Emerging Technologies in Electrophysiology: From Single-Chamber to Biventricular Leadless Pacemakers

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Keywords

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Abstract

Background: Transvenous pacemakers have been shown to improve quality of life and mortality in patients with bradycardia and cardiac conduction blocks. However, they possess inevitable drawbacks as they have a relatively high incidence of lead and device pocket-related complications. Therefore, leadless pacemakers have emerged as a solution to reduce the complications seen with conventional pacemakers. However, there have been no clinical trials to date comparing transvenous to leadless pacemakers. **Summary:** Currently, the Micra™ transcatheter pacing system or AV device has been approved for commercial use worldwide but is limited to single-chamber pacing with single- or dual-chamber sensing. Although the leadless pacemaker Nanostim™ was initially promising, it has been recalled due to concerns of battery failures and is no longer approved in Europe. In addition, the lack of defibrillation capabilities with leadless pacemakers has been a limiting factor; therefore, a leadless pacemaker with the already approved subcutaneous cardioverter-defibrillator system is currently being studied in humans. Moreover, the WiSE cardiac resynchronization

therapy (CRT) device has been approved in Europe, with the capabilities for leadless CRT in patients with unsuitable coronary sinus anatomy. Furthermore, retrieval of leadless pacemakers has been an area of concern; however, clinic data have signaled toward safe extraction of these devices with minimal complications. **Key Messages:** This review will encompass the current literature regarding clinical safety and outcomes of these novel leadless pacemakers and discuss the evolving technologies in the field of cardiac pacing.

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Introduction

It is estimated that more than 700,000 new pacemakers were implanted in 2009 [1]; in recent years, these rates have exponentially increased as greater than 1 million devices are implanted annually [2]. Since their introduction in 1958 [3], transvenous pacemakers have improved quality of life and reduced mortality in patients with bradyarrhythmia or heart block [4–6]. Despite proving to be lifesaving, these devices still possess significant limitations, with reported complication rates of 8–12% in the short- and long-term settings [7, 8]. Complications are typically related to the transvenous leads and subcutaneous device pockets. These consist of pocket hematoma, pneumothorax, cardiac tamponade, lead dislodgement,

Fig. 1. Leadless Pacemakers. Illustration of leadless pacemakers, Nanostim™ (a), Micra™ (b), the left ventricular electrode in the WiSE-CRT™ system (c), and EMPOWER™ (d) with relative size comparisons and accurate measurements.

venous obstruction, systemic infection, or endocarditis [9–13]. Pocket and transvenous lead-related infections are particularly severe, with an associated mortality of up to 12% and 31%, respectively, requiring removal of all hardware [14]. Moreover, leads may also fracture from mechanical trauma, causing malfunction and insulation disruptions, resulting in abnormal pacing and sensory function [15, 16]. Therefore, reducing pacemaker hardware is essential to mitigate these complications.

The concept of a leadless pacemaker that could overcome the limitations of transvenous pacers was first pro-

posed in 1970 by Spickler et al. [17]. In the ensuing years, several studies were conducted in animals, demonstrating the feasibility, efficacy, and safety of leadless pacemakers [18–21]. With technological advances in transcatheter interventions, device miniaturization, communications, and battery longevity, this concept became realistic in humans and has resulted in a paradigm shift in modern medicine. This review will summarize the clinical safety and efficacy of the current leadless devices (Fig. 1) and discuss the emerging technologies in this rapidly advancing field.

Table 1. Comparison of leadless devices

	Nanostim™	Micra™ TPS/AV	EMPOWER™	WiSE-CRT™
Manufacturer	St. Jude Medical/Abbott	Medtronic	Boston Scientific	EBR Systems
Volume, cm ³	1.0	0.8	0.8	0.05
Length, mm	41.4	25.9	31.9	9.1
Diameter, mm	5.99	6.7	6.0	2.7
Battery	Lithium-carbon monofluoride	Lithium silver vanadium oxide/ carbon monofluoride	Lithium-carbon monofluoride	Ultrasound transmitter with left ventricular electrode receiver
Battery life	9.8 years	12 years	Estimated 8.75 years	Estimated 7 years
Device fixation	Screw-in helix	Self-expanding nitinol tines	Active-fixation nitinol tines	5 nitinol tines/anchoring barbs
Pacing mode	VVI	VVI	VVI with anti-tachyarrhythmia defibrillation	CRT in conjunction with right ventricular pacer or Micra™
Associated device	n/a	WiSE-CRT™	EMBLEM MRI S-ICD™	Subcutaneously implanted pulse generator

Leadless Single-Chamber Ventricular Pacemakers

Currently, two leadless devices have been developed with ventricular pacing, sensing, and inhibition pacing (VVI) capabilities. These are Nanostim™, manufactured by St. Jude Medical and Micra™ transcatheter pacing system (TPS), manufactured by Medtronic. The design of these devices is similar as they are entirely self-contained, including pacemaker electronics, lithium batteries, and electrodes. Both are delivered to the right ventricle under fluoroscopic guidance via a deflectable catheter with a sheath system from the femoral vein. Minor differences lie in implantation; Nanostim™ is secured by a single turn (screw-in) into the endocardium with a maximum depth of 1.3 mm [22]. Micra™ TPS is fixated to the endocardium by four nitinol tines. Both devices are connected to the catheter by tethers used to confirm adequate fixation with a tug test before the device is released [23]. Both devices allow response rate programming via a temperature sensor (Nanostim™) or accelerometer (Micra™ TPS) [24]. Details and comparisons between these devices are displayed in Table 1. These devices are only capable of VVI pacing, lacking defibrillation capacity, which limits their utility. Currently, they are suitable for patients with permanent atrial fibrillation with a slow ventricular response, bradycardia-tachycardia syndrome in the setting of sick sinus syndrome, atrioventricular (AV) or sinus node block in which frequent ventricular pacing is not

expected, and recurrent syncope due to vagally induced cardio-inhibition [25]. MRI compatibility is also an important consideration; both devices are MRI-conditional. Micra™ TPS is safe for 1.5T and 3.0T scanners [26, 27]; however, Nanostim™ is only proven safe for 1.5T scanners [28].

Clinical Safety and Efficacy

Nanostim™

The landmark LEADLESS trial [22] was the first-in-man study assessing the feasibility of a leadless pacemaker. This was a multicenter trial conducted in Europe, enrolling 33 patients with a primary safety endpoint defined as freedom from device or implant-related complications at 90 days. As part of secondary performance endpoints, device performance measures (sensing, impedance, R-wave amplitude, and pacing threshold) were also evaluated. In this trial, 32 out of 33 (97%) devices were successfully implanted, and the primary safety endpoint was met as 31 out of 33 (94%) participants were complication-free. Of the 2 complications, 1 patient had a perforation of the right ventricular apex resulting in cardiac tamponade and eventual death. The second patient had incorrect device implantation into the left ventricle (LV) through a patent foramen ovale. The device was successfully retrieved and correctly placed, and the patient did not experience any

further adverse outcomes [22]. In this study, Nanostim™ proved to be safe and efficacious without battery complications and sensing or capturing malfunctions. Therefore, a CE mark for European approval was granted in October 2013. At 1-year follow-up, the results of this trial were sustained in the 31-patient cohort as there was stable device performance (pacing threshold, sensing amplitude, and impedance) with no reported device-related complications [29]. The LEADLESS II IDE (FDA investigational device exemption) [30] was the second trial with Nanostim™ conducted across 3 countries (the USA, Canada, Australia), assessing clinical safety and efficacy. The pacemaker was implanted successfully in 504 out of the 526 participants (95.8%), 300 of which met the minimum follow-up of 6 months. The primary efficacy endpoint of an appropriate pacing capture threshold (≤ 2.0 V at 0.4 ms) and R-wave amplitude (R-wave ≥ 5.0 mV or equal or greater than the value at implantation) were met in 90% of patients (270 out of the 300). The primary safety endpoint (freedom from device-related serious adverse events at 6 months) was met at 93% (280 out of the 300 patients). Twenty-two serious adverse events occurred in 20 (6.7%) of the participants. These events included device dislodgement requiring percutaneous retrieval (1.7%), cardiac perforation (1.3%), pacing threshold elevation requiring replacement (1.3%), and vascular complications (1.3%). Device dislodgement occurred 4 times to the pulmonary artery and twice to the right femoral vein, irrespective of implantation site. However, in total, these results were again favorable as patients saw an improved mean R-wave amplitude from 7.8 ± 2.9 to 9.2 ± 2.9 ($p < 0.01$), increased ventricular pacing, and pacing capture threshold at 0.4 milliseconds (ms) decreased from 0.82 ± 0.69 V to 0.58 ± 0.31 V ($p < 0.01$) at 1-year follow-up [30].

The LEADLESS Observational Study was a post-marketing trial conducted primarily in Europe, evaluating the short- and long-term safety of Nanostim™ in the real-world setting [31]. The primary endpoint of this study was an evaluation of safety as freedom from serious adverse device events (SADE) at 180 days in 300 subjects. Incidents of cardiac perforation resulting in death occurred in 2 out of the 131 initial implants, leading to trial suspension in April 2014. An analysis of events identified a learning curve with device deployment; therefore, additional training and updated protocols were instituted. The trial was resumed after these protocol changes; the subsequent freedom from SADE was 94.6%. A total of 18 SADE occurred in 16 patients; the majority of these events (88.9%) occurred within 30 days of implantation. There

were 8 cardiac perforations, 1 device dislodgement to the right pulmonary artery, and 2 vascular complications. Similar to previous trials, pacing capture thresholds of Nanostim™ were consistent with traditional pacemakers at 6 months. However, in October 2016, St. Jude Medical issued a stop advisory, and implants were halted worldwide after reports of battery failures resulting in loss of pacing output and communications. After the LEADLESS observational trial's conclusion date, 19 battery failures were reported [31]. These concerns prompted the replacement of 1423 Nanostim™ devices with either a transvenous pacemaker or Micra™ device. Of all the implanted devices worldwide, 34 battery failures (2.4%) were identified (Europe = 30, USA = 3, and Australia = 1), occurring at an average of 3 years. Analysis of the retrieved device indicated reduced electrolyte within the lithium-carbon monofluoride battery, causing increased battery resistance and loss of adequate current for device functionality [32]. Moreover, an observational single-center study consisting of 14 patients with a mean follow-up of 33.3 months reported an alarmingly high incidence of battery failure at 40% after 3 years [33]. The increased percentage of failure in this study was likely because of the longer follow-up in these patients compared to the initial trials as battery failure was time-dependent. Currently, Abbott has pivoted away from Nanostim™ to a new ventricular device called Aveir™ leadless pacemaker system. Safety and efficacy will be evaluated in the LEADLESS II IDE study (phase II), which is currently ongoing [34].

Micra™ TPS

Preclinical trials with Micra™ in animals demonstrated performance and safety similar to transvenous pacemakers [35] with accurate measurement of pacing thresholds and R-wave amplitudes [36]. The Micra TPS IDE study [37] was the first-in-man trial evaluating short- (6 months) and long-term performance (1 year) and safety of Micra™ TPS at 70 centers worldwide. The primary safety endpoint was freedom from system-related or procedure-related major complications. The primary efficacy endpoint was defined as pacing capture threshold of ≤ 2 V at 0.24 ms at 6 months, without an increase by more than 1.5 V from implantation time [38]. The device was successfully placed in 719 of 725 participants (99.2%). Both safety and efficacy endpoints were met as adverse events occurred in only 4% of participants, and pacing capture thresholds were met in 98.3% of participants. At 6 months, 28 major complications occurred in 25 patients. Notably, no device dislodgements occurred, and the major complications observed included cardiac per-

forations (1.5%), vascular complications (0.7%), venous thromboembolism (0.3%), and increased pacing thresholds (0.3%). Moreover, a post hoc analysis comparing these 725 patients to 2,667 patients receiving transvenous pacemakers showed a reduced risk of major complications (4.0% vs. 7.4%; HR, 0.49; 95% CI, 0.33–0.75, $p = 0.001$) [37]. At 1-year follow-up, these results were stable as freedom from the complication rate was again 96%, and the efficacy endpoint was met in 93% of participants [39]. Micra™ TPS obtained CE approval in 2015 and subsequently FDA approval in 2016. The initial real-world outcomes of Micra™ were reported by the Micra TPS Post-Approval Registry consisting of 795 participants. The incidence of device-related complications was lower than reported in the Micra TPS IDE trial (2.89%) as the 30-day major complication rate was only 1.51%. Furthermore, the device was successfully placed in 792 of 795 (99.6%) participants. Pacing capture thresholds were also maintained at 97%, consistent with results from the Micra TPS IDE trial [40]. Currently, the largest prospective study Micra CED is ongoing, consisting of a Medicare beneficiary population with an estimated to enrollment of 37,000 participants with a 2-year follow-up [41].

Leadless AV Synchronization

By virtue of the safety and efficacy of Micra™ TPS demonstrated in clinical trials, interest in expanding device capabilities emerged since VVI pacemakers only encompassed 14% of total pacemaker implantations [42]. Dual-chamber pacemakers providing AV synchrony have been shown to decrease pacemaker syndrome, improve stroke volume, and positively influence functional status and quality of life in patients with an AV block [43–45]. Therefore, 3 clinical trials, MASS, MASS II, and MARVEL, were conducted to evaluate the feasibility of an innovative AV synchronous algorithm downloaded into an implanted Micra™ device incorporating ventricularly paced, dual-chamber sensed (VDD) pacing capabilities [46]. In the MASS and MASS II studies, intracardiac accelerometer signals were obtained from the implanted Micra™, which sensed atrial contraction during various patient activities to create a sensing algorithm. This algorithm was based on 3-axis accelerometer signals collected from 4 distinct segments of the cardiac cycle corresponding to isovolumic contraction and mitral/tricuspid valve closure (A1), aortic/pulmonic valve closure (A2), passive ventricular filling (A3), and atrial contraction (A4). Blanking windows in the system rejected signals that were

ventricular in origin (A1, A2), isolating atrial signals. Atrial contraction was detected when the filtered and rectified accelerometer signal exceeded a programmed threshold. The algorithm also incorporated a smoothing feature that maintained AV synchronous pacing during diminished A4 sensing, such as during patient activity [46].

The MARVEL study assessed the feasibility of the algorithm developed in MASS/MASS II studies by downloading the algorithm into patients' implanted Micra™ device for AV synchronous pacing [46]. This study demonstrated that AV synchronous pacing with the algorithm was feasible in tracking atrial contractions. The average synchronous pacing during algorithm application was 87% (95% CI; 81.8–90.9%). In patients with a high-grade AV block, the algorithm improved the AV synchrony percentage from 37.5% to 80% ($p < 0.001$) compared to VVI pacing. Furthermore, left ventricular outflow velocity measured by echocardiography was significantly higher with the algorithm compared to VVI pacing (23.9 vs. 21.8 cm, $p = 0.004$). Holter monitor data from study participants revealed no pauses, pacemaker-mediated tachycardia during algorithm pacing, or adverse events related to the device or algorithm [46]. The MARVEL 2 study built upon previous results as it implemented a similar downloadable accelerometer-based algorithm for VDD pacing with enhanced features, including automated programming and mode switching algorithms that could accommodate changes in the patient rhythm and activity [47]. This study enrolled 75 participants from 12 centers worldwide who were implanted with Micra™ and had the algorithm downloaded [47]. Similar to MARVEL I, the majority of participants completed the study procedures during a single visit. The algorithm was downloaded into the patient's device at these visits, and a specialized Holter monitor capable of storing accelerometer waveforms, device markers, and electrocardiogram data was placed. Information was then collected during VVI and VDD pacing, with the participants assuming various positions and walking velocities. Results were promising as the percentage of AV synchronous pacing increased from an average of 26.8% during VVI pacing to 89.2% during VDD pacing. 38 out of 40 (95%) patients had greater than 70% AV synchrony during algorithm-mediated VDD pacing compared to 0 out of 40 with VVI pacing ($p < 0.001$). AV synchrony was 89.2% at rest and 69.8% while standing [47]. Left ventricular outflow velocity measured by echocardiography was significantly increased by 1.7 cm during VDD pacing from a baseline average of 22.7 cm during VVI pacing ($p = 0.002$). Safety

was similar to MARVEL I as no pauses, episodes of oversensing induced tachycardia, or adverse events related to the algorithm were reported during VDD pacing [47]. The enhanced algorithm proved to be superior to the initial algorithm used in MARVEL I. A key limitation in these studies was the short observation periods used as the majority of procedures were completed during a single appointment, which may not accurately reflect real-world variability. Following this study, the Micra™ AV received FDA approval in January 2020.

Leadless Pacemaker with Subcutaneous Implantable Cardioverter-Defibrillator

Although leadless pacemakers were safe and effective, they lacked defibrillation capabilities, limiting their utility in many patients. Therefore, the concept for a leadless pacemaker with a subcutaneous implantable cardioverter-defibrillator (S-ICD) was explored [48]. The S-ICD system was first introduced in 2008 and consisted of a 3-mm tripolar electrode connected to an electrically active pulse generator. The electrode is positioned 1–2 cm left and parallel to the sternal midline. Its distal end is positioned adjacent to the manubriosternal junction, and the proximal sensing electrode is positioned adjacent to the xiphoid process. The pulse generator is placed over the sixth rib between the anterior and midaxillary lines. The electrode contained an 8-cm shocking coil and 2 sensing electrodes. During operation, the cardiac rhythm is detected by the sensing electrodes and the pulse generator. The system uses feature analysis and rate detection to categorize rhythm types and determine the need for defibrillation, delivered at 80 joules. This device is implanted without fluoroscopy as only anatomical landmarks are needed to guide interventionalists [49]. After demonstrating tremendous efficacy and safety for ventricular tachycardia and fibrillation [50, 51], the Boston Scientific S-ICD (EMBLEM) received CE approval in 2009 and FDA approval in 2012.

Preclinical studies with a combination system, including an S-ICD and leadless VVI pacemaker in an ovine model, demonstrated successful intrabody communication applying galvanic coupling for anti-tachycardia pacing during stimulated ventricular tachycardia [48]. A larger preclinical study assessed the acute and 3-month performance of a similar system in 3 animal models (8 ovines, 5 porcine, and 27 canines). The S-ICD device used was based on the EMBLEM with updated firmware enabling communication with a leadless pacemaker called

EMPOWER, both devices from Boston Scientific. Both devices were successfully implanted in 98% of the animals, and the pacemaker exhibited appropriate VVI functionality at the 3-month follow-up. Unidirectional communication between the devices was successful in 99% of attempts, resulting in 100% anti-tachyarrhythmia pacing delivery by the system. Furthermore, pacing did not negatively impact S-ICD sensing of cardiac rhythms at rest or during simulated ventricular arrhythmias [52]. Interestingly, a novel treatment strategy called modular cardiac rhythm management allows this system to be personalized for specific clinical indications. Both component devices do not need to be simultaneously implanted; if a patient only requires defibrillation, only the S-ICD can be implanted. The leadless pacemaker can then be added in the future if the patient requires pacing for bradycardia in addition to their defibrillator or vice versa. Currently, only animal studies with this system have been completed. However, the first-in-man trials are anticipated to commence in the near future [53].

Leadless Cardiac Resynchronization Therapy

Cardiac resynchronization therapy (CRT) devices have been shown to improve mortality and quality of life in patients with heart failure with reduced ejection fraction and prolonged intraventricular conduction [54–56]. However, about 30–45% of patients eligible for these devices remain untreated because of unresponsiveness to treatment or anatomical constraints with the coronary sinus lead [57–60]. EBR systems manufactured the Wireless Cardiac Stimulation System (WiCS-LV)™, which utilized transcutaneous ultrasound energy to communicate with a leadless left ventricular pacer to overcome these deficiencies. The concept for this device proved to be safe and feasible in preclinical studies [61–63]. The WiCS-LV™ system functions in harmony with a co-implanted transvenous single or biventricular pacemaker (Fig. 2). The system provides wireless pacing by transmitting acoustic ultrasound energy from a pulse transmitter implanted subcutaneously over the ribcage to an implanted receiver electrode in the LV. The LV electrode converts the acoustic energy into an electrical pacing pulse. Biventricular synchrony is accomplished by sensing pacing signals from the co-implanted right ventricular leads and immediately transmitting acoustic energy to the LV electrode [63]. Currently, the device is implanted in a 2-step process carried out on 2 consecutive days. First, the pulse transmitter is surgically implanted subcutaneously in the

Fig. 2. Communication of the WiSE-CRT system. Illustration of the communication sequence for the WiSE-CRT device. The co-implanted transvenous pacemaker transmits a wired pacing signal to the right ventricle (#1) detected by the subcutaneous pulse generator (#2). The subcutaneous pulse generator transmits the signal via ultrasound energy to the left ventricular electrode (#3), resulting in left ventricular pacing (#4).

4th to 6th intercostal spaces lateral to the left parasternal border to deliver unimpeded acoustic signals. Second, a balloon-tipped delivery sheath containing the electrode is introduced by femoral access and advanced into the LV under fluoroscopic guidance, where the electrode is implanted. The system requires a lung- and bone-free acoustic line of sight to communicate optimally [64, 65].

The initial trials with this system were the WiSE-CRT [66] and the SELECT-LV [65] studies, consisting of patients unable to undergo implantation with conventional CRT devices. The WiSE-CRT study was temporarily sus-

pending after 3 out of the initial 17 (18%) implantations resulted in pericardial effusions. After review, these adverse events were noted to be caused by the catheter's delivery sheath rather than the device anchor. However, the device proved to be technologically feasible as biventricular pacing was successful in 83% of patients at 1 month and 92% at 6 months, with shorter QRS duration and improved ejection fraction in these patients [66]. Since pericardial effusions were a device limitation, the SELECT-LV study featured an upgraded version of the WiCS-LV™, now called WiSE-CRT™ which utilized a redesigned

delivery system [65]. The distal portion of the delivery sheath was now equipped with a balloon to facilitate atraumatic engagement with the LV endocardium, which results in zero instances of pericardial effusions in the 35 participants. The primary performance endpoint of biventricular pacing on a 12-lead electrocardiogram was met in 97.1% (33 of 34) of participants at 1 month and 93.9% (31 of 33) at 6 months. Although no pericardial effusions occurred, adverse events related to the device or procedure occurred in 3 participants within 24 h and 8 patients after 1 month. Notably, there was 1 occurrence of catheter-induced ventricular fibrillation, resulting in death and 2 occurrences of infections related to the subcutaneous pulse generator. In 1 patient, the LV electrode embolized to the left tibial artery [65]. Nonetheless, WiSE-CRT™ received CE approval after this trial. Furthermore, data from the WiSE-CRT post-market surveillance registry [67] in Europe redemonstrated the technical feasibility of the device as biventricular pacing was confirmed in 94.4% (85 of 90) of patients, and 70% had improvement in heart failure symptoms. However, the complication rate was still concerning as 4.4% experienced complications in less than 24 h, 18.8% had complications at the 30-day follow-up, 6.7% had complications in the 1–6-month follow-up period, and 5 deaths were reported [67]. Currently, the SOLVE-CRT trial is ongoing; this is a multicenter (the USA, Europe, and Australia), randomized, double-blinded, sham-controlled trial of patients who failed or did not respond to conventional CRT with the intent to enroll 350 participants. All participants will be implanted with the WiSE-CRT™ and randomized to have the device active or turned off to evaluate the safety and performance of the device for CRT [68].

Recently, innovations have been made toward creating a totally leadless CRT system incorporating the WiSE-CRT™ and Micra™ TPS devices, which was described in two published case reports [69, 70]. The implantation procedure for each device is similar to previously described, as both devices are implanted individually. The subcutaneous pulse transmitter from the WiSE-CRT system can synchronize with the RV pacing pulse from the Micra™ TPS and deliver a corresponding acoustic signal to the LV electrode, generating an electrical pulse within 2 ms [71]. In a 2020 observational study at 6 centers in Europe, 8 patients co-implanted with Micra™ TPS and WiSE-CRT™ for CRT were assessed to demonstrate technical feasibility and safety [71]. Implantation was successful in all 8 participants without failed attempts. Seven of the 8 participants reached the 6-month follow-up; one

death occurred 4 months post-implant due to acute heart failure. Investigators noted a significant acute reduction of the QRS duration on electrocardiogram from 204.38 ± 30.26 ms to 137.5 ± 24.75 ms ($p = 0.0012$), which was consistent at 6-month follow-up. LV ejection fraction improved post-implant by $11.29\% \pm 8.46$, $p = 0.018$). However, there was no evidence of LV reverse remodeling and nonsignificant variations in LV end-systolic and diastolic volumes [71]. This study demonstrated that both devices could successfully operate in unison to deliver CRT. However, larger prospective clinical trials are needed to represent the safety and efficacy of this system accurately. Moreover, the first case successfully implanting three co-existing systems, Micra™ TPS, WiSE-CRT™, and Emblem S-ICD, in 1 patient for CRT with defibrillation was recently published [72]. Although technically challenging, this case demonstrated the future possibilities with technological advances and additional device miniaturization. Furthermore, the combination of WiSE-CRT™ with the newly innovated Micra™ AV could be a future prospect with the ability to provide VDD pacing in conjunction with CRT.

Leadless Pacemaker Retrieval

Retrieval Techniques

Although leadless pacemakers have shown promising results in clinical trials, device retrieval at the end of service, especially with chronically implanted devices, has been an area of concern. Both Nanostim™ and Micra™ are designed with unique retrieval mechanisms at their proximal ends (Fig. 1). The Nanostim™ retrieval mechanism is in the form of a docking button on its proximal end. Retrieval is facilitated with the use of an 18-French catheter with a snare of various diameters. The snare is attached to the docking button, and the protective sleeve from the catheter is advanced halfway over the device. After coaxial alignment is confirmed, the retrieval catheter is rotated counterclockwise to unscrew the device from the endocardial tissue [73].

Retrieval of Micra™ can be performed using two approaches, utilizing either the Micra™ delivery catheter (27-French) or steerable sheath. Snares of different sizes (7–10 mm) and shapes (single or multiple loops) are used. Both approaches begin with advancing the delivery catheter or steerable sheath to the proximal retrieval end of the device. For the first approach, the single or triple loop snare is inserted through the central lumen of the device, and the snare is deployed around the proximal retrieval

feature. Tension to the snare and counter traction from the cup release the tines from the endocardial tissue, and the device is withdrawn. However, engagement of the proximal retrieval feature of Micra™ is challenging. This is circumvented by the more adaptable steerable sheath used in the second approach, which allows for superior coaxial alignment. In this approach, a large caliber short sheath (11–16 French) is inserted into the Micra™ introducer sheath, preventing back bleeding. After the short sheath is inserted, the steerable sheath (8.5 French) is inserted into the large introducer sheath and advanced to the device. Next, a single or triple loop snare is advanced using the steerable sheath to engage the proximal retrieval feature, and traction is applied, straightening the tines and detaching the device [74, 75].

Clinical Safety

A small multicenter study including 16 patients implanted with Nanostim™ assessed the feasibility of short-term retrieval at less than 6 weeks and long-term retrieval at greater than 6 weeks. The investigators noted a 100% success rate in the short-term and a 91% long-term, without any procedure-related complications [76]. Moreover, after St Jude Medical issued a worldwide alert of battery malfunctions occurring with Nanostim™, Lakkireddy et al. [32] sought to retrieve 73 implanted devices. A total of 66 out of those devices were successfully retrieved (90.4%), which had been implanted from 0.2 to 4 years. They noted that the docking button of the device was inaccessible in 6 patients, and it had detached in 1 patient. No severe complications occurred after device retrieval; however, there were two instances of tricuspid valve damage [32]. Furthermore, long-term retrieval of Nanostim™ in 34 patients with an average implantation duration of $1,570 \pm 479$ days was evaluated in a single-center study. The retrieval success rate was 85%, with no procedure-related complications. The investigators noted that the retrieval success rate was significantly higher in patients with a more remarkable swinging movement of the docking button on fluoroscopic visualization compared to those without significant swinging. Consistent with previous studies, the docking button was not engageable in 5 patients as it was trapped by the surrounding tissue [77]. Early retrieval of Micra™ has been shown to be safe and feasible [74]; however, there is a paucity of data regarding long-term retrieval. Dar et al. [75] retrospectively compared the safety and efficacy of Nanostim™ and Micra™ retrieval. This study included 73 Nanostim™ and 40 Micra™ retrievals, with a median extraction time of 256 days and 46 days, respectively. The retrieval success rate for

Nanostim™ was 90% and 100% for Micra™. When comparing the devices, the higher success rate with Micra™ retrieval was attributed to the simple disengagement techniques, without reliance on the engagement of a proximal retrieval feature as seen with Nanostim™ [75].

Conclusion

Leadless pacemakers have emerged as a revolutionary innovation to mitigate the complications seen with transvenous pacemakers. Currently, Micra™ TPS or AV with VVI or VDD functionality is the sole leadless pacemakers approved for commercial use worldwide. Although this device has been promising, to date, there have been no randomized trials comparing leadless pacemakers to single chamber transvenous pacemakers. According to the recent 2021 European Society of Cardiology guidelines on cardiac pacing and CRT, leadless pacing should be considered as an alternative to standard transvenous pacemakers when there is an obstruction of the venous route used for standard pacemaker implantation or when the risk for device pocket infection is increased, such as in patients with previous pocket infections or those on hemodialysis [78].

Moreover, a leadless pacemaker with S-ICD system, implementing the novel modular cardiac rhythm management concept, demonstrated excellent feasibility in animal models; human studies are planned to start in the near future. Moreover, the WiSE-CRT™ provides a solution for patients unable to receive CRT due to coronary sinus anatomical constraints. However, this system is still prone to device- and lead-related complications. Therefore, data from ongoing trials will be imperative in establishing this new technology. With this device comes the prospect of a total leadless CRT system when combined with Micra™, which could usher in the new era in cardiac pacing. This combination system has shown efficacy in small studies; however, future trials assessing clinical safety and efficacy of this new system are needed.

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Statement of Ethics

Does not apply.

Conflict of Interest Statement

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