Are Leadless Pacemakers a Niche or the Future of Device Therapy?*

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Pacemakers were developed in the 1950s primarily to treat life-threatening transient heart block after cardiac surgery. These were large external devices connected to epicardial electrodes placed surgically. Although life-sustaining, these devices were plagued by many problems including short battery life, lead failures, and infections, due in part to externalization of part of the system (1). Interestingly, many of these same issues are present today with most left ventricular assist devices, which also are life-sustaining therapies. With advances in technology, size was reduced significantly to allow for the first implantable pacemaker in Sweden in 1958. It was more than 50 years ago, in the early 1960s, that transvenous leads were developed and first used with implantable devices by Parsonnet et al. (2). These early pacemakers had very limited functionality and only performed asynchronous pacing. Rapid advances were made with programmable features, including rate and output, to allow noninvasive communication with devices and improved battery technology to extend pulse generator longevity beyond the approximate 1-year life span of very early devices.

Many of the improvements in pacing technology over the past 5 decades are incremental, but some have certainly been game-changing or revolutionary advances, including dual-chamber pacing to allow maintenance of atrioventricular synchrony, rate responsive pacing, and cardiac resynchronization therapy, with or without defibrillation backup (Figure 1). Despite these developments, certain problems have persisted. Complications that result from the use of implantable devices are the most prominent issue that has persisted over the years. These complications include acute problems involving the implantation procedure, such as pneumothorax and hematoma, as well as more subacute and chronic problems including infection and lead failure. Similar problems have plagued the use of all cardiac implantable electronic devices (CIEDs), although the solutions have differed.

Significant complications with implantable cardioverter-defibrillators (ICDs) have affected their use. Probably the 2 greatest problems are lead failures and infection. Although lead recalls have been the most visible of these issues, all intravascular leads have a disturbingly high failure rate due in part to the chronic stress placed on them in a beating heart (3). Moreover, the extraction of leads, either for infection or failure, is associated with significant costs and additional complications. A recent innovation to address this problem is the development of a subcutaneous ICD. Such a device avoids the problems associated with intravascular lead use and uses a lead likely to have better long-term stability (4). However, this first-generation device is not without limitations. It is larger, has a shorter battery life, lacks remote monitoring capabilities, and has very limited pacing capabilities including the lack of antitachycardia pacing. These limitations will be addressed with further development of this technology, but it is already apparent that the subcutaneous ICD is an important addition to the treatment options for the prevention of sudden cardiac death.

Another CIED that has been limited by persistent lead problems, but with a very different solution, is implantable hemodynamic monitoring for guiding the treatment of heart failure (HF). This promising approach for reducing HF hospitalizations has been

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limited by a high incidence of lead failures (5). To help address this problem, a leadless implantable monitor was developed and is implanted in the pulmonary artery, which eliminates complications associated with a lead or pocket for the device. This was shown to be very effective for reducing HF exacerbations (6). Again, this first-generation device has limitations, including the lack of continuous hemodynamic data, limited parameters measured, and uncertainty regarding the retrievability of the unit in the long term. Nevertheless, this device is a novel approach to the challenges of managing chronic HF.

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In this issue of the Journal, Knops et al. (7) provide intriguing data on the mid-term results of a leadless pacemaker. This device was designed to address the complications associated with implantable pacemakers. Approximately 8% of pacemaker implants are associated with acute complications. There are ~65,000 lead failures annually in the more than 4 million implanted systems worldwide (8). Accordingly, this is a major problem that has persisted despite many improvements in lead and pulse generator design. For this reason, the leadless pacemaker was developed as a self-contained unit placed in the right ventricular apex via femoral vein access. It uses an active fixation mechanism with an extendable helix and has many contemporary features, such as rate response, telemetry, and data logs. The 1-year data presented in this paper shows remarkably stable pacing parameters, including persistent mean pacing thresholds <0.5 V and sensed ventricular signals (R waves) >10 V. Based on these data, the projected longevity of this device is ~10 years, even with 100% pacing. Finally, there were no infections, dislodgments, or other complications noted after the periprocedural period.

Despite the outstanding results noted with this first-in-human experience with a leadless pacemaker, there are limitations of the data that must be acknowledged. The sample size was very small, with only 31 subjects followed in the long term. Moreover, these implantations were performed at a limited number of very experienced European centers. Importantly, there were serious implantation complications, including 1 death from the procedure and 1 case of cardiac tamponade. Ongoing larger multicenter studies in the United States and elsewhere will provide a more accurate estimate of efficacy and risk associated with this approach. Nevertheless, these early results are very encouraging.

As with the other novel CIEDs, there are limitations associated with the first-generation devices. For the leadless pacemaker, the most obvious is the ability to provide only right ventricular pacing. Neither dual-chamber nor left ventricular pacing, to allow for cardiac resynchronization therapy, is available. Remote monitoring is not available, and the usefulness of the temperature-based rate sensor has not been established. Undoubtedly, these issues will be addressed in future generations of leadless pacemakers.

Predicting the role of this device in pacemaker therapy is a challenge, as it is for most new devices. In the United States and most European countries, ~20% to 30% of patients receive ventricular pacemakers primarily for chronic atrial fibrillation, and this was largely the population implanted in the current trial. However, in less developed countries, this proportion is often ≥50% (9). In addition, pacemaker use is limited in many areas of the world, in part because of the lack of implantation expertise. The steep learning curve for the leadless pacemaker implantation and the more common skill set of femoral vascular access and sheath manipulation suggests that this approach could fill an unmet need. Consequently, the adoption of this therapy in such countries could be high, particularly if the cost is competitive with traditional pacing systems.

There are a number of questions that remain to be answered regarding this new technology. Will the device continue to perform at a high level in the long term and match the reliability of current pacemaker pulse generators? Is this device retrievable in the long term, and how are patients managed when systemic infection develops or the device reaches elective replacement? Abandoning the device and implanting a second unit is likely a viable option for many patients at elective replacement, given the small size of the unit, 10-year battery life, and mean age of ~70 years for initial implantation. Finally, will there be any long-term thrombogenic complications associated with an indwelling right ventricular pacemaker?

It is easy to envision an important role of leadless pacing in future CIEDs. The ability to communicate with a second device placed in the right atrium would result in dual-chamber pacing capabilities. Similarly, communication with a subcutaneous ICD would allow for both bradycardia and antitachycardia pacing, and it would likely improve rhythm discrimination, reducing oversensing of T waves, myopotentials, or nonbiologic noise associated with such ICDs. The potential safety of placing a device even this small in the left ventricle in the absence of
A pictorial representation of the evolution of cardiac implantable electronic devices including possible future devices. A single-chamber pacemaker with a right ventricular apical lead and a dual-chamber pacemaker with a second lead in the right atrium are shown. The transvenous implantable cardioverter-defibrillator (ICD) lead in the right ventricular apex. Cardiac resynchronization therapy is most commonly used with ICD backup. There are 3 leads in the heart with pacing leads in the right atrium and left ventricle through the coronary sinus, as well as an ICD lead in the right ventricle. The subcutaneous ICD has leads in the subcutaneous tissue outside the heart. The leadless pacemaker has the pacing system fully implanted in the right ventricular apex. Finally, the future universal device has leadless pacing systems in the right atrium and ventricle, a leadless pacing electrode in the left ventricle, and subcutaneous defibrillation lead and pulse generator.
anticoagulation is unclear, but the development of smaller pellets with a transducer could be coupled with a subcutaneous energy source for cardiac resynchronization with defibrillation therapy if appropriate (Figure 1). All of these possibilities point toward a bright future for leadless pacing with the likely possibility that the devices of the future will largely devoid of intravascular leads, and many will not require subcutaneous pulse generators. As such, these devices should become the future of pacing in many types of devices rather than persist as a niche to compete in the single-chamber pacemaker market.

REFERENCE

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