

Retrieval of the Leadless Cardiac Pacemaker A Multicenter Experience

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Background—Leadless cardiac pacemakers have emerged as a safe and effective alternative to conventional transvenous single-chamber ventricular pacemakers. Herein, we report a multicenter experience on the feasibility and safety of acute retrieval (<6 weeks) and chronic retrieval (>6 weeks) of the leadless cardiac pacemaker in humans.

Methods and Results—This study included patients enrolled in 3 multicenter trials, who received a leadless cardiac pacemaker implant and who subsequently underwent a device removal attempt. The overall leadless pacemaker retrieval success rate was 94%: for patients whose leadless cardiac pacemaker had been implanted for <6 weeks (acute retrieval cohort), complete retrieval was achieved in 100% (n=5/5); for those implanted for ≥ 6 weeks (chronic retrieval cohort), retrieval was achieved in 91% (n=10/11) of patients. The mean duration of time from implant to retrieval attempt was 346 days (range, 88–1188 days) in the chronic retrieval cohort, and nearly two thirds (n=7; 63%) had been implanted for >6 months before the retrieval attempt. There were no procedure-related adverse events at 30 days post retrieval procedure.

Conclusions—This multicenter experience demonstrated the feasibility and safety of retrieving a chronically implanted single-chamber (right ventricle) active fixation leadless pacemaker.

Clinical Trial Registration—URL: <https://www.clinicaltrials.gov>. Unique identifiers: NCT02051972, NCT02030418, and NCT01700244.

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Key Words: device removal ■ heart ventricles ■ humans ■ pacemaker, artificial ■ prostheses and implants

Leadless cardiac pacemakers (LPs) have emerged as a safe and effective alternative to conventional transvenous pacemakers for patients with an indication for single-chamber ventricular pacing. In 2 prospective studies with intermediate follow-up, leadless pacemakers exhibited high acute implantation success rates and stable pacing performance at 6 months.^{1,2} Despite these promising results, the ability to retrieve a chronically implanted leadless pacemaker is an important component of leadless pacemaker management. Instances where removal of a chronically implanted leadless pacemaker may be desirable, or even necessary, include elevations in pacing threshold, reductions in sensing amplitude, development of right ventricular pacing-mediated cardiomyopathy, infection (albeit, none were seen in the trials), and at the end of battery life. Although the feasibility of retrieval of leadless pacemakers has been demonstrated in animal models up to two and a half years, there are no systematic reports of the safety and feasibility of this approach in humans.³ Herein,

we report the results of the acute retrieval (<6 weeks) and chronic retrieval (>6 weeks) of the Nanostim LP in patients who underwent device implantation as part of 3 prospective multicenter trials.

Methods

This analysis included patients who were implanted with a right ventricular active fixation LP (Nanostim; St. Jude Medical) within 3 multicenter clinical trials (www.clinicaltrials.gov, NCT02051972, NCT02030418, and NCT01700244) conducted in Europe, United States, Canada, and Australia and who subsequently underwent a device removal attempt. The local institutional review board for each participating center approved the study, and the subjects gave informed consent. The inclusion criteria and implant technique of the LP have been previously described.⁴ The presence of any serious adverse device effects up to 30 days after device retrieval was documented.

Because it takes ≈6 weeks to develop a fibrous capsule at the lead–tissue interface of steroid-eluting leads, acute retrieval has traditionally been defined as a device implanted for <6 weeks and chronic retrieval if it had been implanted for ≥6 weeks; accordingly, these

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WHAT IS KNOWN

- Two prospective studies have demonstrated that LPs are a safe and effective alternative to conventional transvenous pacemakers for patients with an indication for single-chamber ventricular pacing.
- The ability to retrieve a chronically implanted leadless pacemaker is an important component of leadless pacemaker management.

WHAT THE STUDY ADDS

- This multicenter experience demonstrated that retrieving a single-chamber (right ventricle) helix active fixation leadless pacemaker is feasible.
- The overall leadless pacemaker retrieval success rate was 94%, and there were no procedural related adverse events.
- Nearly one third of the chronic retrieval cohort (>6 weeks) had been implanted for >6 months before the retrieval attempt.

same definitions were used in this analysis.^{5,6} As previously described and shown in Figure 1, the LP retrieval catheter system is inserted via the femoral vein and includes a deflectable tip (>180°) with either a single-loop or triple-loop snare and an integrated protective sleeve.³ There are 3 separate mechanisms that control tip deflection, snare closure, and LP docking to the retrieval catheter. After introduction of the retrieval catheter through the 18F sheath, the system is advanced under fluoroscopic guidance to the junction of the inferior vena cava and right atrium. The protected sleeve is fully retracted exposing the deflectable retrieval catheter with snare. With the snare open, the snare is advanced into position behind the docking feature of the LP with a combination of catheter advancement, deflection of the distal tip, and rotation of the snare. Coaxial alignment of the snare with the docking feature is confirmed with multiplane fluoroscopy. As shown in Figure 2, the snare is closed and locked around the docking feature on the proximal end of the LP. After closing the snare, it is docked to the LP. The protective sleeve is advanced halfway over the LP to facilitate coaxial alignment of the retrieval catheter and the LP. The snare control handle is rotated counter clockwise to unscrew the leadless pacemaker from the endocardium (2 full rotations of the pacemaker, which is confirmed under fluoroscopic visualization of the radiopaque marker). The LP is then fully covered with the protective sleeve, and the system is withdrawn from the body as a single unit.

Statistical calculations were performed with the use of SAS software (SAS Institute). A clinical events committee adjudicated all clinical events. All continuous variables are presented as means±SDs.

Results

As of April 25, 2016, a total of 1197 patients were enrolled within the 3 multicenter trials. A total of 16 patients with a Nanostim LP underwent a retrieval attempt (acute=5 and chronic=11). The clinical characteristics of the 16 patients are shown in the Table. The mean ages of the acute and chronic retrieval cohorts were 73.4±15.8 and 78.2±11.0 years, respectively; the body mass indexes were 27.5±10.3 and 27.2±5.9 kg/m², respectively. More than half of the patients (n=3; 60%) in the acute group and a majority in the chronic retrieval group (n=9; 82%) were men. One patient in the acute and 2 patients in the chronic retrieval cohort had previous cardiac surgery. During the initial implant procedure, 40% (n=2)

of patients in the acute cohort and 54% (n=6) of patients in chronic cohort required ≥1 repositioning attempt to achieve the final pacemaker position.

The retrievals were performed by 9 different operators at 9 centers. The indication for attempted device removal in the acute retrieval patients was elevation in pacing threshold (n=4/5) and need for upgrade to a secondary prevention defibrillator (n=1/5). The indications for device removal in the chronic retrieval group included elevations in pacing threshold (n=4/11; 36%), a decline in left ventricular function and symptoms consistent with the right ventricular pacing cardiomyopathy in 5 of 11 (45%), failure to pace in 1 of 11 (9%), and patient preference in 1 of 11 (9%). The mean duration of time from implant to retrieval attempt was 6 days (range, 1–13 days; median, 6) in the acute cohort and 346 days (range, 88–1188 days; median, 220) in the chronic cohort. In the chronic cohort, nearly two thirds (n=7; 63%) had been implanted for >6 months before the retrieval attempt.

Procedural success, defined as complete retrieval of the leadless pacemaker, was achieved in 100% (n=5/5) of the patients whose device had been implanted for <6 weeks and 91% (n=10/11) of those implanted for ≥6 weeks; for the unsuccessful retrieval case, the implant duration had been 103 days. After attempted device retrieval, 3 of 4 patients of the acute group underwent reimplant of a new leadless pacemaker, 1 underwent implantation of a single-chamber defibrillator (as previously described), and 1 underwent implantation of a dual-chamber transvenous pacemaker.⁴ Of the 11 chronic retrieval patients, 4 underwent implantation of a new leadless pacemaker, 1 underwent implantation of a dual-chamber transvenous pacemaker, and 6 underwent implantation of a transvenous biventricular pacing system to treat left ventricular dysfunction and right ventricular pacing cardiomyopathy. During the unsuccessful retrieval attempt, the operators reported that the docking feature could not be engaged because of its position relative to the subvalvular apparatus (in this patient, the original LP was turned off and a new LP was implanted).

There were no procedure-related adverse events. However, 1 patient had prolongation of hospital course by 3 days after the LP retrieval. This patient, an 83-year-old man, whose device had been implanted for 208 days, was admitted for acute decompensated heart failure and underwent LP retrieval and reimplant of transvenous biventricular pacemaker (same day). The patient was discharged home 3 days later, after diuresis and optimization of medical therapy.

Although not formally quantified, visual inspection revealed fibrous material on either the proximal (docking knob) or the distal (helix) end in 10 of the chronic retrieval patients. However, in only 1 patient was there near-complete encapsulation of the device with a thin layer of fibrous tissue (Figure 3). The other 10 devices showed minimal adherent tissue on the body of the pacemaker. It should be noted that because these devices were withdrawn into a sheath, we cannot rule out the possibility that additional fibrous material adherent to the endocardium was deposited in the vascular system or remained undetected in the retrieval sheath. In addition, it should be noted that for all 16 successful retrieval cases, the device helix was intact after removal from the right ventricle.

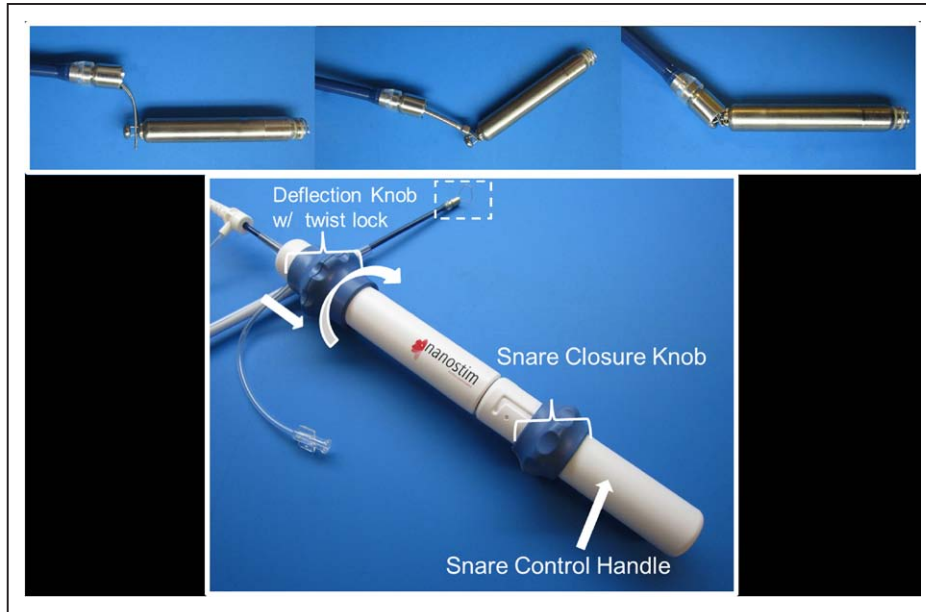


Figure 1. Leadless cardiac pacemaker retrieval catheter (**bottom**) and an example of a single-loop snare engaging and docking the pacemaker (**top**).

Discussion

This multicenter experience demonstrated that retrieving a single-chamber (right ventricle) helix active fixation leadless pacemaker is feasible. The overall leadless pacemaker retrieval success rate was 94% (acute=100%, chronic=91%). In 1 patient (implant duration of 103 days), retrieval was unsuccessful as the docking feature could not be engaged and a new leadless pacemaker was implanted. Of note, in a different patient undergoing device retrieval, a similar situation (ie, inability to engage the docking feature because of its proximity to the valvular apparatus) was encountered, but by introducing a steerable catheter via the contralateral groin, the docking feature of pacemaker was successfully manipulated away from the base of the tricuspid valve apparatus, allowing the snare to engage the pacemaker and the device to be successfully retrieved (Figure 4). It is reassuring that there were no procedure-related serious adverse events (at 30 days) although 1 patient did have a prolongation of hospitalization (3 days)

after LP retrieval (and upgrade to a transvenous biventricular pacemaker) because of acute heart failure symptoms requiring intravenous diuresis. Of the 16 patients included in this study, the mean duration from implant to retrieval was 240 days (range, 1–1188 days), and in nearly one third of these patients (n=5), the LP had been implanted for >1 year.

Given that 2 leadless pacemakers have been studied to date in clinical trials, one has already been approved as standard of care for single-chamber (right ventricular) pacing, and presumably, the other will also be similarly approved, the ability to retrieve these devices is clinically relevant. In our particular series of patients, the indications for device retrieval mirror similar indications for transvenous devices—such as elevations in pacing thresholds, changes in pacing performance, or the need to upgrade to a biventricular pacing system. Furthermore, unlike traditional transvenous pacemakers that usually require replacement of a subcutaneous pulse generator only when a battery reaches end-of-life, the leadless

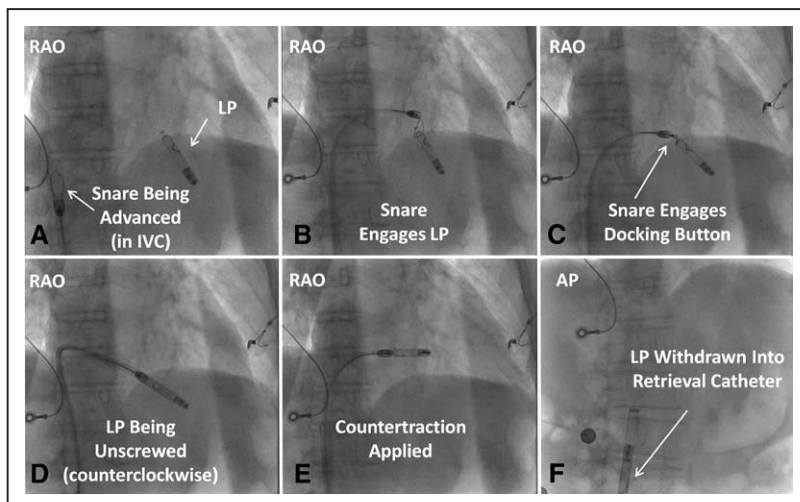


Figure 2. Fluoroscopic views of the leadless cardiac pacemaker (LP) retrieval procedure. **A**, The retrieval catheter and single-loop snare are advanced from the inferior vena cava (IVC) toward the right atrium. **B** and **C**, The snare grabs the leadless pacemaker and by closing the loop engages the docking button (after which the device is docked with retrieval catheter). **D** and **E**, Counterclockwise rotation followed by manual traction is applied to disengage the tip from the endocardium. **F**, The LP is withdrawn into the retrieval sheath. AP indicates anteroposterior; and RAO, right anterior oblique.

Table. Demographics and Procedural Characteristics (Initial Implant)

Variable	Acute (<6 wk; n=5)	Chronic (≥6 wk; n=11)
Age, y	73.4±15.8	78.2±11.0
Male, n (%)	3 (60)	8 (73)
BMI, kg/m ²	27.5±10.3	27.2±5.9
Hypertension, n (%)	3 (60)	9 (82)
Diabetes mellitus, n (%)	2 (40)	3 (27)
Chronic kidney disease, n (%)	1 (20)	0
Previous cardiac surgery, n (%)	1 (20)	2 (18)
Pacing threshold (at implant), V	3.1±1.9	1.5±1.6
Sensing (at implant), mV	5.2±1.6	7.8±3.8
Impedance (at implant), ohms	414±121	590±248
Reposition attempts (at implant)		
0	2	5
1	1	3
2	2	2
3	0	1
Indications for retrieval		
Elevation in pacing threshold	4	4
Decline in LVEF/CHF symptoms	0	5
Other	1	2
Implant duration of implanted LP, d, mean (range)	6 (1–13)	346 (88–1188)
Complete procedural success, n (%)	5 (100)	10 (91)
Adverse events	0	0
Reimplant procedure		
New leadless pacemaker	3	4
New single-chamber ICD	1	0
Transvenous dual-chamber pacing system	1	1
Transvenous biventricular pacing system	0	6

BMI indicates body mass index; CHF, congestive heart failure; ICD, implantable cardioverter-defibrillator; LP, leadless cardiac pacemaker; and LVEF, left ventricular ejection fraction

pacemaker presents a new set of device management challenges because the pacing electrodes and battery are a single component. In fact, management of these devices at end-of-life remains an unsettled concern with leadless cardiac pacemakers.⁷ Some have suggested that the small form factor of leadless pacemakers (≈1-mL displacement) lends itself to a strategy of simply abandoning the old device and placing an additional leadless pacemaker. The average age of patients in the Leadless II study (75.6 years) and the projected battery longevity make it likely that this approach would be applicable to a substantial number of patients. However, this may

be less practical in younger patients or those with smaller ventricular chambers. Also, and although not seen in any of the prospective studies, there remains the possibility of a leadless pacemaker infection that may require device removal to achieve bloodstream clearance.

It should be noted that the 2 clinically available leadless pacemakers differ significantly in their fixation mechanisms and available retrieval tools.⁸ The Nanostim leadless cardiac pacemaker described in this article has a helical fixation mechanism and a retrieval catheter with an integrated snare system. The manufacturer does, however, recommend caution for removal of a Nanostim device implanted for >2.3 years. Our data would suggest that removing a device that has been implanted longer (in 1 case, even 3 years) is feasible. Furthermore, using an *in vivo* ovine model, we recently reported that in a series of 18 animals with chronically implanted Nanostim devices (ranging in implant duration from 5 months to 2.5 years), all devices were successfully retrieved.³ Although encouraging, it is clear that additional confirmatory experience in a larger cohort of patients is necessary before concluding that all Nanostim devices can be extracted, and additional trial and registry data would be expected to further elucidate the safety and efficacy of retrieving chronically implanted leadless pacemakers. Furthermore, there is only limited experience (n=1) that would inform our understanding of the ability to retrieve LPs beyond 3 years—which would be most relevant for device end-of-service management.

When compared with transvenous lead extraction, removal of a leadless pacemaker has the potential to reduce some risks associated with the procedure. For example, although cardiac avulsion/tear is an everpresent concern with removal of any implantable cardiac device, there should be no significant risk of vascular tear (eg, superior vena cava) with removal of a leadless pacemaker. Furthermore, unlike transvenous leads that have multiple sites of fibrous binding that negatively impact the ability to exert countertraction on the tip of the lead, there is inherently less surface area to which the LP can bind.⁹ It is also advantageous that the distal hub of the Nanostim retrieval catheter is designed to lock into the docking port of the leadless pacemaker; this allows for the significant transmission of torque to the pacemaker when the retrieval catheter is rotated. This was evidenced clinically by the observation that the helix on the Nanostim devices was largely intact.

Limitations

Although this represents the largest series of patients who have undergone retrieval of a leadless pacemaker, and the retrieval efficacy compares favorably to transvenous retrieval studies, the overall number of patients studied (n=16) remains small.¹⁰ We have only reported on 1 type of leadless pacemaker (helix screw-in fixation), and the results should not be considered relevant to other types of leadless pacemakers. Furthermore, although the operators in this series did not have experience with leadless retrieval in humans, they did have experience with leadless pacemaker implantation techniques and tools, and some had previous experience with retrieval of the device in animal models. Although the

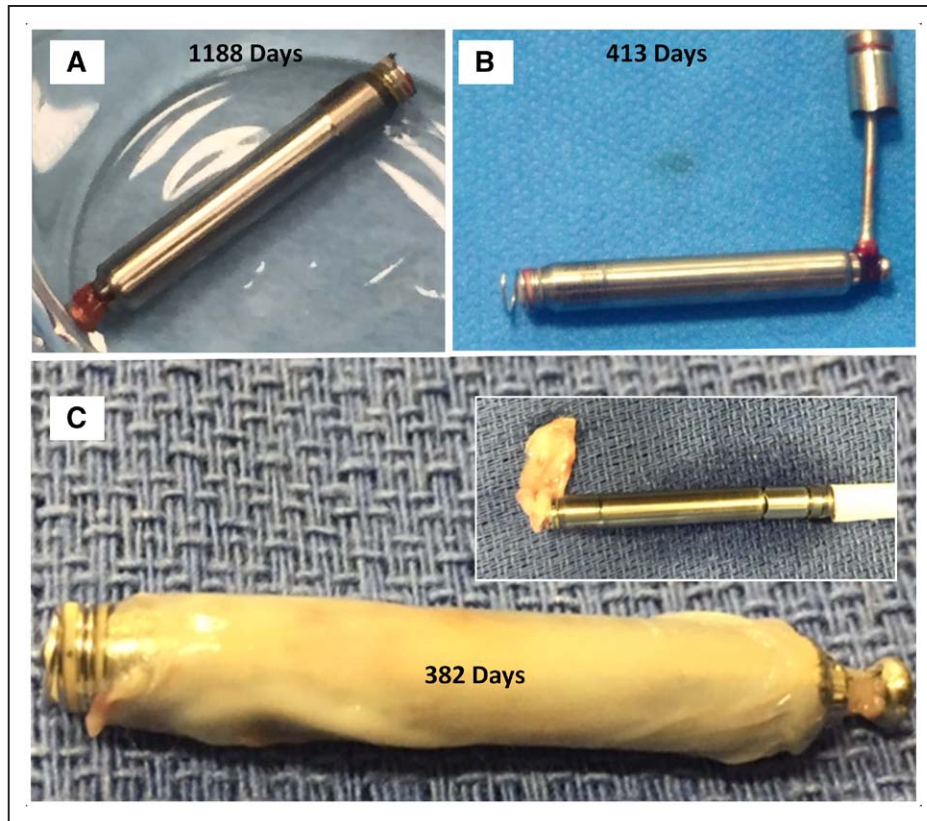


Figure 3. **A** and **B**, Examples of extracted leadless pacemakers demonstrating fibrosis on the docking button at 1188 and 413 d, respectively. **C**, An example of an extracted leadless pacemaker with near-encapsulation at 382 d. On first inspection, the fibrous capsule was attached to the distal end of the leadless pacemaker (inset) and was then placed back over the leadless pacemaker for illustrative purposes.

devices had been implanted for more than a year in one third of patients, it is not known whether results would be similar for longer duration implants—which would be relevant for understanding the feasibility and safety of performing the

retrieval procedure once the battery has reached the end-of-life. Whereas available evidence indicates that fibrosis has developed at the device–tissue interface by 6 weeks, the time course and degree of encapsulation for leadless pacemakers remains unknown. It remains to be seen whether the success of retrieving chronically implanted devices would remain consistent, for devices implanted beyond the time points included in this study, because additional fibrosis could occur over longer periods of time. It is plausible that as leadless pacemakers evolve and more devices are implanted, additional tools and training will be developed to safely and effectively retrieve these devices.¹¹

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Disclosures

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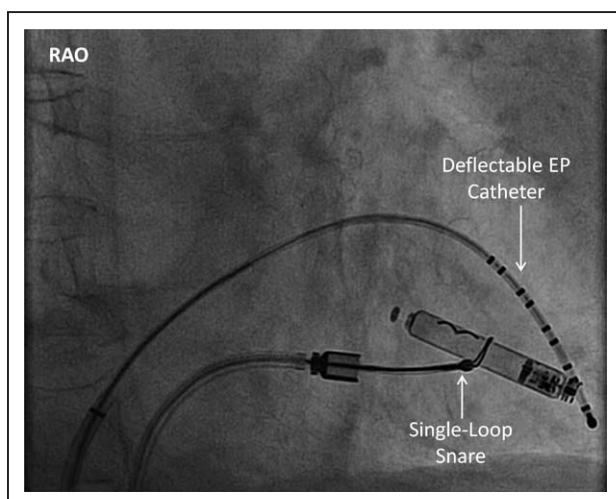


Figure 4. By using an off-the-shelf deflectable catheter to push down on the distal portion of the leadless pacemaker (near the attachment point with myocardium), the proximal portion of the device was successfully manipulated away from the tricuspid apparatus—thereby allowing a single-loop snare to successfully engage the pacemaker. EP indicates electrophysiology; and RAO, right anterior oblique.

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