Miniaturized Leadless Cardiac Pacemakers — Can They Overcome the Problems With Transvenous Pacing Systems? —

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Cardiac pacemakers are among the most successful implantable medical devices and the only treatment for bradyarrhythmias. Despite remarkable progress achieved in the function, longevity and physical characteristics since the first implantation of a pacing system in 1958, several aspects of conventional pacing remain unresolved. The transvenous (TV) leads, in particular, remain the most

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vulnerable component of conventional systems. In the perioperative period, the creation of a pneumothorax is a relatively common complication of the subclavian vein puncture needed to introduce the leads into the cardiac

Table. Characteristics of the Leadless Pacemaker Systems

	Nanostim™ leadless cardiac pacemaker	Micra™ transcatheter pacing system
Manufacturer	St. Jude Medical	Medtronic Inc.
Volume, cm ³	1.0	0.8
Weight, g	2.0	2.0
Pacing mode (sensor)	VVI/VVIR (temperature)	VVI/VVIR (accelerometer)
Fixation mechanism	Screw-in helix	Nitinol tines
Battery longevity, years		
Nominal setting: 60 ppm, 500 Ω, 100% pacing	14.7	9.6
ISO standard: 60 ppm, 600 Ω, 2.5 V/0.4 ms, 100% pacing	9.8	4.7
Pivotal studies	LEADLESS II ^a	Micra Transcatheter pacing system ^a
Study participants, n (%)		
All	526 (100) candidates for permanent VVI pacing	725 (100) candidates for class I or II guideline-based pacing indications
Nationality	Asians: n=10 (1.9)	Japanese: n=38 (5.2)
Control (transvenous pacing studies)		
Safety endpoint	Two studies of 1,660 patients	Five studies of 2,667 patients
Efficacy endpoint	One ongoing study	—
Outcome		
Efficacy	Acceptable pacing threshold and sensing amplitude	Percentage of patients with low and stable pacing capture thresholds
Safety	Freedom from major device-related adverse events	Freedom from major system- or procedure-related complications
Follow-up duration, months	6	6
Results		
Implantation success rate, %	95.8	99.2
Efficacy endpoint, % (95% CI); P value	90.0 (86.0–93.2); P=0.007	98.3% (96.1–99.5); P<0.001
Safety endpoint, % (95% CI); P value	93.3 (89.9–95.9); P<0.001	96.0% (93.9–97.3); P<0.001

CI, confidence interval; ISO, International Organization for Standardization.

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chambers.¹ Shortly after their implantation, leads may dislodge, despite the presence of fixation devices, or perforate the myocardial wall.² Adverse events that may occur in the longer term include lead fractures or infections, insulation breakdown, venous obstructions and tricuspid regurgitation.^{3,4}

The implantation of the pulse generator in a subcutaneous pectoral pocket is another weakness of conventional TV systems, because of complications with pain, limitation of shoulder motion, hematoma, erosion, infection and cosmetic dissatisfaction.^{5,6} It is particularly noteworthy that an infection of the pacing system often requires its total extraction.⁷

Leadless transcatheter pacing (TCP) was conceived over 40 years ago, in the hope of eliminating the complications associated with TV leads, but was initially impractical. Progress in battery technology and innovations in electrical integrated circuits have increased the longevity of the devices, and enabled the introduction of two bipolar, single-chamber, ventricular, rate-responsive, leadless pacing systems into clinical practice. Their efficacy and safety, including success and complication rates of the implant procedures and electrical stability of the systems, have been studied worldwide (Table).^{8,9} In this issue of the Journal, Soejima et al¹⁰ report the results of their study of differences between Japanese patients and patients from other regions of the world for use of cardiac pacemakers. Despite the smaller body dimensions of Asian patients, they found no differences in the rates of major complications or in the electrical pacing characteristics of the 2 study groups. Body size is one determinant of the strategic choice of pacemaker, because a low body mass index increases the risk of postprocedural complications associated with TV lead systems.¹¹ Despite the absence of significant differences in the rates of major complications between Japanese patients and those from other countries, the benefit conferred by TCP compared with conventional TV pacing systems might be greater for Japanese.¹

It is, however, uncertain, whether TCP will be equally accepted by Japanese and non-Japanese patients. International differences have been observed in the implantation rates of new pacing systems. In a worldwide survey, the implantation rate of new pacemakers was 927 per million populations in Germany, 767 per million in the United States, and a much lower 277 per million in Japan.¹² These regional differences in pacemaker implantation rates have been attributed to differences in (a) reimbursement schedules, (b) indications for pacemaker implantation for bradyarrhythmias, and (c) cultural acceptance of device implantations.¹³ One of the most noteworthy observations made by Soejima et al is a significantly lower satisfaction expressed in the recovery phase by Japanese patients, in contrast to the Japanese physicians who were similarly satisfied with the TCP implantation as physicians from other countries.¹⁰ The authors hypothesize that the Japanese patients' dissatisfaction was related to minor complications, such as congestive heart failure or worsening of atrial fibrillation. The prevalence of congestive heart failure was higher and the pacing indications associated with atrial fibrillation were fewer among the Japanese than among the patients from other countries. The reasons for the negative response expressed by the Japanese patients remain, nevertheless, unclear because detailed information regarding these minor complications of TCP are lacking for non-Japanese patients, and because of a relatively shorter follow-up. The incidence

of minor complications and a longer follow-up are needed to clarify the cause of dissatisfaction in Japanese patients.

TVP has several advantages compared with first-generation of TCP systems, namely, capability of physiological atrioventricular and biventricular pacing, reliable long-term function, including battery longevity, advanced operations such as measurements of thoracic impedance to monitor heart failure and respiratory disorders, and a higher rate-adaptive sensor technology.^{14,15} Leadless pacing is, nevertheless, promising, on a road oriented in the direction of multisite stimulation combined with defibrillation. However, its clinical applications should be cautiously selected on a case-by-case basis, especially in patients presenting with congestive heart failure or pacing indications unrelated to atrial fibrillation, such as sinus node disease or atrioventricular block because, for the time being, it remains a single-chamber, non-physiological device.

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