

SUPPLEMENTS

Leadless cardiac pacing: What primary care providers and non-EP cardiologists should know

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Correspondence: Daniel J. Cantillon, MD, FACC, FHRS, Department of Cardiovascular Medicine, J2-2, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; cantild@ccf.org**ABSTRACT**

Over the last 50 years, the use of transvenous pacemakers has been constrained by long-term complications that affect more than 1 in 10 patients, largely attributable to the endovascular leads and surgical pocket. Leadless cardiac pacing involves a self-contained pacemaker deployed directly into the heart without a lead or incisional access. The procedure has shown promise, eliminating pocket-related complications. Other advantages include postprocedural shoulder mobility and the ability to drive, shower, and bathe. Current devices are limited to single-chamber ventricular pacing. Future advances may allow atrial and dual-chamber pacing and combination with a subcutaneous defibrillator to deliver antitachycardia pacing and provide bradycardia backup.

KEY POINTS

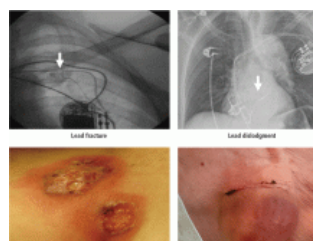
- Leadless cardiac pacing has emerged as a safe and effective alternative involving catheter-based delivery of a self-contained device directly into the right ventricle without incisional access, leads, or a surgical pocket. The procedure typically can be performed in 30 minutes or less, with fewer postprocedure restrictions.
- Leadless pacing is showing promising results, but it is currently limited to single-chamber pacing.
- Future directions include atrial and dual-chamber pacing and combining the procedure with a subcutaneous implantable cardioverter-defibrillator.

WHY LEADLESS PACING?

The first clinical implantation of a cardiac pacemaker was performed surgically in 1958 by Drs. Elmvist and Senning via thoracotomy and direct attachment of electrodes to the myocardium. Transvenous pacing was introduced in 1962 by Drs. Lagergren, Parsonnet, and Welti.^{1,2} The general configuration of transvenous leads connected to a pulse generator situated in a surgical pocket has remained the standard of care ever since. Despite almost 60 years of technological innovation, contemporary permanent transvenous pacing continues to carry significant short- and long-term morbidity. Long-term composite complication rates are estimated at over 10%,³ further stratified as 12% in the 2 months post-implant (short-term) and 9% thereafter (long-term).⁴ Transvenous pacing complications are associated with an increase in both hospitalization days (hazard ratio 2.3) and unique hospitalizations (hazard ratio 4.4).⁵

Short-term complications

Short-term complications include lead dislodgment, pocket hematoma, pericardial effusion, and pneumothorax (**Figure 1**). Pocket hematomas are common with concurrent antiplatelet or anticoagulant administration, with incidence estimates varying from 5% to 33% depending on the definition.⁶ Morbidity associated with pocket hematoma include prolonged



hospitalization, need for re-operation,⁷ and an almost eightfold increase in the rate of device infection over the long term compared with patients without pocket hematoma.⁸ New pericardial effusions after implant may affect up to 10% of patients; they are generally small, including 90% attributable to pericarditis or contained microperforation not requiring intervention. Overt lead perforation resulting in cardiac tamponade occurs in about 1% of transvenous pacemaker implants, of which 10% (0.1% overall) require open chest surgery, with the remainder treated with percutaneous drainage.⁹

Long-term complications

Long-term complications are predominantly lead and pocket-related but also include venous occlusive disease and tricuspid valve pathology.⁴ The development of primary lead failure due to insulation defects, conductor fracture, or dislodgment has been associated with major adverse events in 16% of patients, and an additional 6% if transvenous lead extraction is needed, which can rarely lead to hemorrhagic death by vascular tears involving the heart or superior vena cava.¹⁰ Fibrous tissue growth around the indwelling vascular leads can result in venous obstruction present in up to 14% of patients by 6 months after implant.¹¹ This increases to 26% by the time of device replacement or upgrade, which is typically 5 to 10 years after the original implant, including 17% of patients with a complete venous occlusion.¹² In addition, worsened tricuspid regurgitation due to lead impingement on the valve is seen in 7% to 40% of patients depending on definitions,¹³ with post-implant severe tricuspid regurgitation independently associated with increased mortality risk.¹⁴ The rate of device infection is 1% to 2% at 1 year,^{8,15} and 3% over the lifetime of the initial transvenous system; this increases to more than 10% after generator replacement.¹⁶

LEADLESS PACING TECHNOLOGY

The principal goal of leadless pacing is to reduce short- and long-term pacemaker complications by eliminating the two most common sources of problems: the transvenous leads and the surgical pocket. Discussion of leadless pacing strategies began as early as 1970.¹⁷ Although several preclinical studies demonstrated efficacy with leadless prototypes,^{18–20} clinical implementation of fully leadless technology did not occur until recently. As shown in **Figure 2**, there are now two commercially available leadless pacing devices: Nanostim (St. Jude Medical Inc., St. Paul, MN) and Micra (Medtronic Inc., Dublin, Ireland). At the time of this writing, both have commercial approval in Europe. In the United States, Micra received commercial approval from the US Food and Drug Administration on April 6, 2016, with a similar decision expected on Nanostim. The current approved indications for leadless pacing are chronic atrial tachyarrhythmia with advanced atrioventricular (AV) block; advanced AV block with low level of physical activity or short expected lifespan; and infrequent pauses or unexplained syncope with abnormal findings at electrophysiologic study. Although differences exist between Nanostim and Micra, as shown in **Table 1**,^{21–27} there are fundamental similarities. Both are single-unit designs encapsulating the electrodes and pulse generator with rate-adaptive functionality. Both are delivered via an endovascular femoral venous approach without the need for incisional access, transvenous leads, or surgical pocket (**Figures 3 and 4**).^{21–27}

Nanostim: Landmark trials

As the world's first-in-man leadless pacemaker, Nanostim was evaluated in two prospective, non-randomized, multicenter, single-arm trials abbreviated LEADLESS²² and LEADLESS II.²⁴ The first human feasibility study, LEADLESS, enrolled 33 patients with approved indications for ventricular-only pacing while excluding patients with expected pacemaker dependency. The most common indication was bradycardia in the presence of persistent atrial arrhythmias, thereby obviating the need for atrial pacing. The primary outcome was freedom from serious complications at 90 days. The secondary outcomes were implant success rate and device performance at 3 months. The results demonstrated 94% composite safety (31 of 33 patients) at 3 months. There was one cardiac perforation leading to tamponade and eventually death after prolonged hospitalization, and one inadvertent deployment into the left ventricle via patent foramen ovale that was successfully retrieved and redeployed without complication. The implant success rate was 97%, and the electrical parameters involving sensing, pacing thresholds, and impedance were as expected at 3 months. Results of 1-year follow-up were published for the LEADLESS cohort,²⁵ revealing no additional

Source: Lead fracture and pocket infection images courtesy of Dr. Mohamed Kanj. Hematoma image courtesy of Dr. John Rickard.

FIGURE 1. Common transvenous pacemaker lead and pocket-related complications.

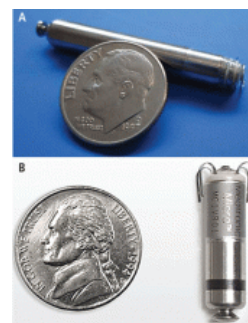


FIGURE 2. Leadless pacemakers (A) Nanostim and (B) Micra.

TABLE 1
Overview of leadless pacemakers Nanostim and Micra based on completed human trials

	Nanostim	Micra
Manufacturer	St. Jude Medical	Medtronic
Size (height × width)	42.0 × 6.0 mm	25.9 × 6.7 mm
Volume	1.0 mL	0.8 mL
Mass	2 g	2 g
Delivery sheath size	18 F	23 F
Primary fixation mechanism	Helix	Tines
Projected battery life*	15.0 years	12.5 years
Remote monitoring	No	Yes
Rate-responsive pacing	Yes	Yes, accelerometer-based
Retrieval system	Yes	No

*Based on reported projections at 3 months. Data from references 21–27.

complications from 3 to 12 months, no adverse changes in electrical performance parameters, and 100% effectiveness of rate-responsive programming.

The subsequent LEADLESS II trial enrolled 526 patients but did not exclude patients with expected pacemaker dependency, and its results were reported in a preplanned interim analysis when 300 patients had reached 6 months of follow-up (mean follow-up 6.9 ± 4.2 months).²⁴ The primary efficacy end point involved electrical performance including capture thresholds and sensing. Initial deployment success was 96% with expected electrical parameters at implant that were stable at 6 months of follow-up. The rate of freedom from serious adverse events was 93%, with complications including device dislodgment (1.7%, mean 8 ± 6 days after implant), perforation (1.3%), performance deficiency requiring device retrieval and replacement (1.3%), and groin complications (1.3%). There were no device-related deaths, and all device dislodgments were successfully treated percutaneously.

There was no prospective control arm involving transvenous pacing in either the LEADLESS or LEADLESS II trial. Thus, in an effort to compare Nanostim ($n = 718$) vs transvenous pacing, complication rates were calculated for a propensity-matched registry cohort of 10,521 transvenous patients, and differences were reported.²⁶ At 1 month, the composite complication rate was 5.8% for Nanostim (1.5% pericardial effusion, 1% dislodgment) and 12.7% for transvenous pacing (7.6% lead-related, 3.9% thoracic trauma, infection 1.9%) ($P < .001$). Between 1 month and 2 years, complication rates were only 0.6% for Nanostim vs 5.4% for transvenous pacing ($P < .001$). This lower complication rate at 2 years was driven almost entirely by a 2.6% infection rate and 2.4% lead-complication rate in the transvenous pacemaker group, nonexistent in the leadless group.

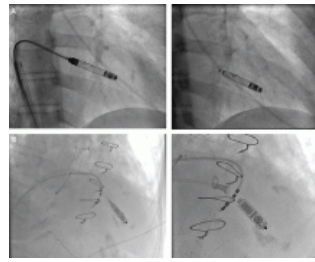


FIGURE 3. Fluoroscopic images depicting catheter-based deployment and subsequent release for the (A) Nanostim and (B) Micra.

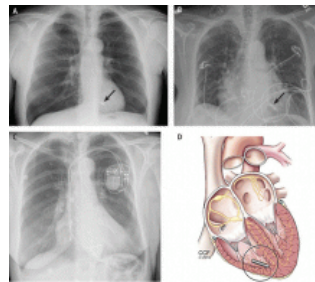


FIGURE 4. Frontal-plane radiographs showing implanted Nanostim (A) and Micra (B) leadless pacing devices and a traditional dual-chamber pacemaker (C). Panel D depicts cardiac deployment.



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