Leadless Cardiac Pacemakers: The Next Evolution in Pacemaker Technology

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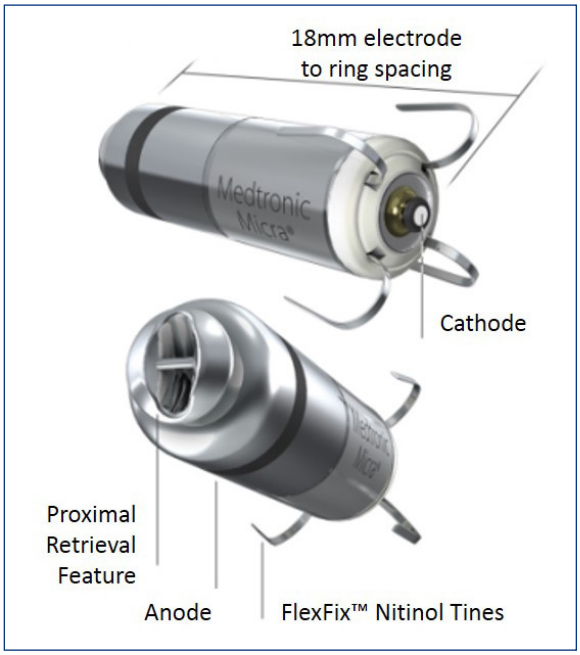
ABSTRACT

Implantable pacemakers stand as a mainstay in our therapeutic arsenal, affording those suffering from advanced cardiac conduction system disease both an improved quality of life and reduced mortality. Annually, over 225,000 new pacemakers are implanted in the United States for bradyarrhythmias and heart block. The first implantable transvenous pacemakers appeared in 1965; they were bulky devices, hobbled by a short battery life, and a single pacing mode. Modern transvenous pacemakers have evolved considerably with significant improvements in battery life, pacing options, and lead technology but are still subject to a spectrum of complications stemming from either the subcutaneous pocket or the leads, including: hematoma, infection, wound dehiscence, pneumothorax, cardiac tamponade, lead dislodgment, upper extremity deep vein thrombosis, lead failure, venous obstruction, tricuspid valve insufficiency, and endocarditis. Single-chamber right ventricular (RV) leadless cardiac pacemakers, a concept from the past, has been revitalized to address these complications. Improvements in battery life, device miniaturization, catheter-based delivery tools, and advanced programming have made leadless cardiac pacemakers a viable option. In this review, we will discuss single-component leadless cardiac pacemaker technology, provide an overview of the two approved devices, and discuss their benefits as well as their limitations.

KEYWORDS: arrhythmias, cardiac; cardiac pacing, artificial; leadless pacing; pacemaker, artificial

Medtronic's Leadless Micra Transcatheter Pacing System (TPS).



INTRODUCTION

Implantable pacemakers stand as a mainstay in our therapeutic arsenal, affording those suffering from advanced cardiac conduction system disease both an improved quality of life and reduced mortality (1-4). Annually, over 225,000 new pacemakers are implanted in the United States for bradyarrhythmias and heart block (5). The first implantable transvenous pacemakers appeared in 1965. They were bulky devices, hobbled by a short battery life, and a single pacing mode. Modern transvenous pacemakers have evolved considerably with significant improvements in battery life, pacing options, and lead technology, but are still inserted similar to the original devices from the 1960s; with a pectoral-placed pulse generator connected to intracardiac transvenous pacing leads (6). Accordingly, while modern pacemakers are significantly more elegant devices, unfortunately they share many complications with their predecessors. In the short term, the subcutaneous pocket, in which the generator lies, is subject to hematoma, infection, and wound dehiscence. Intervention for cutaneous pocket complications increases the infection risk 15-fold (7-9). In addition to the risk posed by the subcutaneous pocket, transvenous leads have both short- and long-term sequelae. In the acute setting, the insertion of transvenous leads can lead to pneumothorax, cardiac tamponade, lead dislodgment, or upper extremity deep vein thrombosis and complication rates may be as high as 8% to 12% (10,11). Long-term complications from transvenous leads include lead failure, venous obstruction, tricuspid valve insufficiency, and endocarditis (11,12). In the simplest of the modern pacing configurations, a subcuta-

neous generator with a single-chamber lead, more than 1 in every 40 implants will require surgical intervention within 3 months of implantation; half of which are attributable to lead issues (12-14). Additionally, over the life of the device, lead failures are associated with significant morbidity (11).

In the 1970s, physicians, in concert with device engineers, developed the idea of a leadless pacemaker. They successfully implanted a self-contained RV cardiac pacemaker in a canine model with induced complete heart block, achieving 66 days of captured pacing. However given the technologic limitations of battery life inherent to the 1970s, the idea was shelved (15). Recently, advances in battery life, device miniaturization, improved catheter-based delivery tools, and advanced programming to optimize power consumption have assisted in making leadless cardiac pacemakers a viable option (16-19). In this review, we will discuss single-component leadless cardiac pacemaker technology, provide an overview of the two main devices, and consider their benefits and limitations.

SINGLE-COMPONENT LEADLESS CARDIAC PACEMAKERS

Currently, there are two single-component leadless cardiac pacemakers: 1) the Micra Transcatheter Pacing System (TPS; Medtronic) which received FDA approval in April 2016 and 2) the Nanostim Leadless Cardiac Pacemaker (LCP; St. Jude Medical) which is currently waiting FDA approval. Both devices are fully self-contained units, transcutaneously deployed via the femoral approach and capable of single-chamber RV pacing, sensing, and rate responsiveness. The Nanostim LCP is longer than the Micra TPS (42 mm versus 25.9 mm), but they displace similar volumes (1.0 and 0.8 mL). While the implantation procedure for both devices is similar, the Micra TPS requires a 27 French delivery sheath, while the Nanostim LCP uses a smaller 21 French delivery sheath. Once the device is advanced to the RV, site selection is accomplished via contrast-enhanced visualization. The pacemaker is then deployed using 4 self-expanding nitinol tines (Micra TPS) or an active screw-in helix with 3 angled nitinol tines perpendicular to the helix (Nanostim LCP). Following anchoring of the pacemaker, electrical parameters are assessed, internal fixation is tested using a gentle tug test, and the device is then deployed from the sheath.

Retrievability is an important consideration for leadless cardiac pacemakers. The Nanostim LCP has a dedicated steerable retrieval system. If a retrieval is warranted, the distal cap of the pacemaker is captured by the snare of the retrieval catheter, then rotated counter-clockwise to release the device from the myocardium. The Micra TPS does not have a dedicated retrieval system, but in several cases has been retrieved by employing a conventional goose-neck snare through a guiding sheath. Neither system has demonstrated long-term retrievability in humans, but has been demonstrated in animal models.

CLINICAL DATA: SAFETY AND PERFORMANCE

The data regarding the safety and efficacy of leadless pacemakers was spearheaded by the LEADLESS Trial. Using the Nanostim LCP device, 33 patients (mean age 77 years, 67% male) at 3 centers were enrolled over a four-month period in 2012-2013. The Nanostim LCP was successfully implanted in 32/33 (97%) patients. Overall, freedom from complications was 94% (31/33) at 90-day follow-up. There was one major complication: a 70-year-old male experienced cardiac tamponade with hemodynamic collapse during Nanostim LCP implantation, requiring emergent cardiac surgery, and died of an ischemic stroke due to a sub-therapeutic INR 3 weeks later (17).

A second clinical study, for safety and efficacy of the Nanostim LCP system, LEADLESS III, was prospectively performed in 56 centers in 3 countries (Australia, Canada, and USA) and enrolled 526 patients (mean age 75 years, 62% male), 300 with a minimum follow-up of 6 months. The Nanostim LCP was successfully implanted in 504/526 (95.8%), mean procedure time was 28.6 ± 17.8 minutes, and 70% of deployed devices did not require repositioning. Device-related serious adverse events occurred in 34 (6.5%) of patients and included pericardial effusion 1.5%, vascular complication 1.2%, dislodgment 1.1% (4 to pulmonary vein, 2 to femoral vein), and device retrieval 0.8% due to elevated pacing thresholds (18). Of note, St. Jude, manufacturer of the Nanostim LCP, issued a battery advisory due to a malfunction in 7/1423 (0.5%) devices, occurring between months 29–37 following implantation. The malfunction caused abrupt battery depletion, eliciting a loss of pacing and failed communication.

The Micra TPS Trial was a global, multicenter prospective study aimed at device safety and efficacy. The study enrolled 725 patients (mean age 75, 58.8% male) who met guidelines for RV pacing. The Micra TPS was successfully implanted in 719/725 (99.2%), with a mean procedure duration of 23.0 ± 15.3 minutes. Device-related serious adverse events occurred in 25 (3.4%) patients and included cardiac perforation 1.5%, vascular complications in 0.7%, venous thromboembolism in 0.3%, and increasing pacing thresholds in 0.3% of patients. No device dislodgment or embolization were observed. There was one major complication: a 77-year-old woman with end-stage renal failure, who underwent concomitant atrioventricular nodal ablation during the Micra TPS implant, died. Her death was likely attributable to a metabolic acidosis from her underlying renal failure and a prolonged procedure time (18).

POTENTIAL BENEFITS/LIMITATION TO LEADLESS CARDIAC PACING

The most obvious benefit of leadless pacing technology stems from mitigation of the short- and long-term risks associated with the traditional subcutaneous pocket with transvenous leads. The Nanostim LCP has a battery life that is

comparable to that of standard, single-chamber transvenous pacemakers. The similarity in battery life, despite the discrepancy in battery size, is directly attributable to the direct contact of the leadless cardiac pacemaker with the myocardium. The resulting reduction in impedance yields a significant reduction in current requirements. For the Nanostim LCP, the per beat requirement is 1.0 µA versus 6.24 µA for a standard transvenous pacemaker from the same device manufacturer (17-22).

On the other hand, the Micra TPS has approximately one half the battery life of the Nanostim LCP. The decreased battery life is based on two differences between the devices; the Micra TPS has a smaller battery (120 vs 248 mAh), and it uses radiofrequency telemetry instead of conductive telemetry. The predicted battery life for the Micra TPS at nominal settings is approximately 9.6 years, while the Nanostim LCP at the same settings would last 14.7 years. However, given that pacing is a dynamic, often user dependent process, there may be some variability in the actual device battery life. Only long-term follow-up will accurately delineate the true life of these devices. Additionally, both devices are believed to be safe for conditional use in magnetic resonance imaging due to a lack of ferromagnetic construction materials. Follow-up studies will need to be conducted to confirm their safety.

The most vexing limitation of the current generation of leadless cardiac pacemakers is their ability to only provide single-chamber RV pacing, barring the devices from placement in individuals requiring dual-chambered pacing or those in need of cardiac resynchronization therapy (23). Single-chamber RV pacing represents a relative minority, 15–30% of patients in Western countries (5). Another potentially concerning, but as of yet unseen complication, is the possibility of chronic device embolization. Also, the relatively large femoral venous sheath size (Nanostim LCP at 21F or Micra TPS at 27F) introduces the potential for both vascular and perforative complications, such as the terminal perforation that happened during the LEADLESS trial. Retrievability or the ability to place multiple devices at end-of-device life is a potential problem that remains to be resolved. While long-term device retrieval has been proven in animal models, it has yet to be done in humans. Lastly, given the relative small displacement by either leadless cardiac pacemaker, ~ 5mL, there is a possibility to deploy multiple devices if retrieval becomes onerous, but again this is a theoretical solution without current supporting clinical data.

CONCLUSION

While leadless cardiac pacemakers offer a potential means to circumvent some of the short- and long-term complications inherent to traditional subcutaneous transvenous pacemakers, many questions remain unanswered. Both the Micra TPS and the Nanostim LCP have demonstrated similar performance and safety. However, since no data is currently available to determine the long-term viability of leadless cardiac pacemakers, we will need to rely on future randomized clinical trials, and registry data to see if the potential benefits of the leadless cardiac pacing systems will supersede their conventional counterparts.

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