

Right Ventricular Anatomy Can Accommodate Multiple Micra Transcatheter Pacemakers

PAMELA OMDAHL, M.B.A.,* MICHAEL D. EGGEN, PH.D.,* MATTHEW D. BONNER, PH.D.,* PAUL A. IAIZZO, PH.D.,† and KENT WIKI, M.S.*

From the *Medtronic, PLC., Mounds View, Minnesota; and †Department of Surgery, University of Minnesota, Minneapolis, Minnesota

Background: *The introduction of transcatheter pacemaker technology has the potential to significantly reduce if not eliminate a number of complications associated with a traditional leaded pacing system. However, this technology raises new questions regarding how to manage the device at end of service, the number of devices the right ventricle (RV) can accommodate, and what patient age is appropriate for this therapy. In this study, six human cadaver hearts and one reanimated human heart (not deemed viable for transplant) were each implanted with three Micra devices in traditional pacing locations via fluoroscopic imaging.*

Methods: *A total of six human cadaver hearts were obtained from the University of Minnesota Anatomy Bequest Program; the seventh heart was a heart not deemed viable for transplant obtained from LifeSource and then reanimated using Visible Heart[®] methodologies. Each heart was implanted with multiple Micras using imaging and proper delivery tools; in these, the right ventricular volumes were measured and recorded. The hearts were subsequently dissected to view the right ventricular anatomies and the positions and spacing between devices.*

Results: *Multiple Micra devices could be placed in each heart in traditional, clinically accepted pacing implant locations within the RV and in each case without physical device interactions. This was true even in a human heart considered to be relatively small.*

Conclusions: *Although this technology is new, it was demonstrated here that within the human heart's RV, three Micra devices could be accommodated within traditional pacing locations: with the potential in some, for even more. (PACE 2016; 39:393–397)*

leadless pacemaker, transcatheter pacemaker, device life-cycle management, retrieval, extraction, right ventricular anatomy, multiple devices

Introduction

The development of transcatheter pacing systems (TPS), or miniaturized pacemakers that are placed directly within a patient's right ventricle (RV) has significantly reduced and in some cases eliminated a variety of complications that have been associated with the pocket and/or the lead placement of traditional pacing systems.¹ These complications may include but are not limited to: infection, erosion, pocket hematoma, lead fracture, and/or lead dislodgement. A

recent clinical trial reported the pocket and lead contributed up to 83% of those complications occurring within the first 2 months after implant.² While the TPS technology has reduced many of these complications,¹ the implantation of the entire device into the heart has raised the important question of how to manage the end of service (EOS) in patients with expected longevities.

In a traditional leaded pacemaker system, at EOS, the pacemaker is replaced with a new device leaving the lead in place. In cases of lead failure, the implanter may choose to either abandon or extract the existing lead. It is generally accepted that two or three leads can be placed in the heart as an acceptable alternative to extraction. Complications with lead extraction have been well documented and the decision to perform extraction requires careful assessment of risks versus the benefits for the patient.^{3,4} In contrast, it has been speculated that any TPS residing in the heart may be difficult to extract after 10 or more years.

To address this issue, the Medtronic TPS (Medtronic, Mounds View, MN, USA) was

Address for reprints: Pamela Omdahl, M.B.A., Medtronic, PLC, 8200 Coral Sea Street NE, MVC52, Mounds View, MN 55112. Fax: 763-526-5848; e-mail: pamelak.omdahl@medtronic.com

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

Received July 14, 2015; revised November 24, 2015; accepted December 23, 2015.

doi: 10.1111/pace.12804

designed so that it can be permanently programmed in an off mode and left in the heart for the life of the patient. This concept provides options for managing patients who may need to receive additional devices when the first device reaches EOS. Thus, the implanter may choose to attempt an extraction or implant another device and turn off the previous one. However, this progression bares the anatomical question as to how many Micra devices can the RV accommodate. In this article, we describe a series of implants in cadaver human hearts, as well as a reanimated one, to demonstrate what might be feasible in clinical situations so to implant up to three devices. This was studied in each of the seven human hearts using both direct visualization and fluoroscopy.

Methods

Medtronic TPS devices were implanted in a total of seven human hearts. Six were from fresh cadavers obtained from the University of Minnesota Anatomy Bequest Program and one was from an organ donor of which the heart was not deemed viable for transplant (via LifeSource, St. Paul, MN, USA).

In each of the six cadaveric hearts, three TPS were implanted employing standard femoral implantation procedures, imaging, and tools.⁵ The devices, tools, and procedure have been described in detail elsewhere.^{5,6} In addition to fluoroscopic imaging, direct intracardiac visualization of the endocardium was used postimplantation, in order to understand the relationships between the size of the right ventricular chamber and the relative positionings of the implanted Micra devices.

In brief, the preparation of six cadavers for perfusion and imaging was as follows: the anterior ribcage was removed and the superior vena cava (SVC) and pulmonary artery (PA) were cannulated. The SVC cannula was connected to a peristaltic pump, which delivered 37° tap water to the heart. The inflow of water in the SVC and the outflow in the PA were balanced such that there was constant flow through the right heart while maintaining an end-diastolic shape. After flushing all remaining blood in the right heart, a flexible 4-mm endoscope was inserted in the bifurcated SVC cannula for visualization.

Following pressurization, three devices were serially implanted in the RV of the human cadaver hearts via the femoral vein and fixated in different positions within the RV, including: the right ventricular apex, septum, and the septal right ventricular outflow tract. The operator was blinded to the direct visualization during device placements to limit bias based on the intracardiac camera. In each of the six perfused cadavers, the device was implanted utilizing the

recommended Micra implant procedure approach outlined below:

- (1) Seldinger technique to access femoral vein
- (2) Insertion of the TPS introducer
- (3) Insertion of the TPS delivery system
- (4) Navigating to the RV
- (5) Deployment of device
- (6) Test device fixation
- (7) Removal of tether and delivery tools

The first pacing capsule was intentionally placed in the RV apex of each heart; active fixation was tested and then the Micra delivery system was removed. The second and third devices were positioned utilizing the identical implant procedure. Fluoroscopic images and cines were obtained in the posterior-anterior, right anterior oblique, and left anterior oblique positions of the device immediately after implant. The seventh heart was reanimated and perfused with a clear Krebs-Henseleit buffer according to previously described Visible Heart[®] methodologies.^{7,8} Endoscopic cameras were positioned once a native sinus rhythm was obtained for direct visualization of the Micra devices. The devices were implanted with the Micra delivery system via the SVC and steps 4–7 outlined above were followed. Unlike the cadaver hearts, for the implants within the reanimated heart only direct visualization with endoscopic cameras were utilized for the implants and positioning of the Micra devices.

Postimplant, endoscopic imaging was performed on all specimens for further verification that the devices were not physically interacting. Following the implantation and imaging of three Micras in each of the cadavers, the hearts were excised from the body and the atrium was removed to view the devices through the tricuspid annulus.

In order to determine the size of the various hearts, each heart was weighed and an approximation of RV volume was determined by holding the heart upright and open at the right atrium and injecting water with a 50cc syringe directly into the RV from the right atrium until the tricuspid annulus was reached. Then, the RV free wall was reflected to obtain a clear image of the devices inside the RV. Finally, the distance between the tricuspid annulus and the RV apex was documented by measuring from the RV apex to the tricuspid annulus (N = 5).

Results

Images from the largest and smallest hearts among the cadaver hearts are shown in Figure 1. An image from the reanimated heart is shown in Figure 2. The perfused cadaver hearts ranged in weight from 433.6 g to 803.2 g and in volume from

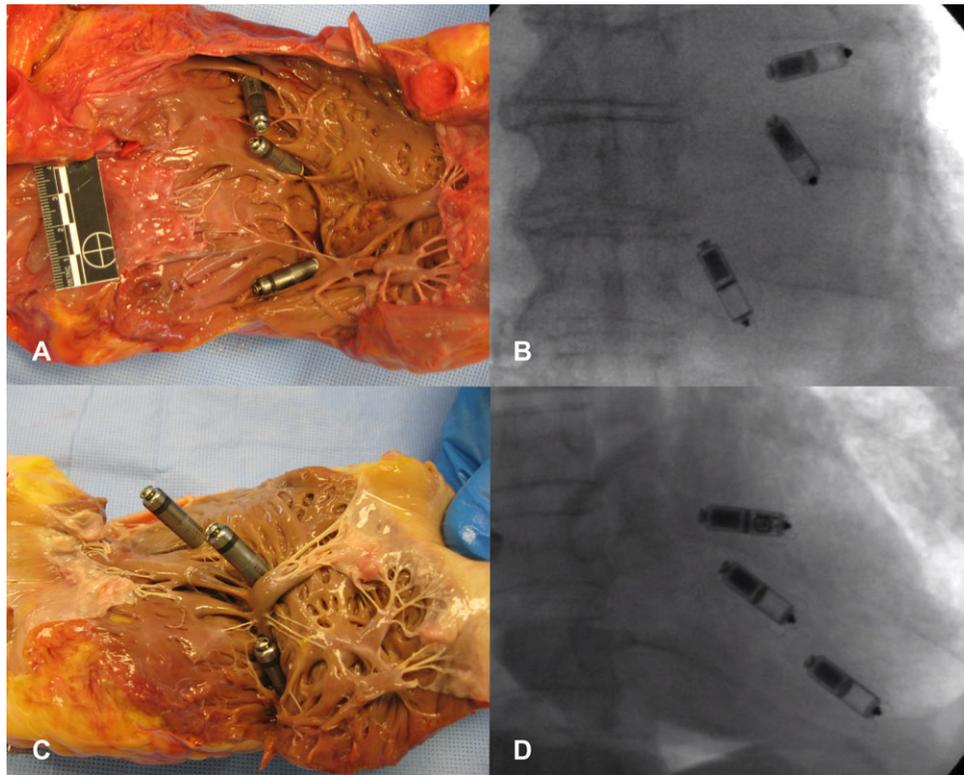


Figure 1. Multiple Micras implanted as shown in photographic and fluoroscopic images. An example of the largest heart is shown in A and B (specimen 10549); an example of smallest heart is shown in C and D (specimen 10550).



Figure 2. Endoscopic view of three Micra devices implanted within the right ventricle of a reanimated human heart.

35 mL to 200 mL, with a range in A-V distance from 6.5 cm to 9.5 cm (Table I). In addition, the body mass index for six cadavers was calculated using the National Institutes of Health calculator and ranged from 20.1 to 26.2 (Table I).

Discussion

The future utilizations of TPSs challenge both implanters and medical device developers to evaluate pacemaker replacements from a new perspective. More specifically, from initial patient selection, to estimating EOS as well as a given patient's life expectancy, considerations must be made to optimize the management of the device life cycle.

While today the average age of a Micra patient is 76 years,¹ the size of the device and the perceived benefits such as preserving vascular access and eliminating lead problems may provoke some physicians to consider a TPS in younger patients. For example, pediatric patients have been noted to elicit higher incidences of lead fracture⁹ and managing lead lengths in growing children can be challenging. The device life cycle questions become elevated in importance as we consider a given patient age, pacing needs, device longevity, and their expected lifespans.

Today, it has been estimated that the average pacemaker patient receives their implant at age 75 years and the average pacemaker now lasts approximately 10 years.¹⁰ Therefore, it is hoped and often the case that many patients receive

Table I.
Specimen Demographics

Specimen ID	Age	Sex	Height (cm)	Weight (kg)	BMI	Heart Weight (grams)	RV Volume (cc)	A-V Measurement (cm)
10523	66	M	190	95	26.2	N/A	N/A	N/A
10543	63	F	170	70	24.3	585.6	N/A	8
10547	59	M	187	81	23.1	498.2	55	9
10549	76	M	172	63	21.3	802.3	200	8.8
10550	79	F	157	49	20.1	433.6	35	6.5
10551	95	M	177	79	25.1	583.3	90	9.5
Reanimated heart						No information available		

BMI = body mass index; RV = right ventricular.

multiple pacemakers and multiple leads in their lifetime. It is a commonly accepted practice that more than one transvenous pacing lead can be implanted in the RV as long as there are minimal physical interactions between the new lead and existing lead(s). The physical limitation to this practice is typically the smaller diameter subclavian venous anatomy, and/or partial to full occlusion of the SVC. It is generally considered that these limitations should be eradicated with Micra and this study shows that even in a relatively small RV chamber (35cc), the implanter successfully placed three Micra devices utilizing fluoroscopic visualization, with no physical interaction between any of the three devices.

Importantly, the average RV volume in end diastole studied across a larger number of subjects using 3D Echocardiography was 80 mL \pm 22 mL for subjects >70 years of age.¹¹ Therefore, in an average pacemaker patient, a single Micra will take up <1% of the RV volume and three Micras implanted in the RV would displace <3% of the total volume.

Pacemaker and lead removal or replacement is not without complications, which have all been well documented.^{3,4} Therefore, the ability to program the Micra device off and implant a new one would allow flexibility in determining the safest procedure for a given patient, i.e., if indeed multiple devices can be left in the human heart, some patients may not need to undergo a Micra extraction procedure.

However, if the device must be removed, whether or not it is encapsulated is an important consideration. Currently, there is not sufficient knowledge regarding the rate of encapsulation with these small devices implanted directly within the heart. To account for these unknowns, the Medtronic TPS was designed with a proximal

retrieval feature that enables removal with a snare, provided the proximal end is free of encapsulation. Animal data at 28 months showed one of four devices fully encapsulated with the remaining three devices safely and successfully removed.¹² In man, there is only one report of the Micra device being retrieved, which was only several weeks postimplant.¹³ As further clinical experience is gained, we will increase our understanding of optimizing patient selection and device management throughout its life cycle.

Limitations

Although the anatomy of each of these seven hearts easily accommodated three Micra devices without physical interaction, it is recognized that this is a very small sample size and physical distances were the only quantified parameters. Yet, ranges of hearts with quite varied ventricular volumes were utilized. In addition, no electrical performance was assessed and the chosen sites were solely based on what typically are known to be acceptable physical locations within the RV. In addition, although physical distances were confirmed, there is potential that within a given beating heart, device interactions would be possible. Therefore, for more representative conclusions to be drawn, additional studies are needed to elucidate whether multiple devices in the RV may impact cardiac function and to what extent as well as if they will alter in any way device performance.

Conclusions

The capability of the human RV to accommodate at least three Micra devices without physical interaction, in seven unique anatomies was demonstrated. The ability to accomplish this through recommended Micra implant procedures via standard fluoroscopic imaging, as well as

verified through endoscopic imaging, indicates that it will likely be feasible to place up to three Medtronic TPS devices into the RVs in most patients.

While the potential benefits of a self-contained miniaturized pacemaker, such as the elimination of both the pectoral device pocket and lead(s), has been demonstrated, the introduction of the TPSs also raises new questions. More data will be necessary to further assess the appropriate

clinical strategy for the TPS at EOS. Nevertheless, the possibility to place three Micra devices within a given patient's heart would provide the possibility of therapeutic pacing for 3–4 decades of life.

Acknowledgments: The authors wish to thank individuals who donated their bodies for the advancement of education and research.

References

1. Reynolds D, Duray GZ, Omar R, Soejima K, Neuzil P, Zhang S, Narasimhan C et al. A leadless intracardiac transcatheter pacing system. *N Eng J Med* 2015 (in press [Epub ahead of print]).
2. Udo EO, Zuithoff NP, van Hemel NM, de Cock CC, Hendriks T, Doevendans PA, Moons KG. Incidence and predictors of short- and long-term complications in pacemaker therapy: The FOLLOWPACE study. *Heart Rhythm* 2012; 9:728–735.
3. Kutalek, SP. Pacemaker and defibrillator lead extraction. *Curr Opin Cardiol* 2004; 19:19–22.
4. Gomes S, Cranney G, Bennett M, Li A, Giles R. Twenty-year experience of transvenous lead extraction at a single centre. *Europace* 2014; 16:1350–1355.
5. Ritter P, Duray GZ, Steinwender C, Soejima K, Omar R, Mont L, Boersma LV, et al. Early performance of a miniaturized leadless cardiac pacemaker: The Micra Transcatheter Pacing Study. *Eur Heart J* 2015; 36:2510–2519.
6. Bonner M, Eggen M, Haddad T, Sheldon T, Williams E. Early performance and safety of the micra transcatheter pacemaker in pigs. *Pacing Clin Electrophysiol* 2015; 38:1248–1259.
7. Hill AJ, Laske TG, Coles JA Jr., Sigg DC, Skadsberg ND, Vincent SA, Soule CL, et al. In vitro studies of human hearts. *Ann Thorac Surg* 2005; 79:168–177.
8. Eggen MD, Bonner MD, Williams ER, Iaizzo PA. Multimodal imaging of a transcatheter pacemaker implantation within a reanimated human heart. *Heart Rhythm* 2014; 11:2331–2332.
9. Fortescue EB, Berul CI, Cecchin F, Walsh EP, Triedman JK, Alexander ME. Patient, procedural, and hardware factors associated with pacemaker lead failures in pediatrics and congenital heart disease. *Heart Rhythm* 2004; 1:150–159.
10. Benkemoun H, Sacrez J, Lagrange P, Amiel A, Prakash A, Himmrich E, Aimè E, et al. Optimizing pacemaker longevity with pacing mode and settings programming: Results from a Pacemaker Multicenter Registry. *Pacing Clin Electrophysiol* 2012; 35: 403–408.
11. Tamborini G, Marsan NA, Gripari P, Maffessanti F, Brusoni D, Muratori M, Caiani EG, 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; 23:109–115.
12. Bonner MD, Neafus N, Byrd CL, Schaerf RH, Goode L. *Extraction of the Micra Transcatheter Pacemaker System*. Heart Rhythm Society Conference, San Francisco, CA, 2014, abstract P004-33.
13. Karim S, Abdelmessih M, Marieb M, Reiner E, Grubman E. Extraction of a Micra™ transcatheter pacing system: First-in-human experience. *Heart Rhythm Case Rep* (in press).