

REVIEW TOPIC OF THE WEEK

Leadless Cardiac Pacemakers

Back to the Future



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ABSTRACT

Despite significant advances in battery longevity, lead performance, and programming features since the first implanted permanent pacemaker was developed, the basic design of cardiac pacemakers has remained relatively unchanged over the past 50 years. Because of inherent limitations in their design, conventional (transvenous) pacemakers are prone to multiple potential short- and long-term complications. Accordingly, there has been intense interest in a system able to provide the symptomatic and potentially lifesaving therapies of cardiac pacemakers while mitigating many of the risks associated with their weakest link—the transvenous lead. Leadless cardiac pacing represents the future of cardiac pacing systems, similar to the transition that occurred from the use of epicardial pacing systems to the familiar transvenous systems of today. This review summarizes the current evidence and potential benefits of leadless pacing systems, which are either commercially available (in Europe) or under clinical investigation. (J Am Coll Cardiol 2015;66:1179-89) © 2015 by the American College of Cardiology Foundation.

Since the first completely endocardial transvenous permanent pacemaker was implanted more than 50 years ago, significant advances have been made in battery longevity, lead performance, and device programming (1-3). Nevertheless, the basic design of cardiac pacemakers has remained relatively unchanged: a (most commonly) pectoral pulse generator connected to 1 or more transvenous leads. Although highly reliable, conventional cardiac pacemakers have several limitations. The subcutaneous pocket has a potential for local complications, such as skin erosion and pocket hematomas, which can be associated with a 15-fold higher risk for subsequent infection if early reintervention is required (4-6). The insertion of transvenous leads can result in acute complications, such as pneumothorax or upper extremity deep vein thrombosis, and the presence

of chronic transvenous leads can lead to central vein obstruction, tricuspid valve insufficiency, and infection (7,8). Even for single-chamber transvenous systems (which are associated with a lower risk than dual-chamber system implants), more than 1 in every 40 implants will result in a complication requiring surgical intervention within the first 3 months, of which more than one-half are lead related (9,10). In the long term, lead failures are associated with significant morbidity (7).

Early recognition that transvenous leads are the weakest link of conventional pacing systems led investigators more than 40 years ago to consider the possibility of leadless cardiac pacing (1). A pre-clinical report in 1970 demonstrated the feasibility of a totally self-contained intracardiac pacemaker. In that study, a canine with an iatrogenic heart block was paced for

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ABBREVIATIONS AND ACRONYMS

CRT = cardiac
resynchronization therapy

LCP = leadless cardiac
pacemaker

TPS = transcatheter pacing
system

more than 2 months. The delivery catheter was inserted through the jugular vein, the leadless pacemaker was passed into the right ventricle under fluoroscopy, and radially directed spiral barbs attached the cylindrical device to the ventricular myocardium. Approximately 2 decades later, additional pre-clinical testing again demonstrated the potential feasibility of this approach (11). Although the field of leadless cardiac pacing remained stagnant for almost 20 years, this has changed with the advent of advancements in several areas, including catheter-based delivery systems, miniaturized high-density energy sources, low-power electronics, novel packaging capabilities, and novel communication technologies. In this review, we strive to summarize the current state of the 2 basic designs of leadless cardiac pacemakers (LCPs). One design uses 2 separate components, an endocardial pacing electrode and a subcutaneous energy transmitter, whereas the second design is a completely self-contained device in which the pulse generator and pacing electrode are a single component.

MULTICOMPONENT (NOT SELF-CONTAINED) LEADLESS PACING

ULTRASOUND-MEDIATED ENERGY TRANSFER.

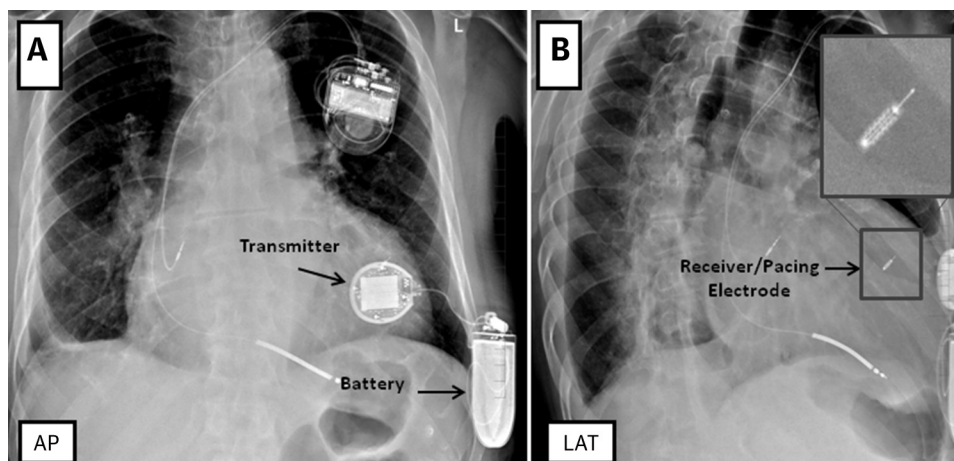
Recently, the results of WiSE-CRT (Wireless Stimulation Endocardially for CRT), a prospective observational feasibility study of leadless ultrasound-based endocardial left ventricular pacing in patients with guideline-directed indication for cardiac resynchronization therapy (CRT) were reported (12). The WiSE-CRT study used a system intended for chronic use with 2 components: a subcutaneous pulse generator and a small receiver electrode. The subcutaneous pulse generator was surgically implanted in the left lateral thorax (subcutaneous) and generated ultrasonic acoustic energy; the small receiver electrode was implanted directly onto the left ventricular endocardium (using a retrograde aortic approach) and converted the acoustic energy to electric pacing pulses (13). All patients in WiSE-CRT had existing implantable cardiac devices (pacemakers or defibrillators) and were considered eligible for enrollment if they: 1) had undergone prior failed coronary sinus lead implantation; 2) had undergone previously successful placement of a coronary sinus lead but were clinical nonresponders; or 3) required an upgrade to a CRT system (12,14). From an efficacy perspective, the results of WiSE-CRT were promising: left ventricular function improved at 6 months (mean pre-implantation left

ventricular ejection fraction of $25 \pm 4.0\%$ vs. mean 6-month post-implantation ejection fraction of $31 \pm 7.0\%$; $p < 0.01$). However, the study was terminated prematurely for safety reasons. Of the 17 patients enrolled (of an intended 100 patients), the device could be successfully implanted in only approximately three-quarters ($n = 13$ [76%]). Most important, 3 patients (18%) developed serious procedure-related pericardial effusions due to either delivery sheath or guidewire manipulation; 1 of these resulted in a patient's death. Additionally, 2 patients (11%) required revision of the transmitter position because of loss of biventricular pacing, and in 1 patient, there was unexpected depletion of the battery.

After WiSE-CRT was terminated because of safety concerns, the delivery system was redesigned to permit atraumatic implantation of the receiver electrode onto the left ventricular endocardial surface. Similar to that studied in WiSE-CRT, the redesigned leadless system is also composed of an implanted battery-powered ultrasonic transmitter and a leadless pacing electrode implanted directly onto the left ventricular endocardium (Figure 1). Again, the system detects a right ventricular pacing pulse from a coimplanted pacemaker or defibrillator and delivers ultrasonic energy to the electrode, which transduces the energy to an electric pacing pulse to stimulate the left ventricle synchronously with the right ventricle. The initial evaluation of this redesigned system in the SELECT-LV (Safety and Performance of Electrodes Implanted in the Left Ventricle) study revealed: 1) adequate acoustic windows to permit implantation in the majority of patients (12 of 14 [86%]); 2) significant cardiac resynchronization in all 12 implanted patients, with QRS shortening by 60 ± 24 ms (vs. right ventricular pacing); and, importantly, 3) no instances of intra-procedural adverse events (15). The SELECT-LV trial continues to enroll patients at multiple centers in Europe.

Although the initial SELECT-LV data suggest that the delivery system modifications have largely addressed the major procedural complication observed in WiSE-CRT, there remain several technology-specific concerns that require consideration. First, although the left ventricular receiver component of this system is indeed leadless, the system does require the use of conventional transvenous leads, because all patients required concomitant conventional implantable right ventricular pacing devices. Second, it is theoretically possible that long-term ultrasound energy exposure to subcutaneous or myocardial tissue in humans may have unintended adverse consequences. Third, there may be untoward

FIGURE 1 The Leadless Endocardial Left Ventricular Pacing System



Anteroposterior (AP) (A) and lateral (LAT) (B) chest radiograph views of the implanted system, including battery, transmitter, and receiver/pacing electrode (inset).

effects of external (environmental) interference and changes in the acoustic window on the system's sensing or pacing performance. In some patients, the availability of an adequate acoustic window may limit the response to resynchronization therapy, because of either the location of the endocardial receiver electrode (anterolateral or lateral-apical) or the target location of the transmitter (intercostal space, because acoustic energy is refracted by bone). Fourth, compared with conventional power sources, energy transfer of current ultrasound-mediated pacing systems is inefficient and might result in a comparatively short battery life (16,17). In fact, in WiSE-CRT, at the 6-month post-implantation follow-up visit, the remaining battery life projection was a mean of 18 months (range: 9 to 42 months). Finally, the endoluminal left ventricular positioning of the receiver electrode could predispose to thromboembolic complications. Indeed, in SELECT-LV, 1 patient with atrial fibrillation in whom oral anticoagulation was interrupted for the procedure sustained a stroke. In subsequent cases, oral anticoagulation was not interrupted (at operator discretion) for the procedure, and no subsequent strokes were observed; however, the safety of this strategy needs to be validated in a larger cohort of patients. However, it should be noted that in a study that used a different approach to left ventricular endocardial pacing (using a transseptal approach), 14% patients (7 of 51) experienced thromboembolic events (stroke or transient ischemic attack) during follow-up (18). However, most of these

patients had subtherapeutic anticoagulation at the time of the event (the goal international normalized ratio was 3.5 to 4.5), and this risk would certainly be expected to be less with the smaller volume leadless electrodes associated with the multicomponent systems. However, this potential for thromboembolic complications remains important to test in large clinical trials.

However, there are compelling data indicating a potentially significant clinical benefit to leadless left ventricular endocardial pacing. Endocardial left ventricular pacing is more physiological (endocardial-to-epicardial transmural activation sequence), may enhance left ventricular diastolic and systolic performance, has the potential to be less proarrhythmic (reduced dispersion of ventricular repolarization), and likely requires lower pacing energy outputs compared with optimally placed coronary sinus leads (19,20). Furthermore, because it is not limited to those coronary sinus branches able to accommodate a transvenous lead, endocardial pacing offers a larger choice of optimal left ventricular stimulation sites; there is also the added benefit of no phrenic nerve stimulation. Leadless left ventricular endocardial pacing might mitigate these limitations and expand our ability to provide optimal CRT. However, there are other variables, such as endocardial scar and adjacent structures, including the papillary muscles, that may affect the ability to pace at the optimal endocardial location (21). Finally, and most important, 2 independent randomized controlled trials, TARGET (Targeted Left

Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy) and STARTER (Speckle Tracking Assisted Resynchronization Therapy for Electrode Region), demonstrated that better targeting of the left ventricular pacing site (at the site of latest contraction or ventricular activation) leads to improvements in clinical response, including freedom from heart failure hospitalization or mortality (22,23). Indeed, because of these various potential advantages to left ventricular endocardial pacing, several investigators have attempted left ventricular endocardial pacing with standard transvenous leads (placed transeptally across the mitral valve directly into the left ventricle) for nonresponders or those with inaccessible coronary sinus anatomy. Although technically feasible, its widespread adoption has been limited by the complexity of the procedure, the need for aggressive chronic oral anticoagulation (with a recommended target international normalized ratio of 3.5 to 4.5), and potential adverse consequences, such as the long-term effect on the mitral valve (24). Leadless left ventricular endocardial pacing might mitigate these risks and expand our ability to provide optimal CRT.

INDUCTION TECHNOLOGY. Leadless pacing using induction (electromagnetic) technology also consists of at least 2 components: a subcutaneous (or sub-muscular) transmitter unit located just above the heart and a receiver unit implanted into the ventricular endocardium (25). Briefly, the transmitter generates an alternating magnetic field, of which a fraction is converted to stimulatory voltage pulses by the receiver unit. Although leadless pacing using induction may be feasible, it has been tested only in animal models (porcine and goat), and further work is needed to determine the effects of alignment, distance, and external interferences on this technology (26).

SINGLE-COMPONENT (FULLY SELF-CONTAINED) LEADLESS PACING

With single-component LCPs, the pulse generator and sensing/pacing electrodes are fully contained within a single unit, thereby eliminating the leads, pectoral surgical pockets, and intrasystem connections. The device is delivered to the right ventricle with a catheter through the femoral vein. At present, 2 types of single-unit leadless pacemakers have been implanted in humans: the Nanostim LCP (St. Jude Medical, Inc., St. Paul, Minnesota) and, more recently, the Micra Transcatheter Pacing System (TPS) (Medtronic, Inc., Minneapolis, Minnesota).

The LCP has CE Mark approval for European use but remains investigational in the United States, whereas the TPS is investigational in both Europe and the United States. Comparatively, the TPS (25.9×6.7 mm) is shorter but wider than the LCP (42×5.99 mm); accordingly, the outer diameter of the delivery sheath for the TPS is larger (24-F) than that for the LCP (18-F). Of course, both devices are significantly smaller than conventional single-chamber transvenous pacemakers (approximately one-tenth the volume); this size discrepancy is further accentuated by the fact that the volume displaced by the pacing lead is typically not factored into these comparisons. Examples of both devices are shown in Figure 2, and the 2 devices are compared in Table 1.

With regard to fixation mechanisms, the LCP uses an active screw-in helix and a secondary fixation mechanism consisting of 3 angled nitinol tines perpendicular to the helix, whereas the TPS uses 4 self-expanding nitinol tines to affix to the myocardium. Figure 3 shows an example of an implantation of an LCP that was repositioned acutely prior to being disconnected from the delivery catheter; it was then

FIGURE 2 The Single-Component (Fully Self-Contained) Leadless Pacemakers



The Micra Transcatheter Pacing System (left) and Nanostim leadless cardiac pacemaker (right) are shown next to a ruler.

positioned at an alternative apical septal location to achieve stable and durable sensing and pacing parameters. **Figure 4** shows an example of the protective sleeve, fixation mechanism, and bipolar sensing and pacing configuration of the TPS. Both devices use a tethering mechanism to maintain a connection between the delivery catheter and the device to test positional integrity before final deployment. **Figure 5** shows an example of a TPS implantation. Finally, both devices are reportedly retrievable, although only animal data with the LCP exist to demonstrate the feasibility of chronic extraction. **Figure 6** shows fluoroscopic images from a clinical case of acute retrieval of an LCP that had been inadvertently implanted in the left ventricle (through a patent foramen ovale). To minimize the possibility of inadvertent placement of the device into the left ventricle through a patent foramen ovale, left anterior oblique fluoroscopic imaging should be performed prior to device release.

The LEADLESS trial, a first-in-human, single-arm, multicenter study of the safety and clinical performance of the LCP, was recently reported (27). Briefly, patients were considered eligible if they had indications for single-chamber, right ventricular pacing (VVI [R]). Indications included: 1) permanent atrial fibrillation with atrioventricular block (including atrial fibrillation with a slow ventricular response); 2) normal sinus rhythm with second- or third-degree atrioventricular block with a low level of physical activity or short expected life span; and 3) sinus bradycardia with infrequent pauses or unexplained syncope with electrophysiologic findings. Exclusion criteria comprised pacemaker dependency, significant pulmonary hypertension, or pre-existing mechanical tricuspid valve prosthesis, pacemaker/defibrillator leads, or inferior vena cava filter. Thirty-three patients were enrolled in the LEADLESS trial. The implantation success rate was 97% (32 of 33 patients), the mean procedure duration was 28 ± 17 min, and the overall complication-free rate was 94% (31 of 33 patients). The 2 complications were right ventricular perforation/cardiac tamponade (the patient subsequently died of a stroke) and inadvertent placement of the device through a patent foramen ovale (the device was retrieved in the same procedure, and no disability resulted). After 3 months of follow-up, all measures of pacing performance (lead impedance, pacing, and sensing threshold) either improved or were stably within the acceptable range.

The 1-year follow-up results of the LEADLESS trial were recently reported and demonstrated that: 1) performance measures (pacing threshold, impedance, and sensing) remained stable; 2) there were further

TABLE 1 Characteristics of the LCP and TCP

| Parameter | LCP | TCP |
|-------------------------------------|------------------------------|---|
| Polarity | Bipolar | Bipolar |
| Pacing modes | VVI (R) | VVI (R) |
| Rate modulation mechanism | Blood temperature | 3-axis accelerometer |
| Battery technology | Lithium carbon monofluoride | Lithium silver vanadium oxide / carbon monofluoride |
| Programmer | St. Jude Medical, model 3650 | Medtronic, model 2090 |
| Energy capacity (mAh) | 248 | 120 |
| Estimated longevity | | |
| ISO standard, yrs* | 9.8 yrs | 4.7 yrs |
| Alternative setting, yrs† | 14.7 yrs | 9.6 yrs |
| Size (h × w), maximum thickness, mm | 42 mm × 5.99 mm | 25.9 mm × 6.7 mm |
| Volume (cc) | 1.0 | 0.8 |
| Fixation mechanism | Helix (screw-in) | Tines |

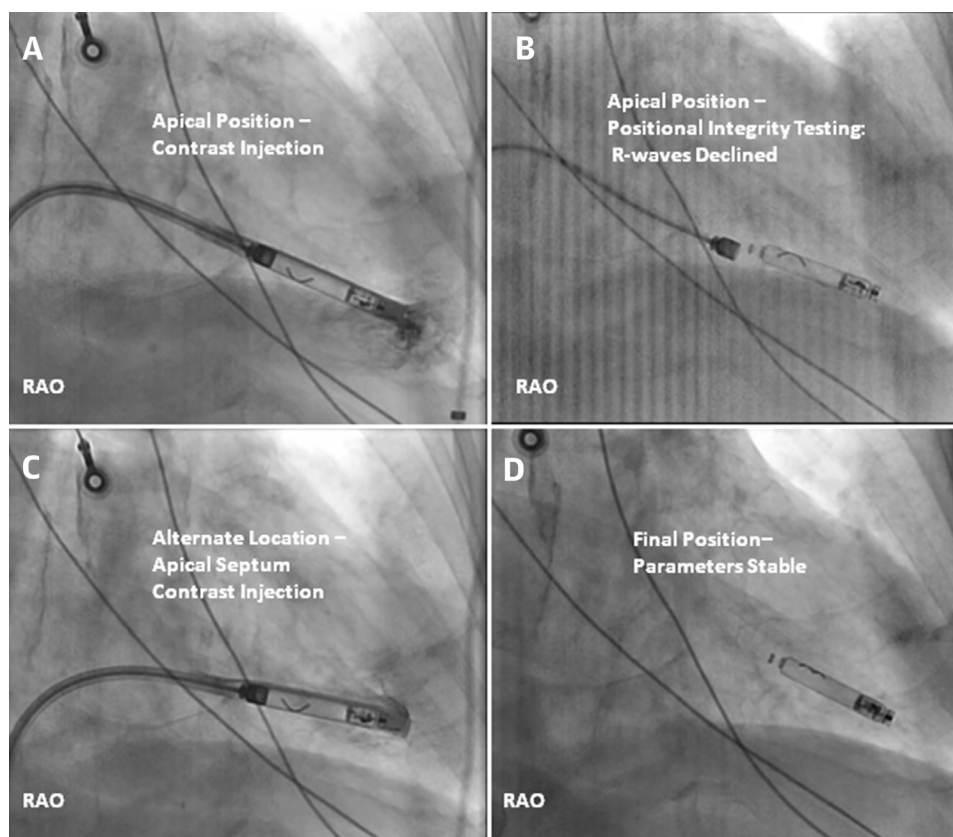
*Longevity based on fixed programming at the ISO International Organization for Standardization (ISO 14708) standard guidelines for reporting pacemaker battery duration longevity: 2.5 V, 0.4 ms, 600 Ω , 60 beats/min, and 100% pacing. †Longevity based on nominal settings (for the TCP): 1.5 V, 0.24 ms, 60 beats/min (with an impedance load of 500 ohms and 100% pacing).

LCP = leadless cardiac pacemaker; TCP = transcatheter pacing system.

no complications related to the device (beyond the index procedure); 3) there were no premature battery depletions or under/oversensing issues; and 4) adequate rate response, defined as 80% of the predicted maximal heart adjusted for age, was observed in those patients for whom it was activated ($n = 19$ of 30) (28). LEADLESS II is a large ($n = 600$) prospective, nonrandomized, single-arm, multicenter trial that has recently begun to assess the clinical safety and effectiveness of the LCP. This trial is intended to provide sufficient safety and long-term effectiveness data to gain U.S. Food and Drug Administration regulatory approval. Similarly, a single-arm, multicenter clinical trial assessing the TPS is also ongoing, and although no results are yet available, the investigators intend to enroll up to 780 patients. Again, these data will be used to support Food and Drug Administration approval.

The early results of the Micra Transcatheter Pacing System Study, a prospective, multicenter, single-arm trial were recently reported. Similar to the LEADLESS trial, patients were eligible if they had a Class I or II indication for single-chamber right ventricular pacing. The device was successfully implanted in all patients ($n = 140$ implanted patients). With regards to early safety performance, 26 patients (18.6%) experienced either a protocol-defined procedure or system-related adverse event, including 4 patients with transient atrioventricular block, 2 with ventricular tachycardia, 1 with ventricular fibrillation and 1 with pericardial effusion without tamponade. There were no procedure-related deaths or unanticipated serious

FIGURE 3 Implantation of the LCP



(A) The delivery catheter and leadless cardiac pacemaker (LCP) positioning in the right ventricular (RV) apex in the right anterior oblique (RAO) view (contrast injection through the delivery sheath). **(B)** Positional integrity testing with traction applied to the LCP (tug test), while the device remains tethered to the delivery catheter. After this maneuver, it was noted that the R waves declined from a baseline of 8.0 to 3.0 mV. Accordingly, the LCP was redocked, and a new position was chosen (higher on the apical septum). **(C)** Delivery catheter and LCP positioning at the RV apical septum (contrast injection through delivery sheath). **(D)** Final positioning of the LCP in the RAO view. At this location, the R waves remained stable (>12.0 mV) at the end of the procedure and through 6 months of follow-up.

adverse device events. With regards to early efficacy ($n = 60$ patients, who had been followed for 3 months), as compared to baseline, the mean electrical values for R-wave sensing amplitude, pacing impedance, and pacing capture threshold were stable at 3-months. The full trial results ($n = 720$ implanted patients) are anticipated in 2016 (29).

POTENTIAL BENEFITS OF LEADLESS CARDIAC PACING

As its name implies, the most obvious potential benefit of leadless cardiac pacing is the absence of a transvenous lead. Because the majority of acute and chronic complications of conventional pacemakers are attributable to the transvenous lead, a system that

eliminates this component is desirable (30). In addition to mitigating the risk of well-recognized complications, such as lung injury during subclavian access or chronic venous occlusion, there is also the inherent benefit of preventing intrasystem connection errors (albeit an uncommon cause of acute procedural complications), because the pulse generator pace/sense electrodes are a single unit. The single-component systems do not require a surgical incision/subcutaneous pocket, which mitigates the risk of surgical complications and may provide a more favorable cosmetic profile.

Despite their smaller size, LCPs have projected battery longevity that is comparable to that of standard single-chamber transvenous pacemakers. One of the most important determinants of battery

longevity is the internal current drain. The current drain for the LCP is only approximately 1 μ A, which is significantly less than for a standard single-chamber transvenous pacemaker (6.24 μ A) from the same manufacturer (31-33). Additional factors accounting for the extended longevity of the leadless pacemakers include the lack of “lost” energy through the lead, the high-density lithium carbon monofluoride battery, and, importantly, for the LCP, the use of energy-efficient conductive (vs. inductive) telemetry.

The battery life of the TCP, based on the International Organization for Standardization (ISO) standard for reporting battery longevity (2.5 V, 0.4 ms, 600 Ω , 60 beats/min, and 100% pacing) is approximately one-half that of the LCP (Table 1) largely because: 1) its smaller form factor also results in less battery capacity (248 vs. 120 mAh); and 2) instead of conductive telemetry, it employs radio-frequency telemetry which results in a greater background current drain. However, the TCP employs various energy-efficient approaches to minimize battery drain, such as capture management, which would increase battery longevity. As an example, the projected battery life for the TCP at the nominal settings (1.5 V, 0.24 ms, 60 beats/min with an impedance load of 500 ohms and 100% pacing) increases to 9.6 years. In comparison, the LCP device at the same settings has a projected battery life of 14.7 years. Finally, it should be also noted that the energy efficiency of both the LCP and TCP are partly related to the fewer enhancements (e.g., electrogram



storage) in these devices, as compared with conventional pacemakers.

The power source of the TPS device is lithium-silver vanadium oxide/carbon monofluoride, commonly used in transvenous systems. A high-density

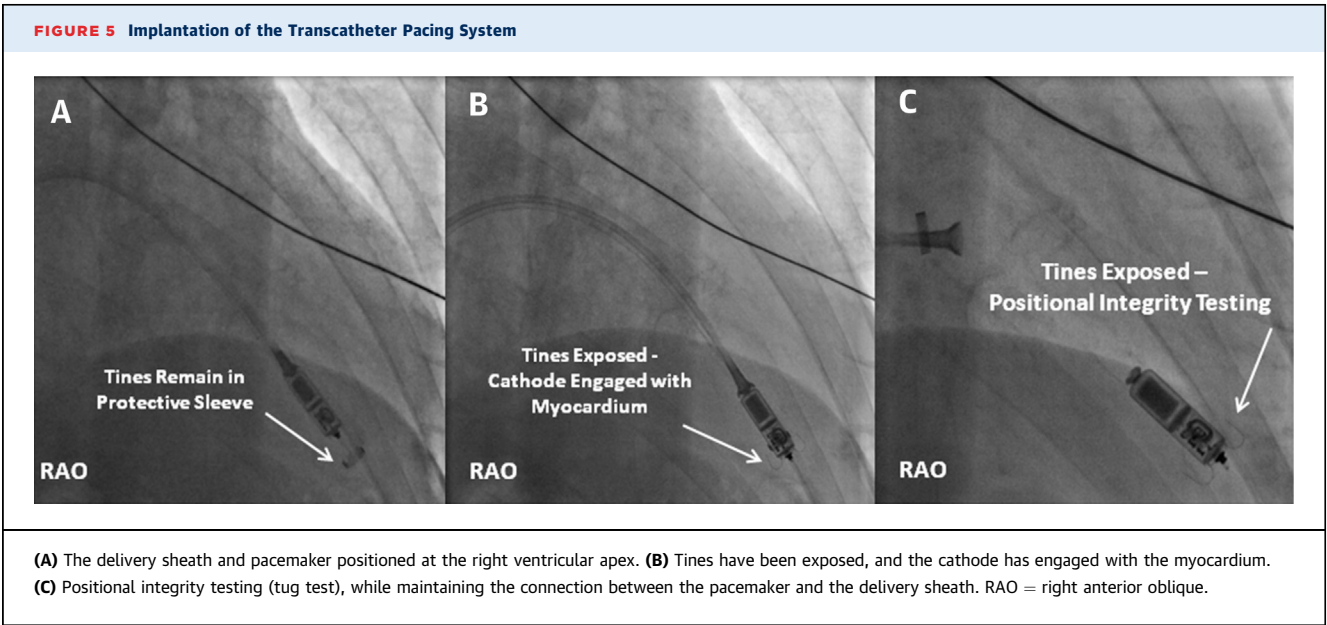
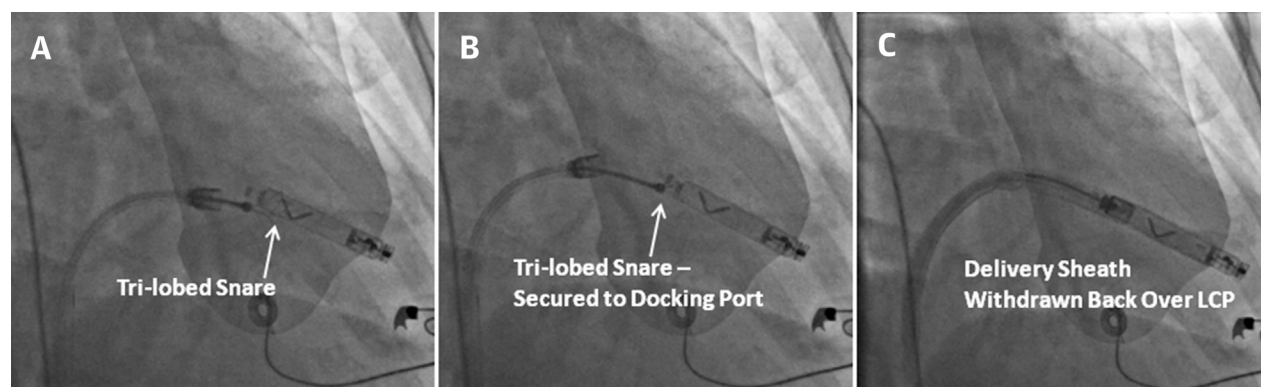


FIGURE 6 Retrieval of a Deployed LCP Device



The leadless cardiac pacemaker (LCP) had been inadvertently deployed within the left ventricle through a patent foramen ovale and thus required removal. **(A)** A trilobed retrieval snare was advanced through the patent foramen ovale, across the mitral valve, and looped around the body of the LCP within the left ventricle. **(B)** The trilobed snare was secured to the docking port on the distal end of the LCP. **(C)** After re-engagement of the delivery catheter to the docking port, the delivery sheath was drawn back over the LCP. Subsequently, the LCP was unscrewed from the myocardium and removed from the left ventricle, and a new LCP was placed in the right ventricle.

lithium carbon monofluoride battery powers the LCP. Although this is an ideal power source for miniaturized leadless pacemakers because of its high energy capacity, prior applications were limited by concerns for abrupt end-of-service characteristics. However, technological developments (including a proprietary algorithm fuel gauge to accurately predict the remaining energy capacity of the cell) have ensured that the leadless pacemaker conforms to the International Organization for Standardization requirement that the device provide pacing function for at least 6 months from the recommended replacement time to end of service (34,35). The LCP and TPS are also believed to be safe for use with magnetic resonance imaging (conditionally), because of their lack of ferrous material; however, additional pre-clinical and clinical testing is necessary to confirm this. Finally, because of the greater distance between the radiograph source and the operator (located at the femoral insertion site) during LCP implantation, there is potentially less radiation exposure for the implanting physician. However, there are currently no comparisons in total radiation exposure between leadless pacemaker implants and conventional transvenous systems.

POTENTIAL LIMITATIONS OF LEADLESS CARDIAC PACING

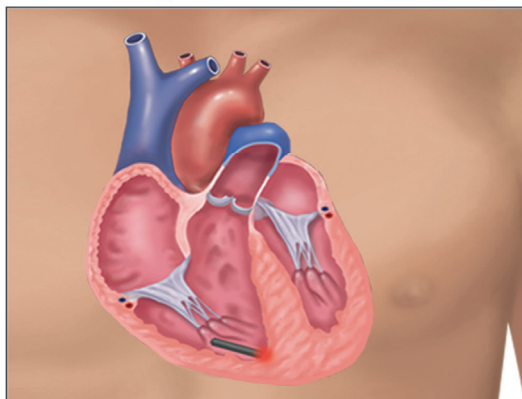
For the current generation of single-unit LCPs, the most important limitation is their ability to perform only single-chamber pacing, specifically

right ventricular pacing. Therefore, these devices would not be appropriate for most patients with sinus node dysfunction, who derive significant clinical benefit from dual-chamber sensing/pacing (30). Although multichamber systems (atrioventricular and biventricular) are in development, there are currently no available data on the feasibility of these systems. Device-device communication and fixation mechanisms (in the morphologically distinct right atrium) are just a few of the challenges that must be overcome before multicomponent systems can become a reality (Central Illustration). To our knowledge, there have not been any chronic device embolizations with single-component systems, but this remains a potential source of concern. The optimal fixation mechanism, with regard to both chronic performance and the need for future extraction, remains to be seen. The long-term reliability and accuracy of rate-responsive features, now that the sensor has been relocated from the subcutaneous pulse generator to the intraventricular space, is not yet known. However, the ongoing LEADLESS II trial is assessing rate-response characteristics (as a secondary endpoint) in a series of patients undergoing graded exercise testing. Furthermore, although the single-component systems are, by volume, significantly smaller than conventional cardiac pacemakers, the portion of the device that interacts with the endocardium has a wider diameter, which has raised the possibility of proarrhythmia. The delivery system for single-unit leadless pacemakers includes a large venous sheath

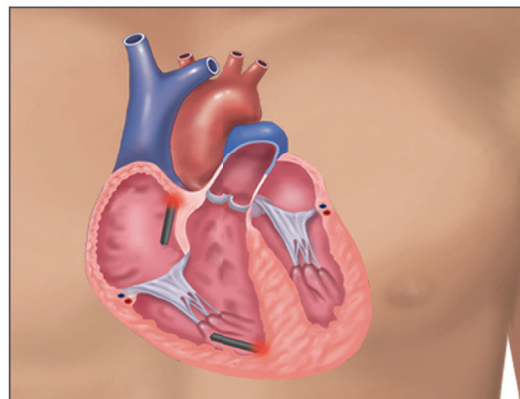
CENTRAL ILLUSTRATION Leadless Cardiac Pacemakers

Bradycardia

Single-Chamber Pacemaker

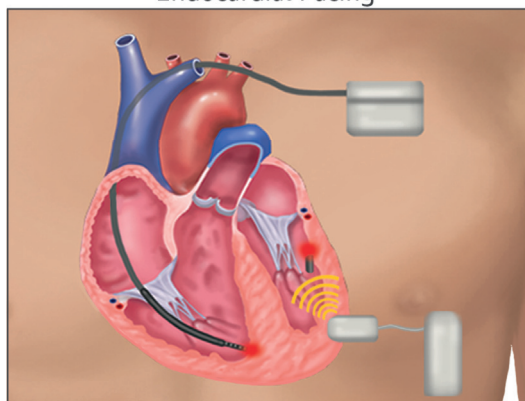


Dual-Chamber Pacemaker



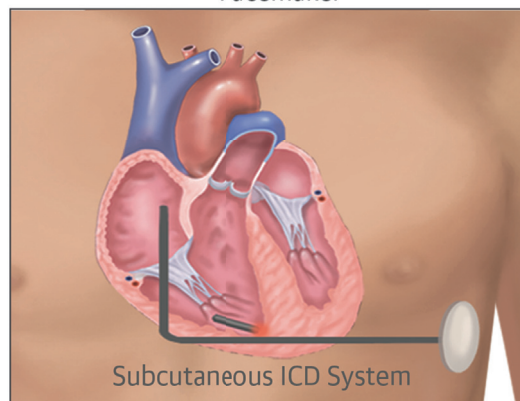
Congestive Heart Failure

Ultrasound-Mediated Left Ventricle Endocardial Pacing



Sudden Cardiac Death

Subcutaneous ICD and Leadless Pacemaker



Miller, M.A. et al. J Am Coll Cardiol. 2015; 66(10):1179-89.

ICD = implantable cardioverter-defibrillator.

(24-F for the TPS and 18-F for the LCP) and delivery catheter. The larger caliber of the delivery units has the potential to increase complications related to either the femoral access site or catheter manipulation within the right ventricle. Indeed, in the LEADLESS study, the one and only major procedural complication (cardiac perforation and subsequent death) was related to the delivery catheter. Further refinements in technique and technology are likely to mitigate the chance of this complication. Although leadless

pacemakers are reportedly retrievable acutely, the ability to remove a chronically-implanted device remains untested in humans. As such, the strategy for device management (retrieval vs. abandonment) once the battery has been depleted remains to be determined. As with any emerging technology, special training will be required to develop proficiency in LCP implantation. On one hand, many of the technical and cognitive skills overlap with those used in common electrophysiologic procedures (e.g.,

fluoroscopic imaging, manipulation and implantation of devices within the right ventricle); on the other hand, additional skills will undoubtedly require further proctoring/training (e.g., large venous sheaths, intraprocedural positional integrity testing). Future clinical competency statements will likely address this matter (36).

CONCLUSIONS

As with any transformative technology, a number of questions remain unanswered with each of these leadless pacing systems. Randomized clinical trials will be necessary to definitively determine whether

the theoretical benefits of leadless systems will be superior to those of conventional pacemakers both from a safety perspective (fewer acute and chronic complications) and in terms of long-term pacing and sensing performance. However, it certainly seems possible that the future of cardiac pacing will see the minimization, if not eventual extinction, of all pacing leads.

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