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Leadless Pacemakers: Recent and Future Developments

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Abstract

Purpose of review Leadless pacemakers were developed to reduce complications associated with transvenous pacemaker implant and long-term follow-up. Since initial market release, however, there have been registry and single-center reports documenting improvements in implant technique, reduced complication rates, and new patient populations studied.
Recent findings Most studies have demonstrated a further reduction in complication rates and safe implant in those on continuous anticoagulation. Perforation rates are decreasing but still occur and risk factors include BMI < 20 kg/m2, age ≥ 85 years, females, history of heart failure, indication not including atrial fibrillation, and chronic lung disease. Device infections are exceedingly rare, even in those undergoing infected transvenous devices at the same time.
Summary For appropriate patients, leadless pacing is a safe and reasonable option, especially if atrial-based sensing or pacing is not needed. Future iterations may include VDD pacing, atrial pacing, dual-chamber pacing, biventricular pacing, and device-device communication.

Introduction

Over one million cardiac pacemakers are implanted yearly worldwide [1]. This number is only expected to increase as the population ages. Pacemakers have undergone rapid advancements in technology since their initial inception in the 1950s, with continual improvements to increase battery longevity, decrease generator size, refine pacing algorithms, and ensure lead fidelity. However, despite these technological changes, the two

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points of weakness for the transvenous system remain the lead and the subcutaneous pocket, which can lead to complications including lead dislodgement, cardiac perforation, pneumothorax, venous occlusion, lead fracture, endocarditis, pocket infection, and pocket hematoma, to name a few. The leadless pacing system was developed as an option to circumvent these areas of weakness.

History of the leadless pacemaker

Leadless pacing systems were initially conceptualized, designed, and implanted in dogs with a mercury battery–powered capsule in the 1970s [2], but not until technological improvements were made in regard to battery energy, endocardial fixation, communication capacity, and delivery systems did the first human leadless pacing systems come to fruition [3, 4••].

There are currently two developed leadless pacing systems, the Micra Transcatheter Pacing System (Medtronic, Minneapolis, MN) and the Nanostim Leadless Cardiac Pacemaker (Abbott, Lake Bluff, IL). Both the Micra and the Nanostim were developed as novel technologies to address the known pitfalls and potential complications associated with traditional transvenous pacing systems. The initial iterations of both are right ventricular, single-chamber, self-contained, miniaturized pacemakers that are approximately 90% smaller than traditional transvenous devices. The Micra measures 25.9 mm in length, has a volume of 0.8 cm3, and a weight of 2.0 g. The Nanostim measures 41.4 mm in length, has a volume of 1 cm3, and a weight of 2.0 g. Both devices successfully eliminate the need for a subcutaneous pocket and leads within the vasculature. Additionally, both are designed to be permanently retained devices but can be retrieved if necessary. They displace less than 1% of right ventricular blood volume [5] with expected encapsulation of the device within the right ventricle over time [6]. It is thought that at least three devices could be implanted if necessary [5], and we have had patients with two implanted without difficulty (Fig. 1). The Micra received Food and Drug Association (FDA) approval in April 2016, while the Nanostim is not available at this time due to two major recalls. One was the result of spontaneous detachment and potential embolization of the docking button and the other was due to premature battery failure [7].

Patient selection criteria

The best candidates for leadless pacemaker insertion are symptomatic patients with persistent or permanent atrial fibrillation with high-grade AV block who only need single-chamber pacing, as would be true for single-chamber transvenous pacing also. In addition, those with high-grade AV block in the absence of atrial fibrillation in whom atrial lead placement is considered too difficult, high risk or not necessary for therapy are reasonable candidates. Even for patients who have sinus node dysfunction who require infrequent pacing or who have limited functional capacity, leadless pacing may be a good alternative [8]. Leadless pacing has been described for patients with recurrent vasovagal syncope [9], though there is some question whether this will work on all patients due to the lack of increased rate at the time of the vasovagal episode. Patients with short-term indications for pacing such as post transcatheter aortic

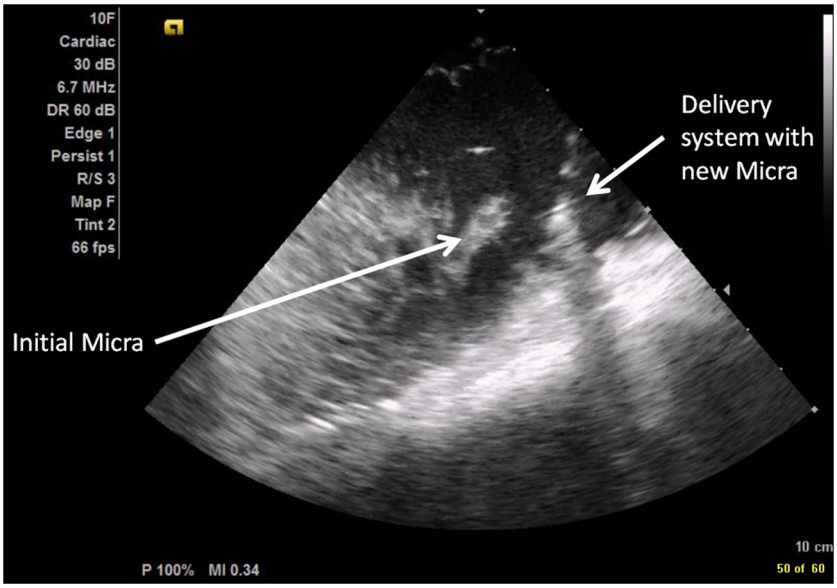

Fig. 1. Intracardiac echocardiogram image of the right ventricle in a 37-year-old male with muscular dystrophy who had a rising threshold and loss of capture with high output pacing of a Micra placed 6 months earlier. A second Micra was placed using intracardiac echo because of significant musculoskeletal abnormalities which affected cardiac rotation.

valve replacement or Lyme carditis with heart block may be reasonable candidates as conduction may recover and there may only be a brief window for therapy needed [10]. Those with renal disease may also want this device because of an increased risk of infection and desire to preserve venous access [11]. Patients with single or recurrent pocket infections could be considered candidates, as well as patient preference for implantation of a leadless system.

Conversely, patients who would be unlikely to benefit from a leadless pacemaker system based on currently available device technology are those who require AV synchrony due to symptoms of pacemaker syndrome and those who qualify for cardiac resynchronization therapy. Presence of a mechanical tricuspid valve is a contraindication. There may be concerns in those with morbid obesity which may prevent the device from obtaining telemetry communication within < 12.5 cm from the chest wall, though the distance from the wand to the device may be less if the wand is placed in the axilla. A prior IVC filter is not necessarily a contraindication to device implant [12].

Newer implantation techniques of a leadless pacemaker

The implantation technique for both the Micra and the Nanostim are similar in conceptual design—both are delivered percutaneously with a catheter-based approach through central venous access (traditionally the right femoral vein). The Nanostim introducer sheath has an 18 French inner diameter and 21 French outer diameters, and the Micra sheath is slightly larger with a 23 French inner sheath diameter and 27 French outer sheath diameters. The delivery systems are designed for navigation across the tricuspid valve, and enable device positioning on the septum of the RV. The devices do differ in fixation method, with the Micra achieving fixation to the trabeculated RV myocardium with 4

nitinol tines, and the Nanostim using an active fixation helix. After appropriate attachment is confirmed, sensing and capture thresholds are verified, the device is released, and delivery systems are withdrawn.

We have had difficult cases due to tortuosity of the venous system, and in these situations, switching access to the left groin may make implant easier. In addition, where there was difficulty advancing the stiff wire to the superior vena cava (SVC) through a short sheath, we have used a JR4 or SL0 sheath over a floppy wire into the SVC, at which point the stiff wire can be exchanged for the floppy wire through the sheath and the Micra sheath advanced. In those with inability to access the femoral vein or inferior vena cava, a superior vena cava approach is possible [13]. Lastly, we have found intracardiac echo useful on rare occasions to appropriately place the device, especially, for those with complex anatomy (Fig. 1).

Because of the large size of the delivery system, the best management strategy in those on anticoagulation has been in question. If appropriate, anticoagulation can be stopped, however, this is frequently not possible. Implantation with continuous anticoagulation, or holding only one dose, can be done safely with a low rate of bleeding complications [14, 15].

There are a few different strategies for closure of the venous access site. While manual compression is an option, it is a large bore sheath that requires a prolonged period of time with pressure. Many operators have used a figure-of-eight suture of the skin and subcutaneous tissue to provide hemostasis, but using a vascular closure device such PerClose ProGlide (Abbott Vascular, Santa Clara, CA) is also an option, though usually two sutures are used which increases cost [15].

Complications

The LEADLESS II Nanostim study had 6.7% complication rate and 1.3% perforation rate [3], while the Micra Transcatheter Pacing Study Group had 4.0% complication rate and 1.6% perforation rate [4••]. Follow-up studies of leadless pacing had complication rates of up to 4%, with a risk of cardiac perforation and effusion of up to 1.5% [16]. Risk factors for perforation include BMI < 20 kg/m2, age ≥ 85 years, females, history of heart failure, indication not including atrial fibrillation, and chronic lung disease [17]. In the Micra post-approval study, this perforation rate decreased to 0.6%, though only 0.25% required pericardial drainage [18]. Further evaluation in a real-world registry of Micra demonstrated an effusion event rate of 0.77%, with 0.55% needing pericardiocentesis or surgery [19]. This improvement is likely due to the understanding that trying to implant the device on the septum, rather than the apex, will reduce the chances of a right ventricular free wall perforation. However, in a recent study of 51 patients where operators purposely planned to implant in the mid septum, it was only achieved 90% of the time, and one patient developed a pericardial effusion when the first implant location was inadvertently against the RV free wall [20]. They noted that using the left lateral view can be helpful to assess free wall versus septal location as the left anterior oblique view may give a false sense that it is implanted in the septum.

One of the other major benefits of leadless pacing is the absence of a pocket and a reduction in foreign material, making infection exceedingly low [16]. In

fact, there have only been rare reports of leadless pacemaker infection [21]. Several studies have now shown that leadless pacemakers can be implanted in those with a prior device infection without a leadless pacemaker infection occurring [22–24]. Some have even safely completed leadless pacemaker implant during the same session as the lead extraction of an infected transvenous device with no leadless pacemaker infection [23, 24••].

Device removal

Leadless pacing devices are designed to be a permanently retained device, but retrieval is a possibility. Given the intrinsic design features of leadless systems, they are less likely to require system revision or extraction then traditional transvenous systems. In one study, the need for system revision within the first 24 months post-implant was 75% lower for Micra than for revision of traditional transvenous systems [6]. However, the need for extraction or system revision does still occur.

Retrieval of the Micra leadless pacing system can be achieved using two different approaches. A 7-mm loop snare can be introduced through the Micra delivery system, and once the Micra has been successfully captured with the snare, the retrieval cup is used for device recapture [25]. This approach gives the ability to deliver counter traction with the Micra sheath. In the second approach, a steerable sheath is used in conjunction with a 20-mm snare. This provides the advantage of a larger snare size, with the downside of no ability to provide counter traction which could lead to potential myocardial damage [25].

The data for device retrieval of the Micra leadless pacing system is limited at this time. In one study, 29 Micra devices were retrieved, 11 of which were removed during the initial implantation procedure, and an additional 18 devices were snared at a median of 46 days post-implantation [25]. Data from post-mortem autopsy studies have noted the potential for encapsulation of the device and noted to be tightly adherent to an adjacent papillary muscle occurring as soon as 1 year post-implantation [26]. Recently, successful extraction of a Micra 4 years post-implantation was described using the technique of the steerable sheath and large snare without any complications [27]. While at this point, successful retrieval and explantation of longer-term indwelling Micra devices remain anecdotal in a few case studies, it can be completed successfully.

Future developments in leadless pacing

One of the biggest limitations in patient selection for the Micra is that it is currently only a VVI(R) device. However, advancements to the Micra programming algorithm and battery capability have allowed for testing of a system which performs VDD pacing with atrial tracking based on intracardiac accelerometer data [28]. The algorithm developed for the Micra in the MASS and MASS2 studies utilized data from the internal device accelerometer in which 4 distinct segments of the cardiac cycle can be recognized: isovolumic contraction and mitral/tricuspid valve closure (A1), aortic/pulmonic valve closure (A2), passive ventricular filling (A3), and atrial contraction (A4) [28]. Segments A3

and A4 were associated with mitral flow E and A-wave segments and were utilized to develop the algorithm to recognize atrial contraction and set timing cycles for VDD pacing. The MARVEL study showed feasibility and success of VDD programming of the Micra device with an improvement in AV synchrony from 37.5 to 80% in patients with high-degree AV block [28]. The advent of atrial tracking and effective VDD pacing for Micra would expand the patient indications to include those normal sinus node function and AV block, though this device is not FDA-approved as of this writing.

Another proposed advancement in leadless pacemakers is dual-chamber pacing. In a prototype, this was achieved through two small leadless devices, one implanted in the atrium and one in the ventricle which are able to efficiently and effectively communicate with each other to be able to achieve synchrony within each cardiac cycle [29]. Intrabody communication was developed and validated as proof of concept in 3 in vivo implantations that were able to successfully deliver dual-chamber pacing. Dual-chamber leadless pacemaker systems are expected to come to market at some point to allow for atrial-based pacing.

Just as leadless pacemakers have added a novel development to Brady device therapy, the subcutaneous implantable cardioverter defibrillator (S-ICD) (Boston Scientific, Marlborough, MA) has offered a novel device option for antitachycardia therapy. However, currently, the S-ICD is only offered in patients without pacing indications and is not able to offer antitachycardia pacing (ATP) [30]. Combined use of a modular cardiac rhythm management system, utilizing the S-ICD as well as a leadless pacemaker, is currently being studied with promising initial results [30]. The system, as being developed, will have the S-ICD send low-voltage 25 kHz signals in a proprietary pattern from the shocking coil to the can that the leadless pacemaker will be able to sense [30]. In the initial iteration, there is only one-way communication from the S-ICD to the leadless pacemaker. There is some concern that the spatial orientation of the leadless pacemaker will make it difficult to sense this communication signal, however, it is thought that most of the time, the device will be placed in a location and angle for good sensing or that motion of the heart and lungs will improve the sensing enough for good communication to occur. ATP before or during S-ICD charging will be one of the main benefits of having the leadless pacemaker, as well as bradycardia pacing. Human studies of the combined system are expected to be started this year.

Lastly, a totally leadless biventricular pacing system has been recently described [31]. A Micra was placed in the right ventricular and a WISECRT system (EBR Systems, Sunnyvale, CA) was used for left ventricular endocardial pacing in a patient with permanent atrial fibrillation and prior pacemaker infections. It is likely that there will be leadless biventricular pacing systems developed expressly for this purpose in the future.

Conclusion

Leadless pacing is one of the major advancements in pacemaker technology and complications rates are decreasing with improved implant technique. Improved

groin management techniques and access site options are opening up further safety and implant choices. Future iterations may include VDD pacing, atrial-based pacing, dual-chamber pacing, biventricular pacing, and device-device communication.

Compliance with Ethical Standards

Conflict of Interest
The author declares that they have no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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