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RESEARCH LETTER

Leadless epicardial pacing at the left ventricular apex: an animal study

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Aims State-of-the-art pacemaker implantation technique in infants and small children consists of pace/sense electrodes attached to the epicardium and a pulse generator in the abdominal wall with a significant rate of dysfunction during growth, mostly attributable to lead failure. In order to overcome lead-related problems, feasibility of epicardial implantation of a leadless pacemaker at the left ventricular apex in a growing animal model was studied.

Methods and results Ten lambs (median body weight 26.8 kg) underwent epicardial implantation of a Micra transcatheter pacing system (TPS) pacemaker (Medtronic Inc., Minneapolis, USA). Using a subxyphoid access, the Micra was introduced through a short, thick-walled tube to increase tissue contact and to prevent tilting from the epicardial surface. The Micra's proprietary delivery system was firmly pressed against the heart, while the Micra was pushed forward out of the sheath allowing the tines to stick into the left ventricular apical epimyocardium. Pacemakers were programmed to VVI 30/min mode. Pacemaker function and integrity was followed for 4 months after implantation. After implantation, median intrinsic R-wave amplitude was 5 mV [interquartile range (IQR) 2.8–7.5], and median pacing impedance was 2235 Ω (IQR 1725–2500), while the median pacing threshold was 2.13 V (IQR 1.25–2.9) at 0.24 ms. During follow-up, 6/10 animals had a significant increase in pacing threshold with loss of capture at maximum output at 0.24 ms in 2/10 animals. After 4 months, median R-wave amplitude had dropped to 2.25 mV (IQR 1.2–3.6), median pacing impedance had decreased to 595 Ω (IQR 575–645), and median pacing threshold had increased to 3.3 V (IQR 1.8–4.5) at 0.24 ms. Explantation of one device revealed deep penetration of the Micra device into the myocardium.

Conclusion Short-term results after epicardial implantation of the Micra TPS at the left ventricular apex in lambs were satisfying. During mid-term follow-up, however, pacing thresholds increased, resulting in loss of capture in 2/10 animals. Penetration of one device into the myocardium was of concern. The concept of epicardial leadless pacing seems very attractive, and the current shape of the Micra TPS makes the device unsuitable for epicardial placement in growing organisms.

Keywords Leadless pacemaker • Micra • Children • Epicardial pacing

What's new?

- Epicardial insertion of a leadless pacemaker (Micra, Medtronic Inc) at the left ventricular apex in lambs was technically feasible.
- Initially after implantation, capture thresholds and sensing were favorable but deteriorated during mid-term follow-up of 4 months in most animals while 2/10 devices lost ventricular capture.
- Penetration of one of the devices into left ventricular myocardium was of major concern.

Background

Indication for permanent cardiac pacing in the young implies life-long need for cardiac pacing with a life expectancy of >50–70 years. Because transvenous pacemakers have a high risk of venous thrombosis and vessel occlusion in small children,[1] it is recommended to place pacing leads at the epicardium in subjects ≤15 kg.[2,3] However, this implantation technique is more invasive compared with transvenous systems and has a higher risk for lead failure due to fracture or dislodgement.[4] As initial results after epicardial placement of a leadless pacemaker were unfavourable,[5] we modified our implantation technique

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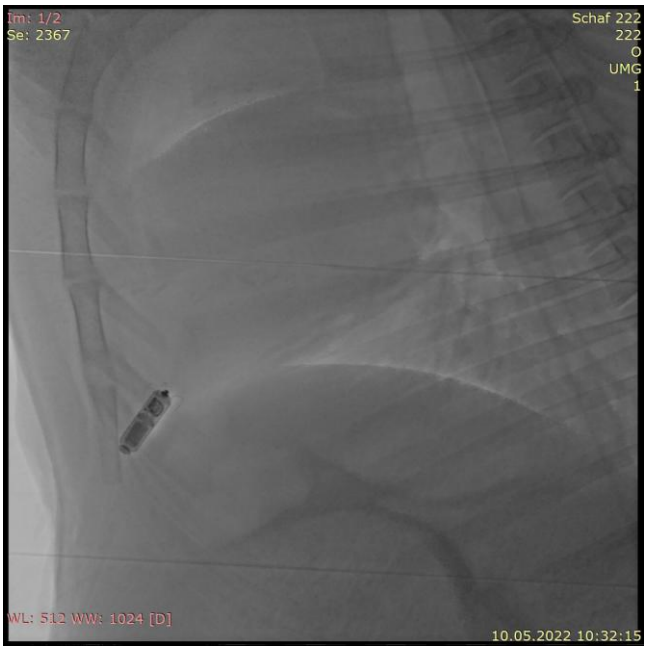

Figure 1 Fluoroscopy after Micra implantation. The animal is still in the right-sided position with a horizontal path of X-ray, resulting in a lateral projection. The electrode of the Micra is still placed at the LV apex with fixation of the tines within the epimyocardium. The body of the device is embedded in the space between the diaphragm, sternum, and apex.

in order to improve midterm performance. This report describes our experience using a modified, minimally invasive implantation technique for epicardial leadless pacemaker implantation at the left ventricular (LV) apex in lambs.

Animals, methods, and results

Ten lambs (German 'Schwarzkopf' sheep, median body weight 26.8 kg) were used. Under general anesthaesia, lambs were placed in a right-sided position and a 2 cm incision was performed just beneath the xyphoid process. Chest wall, diaphragm, and connective tissue were carefully dissected until the surface of the pericardium and the LV apex became visible. Two sutures (4.0 Prolene, Ethicon, USA) were stitched through the pericardium at the LV apex, and the pericardium was opened between these sutures. As the Micra within its proprietary delivery system could not obtain a stable position at the beating apex of the heart (see supplementary fluoroscopy), the delivery system was advanced through a 3–4 cm long portion of an 8.0 mm endotracheal tube to the LV apex. The tube was firmly pushed against the LV apex resulting in a visible impression on fluoroscopy (see schematic diagram—Supplementary material online, *Figure S1*). Subsequently, the Micra was slowly advanced out of the delivery system, while the endotracheal tube was withdrawn. This manoeuver allowed the tines of the Micra to penetrate the epimyocardial aspect of the LV apex and to keep the pacemaker in a perpendicular position towards the LV surface (see *Figure 1*). After confirmation of a pacing threshold < 3 V at 0.24 ms impulse width, the chest was closed. Pacemakers were programmed to VVI 30/min mode, and animals were extubated after recovery from anaesthesia.

Following implantation, median R-wave amplitude was 5.0 mV [interquartile range (IQR) 2.8–7.5] and median pacing threshold was 2.1 V (IQR 1.25–2.91) at standard impulse width of 0.24 ms. After 7 days, median R-wave amplitude dropped to 2.85 mV (IQR 2.0–4.8). Pacing threshold exceeded maximum amplitude (>5 V) at standard impulse width of 0.24 ms in 1/10 animals, while median threshold was 1.63 V (IQR 1.3–2.9) at 0.24 ms in the remaining 9/10 animals. After 20 days, pacing threshold exceeded maximum amplitude in another animal (see Supplementary material online, *Figure S2*). After maximum follow-up of 120 days, median R-wave was 2.25 mV (IQR 1.2–3.6) and median pacing threshold was 3.1 V (1.8–4.5) at an impulse width of 0.24 ms in 8/10 animals, while loss of capture at maximum output of 5 V was still present in 2/10 animals. At that time, animals had reached a median weight of 53.8 (IQR 50.4–55.6) kg. Explantation of a Micra was attempted in one animal. However, as the device was found to have deeply penetrated the LV myocardium, the respective animal suffered from severe bleeding and had to be sacrificed. The heart together with the Micra was explanted for histological analysis (see Supplementary material online, *Figure S3*). Explantation of more than one device together with the respective heart had been banned by the animal protection authorities, and the remaining animals were given to an animal sanctuary after pacemakers were programmed to OVO.

Discussion

Moore's law significantly impacts our way of life with new and mostly miniaturized technologies becoming part of our daily life. However, in our professional care, we use pacemaker systems in small children implementing a technique that has not significantly changed during the last 4 decades.[5] Because the market share of specifically paediatric pacemakers is not large enough to pay the cost for development, advancement, and certification of such badly needed devices, our youngest patients depend on devices that are developed for elderly subjects. As we know that strain on the lead and the connectors are the Achilles' heel of extracardiac pacemaker systems,[3,4,6] it seems to be crucial to investigate the feasibility of new leadless and miniaturized

techniques. Currently available leadless pacing systems though are designed for transvenous implantation and therefore are bullet-shaped with the electrode located at the distal tip of the device.[7] As the epicardial surface of the heart has a convex shape, implantation at this location necessitates a perpendicular position of the pacemaker with a small contact area between electrode and epicardium and a much larger contact zone of the device's body with surrounding structures. In a previous animal study, we implanted leadless Micra pacemakers at the lateral aspect of the ventricular epicardium and found that adhesions of the device with the thoracic wall were responsible for failure of the pacemakers during midterm follow-up.[5]

With the herein described modified approach, we used a subxyphoidal access allowing the Micra to be nested in the pericardial recess at the left ventricular apex which has been reported to be the most favourable epicardial pacing site in infants and small children.[8] This approach was technically easy to perform and resulted in reasonable initial results. However, during mid-term follow-up, pacing threshold increased in most animals to unacceptable high values as in our previous study.[5]

Explantation of one of the devices revealed deep ingrowth of the electrode tip into the left ventricular myocardium most probably due to perpendicular push and pull of the device. This observation may result in abandoning device Micra implantation in the current shape at the epimyocardium. Moreover, this finding must be considered whenever implanting a leadless pacemaker endocardially in young subjects, as the retrieval of the device after battery depletion or the implantation of additional devices remain arguable. It is another approach to use the miniaturized body of the Micra pacemaker in combination with a short lead that connects to an epicardial electrode.[9] Though this would be a great leap forward to a pacemaker designed for children, it still carries all the disadvantages of the lead. To overcome this limitation and to create a leadless epicardial pacemaker, a different device shape with enhanced contact zone, a low profile like a coin, and an active fixation of the electrode (e.g. with a helix) seems preferable.

Supplementary material

Supplementary material is available at *Europace* online.

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Conflict of interest: None declared.

Data availability

All data are with the corresponding author (D.B.) and could be shared upon reasonable request.

References

1. Haghjoo M, Nikoo MH, Fazelifar AF, Alizadeh A, Emkanjoo Z, Sadr-Ameli MA. Predictors of venous obstruction following pacemaker or implantable cardioverter-defibrillator implantation, a contrast venographic study on 100 patients admitted for generator change, lead revision, or device upgrade. *Europace* 2007;**9**:328–32.
2. Brugada J, Blom N, Sarquella-Brugada G, Blomstrom-Lundqvist C, Deanfield J, Janousek J *et al.* Pharmacological and non-pharmacological therapy for arrhythmias in the pediatric population: EHRA and AEPC-arrhythmia working group joint consensus statement. *Europace* 2013;**15**:1337–82.
3. Glikson M, Nielsen JC, Kronborg MB, Michowitz Y, Auricchio A, Barbash IM *et al.* 2021 ESC guidelines on cardiac pacing and cardiac resynchronization therapy. *Europace* 2022;**24**:71–164.
4. 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**:150–9.
5. Backhoff D, Betz T, Eildermann K, Paul T, Zenker D, Bonner M *et al.* Epicardial implantation of a leadless pacemaker in a lamb model. *Pacing Clin Electrophysiol* 2020;**43**:1481–5.
6. Defaye P, Biffi M, El-Chami M, Boveda S, Glikson M, Piccini J *et al.* Cardiac pacing and lead devices management. *Europace* 2023;**25**:euad202. doi:10.1093/europace/euad202
7. Tjong FVY, Reddy VY. Permanent leadless cardiac pacemaker therapy: a comprehensive review. *Circulation* 2017;**135**:1458–70.
8. Janoušek J, van Geldorp IE, Krupičková S, Rosenthal E, Nugent K, Tomaske M *et al.* Permanent cardiac pacing in children: choosing the optimal pacing site: a multicenter study. *Circulation* 2013;**127**:613–23.
9. Berul CI, Dasgupta S, LeGras MD, Peer SM, Alsoufi B, Sherwin ED *et al.* Tiny pacemakers for tiny babies. *Heart Rhythm* 2023;**20**:766–9.