

REVIEW ARTICLE

Leadless Cardiac Pacemaker Therapy. An Overview for the HospitalistRichard Weachter¹¹Division of Cardiovascular Medicine, Department of Medicine, University of Missouri, Columbia, MO

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Am J Hosp Med 2018 Jul;2(3):2018.016 <https://doi.org/10.24150/ajhm/2018.016>**INTRODUCTION**

Each year, approximately 200,000 permanent pacemakers are implanted in the United States and 1,000,000 worldwide.^{1,2} Since the initial transvenous pacemaker implantation 6 decades ago, improvements in battery longevity, lead performance and device programming have occurred.³ However, the basic components of and implantation technique for permanent transvenous pacemakers have remained essentially unchanged. Of the 2 pacemaker system components – pulse generator and lead – the lead has been considered the “weakest link”.³ While the concept of leadless pacing was first proposed in 1970, not until 2012, with implantation of the St. Jude leadless pacemaker, did practical application of this concept come to fruition.^{4,5}

TRANSVENOUS PACEMAKER IMPLANTATION AND COMPLICATIONS

Over the past 6 decades, transvenous pacemaker implantation techniques have changed little. Following the initial infraclavicular incision and subcutaneous pocket formation, access to the axillary-subclavian vein is obtained, most commonly using a modified Seldinger technique.

Leads are then fluoroscopically advanced to the desired cardiac chamber and either actively or passively fixated (Figure 1).

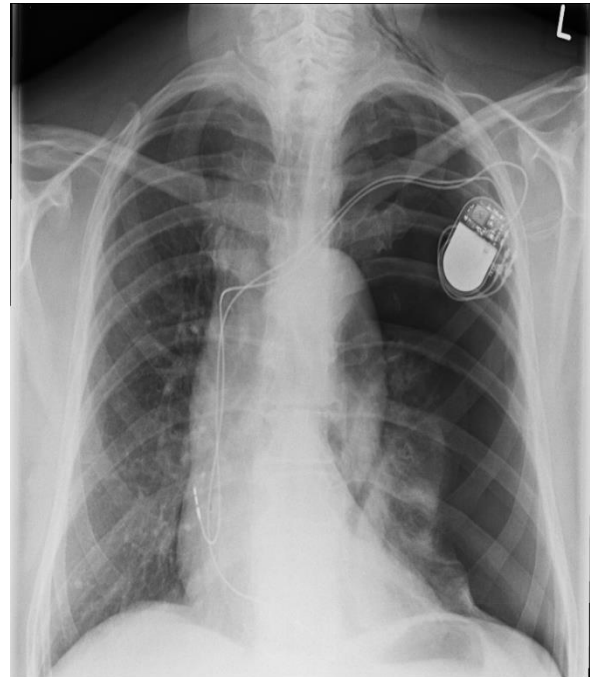


Figure 1. Transvenous dual chamber pacemaker

Complications due to transvenous pacemakers involve either the subcutaneous pacemaker pocket or the transvenous leads. Subcutaneous pocket complications, with an incidence of 0.7 – 2.4%, include skin erosion of pulse generator and/or leads, pocket hematoma and pocket infection.^{6,7,8} Transvenous lead complications are classified as acute and chronic. Acute lead

complications include pneumothorax, upper extremity deep vein thrombosis, cardiac perforation with risk of tamponade, and lead dislodgement. Chronic lead complications include central vein obstruction, tricuspid valve regurgitation, lead endocarditis and lead failure.^{9,10,11} Short-term (<3 months) complications from transvenous lead placement have an 8-12% incidence.^{9,12}

Transvenous lead endocarditis has a 12-31% mortality risk.^{13,14} One in 40 single-chamber transvenous pacemaker systems will have a complication requiring surgical intervention within 3 months.¹² The concept of leadless pacing was developed in an attempt to minimize these transvenous pacemaker associated complications.

LEADLESS PACEMAKER SYSTEMS

Two leadless pacemaker systems have been implanted worldwide – the St. Jude Nanostim leadless cardiac pacemaker (LCP), first implanted in 2012, and the Medtronic Micra transcatheter pacing system (TPS), first implanted in 2013 (Figure 2.).^{5,15}

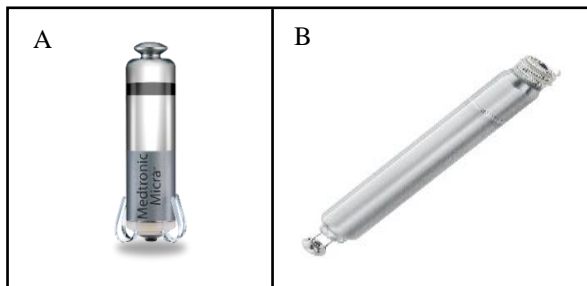


Figure 2. A. Medtronic Micra TPS (*Reproduced with permission of Medtronic, Inc.*) B. St. Jude Nanostim LCP (*Reproduced with permission of St. Jude Medical, LLC.*)

Both leadless pacing systems have similar implantation techniques. Initially, vascular access is gained at either femoral vein using a large diameter 2 component delivery catheter – 21 F outer diameter for the St. Jude Nanostim LCP and 27F outer

diameter for the Medtronic Micra TPS. The leadless pacemaker, contained at the distal end of the inner delivery catheter, is fluoroscopically advanced to the right ventricle (RV). Following venogram confirmation of optimal catheter – RV endocardial interface, most commonly along the RV septum, the pacing electrode is deployed – the St. Jude Nanostim LCP using a screw-in helix fixation mechanism and the Medtronic Micra TPS using a 4 tine fixation mechanism (Figure 3).

Once acceptable electrical parameters are confirmed, both pacing electrodes are untethered and fully deployed.^{5,15} Following removal of the delivery catheter, care is taken to achieve hemostasis at the femoral vein access site. Postoperative care is confined to the femoral vein access site and consists of short-term restrictions in lifting, walking, bathing and application of local counterpressure with standing or Valsalva.

LEADLESS PACEMAKER COMPARISON

While both systems are implanted in a similar manner, currently pace only the RV, and are similarly shaped, some significant differences exist. The St. Jude Nanostim LCP, measuring 42 mm in length/6mm in diameter, uses a screw-in helix fixation mechanism and blood temperature within the RV as its rate responsive sensor. The Medtronic Micra TPS, measuring 26mm in length/6.7 mm in diameter, uses nitinol tines for fixation and an accelerometer as its rate responsive sensor.^{5,15}

While the 2 devices have not been compared head-to-head, some comparisons can be made. Both have similar implantation success rates, acute and chronic thresholds, and while overall complication rates are similar, the device dislodgement rate for the St. Jude Nanostim LCP has been greater.

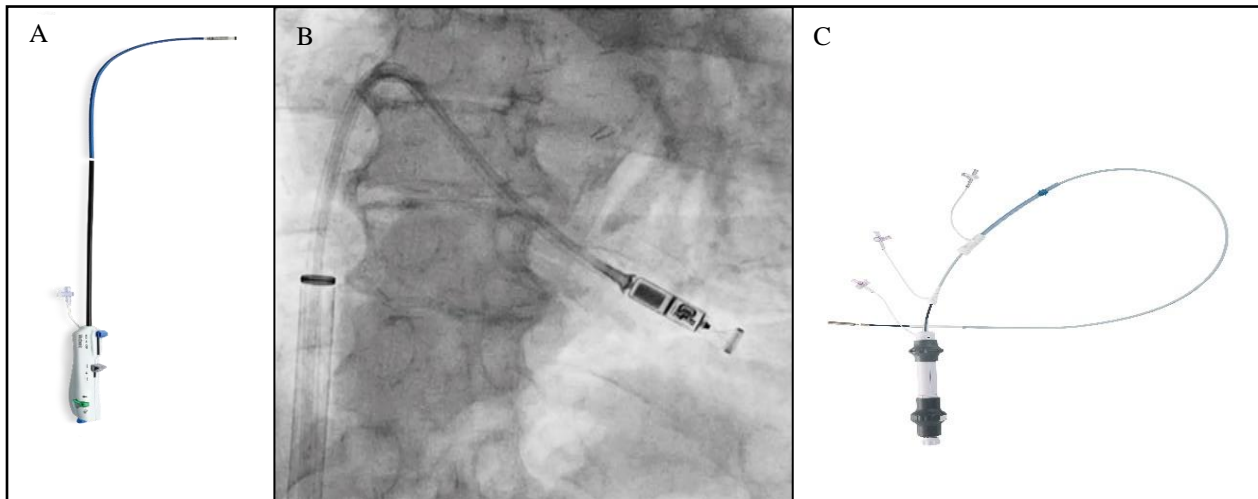


Figure 3. A. Medtronic Micra TPS inner delivery catheter B. Medtronic Micra TPS delivery within RV C) St. Jude Nanostim LCP delivery catheter. *Reproduced with permission of Medtronic, Inc. (images A and B) and St. Jude Medical, LLC (image C).*

Battery longevity, dependent upon standards used, are for the St. Jude Nanostim LCP between 9.8 and 14.7 years and for the Medtronic Micra TPS between 4.7 and 10 years.¹⁶

In October 2016, a battery advisory was issued by St. Jude for the Nanostim LCP. Abrupt battery depletion with loss of telemetry and pacing was found in 2.4% of device implants occurring 29 to 37 months post-implant. The St. Jude Nanostim LCP has yet to receive FDA approval for implantation.

LEADLESS VS. TRANSVENOUS PACEMAKER

No long-term performance data are yet available for leadless pacemakers. However, both short-term (<3 months) and intermediate-term (12 months) comparisons of leadless and transvenous pacemakers have been reported.^{17,18}

Both leadless and transvenous pacing systems have similar short-term complication rates but different types of complications. Mostly commonly reported short-term complications of leadless pacemakers include:

- Cardiac perforation (1.5%)
- Vascular complication (0.9%)
- Pacing threshold rise requiring re-intervention (0.5%)
- Device dislocation (0.5%)¹⁷

Most commonly reported short-term complications of transvenous pacemakers include:

- Pneumothorax (0.6-0.9%)
- Lead dislodgement (0.4-1.7%)
- Pocket hematoma (0.2-0.7%)
- Cardiac perforation (0.1-0.3%)¹⁷

Intermediate-term (12 months) comparisons of leadless and transvenous pacing systems have been recently published. In the 12 month follow-up of the St. Jude LEADLESS trial, from 3 to 12 months there were no pacemaker-related adverse events. When compared to historical transvenous pacemaker controls, there was a 71% reduction in complications with St. Jude Nanostim procedures.^{18,19} A similar intermediate-term performance comparison of the Medtronic Micra TPS and historical transvenous controls found a 48% lower risk of major complications predominantly from 48% fewer hospitalizations and an 82% reduction in pacemaker revision.²⁰

When comparing complication rates of leadless and transvenous pacing systems it is important to note that transvenous pacemaker implantation has matured over several decades whereas leadless pacemaker implantation is a new procedure with an expected learning curve. Additionally, there are no long-term data yet available for leadless pacing systems. This is relevant since the long-term complications associated with transvenous pacemakers from both pocket and leads are not expected with the leadless pacing system.¹⁹

RETRIEVE VS. ABANDON

Both leadless pacing systems are retrievable. Retrieval, which requires use of a snare technique, can be technically challenging. Limited experience to date has suggested successful retrieval rates of 80 to 90% up to 4 years following device implantation.^{21,22}

Currently, due to the unknown long-term ability to retrieve a leadless pacemaker, the optimal end-of-life strategy is unclear. Two options are available – abandon the previously implanted end-of-life pacemaker and implant an additional device in the RV or extract the previously implanted leadless pacemaker at the time of replacement. Rationale for simply abandoning the previously implanted device include, the devices occupy small volumes (0.8-1.00 cc) representing <2% of the normal RV volume (and thereby unlikely to compromise RV function) and 3 Medtronic Micra TPS devices have been successfully implanted within the pig heart without ill-effect. Rationale for explanting the previously implanted device include, avoiding the potential risk of device-device interaction, the unknown long-term risk of multiple devices, and making the RV more accessible should an additional device need to be implanted at a later date.^{23,24,25}

INDICATIONS/ CONTRAINDICATIONS

The most common indications for the current generation leadless pacing systems are in most instances comparable to standard transvenous single chamber (VVI) pacemaker indications and include:

- Permanent atrial fibrillation with atrioventricular (AV) block or significant pauses
- Sinus rhythm with intermittent advanced heart block in patients of limited life span or very low levels of physical activity
- Sinus bradycardia with infrequent pauses
- Syncope with electrophysiologic study findings concerning for increased risk of heart block

Other potential indications unique to the leadless pacing systems include:

- Renal failure requiring hemodialysis (due to increased risk of device-related infections)
- Recurrent device infections
- Venous occlusion from prior pacemaker implantation¹⁷

Contraindications to leadless pacemaker implantation are few but may include:

- Mechanical tricuspid valve
- Pre-existing pacemaker or defibrillator leads
- Inferior vena cava filter
- Unfavorable venous anatomy
- Morbid obesity preventing telemetry communication
- Concern for loss of AV synchrony resulting in a pacemaker syndrome
- Severe pulmonary hypertension¹⁷

SAFETY CONCERNS

There are relatively few safety concerns for leadless pacing systems. Both leadless pacing systems are magnetic resonance

imaging (MRI) compatible – the Medtronic Micra for 1.5T and 3.0T MRI scans and the St. Jude Nanostim for 1.5T MRI scans.^{17,26} To date, no significant adverse effects have been reported following delivery of radiotherapy or external defibrillation therapy on leadless pacemaker function.^{27,28} The Medtronic Micra has been proven safe for cremation.²⁹

FUTURE

There is a bright future for the leadless pacing system. The current first generation of leadless pacing system is limited to simply single chamber RV pacing. However, the foreseeable future will almost certainly include multi-chamber leadless pacing and combination with the subcutaneous defibrillation system (to allow for backup bradycardia pacing and anti-tachycardia pacing for monomorphic ventricular tachycardia).¹⁹

SUMMARY

1. The basic design of the transvenous pacing system has been essentially unchanged since inception 6 decades ago with the weakest link being the transvenous lead.
2. The most common indication for the current generation of leadless pacing system is permanent atrial fibrillation with pauses but other indications include patients with sinus rhythm who will require infrequent pacing, have low levels of physical activity or limited life span, and those patients at high risk for device infection.
3. Short-term complication rates for leadless pacing systems are comparable, but different, than for transvenous pacing systems. Intermediate – term complication rates for the leadless pacing system are lower and long-term

complication rates are expected to be lower.

4. Unanswered questions include long-term complication rates of the leadless pacing system and the optimal end-of-life strategy.
5. A bright future for the leadless pacing system is expected with the potential for future multi- component leadless devices.

Notes

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References

1. Greenspon AJ, Patel J, Lau E, et.al. Trends in Permanent Pacemaker Implantation in the United States from 1993 to 2009: Increasing Complexity of Patients and Procedures. *J Am Coll Cardiol* 2012; 60:1540-5.
2. Mond HG, Irwin M, Ector H, et.al. The World Survey of Cardiac Pacing and Cardioverter Defibrillators: Calendar Year 2005 an International Cardiac Pacing and Electrophysiology Society (ICPES) Project. *Pacing Clin Electrophysiol* 2008; 31:1202-12.
3. Miller MA, Neuzil P, Dukkipati S, et.al. Leadless Cardiac Pacemakers. Back to the Future. *J Am Coll Cardiol* 2015; 66:1179-89.
4. Spickler J, Rosor N, Kezdi P, et.al. Totally Self-Contained Intracardiac Pacemaker. *J Electrocardiol* 1970; 3:325-31.
5. Reddy V, Knops R, Sperzel J, et.al. Permanent Leadless Cardiac Pacing: Results of the LEADLESS Trial. *Circulation* 2014; 129:1466-71.
6. Klug D, Balde M, Pavin D, et.al. Risk Factors Related to Infections of Implanted Pacemakers and Cardioverter-Defibrillators: Results of a Large Prospective Study. *Circulation* 2007; 116:1349-55.
7. Lekkerkerker J, Van Nieuwkoop C, Trines S, et.al. Risk Factors and Time Delay Associated with Cardiac Device Infections: Leiden Device Registry. *Heart* 2009; 95:715-20.
8. Essebay V, Healey J, Ayala-Paredas F, et.al. Clinically Significant Pocket Hematoma

- Increases Long-Term Risk of Device Infection: BRUISE CONTROL INFECTION Study. *J Am Coll Cardiol* 2016; 67:1300-8.
9. Udo E, Zuithoff N, Van Hamel N, et.al. Incidence and Predictors of Short- and Long-Term Complications in Pacemaker Therapy: The FOLLOWPACE Study. *Heart Rhythm* 2012; 9:728-35.
 10. Hauser R, Hayes D, Kallinen M, et.al. Clinical Experience with Pacemaker Pulse Generators and Transvenous Leads: An 8-Year Prospective Multicenter Study. *Heart Rhythm* 2007; 4:154-60.
 11. Haghjoo M, Nikoo M, Fazelifar A, et.al. Predictors of Venous Obstruction Following Pacemaker or Implantable Cardioverter-Defibrillator Implantation: A Contrast Venographic Study on 100 Patients Admitted for Generator Change, Lead Revision or Device Upgrade. *Europace* 2007; 9:328-32.
 12. Kirkfeldt, R, Johansen J, Nohn E, et.al. Complications after Cardiac Implantable Electronic Device Implantations: An Analysis of a Complete, Nationwide Cohort in Denmark. *European Heart Journal* 2014; 35:1186-94.
 13. Tarakji K, Wazni O, Harbs, et.al. Risk Factors for 1-Year Mortality among Patients with Cardiac Implantable Electronic Device Infection Undergoing Transvenous Lead Extraction: The Impact of the Infection Type and the Presence of Vegetation on Survival. *Europace* 2014; 16:1490-5.
 14. Brunner M, Cronin E, Wazni O, et.al. Outcomes of Patients Requiring Emergent Surgical or Endovascular Intervention for Catastrophic Complications during Transvenous Lead Extraction. *Heart Rhythm*. 2014; 11:419-25.
 15. Reynolds D, Duray G, Omar R, et.al. A Leadless Intracardiac Transcatheter Pacing System. *N Engl J Med* 2016; 374:533-41.
 16. El-Chami M, Merchant F, and Leon A. Leadless Pacemakers. *Am J Cardiol* 2017; 119:145-8.
 17. Lee J, Mulpuru S, and Shen W. Leadless Pacemaker: Performance and Complications. *Trends in Cardiovascular Medicine* 2018; 28:130-141.
 18. Knops R, Rjong F, Neuzil P, et.al. Chronic Performance of a Leadless Cardiac Pacemaker: 1-year Follow-up of the LEADLESS Trial. *J Am Coll Cardiol* 2015; 65:1497-504.
 19. Tjong F and Reddy V. Permanent Leadless Cardiac Pacemaker Therapy: A Comprehensive Review. *Circulation* 2017; 135:1458-70.
 20. Duray G, Ritter P, El-Chami M, et al. Long-term Performance of a Transcatheter Pacing System: 12-month Results from the Micra Transcatheter Pacing Study. *Heart Rhythm* 2017; 14:702-9.
 21. Lakkireddy D, Knops R, Atwater B, et.al. A Worldwide Experience of the Management of Battery Failures and Chronic Device Retrieval of the Nanostim Leadless Pacemaker. *Heart Rhythm* 2017; 14:1756-63.
 22. Micra Transcatheter Pacing System (TPS). FDA Panel Pack for Circulatory Systems Devices Panel, meeting date February 18, 2016
<http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/UCM485094.pdf> Accessed June 9, 2018.
 23. Tamborini G, Marsan N, Gripari P, et.al. Reference Values for Right Ventricular Volumes and Ejection Fraction with Real-Time Three-Dimensional Echocardiography: Evaluation in a Large Series of Normal Subjects. *J Am Soc. Echocardiogr* 2010; 23:109-15.
 24. Beurskens N, Tjong F, Knops R. End-of-Life Management of Leadless Cardiac Pacemaker Therapy. *Arrhythmia and Electrophysiology Review* 2017; 6:129-33.
 25. Omadahl P, Eggen M, Bonner M, et.al. Right Ventricular Anatomy Can Accommodate Multiple Micra Transcatheter Pacemakers. *Pacing Clin Electrophysiol* 2016; 39:393-7.
 26. Soejima K, Edmonson J, Ellingson M, et.al. Safety Evaluation of a Leadless Transcatheter Pacemaker for Magnetic Resonance Imaging Use. *Heart Rhythm* 2016; 13:2056-63.
 27. Martinez-Sande J, Garcia-Seara J, and Rodriguez-Maners. Radiotherapy in a Leadless Pacemaker. *EP Europace* 2018; 20:81.
 28. Venier S, Jacon P, and Defaye P. Direct Electrical Shock on a Leadless Pacemaker. *J Interv Card Electrophysiol* 2017; 49:39.
 29. Cheung L, Chan G, Chan J, et.al. Cremation of Leadless Pacemaker. *Pacing Clin Electrophysiol* 2017; 40:629-31.