up**

Patients were discharged an average of 2.9 +/- 4 days following the implantation, after confirming normal function of the pacemaker and obtaining an X-ray chest film. Follow-up was performed on average about 16.5 +/- 18 days after the procedure in the outpatient pacemaker clinic.

**Discussion**

This proof-of-concept study demonstrated that TEE as a supplemental imaging modality to guide LP implantation is feasible. The LP guide catheters and the cardiac markers (TV, PV and papillary muscles) were adequately visible and beneficial for localization.
throughout the procedure. In this study period, a total of 77 LP implantations (38 VR and 39 AV) were performed in our institution and 21 of the implantations had only fluoroscopy, most of which were at the initial phase of the procedural implantation at our institution, thus we did not perform comparisons between the fluoroscopy guided only cohort and the TEE/fluoroscopy guided cohort, as the numbers were too small and implanter’s learning curves were screwed.

This was the first time intra-procedural TEE was used to define the TV-LP, PV-LP, and RV Apex-LP distances to the best of our knowledge. These parameters had several advantages over using contrast to determine RV non-apical location. First, using the TV-LP and PV-LP distances allowed the operator to determine how far the LP device was from the RV apex. This was crucial as the RV apex is the thinnest part of the RV and most vulnerable for perforation. It provided an additional layer of monitoring for intra-procedural complications during LP placement. Secondly, we found the septal papillary muscle of the tricuspid valve apparatus was reliably visualized in majority of the cases in the gastric 90-130° RV long axis view. This important landmark on the RV side of the IVS could serve as an important landmark for septum localization (17). We used this septal papillary muscle as the reference point but did not aim to implant the LP onto the papillary muscle as it might reduce the stability and negatively influenced the LP pacing parameters. Numerically, the LP was found to be closer to the PV (4.2 cm) than the TV (4.9 cm) in keeping with suggested non-apical implantation. Thirdly, we found that the TEE trans-gastric (0-40/90-130°) biplane view was the optimal view to visualize device position, especially the LP relationship with the IVS and the RV apex.

We used TEE to assist LP implantation only with patients under general anesthesia. The type of sedation used for the implantation of LP was decided jointly by the patients and procedural physicians clinically. In this study period, most of the LP implantation were under general anesthesia to ensure patient safety as it was a new procedure to our institution. As the procedure matured and the procedural sedation transitioned from general anesthesia to MAC (monitored anesthesia care) sedation which is also known as conscious sedation. TEE might add additional patient discomfort and the risk-benefit
assessment needs to be evaluated on an individual basis. Alternatively, Intra-cardiac

echocardiography (ICE) might be used to guide the procedure. Indeed, we had three

patients where ICE was used, we found the RV septum and the LP device were best

visualized with ICE with the ICE probe was in the RV cavity instead of the RA (data not

shown), but the numbers were too small for comparison. Traditionally, RAO/LAO

orthogonal views in fluoroscopy are used for pacemaker lead positioning within the IVS

and IV contrast are used to visualize the RV landmarks such as the RV apex (12). We

used IV contrast in majority of our cases besides the intraprocedural TEE, yet the final

LP position with relationship to the fluoroscopic RV landmarks were difficult to

quantitate, we did not perform any comparison of the TEE RV-LP landmarks and

fluoroscopic RV landmarks.

Although the mid-esophageal 60–90-degree short axis view allowed visualization of the

LP, TV and PV at the same 2D imaging plane, the IVS was not visible in this view. (15)

In the mid-esophageal 0–30-degree four chamber view, there was good visualization of

the IVS, the LP and the pulmonic valve were rarely visible, and the PV was usually

absent. (13) Finally, intraprocedural TEE allowed real time monitoring for early

identification of an iatrogenic pericardial effusion if present.

The periprocedural complication rate of LP implantation was low with rates of pericardial

effusion or tamponade observed in 1% to 2% of cases. (6, 9) Previously described

septal positioning of the LP device was suggested to have a favorable effect on the risk

of perforation. (6, 7) However, in many relevant studies, devices which were thought to

be septally implanted under fluoroscopy were implanted in the RV apex. (6, 9, 11, 14)

Surprisingly, in 4 out of the 5 patients with LP- related pericardial effusion or

tamponade, the devices were implanted in the septal position. (11) In a study by

Kaczmarek et al, who investigated septal implantations of LP devices, a single heart

perforation occurred when a delivery sheath was directed to the free wall of the RV (15).

Prior experience with conventional pacemakers suggests that fluoroscopy might be

insufficient for guiding precise lead implantation in the IVS, therefore, use of

intraprocedural TEE seems to be advisable.(3, 16) Contrary to the study by Kaczmarek
et al, who suggested that the upper- mid- esophageal position of the TEE probe was the best location to visualize and facilitate septal positioning of the LP during implantation (15), our study favored the TEE trans-gastric (0-40/90-130°) biplane view as it was reproducible in all study participants.

RV pacing induced QRS widening is a well-known phenomenon. In our study, we found no statistical correlation between the TEE defined the TV-LP, PV-LP, LP-Apex distances and the native and paced QRS complexes. However, our study showed that the wider the native QRS at baseline, the wider the QRS post LP-pacing. This was consistent with the notion that intraventricular conduction system disease was a diffuse process, the pre-existing conduction system disease is an important contributor to determine the post pacing QRS width. Moreover, there is also significant QRS axis shift post LP pacing. Preliminary analysis of our study cohort demonstrated that LP pacing resulted in the QRS complexes shifted right-wards in the frontal plane and posteriorly in the horizontal plane (date not shown). Further analysis of the relationship of LP anatomical position and QRS shift is under way.

Lastly, the average length of hospital stay was 2.9 days post LP implantation, which was longer than expected, this was likely due to the higher proportion of inpatients in our study cohort.

Limitations
This study had several limitations that restrict the generalizability of the results. First, this was a retrospective study involving a small sample with inherent biases. Due to the small sample size, there was a risk of Type II statistical error and we could not perform adjusted analyses. Also, there was no control group of patients who underwent fluoroscopic only implantation of LP to serve as a comparison. As such, no clinical inference can be made. Given this was a single-center study, there was an inherent lack of external validity to support widespread changes in clinical practice. The study duration was short, and number of participants was too small to detect rare, previously reported complications. Finally, we were unable to account for repositioning due to the
Conclusions
This study represented the first report of a systematic intraprocedural TEE protocol to guide non-apical mid RV implantation of LPs. Important cardiac landmarks to LP distances (which are considered surrogates for mid-ventricular and non-apical implantation) were measured and reported. This study suggested TEE may be useful to navigate the mid-ventricular and non-apical implantation of LPs while perhaps avoiding perforation. Our preliminary study proposed a method to protocolize intraprocedural imaging for LP implantation procedures. The use of ICE may be considered on a case-by-case basis to avoid risks of GA. Larger studies, comparing the different echocardiographic modalities to traditional fluoroscopy are needed to conclusively determine the cost-effectiveness and patient safety concerns of utilizing various imaging modalities to guide LP implantation. Additionally, more data is needed to study whether TEE will lead to fewer intraprocedural complications.

References


10.5772/intechopen.95799

FIGURE LEGENDS:

Figure 1: Standard fluoroscopic views of LP implantation views: AP view (A) and LAO 40 degrees view (B) and standard 12-lead ECG monitoring (C), QRS complex width were measured before (first 3 QRS complexes) and after (last 4 QRS complexes) LP pacing

Figure 2: Transesophageal echocardiographic images in the deep gastric (130-140 degrees) with obtained PV-LP (A), TV-LP (B), the derived RV Apex -LP (D), as illustrated (C), and IVS length measurement in the mid-esophageal view at 0 degrees. The post implant x-ray (F), PV: Pulmonic valve, TV: Tricuspid valve, LP: Leadless pacemaker, RV: Right ventricle, IVS: Intraventricular septum, Figure 1C was adapted from Stephenson, R.S., Atkinson, A., Kottas, P. et al. High resolution 3-Dimensional imaging of the human cardiac conduction system from microanatomy to mathematical modeling. Sci Rep 7, 7188 (2017). https://doi.org/10.1038/s41598017-07694-8
<table>
<thead>
<tr>
<th>Table 1. Demographic Characteristics (N = 56)</th>
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<tr>
<td><strong>Age (years)</strong></td>
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<tr>
<td><strong>Male</strong></td>
</tr>
<tr>
<td><strong>Indication for pacing</strong></td>
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<tr>
<td>Grade 2 or 3 atrioventricular block</td>
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<td>Sick sinus syndrome</td>
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<td><strong>Comorbidities</strong></td>
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<td>Ischemic heart disease</td>
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<td>Previous myocardial infarction</td>
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<td>Chronic kidney disease</td>
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<tr>
<td>Heart failure</td>
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<td>Left ventricular ejection fraction</td>
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Table 2. Pearson Correlation Coefficients of the obtained measurements with p-value (N = 56)

<table>
<thead>
<tr>
<th></th>
<th>Inherent QRS</th>
<th>Paced QRS</th>
<th>IVS Length (TEE)</th>
<th>TV-LP (TEE)</th>
<th>PV-LP (TEE)</th>
<th>LP-Apex average (TEE)</th>
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<tr>
<td><strong>Native QRS</strong></td>
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<td>0.57</td>
<td>0.41</td>
<td>0.31</td>
<td>0.32</td>
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<td></td>
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<td>(0.02)</td>
<td>(0.02)</td>
<td>(0.18)</td>
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<tr>
<td><strong>Paced QRS</strong></td>
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<td>0.28</td>
<td>0.48</td>
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<td>(0.06)</td>
<td>(0.04)</td>
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<td>(0.61)</td>
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<tr>
<td><strong>IVS Length (TEE)</strong></td>
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<td>0.51</td>
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<td></td>
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<td>(&lt;.0001)</td>
<td>(0.0003)</td>
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<tr>
<td><strong>TV-LP (TEE)</strong></td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>(&lt;.0001)</td>
<td>(0.36)</td>
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<tr>
<td><strong>PV-LP (TEE)</strong></td>
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KEY FINDINGS

• Currently, fluoroscopy imaging is standard practice for leadless pacemaker (LP) implantation, but transesophageal echocardiography (TEE) is a reasonable alternative.

• This proof-of-concept study demonstrates the use of TEE cardiac landmarks and electrocardiographic gating guide to optimal LP placement.

• We propose a protocol for intraprocedural imaging for LP implantation procedures.

• Further studies are required to establish whether this reduces implant complications when compared with conventional fluoroscopy and/or intracardiac echocardiography (ICE).