ORIGINAL ARTICLE

Minimally Invasive Implantation of a Micropacemaker Into the Pericardial Space

BACKGROUND: Permanent cardiac pacemakers require invasive procedures with complications often related to long pacemaker leads. We are developing a percutaneous pacemaker for implantation of an entire pacing system into the pericardial space.

METHODS: Percutaneous micropacemaker implantations were performed in 6 pigs (27.4–34.1 kg) using subxyphoid access to the pericardial space. Modifications in the implantation methods and hardware were made after each experiment as the insertion method was optimized. In the first 5 animals, nonfunctional pacemaker devices were studied. In the final animal, a functional pacemaker was implanted.

RESULTS: Successful placement of the entire nonfunctional pacing system into the pericardial space was demonstrated in 2 of the first 5 animals, and successful implantation and capture was achieved using a functional system in the last animal. A sheath was developed that allows retractable features to secure positioning within the pericardial space. In addition, a miniaturized camera with fiberoptic illumination allowed visualization of the implantation site before electrode insertion into myocardium. All animals studied during follow-up survived without symptoms after the initial postoperative period.

CONCLUSIONS: A novel micropacemaker system allows cardiac pacing without entering the vascular space or surgical exposure of the heart. This pericardial pacemaker system may be an option for a large number of patients currently requiring transvenous pacemakers but is particularly relevant for patients with restricted vascular access, young children, or those with congenital heart disease who require epicardial access.

VISUAL OVERVIEW: An online visual overview is available for this article.

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WHAT IS KNOWN?

- Patients who are unable to undergo transvenous pacemaker placement require invasive epicardial pacemaker implantations.
- Complications continue to occur related to long pacemaker leads with both transvenous and epicardial pacemaker implantation.

WHAT THE STUDY ADDS?

- A novel pericardial micropacemaker system allows cardiac pacing without entering the vascular space and avoids surgical exposure of the heart.
- Early animal studies demonstrate the potential feasibility of implanting this system into the pericardial space using a securable sheath.

Permanent cardiac pacing is usually performed through the implantation of myocardial leads attached to a remote pacing device. These systems continue to be the mainstay of cardiac pacing, but lead issues may result in significant complications and impact system longevity.[1,2] More recently, leadless pacemakers have been added to the palette of permanent pacing options.[3,4] With these systems, the pacing devices are directly attached to the right ventricular myocardium and reside in the endovascular space of the heart. Complications have been seen with these systems, however, and residual concerns include device dislodgment.[5,6]

Although transvenous pacing is the primary modality for permanent pacing, many patients are not candidates for endovascular devices and require thoracotomies for implantation of epicardial systems. This includes a relatively large proportion of children and those with congenital heart disease, plus a number of adult patients with contraindications to transvenous pacemakers, including tricuspid valve pathology, venous access issues, right to left shunts, endocardial infection, and clotting disorders. These patients undergo far more invasive pacemaker implantations with the associated morbidities related to thoracotomy, including difficult surgical recovery, longer hospitalization time, and large surgical scars.

We have previously developed a novel micropacemaker for anticipated use in the human fetus.[7,8] This is an integrated, single-chamber pacing system that can be implanted percutaneously into the fetal chest without the need for open uterine surgery. Experience from that work has led to the development of a similar system and technique for implanting a pacing system for postnatal pediatric and adult use. By inserting the implantation sheath directly into the pericardial space via subxyphoid approach, the entire pacing system can be placed within the pericardial space. This approach may not only eliminate the need for thoracotomy in patients requiring epicardial pacing systems but may also provide a safer and more robust alternative to transvenous pacing systems. We describe our experience with developing a novel micropacemaker and implantation scheme in a series of pigs.

METHODS

Because of the proprietary nature of the reported device, the data, analytic methods, and study materials will not be made available at this time to other researchers for purposes of reproducing the results or replicating the procedure.

System Design

Micropacemaker

The micropacemaker used in our system is modeled after our fetal micropacemaker, which is a cylindrical structure 3.2 mm in diameter and 2.4 cm in length. For purposes of these experiments, which have focused on the implantation technique and feasibility of our system, we used either dummy devices that did not emit electrical pulses for cardiac stimulation or we encapsulated our small fetal device with medical-grade epoxy for a larger dimension. Because of the relatively large space afforded in a child or adult's pericardium (compared with a fetal chest) and the desire for a larger pacing device that could accommodate both a longer battery longevity and more sophisticated circuitry, we used a cylindrical device that would fit through a traditional 18F sheath. The device measured 5.2 mm in diameter and 2.0 cm in length for the dummy device and 5.0 mm in diameter and 2.4 cm in length for the encapsulated functional micropacemaker (Figure 1).

Interjoining Flexible Lead

The interjoining lead is a short (7.5–10 mm long) open-coil spring (1.5 mm diameter) made of highly elastic stainless steel (spring tempered SS304 Stainless Steel, wire diameter d=152.4 µm). The lead is insulated with a thin layer of highly flexible and biocompatible polymer Parylene C (thickness, 20 µm).[9] This design was used to allow for the infiltrated, living connective tissue matrix to serve as a mechanical support matrix, rather than having the conductor embedded in a synthetic polymer that can degrade over time. Because of the many million cardiac cycles expected to be endured with permanent cardiac pacing, we have theorized that this biological support may allow a longer longevity of the lead integrity.[10]

Hinged Electrode Mechanism

The hinged electrode mechanism was developed to accommodate the anatomic constraints of implanting the screw electrode perpendicular to the myocardial surface, while ultimately needing the micropacemaker system to lie parallel to the epicardial surface after implant. In our design, the flexible lead acts as a spring-loaded hinge between the body of the pacemaker and a corkscrew electrode that is implanted perpendicularly into the myocardial surface. During implantation through a pericardial sheath, the entire assembly is contained within a thin-walled plastic sleeve that holds the corkscrew electrode in a coaxial orientation and allows it to be screwed into the myocardium (see Figure 1

and System Implantation below). The epoxy disk at the base of the corkscrew electrode is wedged into the sleeve and then pushed free. After deployment, the hinge returns to its passive position (90° angle) as the micropacemaker is free to orient itself in a manner that minimizes the mechanical forces on the entire system. Preliminary benchtop testing determined optimal flexibility and stability before use, but long-term viability of the hinged lead depends on distribution of stresses in its open coils and the connective tissue that infiltrates and supports these coils as described in our preliminary work.[10] For the final implant that used a functional pacing system, a steroid-eluting plug was added at the proximal end of the electrode screw.

System Implantation

Implantation experiments were performed on 6 pigs (white farm pigs, Yorkshire and Landrace) with implant weight 31.7±3.2 kg. The protocol conformed to the Guide for the Care and Use of Laboratory Animals and was approved by the Institutional Animal Care and Use Committees at the University of Southern California.

The pigs were anesthetized using telazol 2.0 to 4.4 mg/kg IM, xylazine 2 to 4 mg/kg IM, and atropine 0.04 mg/kg followed by isoflurane 1% to 3% IH continuously during procedures. Prophylactic lidocaine 10 mg/kg per hour was given to the first 4 pigs (per veterinary team) but not to the last 2 pigs. With the pig in the supine position, the subxyphoid region was cleaned, sterilized, and draped. The procedure was performed using single-plane fluoroscopy in all of the implant procedures (with a movable arm to allow various thoracic views). An 18-gauge Tuohy needle was used for these procedures to allow for easier extrusion of the guidewire into the pericardial space. The needle was advanced from the subxyphoid region to the pericardial sac, with small injections of contrast dye (Optiray 350; Liebel-Flarsheim Company LLC, Raleigh, NC) given until movement of contrast suggested that the needle tip was in the pericardial space. Once needle tip placement in the pericardial space was assumed, a guidewire (0.018 inches in early experiments and 0.035 inches in later experiments) was advanced into the space. When the 18-gauge wire was used, this was followed by placement of a Micropuncture Kit (B. Braun Interventional Systems, Inc, Bethlehem, PA) to change to the larger 0.035-inch wire. Thereafter, a standard 18F implantation sheath and dilator (Cook Incorporated, Bloomington, IN) were implanted over the wire into the pericardial space. With early experiments, a series of dilators (5–18F) were used to gradually stretch the entire length of the tissue tunnel. After the third procedure, however, it became clear that this was not necessary, and the conventional 18F sheath and dilator were passed over the 0.035-inch wire without additional dilation. Ultimately, a new sheath was developed (prototype produced by Via Biomedical, Maple Grove, MN) and used in the final 3 experiments, which allowed for secure retention of the sheath in the pericardial space (Figure 1). Once the implantation sheath tip was in the pericardial space, it was manipulated to allow perpendicular force onto the myocardial surface in order for the screw electrode to be screwed in. With the last 3 experiments, a miniature camera with fiberoptic lighting (Micro ScoutCam; Medigus, Ltd, Omer, Israel) was inserted temporarily into the
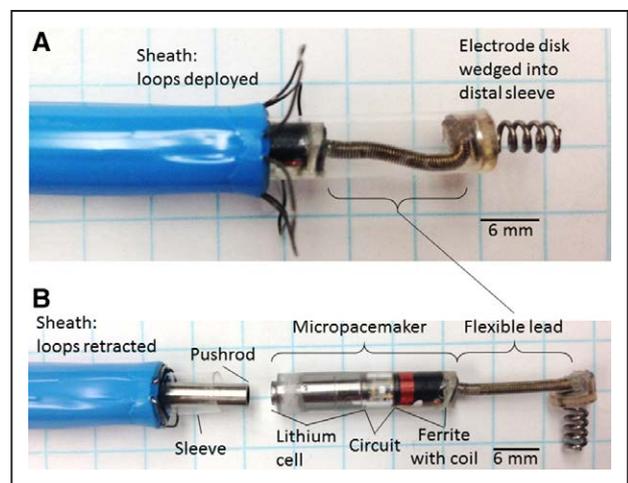

Figure 1. Epicardial micropacemaker system.
A, During implantation, the sheath is held inside the pericardial membrane by the extended wire loops while the corkscrew iridium electrode (far right) is screwed into the myocardium by rotating the plastic sleeve that grips its disc-shaped base. **B**, The micropacemaker and its coil-spring flexible lead are deployed by pushing it out of the sleeve and into the pericardial space, followed by retracting the loops of the sheath and removing it with the sleeve and pushrod. The micropacemaker includes an epoxy-encapsulated, relaxation-oscillator circuit that generates fixed-rate pulses, a lithium ion cell, and an inductive coil that captures energy from an extracorporeal radiofrequency electromagnetic field (6.78 MHz) to recharge the cell as required.

sheath to visualize the proposed electrode location to avoid any large coronary vessels. After the implanting sheath was in position, the smaller implantation sleeve (housing the micropacemaker device, the flexible lead, and the corkscrew electrode) was placed into the implantation sheath and advanced until the electrode contacted the epicardial surface (confirmed by mechanical resistance and by fluoroscopy). The implantation sleeve was then rotated clockwise until the electrode was felt by increased resistance to be firmly implanted into the myocardium (usually 4 complete turns). The micropacemaker system was released by slowly withdrawing the sleeve while advancing the device with a pushrod. When the retention sheaths were used in later experiments, the micropacemaker was pushed into the pericardial space while pulling on the sheath while the retaining loops were extended (to maximize the pericardial space to accommodate the device and allow more free movement to a position minimizing strain on the lead/system). The loops were retracted, the sheath removed, and the small entry wound closed with a single suture and tissue adhesive. Postoperative transthoracic echocardiography was performed to assess ventricular function and rule out a pericardial effusion, as well as to attempt visualization of the lead implantation site and position of the micropacemaker.

Follow-Up and Device Explantation

Animals were followed by the veterinary team with ultrasound/fluoroscopy follow-up performed intermittently. The animals were euthanized (pentobarbital/phenytoin solution) after the follow-up period was completed (27–56 days), and a thoracotomy was performed to determine the hardware location (micropacemaker, flexible lead, and electrode). In addition, injury and inflammation of the surrounding tissues were evaluated, and necropsy specimens were sent

for histological evaluations. In the last animal, recharging of the micropacemaker was attempted using an external recharging ring that was specifically developed for the micropacemaker.[11] Device position and orientation were evaluated by fluoroscopy and transthoracic echocardiography to determine the optimal orientation of the recharging ring to recharge the micropacemaker battery. After implantation in the last animal, prolonged single-channel Holter monitoring (Ziopatch; iRhythm Technologies, Inc, San Francisco, CA) was performed to determine pacing and capture over time.

RESULTS

Evolution of Implantation Technique

Device implantations were performed in 6 adult pigs. The Table summarizes the procedure results. With experience gained from each procedure, the pacing system and implantation techniques evolved to maximize the chance for success. Difficulty entering the true pericardial space was encountered in earlier animals because of wire positioning suggesting pericardial access when in fact the pleural space was entered. Once the sheath was successfully placed into the pericardial space, our initial strategy was to apply lateral force on the delivery sheath to indent the epicardial surface so that the corkscrew electrode could be screwed in nearly perpendicular to its resting surface, but this was unsuccessful. With the recognition that achieving a perpendicular placement of the sheath to the myocardium was required, it became clear that the sheath would need to be only slightly inside the pericardial space at the time of implantation. Because of concern that the sheath could

fall out of the pericardial space before implantation was complete, we initially addressed this issue (pig No. 3) by leaving a wire inside the sheath and into the pericardial space at the time we inserted the implantation cannula. This was ultimately successful, but we improved on this approach for pig No. 4 by developing a sheath (Figure 1) with retractable loops that allowed the sheath tip to remain securely in the pericardial space during implantation of the micropacemaker. However, because of partial failure of the initial sheath loops after repeatedly extending and retracting the loops in pig No. 4, the sheath ultimately pulled back out of the pericardial space and resulted in inappropriate device positioning. Significant refinements were subsequently made to the sheath design, which ultimately functioned correctly. In addition, starting with pig No. 4, we benefitted from the additional step of directly viewing the myocardium with the miniature camera to avoid implanting the electrode into a large coronary vessel. Figure 2 demonstrates a fluoroscopic view of the implantation system and micropacemaker just after successful implantation and deployment. Postoperative transthoracic echocardiography confirmed normal ventricular function and absence of a pericardial effusion (hemopericardium) and gave basic visualization of the lead implantation site and position of the micropacemaker within the pig chest.

Implantation of Functional Pacing Device

With our last device (Figure 3), a functional micropacemaker was implanted and pacing confirmed via electrocardiography. This device demonstrated successful

Table. Summary of Procedure Results

Pig No.	Weight at Implant, kg	Weight at Explant, kg	Device Follow-Up Time, d	Procedure Time, h	Location of Electrode	No. of Devices Attempted	Successful Implant	Comments
1	27.8	40.5	33	1:24	NA	2	No	2 device implants attempted, but both outside of pericardial space.
2	33.6	33.6	NA	1:05	Anterior of RV apex	2	No	Both implants in pericardial space, but electrode not into myocardium.
3	32.7	50	56	1:00	Near LV apex	2	Yes	First device in pericardium. Second device outside pericardium, but electrode in epicardium.
4	34.4	43.5	27	1:35	Diaphragmatic surface	1	No	Electrode in myocardium, but device outside of pericardial space.
5	34.1	46	30	1:28	Near LV apex	1	Yes	Appropriate placement.
6	27.4	45.1	28	0:50	Near RV apex	1	Yes	Appropriate placement of functional device.

LV indicates left ventricle; NA, not available; and RV, right ventricle.
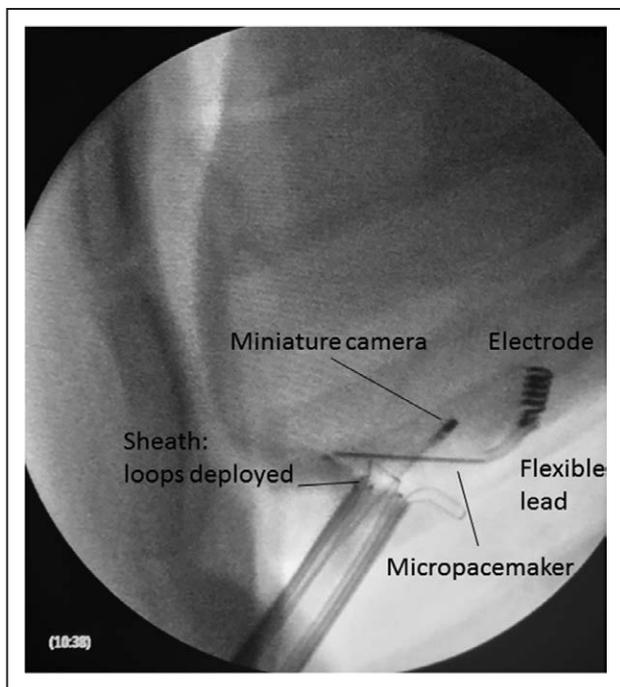
Figure 2. Fluoroscopic view (lateral) of dummy micropacemaker system just after implantation.
The securable sheath is seen with loops extended. The miniature fiberoptic camera was advanced through the sheath to view the device after placement.

ventricular capture (pacing at ≈140 beats per minute depending on capacitance) for 3 days. Intermittent loss of capture was seen at 3 days, with ultimate loss of capture at 5 days and loss of pacing spikes (pacing output) at 5.6 days as anticipated from previous experiments and the lithium cell charge capacity. An attempt to recharge the device was performed on the day of explant (28 days after implant). Transthoracic
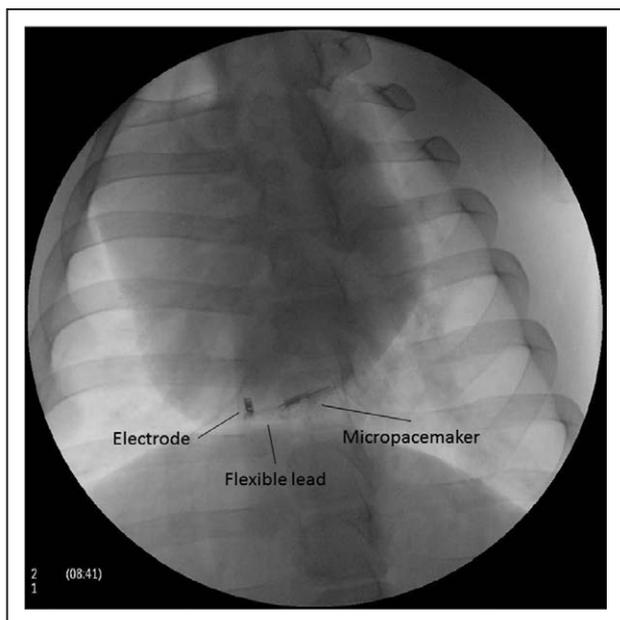

Figure 3. Fluoroscopic view (anteroposterior) of micropacemaker system just after implantation.
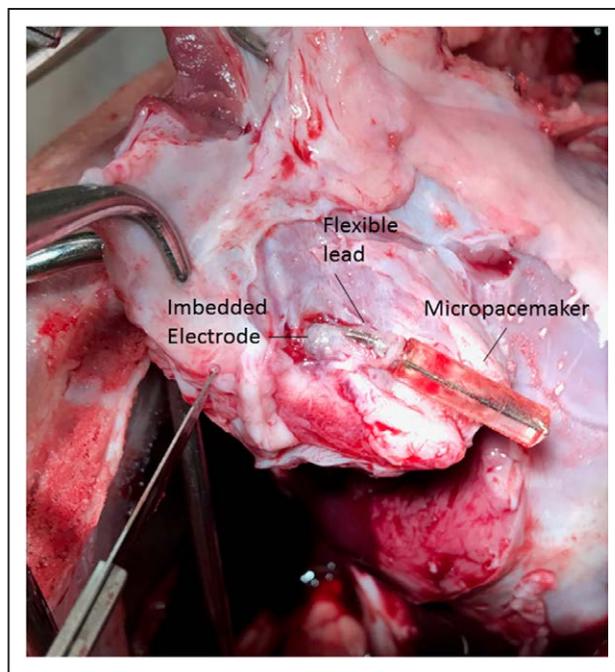

Figure 4. View at necropsy of dummy micropacemaker device with electrode implanted into epicardial surface.

echocardiography at that time demonstrated normal cardiac function with no pericardial effusion, and the pacemaker lead appeared to be in stable position by both echocardiography and fluoroscopy. Sufficient cell voltage was restored to generate pacing output artifacts without ventricular capture soon after the wireless recharging was initiated. Recharging was much slower than anticipated, which was later traced to a poor connection in the external recharging system hardware. The absence of ventricular capture during recharging was assumed to be related to the combination of low pulse charge with a minimally recharged cell and post-implant inflammation/fibrosis around the electrode. We had attached a steroid-eluting plug at the proximal aspect of the electrode coil to attempt to modulate the inflammatory process in this pig, but we suspect that the material was covered by silicone adhesive and was, therefore, unable to reach the myocardium.

Follow-Up and Necropsy

No symptoms were seen for any animal after the immediate postoperative period, and all animals survived follow-up until the planned explant date (pig No. 2 was explanted at the end of the implant procedure because of suspicion that neither device was successfully implanted). Necropsy was performed at the conclusion of all 6 experiments to evaluate for potential injury to the animal, as well as to assess the location and integrity of the micropacemaker system. Skin evaluation of the subxyphoid region demonstrated good healing in all animals, and there was no evidence for abdominal

organ trauma from the implantations or infection. In some cases, an inflammatory reaction was grossly suggested inside the pericardial space as manifested by small adhesions. Determination of device and electrode location was made in each case (Table). In all cases, the electrode/flexible lead/micropacemaker system was intact without evidence for lead breakage (Figure 4). In pig No. 1 and 4, the electrode and devices were seen to be outside of the pericardial space (such that the sheath tip had not been appropriately inside the pericardium at the time of electrode implantation and device deployment). In pig No. 3, 2 devices were implanted. For the first, the electrode and device were appropriately positioned. For the second device, the electrode was inside the myocardium, but the device was positioned outside the pericardial space with the lead remaining intact in this configuration. Histology of the pacing electrode site after 28 days in pig No. 6 shows the foreign body reaction at the electrode insertion (Figure 5).

DISCUSSION

Transvenous pacemaker systems are the mainstay of permanent pacing, with a much smaller fraction of patients undergoing implantation of an epicardial system. In both of these scenarios, pacing leads connect a myocardial electrode to a remotely placed pacing device and travel long distances either through the vascular space or across tissue planes. Although transvenous pacing has been successful in a large number of patients, lead failure is an important challenge for these patients,[1,2,12,13] and efforts toward leadless pacing have sought to eliminate pacing leads.[3,4] Although leadless pacing systems also eliminate the need for surgical incisions for device placement, there have been concerns about their placement in the intravascular space.[5,6] In addition to both cardiac perforation and dislodgment and embolization of devices, these leadless pacemakers require transvenous placement that is not always feasible in those with venous access issues, endocardial infections and clotting issues. Small children and those with congenital heart disease also make up an important group of patients for whom transvenous pacemakers are not advised because of size, as well as concern for intracardiac shunting and risk for cerebrovascular accidents.

Our team is developing a fetal micropacemaker device to allow percutaneous placement of an entire pacemaker system into the fetal chest. Here, we describe adaptation of our micropacemaker system and implantation scheme to address the above challenges of chronic pacing in children and adults. Our pacing system allows for the entire pacemaker system to reside within the pericardial space through a minimally invasive percutaneous approach and accomplishes the following: (1) elimination of surgical incisions, (2) complete avoidance of the vascular space, (3) placement of the device in near proximity to the electrode so that the short lead does not cross tissue planes, and (4) ability to pace from the left ventricular (LV) myocardium.

This novel approach can address the above problems for all patients who are candidates for transvenous, epicardial, or leadless pacemakers; however, pediatric patients and those with congenital heart disease who currently require epicardial pacing may be the best initial candidates for this pericardial pacing approach. This is because of the far more invasive epicardial surgery currently required for these patients, as well as the higher lead complication rates seen for epicardial systems.[3] One potential challenge for implanting our system in patients with congenital heart disease, however, is that the pericardial space is often fibrosed or otherwise not intact in patients who have undergone congenital heart disease surgery. We have hypothesized that our implantation scheme may be adapted further to address these patients by implanting the electrode directly through the pericardial membranes (even if they are adherent to the epicardium). In such cases, the micropacemaker device can be deployed in the pleural or even subdi-
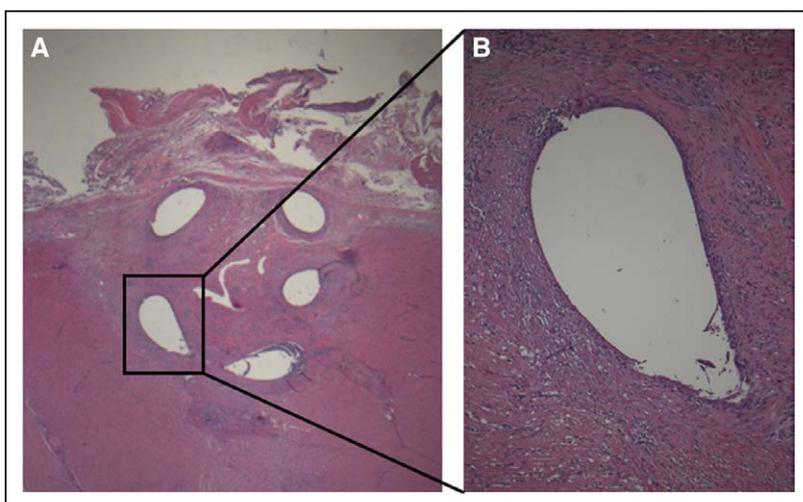

Figure 5. Myocardium at site of implantation from pig No. 6 demonstrating the path of the electrode (seen as round/elliptical voids).
A, The histology demonstrates histiocytes, fibrosis, and chronic inflammatory changes consistent with a foreign body reaction. **B**, Magnification of histology.

aphragmatic space. We studied this possibility in our third pig in which a second pacing device was deployed outside of the pericardial space. Although conclusions cannot be made after a single experiment with relatively short follow-up and no testing of lead capture or sensing performed, the lead and system were intact after 54 days of observation. It remains to be seen whether the lead stresses that we analyzed previously[10] would be low enough to avoid long-term stress fatigue for such a placement. Although we had not used our miniature camera visualization system by that point in the experiments, the ability to visualize the location where the electrode would be implanted and the space where the device would be deployed (by expanding of any potential spaces with the sheath loops deployed) could be beneficial in implanting such a system in a patient with congenital heart disease. It is important to note that the pigs we used were growing rapidly at the time of our experiments (implantation at ≈30 kg with ≈10 kg per month of growth after implant). Although using this less-than-adult size gave us some information related to the consequences of growth over time, it did not allow an adequate size representation to study the potential of implanting our device in the infants and small children who could theoretically be the biggest beneficiaries of our pacing system.

The potential fibrotic reaction in the pericardial space from implanting a pericardial micropacemaker is not yet defined, and methods of removing an infected or dysfunctional device without open thoracotomy have not yet been devised. In addition, although the current scheme allows for the possibility of implanting a second or third device into the pericardial space after normal battery depletion, the as-yet-undefined fibrotic reaction from the device as it remains in situ for years could preclude easy access back into the pericardial space. If significant fibrosis did occur, however, this could be analogous to the postheart surgery discussion above, and placement of an additional device outside of the pericardial space may be feasible.

The focus of our experiments was on the implantation scheme, hence the use of nonfunctional pacing devices for the first 5 experiments. However, we used a functional pacemaker for the final procedure. Successful capture was demonstrated, but because of the constraints of our rudimentary pacemaker, we were not able to determine capture thresholds during the follow-up period. Capture became intermittent before pacing ceased, suggesting that the threshold was close to the minimal output pulse of 2.8 µC (electric charge in Coulombs) rather than the 4.0 µC maximal output of this charge-regulated device. This would be substantially larger than the ≈1 µC thresholds noted for somewhat smaller epicardial corkscrew electrodes studied previously with a similar charge-regulated device.[7] Recognizing that inflammation and fibrosis result in increasing capture thresholds over time, we had attempted to place a steroid-eluting plug at the proximal end of the electrode screw to attenuate the inflammatory process.[14–16] However, it appeared that the steroid plug was coated with silicone adhesive during the fabrication process, thereby effectively making the steroid inert. For future experiments, we anticipate that a functional steroid component is mandatory to mitigate the electrical consequences of inflammation.

In addition to eliminating the need for a surgical incision via our percutaneous implantation scheme, our system removes the need for long pacing leads that are a primary reason for pacing system failures.[1,2] Our system integrates a short pacing lead that allows the micropacemaker impulses to conduct to the electrode screw and absorbs the small amount of bending between micropacemaker body and intramyocardial electrode that is likely to occur with each ventricular contraction. In our intended implantation scheme of placing the entire pacing system inside the pericardial space, this short lead would not be exposed to the significant stresses caused by crossing tissue planes. In addition, our lead design allows the formation of a biological support matrix resulting from the natural fibrosis that occurs. We have begun to test this model and have theorized advantages over traditional pacemaker leads.[10] However, with our most recent implantation model using the retention sheath, even a short lead may not be required. The retention sheath allows the operator to pull the pericardial membrane away from the epicardium and create a temporary pericardial space to deploy a device directly connected to an electrode using a hinge mechanism.

A final benefit of our implantation method is the ability to pace the LV myocardium. Pericardial access via a subxyphoid approach is well suited for targeting the area overlying the LV, and our implantation method is, therefore, well suited for LV pacing. There is a growing body of literature demonstrating the benefits of LV over right ventricular pacing in terms of cardiac synchrony and the potential for ventricular dysfunction.[17] As a result, a percutaneous epicardial pacing approach may mitigate this additional known complication of chronic pacing from the right ventricle.

In addition to efforts to place leadless pacemakers inside the heart, others have attempted to place percutaneous leads into or on the epicardial surface. Jordan et al[18] demonstrated the feasibility of implanting a standard transvenous pacing lead (SelectSecure lead; Medtronic, Minneapolis, MN) directly onto the epicardial surface using thorascopic guidance. John et al[19] developed and implanted an intrapericardial pacing lead in 12 dogs using a novel passive fixation lead system. Similarly, Clark et al[20,21] demonstrated feasibility of implanting a defibrillator lead with a side biting tine through a pericardial sheath. An additional approach

toward extravascular pacing demonstrated successful ventricular capture using a substernal electrode.[22] Although all of these approaches targeted extravascular lead placements, our system is the first to implant the entire pacing system (pulse generator, lead, and electrode) in the pericardial space.

CONCLUSIONS

A minimally invasive micropacemaker can be percutaneously implanted in the pericardial space and allows cardiac pacing without surgical incisions while avoiding the intravascular space. This novel pacing system can most dramatically benefit patients currently dependent on invasive epicardial pacemaker procedures, but it may also provide a minimally invasive alternative to conventional pacemakers. Our experiments were an iterative process whereby our implantation tools and techniques were improved from one experiment to the next to reach the goal of implanting an entire functional pacing system in the pericardial space with up to 5 days of pacing.

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Disclosures

Issued and pending patents assigned to the affiliated institutions and related to the micropacemaker device and implantation methods and equipment.

REFERENCES

1. 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. doi: 10.1016/j.hrthm.2011.12.014.
2. Hauser RG, Hayes DL, Kallinen LM, Cannom DS, Epstein AE, Almquist AK, Song SL, Tyers GF, Vlay SC, Irwin M. Clinical experience with pacemaker pulse generators and transvenous leads: an 8-year prospective multicenter study. *Heart Rhythm*. 2007;4:154–160. doi: 10.1016/j.hrthm.2006.10.009.
3. Reddy VY, Knops RE, Sperzel J, Miller MA, Petru J, Simon J, Sediva L, de Groot JR, Tjong FV, Jacobson P, Ostrosff A, Dukkipati SR, Koruth JS, Wilde AA, Kautzner J, Neuzil P. Permanent leadless cardiac pacing: results of the LEADLESS trial. *Circulation*. 2014;129:1466–1471. doi: 10.1161/CIRCULATIONAHA.113.006987.
4. Ritter P, Duray GZ, Zhang S, Narasimhan C, Soejima K, Omar R, Laager V, Stromberg K, Williams E, Reynolds D; Micra Transcatheter Pacing Study Group. The rationale and design of the Micra Transcatheter Pacing Study: safety and efficacy of a novel miniaturized pacemaker. *Europace*. 2015;17:807–813. doi: 10.1093/europace/euv026.
5. Reddy VY, Exner DV, Cantillon DJ, Doshi R, Bunch TJ, Tomassoni GF, Friedman PA, Estes NA III, Ip J, Niazi I, Plunkitt K, Banker R, Porterfield J, Ip JE, Dukkipati SR; LEADLESS II Study Investigators. Percutaneous implantation of an entirely intracardiac leadless pacemaker. *N Engl J Med*. 2015;373:1125–1135. doi: 10.1056/NEJMoa1507192.
6. Reynolds D, Duray GZ, Omar R, Soejima K, Neuzil P, Zhang S, Narasimhan C, Steinwender C, Brugada J, Lloyd M, Roberts PR, Sagi V, Hummel J, Bongiorni MG, Knops RE, Ellis CR, Gornick CC, Bernabei MA, Laager V, Stromberg K, Williams ER, Hudnall JH, Ritter P; Micra Transcatheter Pacing Study Group. A leadless intracardiac transcatheter pacing system. *N Engl J Med*. 2016;374:533–541. doi: 10.1056/NEJMoa1511643.
7. Loeb GE, Zhou L, Zheng K, Nicholson A, Peck RA, Krishnan A, Silka M, Pruetz J, Chmait R, Bar-Cohen Y. Design and testing of a percutaneously implantable fetal pacemaker. *Ann Biomed Eng*. 2013;41:17–27. doi: 10.1007/s10439-012-0631-3.
8. Bar-Cohen Y, Loeb GE, Pruetz JD, Silka MJ, Guerra C, Vest AN, Zhou L, Chmait RH. Preclinical testing and optimization of a novel fetal micropacemaker. *Heart Rhythm*. 2015;12:1683–1690. doi: 10.1016/j.hrthm.2015.03.022.
9. Loeb GE, Bak MJ, Salcman M, Schmidt EM. Parylene as a chronically stable, reproducible microelectrode insulator. *IEEE Trans Biomed Eng*. 1977;24:121–128. doi: 10.1109/TBME.1977.326115.
10. Zhou L, Bar-Cohen Y, Peck RA, Chirikian GV, Harwin B, Chmait RH, Pruetz JD, Silka MJ, Loeb GE. Analytical modeling for computing lead stress in a novel epicardial micropacemaker. *Cardiovasc Eng Technol*. 2017;8:96–105. doi: 10.1007/s13239-017-0292-3.
11. Vest AN, Zhou L, Huang X, Norekyan V, Bar-Cohen Y, Chmait RH, Loeb GE. Design and testing of a transcutaneous RF recharging system for a fetal micropacemaker. *IEEE Trans Biomed Circuits Syst*. 2017;11:336–346. doi: 10.1109/TBCAS.2016.2620805.
12. Fortescue EB, Berul CI, Cecchin F, Walsh EP, Triedman JK, Alexander ME. Comparison of modern steroid-eluting epicardial and thin transvenous pacemaker leads in pediatric and congenital heart disease patients. *J Interv Card Electrophysiol*. 2005;14:27–36. doi: 10.1007/s10840-005-3797-x.
13. Odim J, Suckow B, Saedi B, Laks H, Shannon K. Equivalent performance of epicardial versus endocardial permanent pacing in children: a single institution and manufacturer experience. *Ann Thorac Surg*. 2008;85:1412–1416. doi: 10.1016/j.athoracsur.2007.12.075.
14. Singarayar S, Kistler PM, De Winter C, Mond H. A comparative study of the action of dexamethasone sodium phosphate and dexamethasone acetate in steroid-eluting pacemaker leads. *Pacing Clin Electrophysiol*. 2005;28:311–315. doi: 10.1111/j.1540-8159.2005.40055.x.
15. Mond HG, Stokes KB. The steroid-eluting electrode: a 10-year experience. *Pacing Clin Electrophysiol*. 1996;19:1016–1020.
16. Horenstein MS, Hakimi M, Walters H III, Karpawich PP. Chronic performance of steroid-eluting epicardial leads in a growing pediatric population: a 10-year comparison. *Pacing Clin Electrophysiol*. 2003;26(7 pt 1):1467–1471.
17. Janoušek J, van Geldorp IE, Krupičková S, Rosenthal E, Nugent K, Tomaske M, Früh A, Elders J, Hiippala A, Kerst G, Gebauer RA, Kubuš P, Frias P, Gabbarini F, Clur SA, Nagel B, Ganame J, Papagiannis J, Marek J, Tisma-Dupanovic S, Tsao S, Nürnberg JH, Wren C, Friedberg M, de Guillebon M, Volaufova J, Prinzen FW, Delhaas T; Working Group for Cardiac Dysrhythmias and Electrophysiology of the Association for European Pediatric Cardiology. Permanent cardiac pacing in children: choosing the optimal pacing site: a multicenter study. *Circulation*. 2013;127:613–623. doi: 10.1161/CIRCULATIONAHA.112.115428.

18. Jordan CP, Wu K, Costello JP, Ishibashi N, Krieger A, Kane TD, Kim P, Berul CI. Minimally invasive resynchronization pacemaker: a pediatric animal model. *Ann Thorac Surg*. 2013;96:2210–2213. doi: 10.1016/j.athoracsur.2013.07.057.

19. John RM, Morgan K, Brennecke LH, Benser ME, Jais P. Acute and chronic performance evaluation of a novel epicardial pacing lead placed by percutaneous subxiphoid approach in a canine model. *Circ Arrhythm Electrophysiol*. 2015;8:659–666.

20. Clark BC, Opfermann JD, Davis TD, Krieger A, Berul CI. Single-incision percutaneous pericardial ICD lead placement in a piglet model. *J Cardiovasc Electrophysiol*. 2017;28:1098–1104. doi: 10.1111/jce.13263.

21. Clark BC, Davis TD, El-Sayed Ahmed MM, McCarter R, Ishibashi N, Jordan CP, Kane TD, Kim PC, Krieger A, Nath DS, Opfermann JD, Berul CI. Minimally invasive percutaneous pericardial ICD placement in an infant piglet model: head-to-head comparison with an open surgical thoracotomy approach. *Heart Rhythm*. 2016;13:1096–1104. doi: 10.1016/j.hrthm.2015.12.015.

22. Sholevar DP, Tung S, Kuriachan V, Leong-Sit P, Roukoz H, Engel G, Kutalek SP, Akula D, Thompson AE, Christie MGT, Ostanniy M, Molin F; SPACE Study Investigators. Feasibility of extravascular pacing with a novel substernal electrode configuration: the substernal pacing acute clinical evaluation study. *Heart Rhythm*. 2018;15:536–542. doi: 10.1016/j.hrthm.2017.11.030.

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