Multifunctional Pacemaker Lead for Cardiac Energy Harvesting and Pressure Sensing

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Biomedical self-sustainable energy generation represents a new frontier of power solution for implantable biomedical devices (IMDs), such as cardiac pacemakers. However, almost all reported cardiac energy harvesting designs have not yet reached the stage of clinical translation. A major bottleneck has been the need of additional surgeries for the placements of these devices. Here, integrated piezoelectric-based energy harvesting and sensing designs are reported, which can be seamlessly incorporated into existing IMDs for ease of clinical translation. In vitro experiments validate the energy harvesting process by simulating the bending and twisting motion during heart cycle. Clinical translation is demonstrated in four porcine hearts in vivo under various conditions. Energy harvesting strategy utilizes pacemaker leads as a means of reducing the reliance on batteries and demonstrates the charging ability for extending the lifetime of a pacemaker battery by 20%, which provides a promising self-sustainable energy solution for IMDs. The additional self-powered blood pressure sensing is discussed, and the reported results demonstrate the potential in alerting arrhythmias by monitoring the right ventricular pressure variations. This combined cardiac energy harvesting and blood pressure sensing strategy provides a multifunctional, transformative while practical power and diagnosis solution for cardiac pacemakers and next generation of IMDs.

1. Introduction

Among various implantable medical devices (IMDs), cardiac pacemakers and implantable cardioverter defibrillators (ICDs) are some of the most effective tools for treatments of heart block and ventricular dysrhythmias. Typical cardiac pacemakers and ICDs can last 5–10 years before the replacement of the depleted of batteries according to manufacturers’ datasheets. A recent study assessed ICD longevity among 685 consecutive patients over the last 20 years, and found that real life longevity was often significantly less than the stated values. The ICDs have a typical limited longevity of 4.9 ± 1.6 years, and 8% demonstrated premature battery depletion by 3 years. Early failure leads to battery replacement surgeries, which can result in infection especially for pediatric and geriatric patients. Biomedical self-sustainable energy generation represents a new frontier to greatly extend the lifetime and effectiveness of IMDs, such as cardiac pacemakers and ICDs. The present work is an effort to develop strategies for biomedical energy harvesting (EH) and sensing simultaneously in vivo by using energy nanomaterials.

Most IMDs consume less than 1 mW over their lifetime, with a typical cardiac pacemaker providing 0.5–2 Ah over 5–10 years (10–100 µW power consumption per year). Given the steadily decreasing power requirements for new generations of IMDs, EH provides a compelling alternative power solution to batteries, converting the mechanical energy of the hearts motion into electrical power. In the human body, thermal or biomechanical energy can be harvested from skeletal motion or the periodic expansions and contractions of organs such as the heart or the lungs. Recent studies on implantable energy harvesters/sensors and self-powered implantable electronic devices research have been summarized. Engineering approaches have been explored for various EH mechanisms. In general, there are five major reported cardiac EH approaches: piezoelectric, triboelectric, mass imbalance oscillation, electrostatic, and electromagnetic methods (Table S1, Supporting Information). However, almost all those in vivo cardiac EH strategies require thoracotomies to place the devices directly onto the heart. From a clinical perspective, these suture-based approaches are invasive and are not acceptable for clinical translation.

From materials perspective, various piezoelectric materials have been used to investigate cardiac EH approaches in vivo, including polycrystalline ceramic of lead zirconate titanate...
Figure 1. Energy harvesting and sensing strategy on a pacemaker lead. The design is using the multiple layers of porous thin film. Both energy harvesting and sensing devices are seamlessly incorporated with the existing pacemaker. The energy harvester converts energy from lead motion into an electrical power to ultimately charge a cardiac pacemaker or any other battery-based IMDs, and right ventricular pressure sensing data provides diagnosis information for patients.

(PZT)$^{[10,11]}$ and single crystalline $(1-x)$Pb(Mg1/3Nb2/3)O3–xPbTiO3 (PMN-PT)$^{[12–14]}$ In vivo studies were performed in large animal models, such as bovine$^{[10]}$ and porcine models.$^{[11]}$ The EH devices were directly sutured onto the animals’ epicardium$^{[10,11,13]}$ or pericardium.$^{[14]}$ The energy from a porcine heart has been used to power wireless data transmission.$^{[13]}$ More recently, Li et al. developed an EH device to pace the porcine heart in vivo without using an external energy storage element.$^{[14]}$ Implantable triboelectric EH approaches have used various materials, such as ZnO$^{[15]}$ and PTFE film.$^{[16,22]}$ However, their affixing/suturing methods all require thoracotomies. Recently, a mechanical approach using mass imbalance oscillation has been shown to generate about 82.0 ± 4.4 µW (apical) and 90.1 ± 0.7 µW (basal) of power from a beating heart by fixing a device (diameter 27 mm and height 8.3 mm) directly on a pig’s heart.$^{[21]}$ An electrostatic EH mechanism has also been employed by using a honeycomb type variable capacitor with coil springs; however, the device was too large to implant into the thoracic cavity of a laboratory animal.$^{[24]}$ In addition, an electromagnetic approach using neodymium permanent magnets with a flux density of 1.43 T and an array of copper coils has been tested with a mean power output of 0.78 µW at 84 beats per minute (bpm).$^{[25]}$ However, their device can only provide a short-term protection from body fluids, and the induced strong magnetic field may interfere with normal cardiac physiology.

There is a lack of promising technologies that can be seamlessly incorporated into current clinical devices to harvest energy without exposing the patient to unnecessary risk. Here, we demonstrate a compact energy harvesting design using the advanced porous thin film energy conversion material, and EH device is integrated with existing pacemaker or ICD leads to convert cardiac motion into electrical energy (Figure 1). The energy source is from the mechanical motion of the lead due to heart’s contraction and relaxation. The design is using multiple layers of thin film, and the porous piezoelectric materials deforms with the lead and transfers the bending and twisting motion of the heart into strain due to the piezoelectric effect, which in turn generates electrical energy.

Replacing the existing batteries is the ultimate goal, and super capacitors have been used for an energy storage role in EH system given the advantage of high cycle efficiency and high power density. Additional self-powered pressure sensing functionality was added to the same pacemaker lead using the piezoelectric porous thin film (Figure 1; Figure S1, Supporting Information). Those right ventricle (RV) sensing data provided important physiological information for patients for real-time monitoring and diagnosis, such as pulmonary hypertension. Both energy harvesting and sensing approaches are compatible with the existing lead implantation methods, and thus it is ideal for clinical translation either incorporated into current leads or as a standalone multifunctional lead as a source of energy for powering cardiac pacemakers and sensing blood pressure for diagnosis applications.

2. Results and Discussions

2.1. In Vitro Evaluation of Prototype Energy Harvesting Lead

The flexible and biocompatible$^{[26]}$ polymer-based piezoelectric material of polyvinylidene fluoride-trifluoroethylene (P(VDF-TrFE)) was employed to utilize the bending and twisting motion of the lead of a cardiac pacemaker. The EH device was developed by using multiple functional layers of porous P(VDF-TrFE), and the sandwich structure of single functional porous piezoelectric thin film included one layer of porous P(VDF-TrFE), one layer of solid P(VDF-TrFE) as isolation layer, two electrodes layers, and additional adhesive layers of polydimethylsiloxane (PDMS) (Figure 2A). Inspired by the nature’s tendrils and twisting leaves, the strain effect was employed to form a self-assembly of the helical structure, which aided in the device’s attachment to the
flexible pacemaker leads. The geometries from a ring shape to a helix were tuned by varying the misorientation between layers of PDMS. (Figure 2B,C). Specifically, the sandwiched porous P(VDF-TrFE) thin film was attached onto the stretched PDMS layer at a given angle \( \alpha \) to the stretching direction (Figure 2B). A second layer of PDMS was then spin-coated on top of the piezoelectric film as an additional encapsulation layer. Once the sandwiched PDMS/P(VDF-TrFE)/PDMS film was released from the stretching, a self-wrapping helical structure was formed due to the strain effect between PDMS layers. The shapes of helical ribbons subject to residual strain were obtained by employing elasticity theory with stationarity principles and differential geometry.\(^{[27]} \)

Finite element analysis (FEA) was performed by using ABAQUS to simulate the various helical structures at different initial misorientation angles using the strain engineering method (Figure S2, Supporting Information), and those FEA results were used to guide and tune the shape of stress-driven helical structures. At an angle of 45°, the helical EH structure showed the best integration with current pacemaker leads for a compact design and transferred the bending and twisting motion of the heart. Scanning electron microscopy (SEM) images showed the multilayers EH devices’ cross-section (Figure 2D). The adhesive layers of PDMS (30 µm thick) were sandwiched between the porous P(VDF-TrFE) materials (50 µm thick), in which an average pore size of 8 µm in diameter was measured. P(VDF-TrFE) material was characterized using an X-ray diffractometer (Rigaku Rotating Anode XRD) with a characteristic peak at 19.9° associated with highly piezoelectric crystalline \( \beta \)-phase (Figure 2E).

Energy outputs of the device were designed to seamlessly couple with the lead, and to best make use of the complex motion of the lead during heart beating. The helical structure transfers the bending and twisting motion into strain within the piezoelectric material, which then in turn produces an electric charge. To demonstrate this concept, in vitro tests were designed to mimic heart environment by using a shaker/motor-based platform (Figure 3A). The distal of the pacemaker lead was connected to a motor on a shaker table to simulate the bending and twisting motion during heart cycle. Based on the previous studies,\(^{[28]} \) a displacement amplitude of 5 mm with excitation frequencies between 1 and 2 Hz were provided by a function generator with a power amplifier (Figure S3 and Video S1, Supporting Information). The results in Figure 3B show the electrical outputs generated from the EH device by mimicking various heart motions. The energy harvested from bending and twisting motion was significantly larger than the outputs from either vibration or twisting motion alone from the lead. The motion of the lead in heart is consistent with surgical implantation techniques, such as anchoring approaches. These results demonstrated the anchor effect on the EH device performance, where the anchored leads (Figure 3C, bending and twisting motion from heart) yield higher electrical output than the contribution from unanchored leads (Figure 3D, vibration/free floating in the heart). The anchored leads have a larger relative bending motion due to the heart’s contraction and
relaxation than the free-floating leads, which show little bending. In addition, the stability of the helical EH device was tested in saline water, and the results in Figure 3E showed that device was functioning very stably with no significant degradation over $10^4$ cycles.

The scalability of EH devices by employing multiple layers were further evaluated. The EH devices were tested with single and multiple layers of the piezoelectric polymer film, which is made of a mesoporous structure. In Figure 4A, the multilayer porous P(VDF-TrFE) EH devices were shown to generate higher voltages with an increasing number of layers, up until a point (eight layers) in which the increased stiffness reduces flexibility enough to inhibit energy output. The results in Figure 4B showed that the 6-layer porous P(VDF-TrFE) EH device was able to produce an output of 2.1 V, which was feasible to provide a pacing pulse at an amplitude of 2 V, significantly higher than the voltages
Figure 4. Electrical output generated by various piezoelectric layers of EH device and the pressure sensing ring, charging capability, and biocompatibility of the devices. A) In vitro results of voltage generated by the single layer, 4-layer, 6-layer, and 8-layer porous P(VDF-TrFE) EH devices, and the inset is a schematic of single functional layer porous P(VDF-TrFE) device with two layers of gold electrodes, a protection layer of solid P(VDF-TrFE), and two encapsulation layers of PDMS. B) The correlation between the generated voltage output from EH device and the increasing layers of porous P(VDF-TrFE) thin film. C) Picture of lighting up an LED by manually bending the device, mimicking the lead motion in vivo. Inset is a schematic of an equivalent circuit by connecting with a bridge rectifier and an LED. D) Charging curve of the EH device by connecting with a microbattery. Inset shows the charging test connection with a rectifier and a microbattery. E) In vitro experimental method to mimic right ventricle blood pressure variations. F) Electrical signal measured by the P(VDF-TrFE) sensor ring with the variations of RV pressure. Inset shows the linear fitting between average voltage output peaks and RV pressure from the commercial sensor. G) Fluorescent images of mouse fibroblasts L929s cultured on the cell culture dish as control (upper) and encapsulated EH devices (lower), showing cytoskeleton (red) and nuclei (blue). H) Viability of L929s after 3 days of cell culture of both control and device groups.
generated by the single layer device. Note that the layers here refer to the functional film of porous piezoelectric material, and the 6-layer porous P(VDF-TrFE) EH device was a total 31 layers of sandwiched structure, including gold electrodes, encapsulation layers of PDMS, and protection layers of solid P(VDF-TrFE). By mimicking the bending motion of the heart, the energy generated by the energy harvester was shown to light up an LED (Figure 4C; Video S2, Supporting Information). The charging ability of the six layers EH device was characterized in vitro by connecting the device with a Schottky bridge rectifier (MB12S, Micro Commercial) and a 50 µF capacitor. The practical power on the capacitor was estimated as 0.3 µW. Given a typical cardiac pacemaker battery capacity of 1 Ah with a longevity of 10 years, an average energy consumption is determined to be 24.15 µW at 2.1 V pulse amplitude. By considering the energy harvested by the EH devices with a total energy requirement of 1 Ah, therefore, 15 six-layer EH devices on a pacemaker lead would extend the lifetime of pacemaker battery by 2.3 years theoretically, suggesting a practical self-sustainable energy solution for IMDS. The EH device was additionally connected with a rechargeable microbattery, and the voltage output across the battery was measured in Figure 4D.

As the heart beats, the right ventricle pumps the blood up as the tricuspid valve shuts, and the deoxygenated blood flows into the right atrium and passes into the ventricle. In vitro sensing testing platform was designed to simulate the blood flow within right ventricle and right atrium of the heart, and the add-on coupled P(VDF-TrFE) sensing functionality was tested in a saline environment (Figure 4E; Video S3, Supporting Information). In this pumping system, an air control unit was used to mimic the pressure variations within the right ventricle and right atrium of the heart. From a practical perspective, in vivo studies are still needed to better understand the sensing performance of the devices, since the in vitro testing system is always difficult to completely replicate and mimic the heart’s natural motion and complex environment. A commercial pressure sensor was integrated with a second pacemaker lead as a reference and immersed in the RV water bag together with the P(VDF-TrFE) sensor lead. Sensing signals were monitored for two devices (Figure 4E, a P(VDF-TrFE) sensor ring and a commercial pressure sensor). The voltage output from the P(VDF-TrFE) sensor ring was measured at different pressure levels. It was observed in Figure 4F that the sensing signals from the P(VDF-TrFE) sensor ring increased with the increasing pressure from 50 to 220 mmHg with a linearity of $R^2 = 0.973$ achieved.

Excellent biocompatibility is essential for the EH devices to be implanted in the heart, and the material of PVDF has proved its biocompatibility in previous studies. The porous P(VDF-TrFE) used in this study was further encapsulated within additional layers of PDMS, whose biocompatibility has been systematically evaluated via the studies on hemocompatibility, the flow velocity of the circulating blood, the time of exposure, and the blood cell adhesion or activation at the surface of the material. The encapsulation layer of PDMS appeared to be an excellent biocompatible material for in vivo studies. In addition, the encapsulated EH device was cocultured with mouse fibroblast cell line L929 to study cytotoxicity, morphology of cells. It was observed in Figure 4G that L929s have similar detectable cellular structures in both control (cell culture dish) and experimental groups. The viabilities of L929 cells in experimental group (grew on the encapsulated EH devices) also demonstrated good biocompatibility by comparing with the control group after 3 days of cell culture (Figure 4H).

### 2.2. In Vivo Evaluation of Multifunctional Lead

The real-time in vivo electrical outputs from the helical energy harvester is shown in Figure 5A, and the electrocardiogram (ECG) and arterial pulse (AP) pressure in the descending thoracic aorta in a porcine model were simultaneously measured. An open-circuit voltage of 2 V (peak-to-peak) was generated from a 6-layer porous P(VDF-TrFE) device during the heart contraction and relaxation. The anchoring positions of the lead in heart were consistent with surgical implantation techniques, and thus resulted in variations of lead motion and deformations. Different anchor points were optimized to generate the highest voltage output when implanted. The results in Figure 5B show the electrical outputs generated by the same EH device on the harvesting lead, which was anchored at five different positions in a porcine heart. The maximum generated voltage was 2.1 V by the energy harvester at the anchor position 4, where the distal 5 cm of the pacemaker lead was initially bended when anchoring the lead to the heart wall during the implantation. This result confirmed that the EH device could generate significant electrical energy from the motion of a pacemaker lead to supply pacing energy, and ultimately to recharge the battery of the pacemaker using the accumulated harvested energy. X-ray images in Figure 5C in the Supporting Information illustrated the five anchor positions in the right ventricle of porcine heart.

In vivo evaluation of two helical EH devices (single layer and 6-layer device) was performed in $n=4$ different porcine right ventricles. From the results shown in Figure 5C, variability of the anchoring location of the pacemaker leads in different animal models significantly affected the generated electrical output from the energy harvester. The slack left on the lead was depending on surgical implantation approaches and may also affect EH performance. The maximum peak-to-peak open-circuit voltage of the energy harvester 2 (a 6-layer device) in Animal C was found about 1.9 V. Those in vivo results were consistent with in vitro experimental results by using a shaker-based testing platform, suggesting that the bending and twisting motion of the pacemaker lead contributed to the energy harvesting and conversion process. The results demonstrated the energy harvester’s capability to provide electrical energy directly from the harvesting lead in $n=4$ different porcine hearts. The scalability of using multiple EH devices on the same pacemaker lead will be explored in the future for design optimization. The influence of cardiac contraction was further investigated by injection dobutamine (2–5 mcg kg$^{-1}$ min$^{-1}$) to increase cardiac contractility. It was found in Figure 5D that in vivo voltage generated by the energy harvester increased from 0.9 to 3.5 V (peak-to-peak) with a peak increase in arterial pulse pressure during the drug treatment, while there was no significant ECG fluctuation observed. An enlarged illustration within 5 s during the drug treatment is shown in Figure 5E. The device was tested in a porcine heart for one and half hours, and it showed very stable performance with no degradation of energy.
Figure 5. In vivo electrical outputs from the energy harvester, and effect of anchor positions and drug treatment on the harvesting performance. A) Real-time electrical output generated by an EH device via motion of a pacemaker lead in a porcine model with simultaneously monitored ECG and AP pressure of the porcine during the EH process. B) Voltage generation at five different anchor positions by the same lead in a porcine model. C) Performance evaluation of energy harvesters in $n = 4$ different porcine right ventricles. (Device 1 is single layer and Device 2 is six layers porous P(VDF-TrFe) film.) D) In vivo measurements of voltages generated by the energy harvester, and simultaneously monitored ECG and AP pressure by changing porcine cardiac contractility via dobutamine. E) An enlarged illustration of the electrical output from the EH device with simultaneously monitored ECG and AP pressure within 5 s.
generation observed, suggesting that the encapsulated EH device was successfully isolated from body fluids.

To demonstrate clinical translation of self-powered blood pressure sensor for diagnosis application, in vivo sensing studies were performed in a porcine model (female, aged 6 months old and a weight of 244.4 lbs). Using the standard implantation techniques for pacemaker leads, a prototype multifunctional lead (Figure 6A) was implanted in right ventricle of a porcine heart, and a commercial pressure transducer catheter (model fdh-5011b-0045b) was inserted to monitor the blood pressure as a reference. Both the porous P(VDF-TrFE) sensor ring and the pressure transducer catheter were in the same position (RV) of the porcine heart. The RV pressure by the porous P(VDF-TrFE) sensor was from the right side of the heart when it pumped out the blood. The pressure transducer catheter was used to scrutinize the sensory functionality of the P(VDF-TrFE) sensor, and the catheter was plugged into the Scisense ADVantage pressure volume measurement system, and the data was collected by ADInstruments PowerLab. The enlarged illustration of signals from both P(VDF-TrFE) sensor ring and commercial catheter is shown in an overlapping manner in Figure 6B, demonstrating the excellent consistency. The arterial pulse pressure and electrocardiogram were simultaneously measured for monitoring cardiac contractility and heart rates in the procedure (Figure 6C). It is worth noting that an abnormal electrical impulse was observed and detected by the P(VDF-TrFE) pressure sensor during the in vivo sensing process, suggesting the potential in alerting arrhythmias by monitoring the RV pressure variations (Figure 6C). Since the real time sensing signals generated by the P(VDF-TrFE) sensor change periodically as an indicator of right ventricular pressure due to the cardiac cycles, those sensing data carried significant information of physiological parameters of patients. For example, it provides real time monitoring for people with elevated right ventricle systolic pressure and pulmonary hypertension. The long-term in vivo RV sensing tests were further performed by leaving the prototype multifunctional lead in right ventricle of the porcine heart for over 80 min, and the stable sensing signals from the RV ring sensor are shown in Figure 6D,E, suggesting an excellent long-term sensing performance of porous P(VDF-TrFE) device in response to the changes of RV blood pressure in a porcine heart. In vivo evaluation of the effect of various heart rates on the sensing performance was performed by connecting an external pulse generator to the prototype lead. The right ventricle was paced from the baseline rate of 68 bpm up to 160 bpm. The electrical output by the porous P(VDF-TrFE) RV sensor ring and the pressure from the transducer catheter were collected during the cardiac pacing process (Figure 6F). The results showed that the voltages generated by the RV sensor were consistent with the right ventricular pressure (RVP) from the transducer catheter, and both sensing signals exhibited similar and complex patterns with RV pacing. ECG was monitored and the arterial pulse pressure was measured simultaneously as an indirect measure of cardiac contractility. Figure 6G presented an enlarged illustration at a heart rate of 140 bpm during a period of 0.7 s in the pacing process.

In vivo studies demonstrated the feasibility of cardiac EH approach of a noncontact harnessing energy of a heart and self-powered blood pressure sensing strategy. Optimization steps and miniaturization of the overall EH and sensing designs will be explored as a next step. Here, we have shown the EH device as an externally self-wrapped structure with an encapsulation coating, adding a minimal increase in diameter to the leads. The functional material in both EH and sensing devices has a thickness less than 100 µm, leaving the possibility of these devices being fully internalized in the dead space within current pacemaker leads, allowing for energy generating leads with no additional size increase. In addition, the EH devices show potentials for the development of stand-alone energy leads that would act as a sustainable power supply for other IMDs.

3. Conclusions

Self-sustainable energy generation could significantly extend the lifetime of IMDs. Previous attempts at improving pacemaker battery life by making use of mechanical energy harvesting have had limited clinical feasibility, requiring a thoracotomy to suture the devices onto the epicardium. In this work, we have developed novel piezoelectric-based EH and sensing devices, which can be easily incorporated into current pacemaker leads for ease of clinical translation. The energy harvester is helically shaped to efficiently convert mechanical energy into electrical power, while common EH structures have been widely used in the literature such as beams,[10,11,13–13] cantilevers,[28,34–36] and patches/membranes.[15,16,22,37–42] This helical structure shows significant advantages for capturing the complex motion (bending, twisting, and kinetic motion) of a pacemaker lead while also seamlessly integrating with the lead for clinical translation.

Energy harvesting strategy utilizes pacemaker leads as a means for reducing the reliance on batteries for powering pacemakers and other IMDs. Lead implantation is consistent with current clinical practice, with an incision and subsequent implantation through the brachiocephalic vein. Therefore, the use of the pacemaker lead as the carrier for the EH and sensing device allows for no additional changes in implantation procedure for the clinician or patient. Using the same porous thin film, an additional self-powered pressure sensor is coupled to the pacemaker lead, and those sensing data carries significant physiological information. Since the porous P(VDF-TrFE) sensor ring is integrated on the existing pacemaker lead, it does not require an additional catheter implanted for pressure measurements for patients. Especially, the add-on coupled sensor ring could provide continuous real-time blood pressure monitoring for diagnosis and treatment, while commercial pressure transducer catheters are only used temporarily and implanted into patients’ bodies during the surgeries. Furthermore, by adding multiple porous P(VDF-TrFE) sensing units along the lead allows for further determining the average velocity of blood flow either in right ventricular or right atrium of the heart. Recently, multifunctional and high-sensitivity sensors and bionic sensing devices have been widely investigated.[41–46] In addition to harvesting energy from motion of the heart and internal organs, implantable piezoelectric and triboelectric devices function as self-powered sensors that monitor important physiological and pathological characteristics. For example, cardiac arrhythmias such as ventricular fibrillation and ventricular premature contraction has been detected by a self-powered endocardial pressure sensor for diagnosis of cardiovascular diseases.[47]
Figure 6. In vivo evaluation of the sensing lead in a porcine heart. A) Schematic and a photograph of a pacemaker lead coupled with a porous P(VDF-TrFE) RV sensor ring. B) Real-time measurements of voltages generated by the RV sensor with simultaneously monitored ECG, arterial pulse pressure (AP pressure), and compared with signals of pressure catheter in a porcine heart. An abnormal electrical impulse during sensing process was detected by the porous P(VDF-TrFE) pressure sensor. C) Comparison of the voltage output from porous P(VDF-TrFE) RV sensor and the pressure sensed by a commercial pressure catheter. D) Long-term in vivo RV sensing performance of the P(VDF-TrFE) sensor ring in a porcine model. E) An enlarged illustration of the voltage output by the RV sensor within 1 min. F) In vivo measurements of the electrical signal generated by P(VDF-TrFE) RV sensor as a function of time by changing the heart rate from the baseline of 68 bpm up to 160 bpm. ECG, RV pressure from commercial catheter, and arterial pulse pressure (AP pressure) of the porcine are simultaneously monitored during the pacing process. G) An enlarged illustration of in vivo voltage output from P(VDF-TrFE) RV sensor, with simultaneously monitored ECG, RVP, and AP pressure at a heart rate of 140 bpm during 0.7 s.
Clinical translation has been demonstrated in four porcine in vivo hearts. The charging ability of the energy harvester was calculated to be suitable for extending the lifetime of pacemaker battery by 20% or more, which provides a promising self-sustainable energy solution for IMDs. For long-term clinical translation, both energy harvesting and sensing devices will be incorporated inside the pacemaker lead. The minimized energy harvester and sensor will fit within the lead space between wire and the silicone coating to contribute a stand-alone multifunctional lead as a sustainable source of energy for pacemakers and other IMDs.

4. Experimental Section

Prototypes and In Vitro Experimental Method: Fabrication of a porous piezoelectric thin film started from spin coating the P(VDF-TrFE) solution, which was prepared from polyvinylidenedifluoride-trifluoroethylene powder (molar ratio: 75:25) and followed by dissolving at a 15 w/w% in N,N-dimethylformamide solvent over 8 h. The solid P(VDF-TrFE) thin film was first made through consecutive spin coating approach (1000 rpm, 30 s). After evaporation for 10 min at a temperature of 50 °C, the cast solid film was formed. This spin-coating process was repeated to fabricate porous P(VDF-TrFE) thin film. By controlling relative 90% humidity condition, the P(VDF-TrFE) film completes phase separation between solvent and nonsolvent by a water vapor phase-separation method. The material’s porous structure and electromechanical coupling efficiency were finely controlled.[48,49] To increase P(VDF-TrFE) crystallinity, the material was annealed at a temperature of 135 °C for 2 h, following by electrical poling process at 100 °C by applying 80 V µm−1 electrical field for 1 h. To fabricate multilayer porous P(VDF-TrFE) thin film, 30 µm thick of PDMS was coated as the adhesive layer, sandwiched between the functional piezoelectric layers. The gold electrodes (10 nm) were sputter coated on the top and bottom of the sandwiched multilayer device. Additional biocompatible layers of PDMS (thickness of 20 µm) were spin coated to encapsulate the device completely to isolate the body fluid for in vivo studies. Integration of sandwiched energy harvester and sensor with the lead was performed at the bottom 7 cm of the pacemaker lead, which is the area contributed to maximum bending/twisting energy in right ventricular of the heart. The self-wrapping helical and rings shape aid in the devices’ attachment to the pacemaker leads. The device’s wiring runs up along the entire length of the pacemaker lead and are encapsulated within a soft silicon tubing. Additional two-parts curable liquid silicon rubber was used to seal the EH device to isolate blood for animal studies.

In vitro experiments were designed to mimic heart environment by using a microfluidic-based platform (Figure 3A). The distal of the pacemaker lead (Bitronik Solia S53 ProMRI) was connected to a motor (Make block DC motor) on a shaker table (2025E from The Modal Shop). Since the tip of lead is anchored, it moves in both axial and torsional directions driven by the shaker and motor, respectively. The motor was controlled by a DC power supply (Agilent E3630A), while the shaker excitation was generated by a function generator (Keysight 33500 B) with an amplifier (21002E1-400 from The Modal Shop). To simulate the bending and twisting motion during heart cycle, the input frequencies (both angular and linear frequencies) were controlled within 2 Hz with an amplitude less than 1 cm, given by the clinical analyses from X-ray videos. A low noise preamplifier from Stanford Research (SR560) was used to extract the signal from the EH and sensing devices without significantly degrading the intrinsic signal-to-noise ratio. Real-time electrical outputs generated by energy harvesting devices were collected via a data acquisition system (National Instruments, model NI USB-6008).

In Vivo Experimental Method: Using standard implantation techniques for pacemaker leads, the encapsulated EH device and sensor were inserted and advanced into the right ventricle of porcine hearts under fluoroscopic guidance. In Figure S1 and Video S4 in the Supporting Information, a fluoroscopy shows a porcine heart with an implanted pacemaker lead coupled with an energy harvester and a sensor in the right ventricle. All animal procedures were approved by the Institutional Animal Care and Use Committee at the University of Texas Health Science Center at San Antonio. Studies (n = 4) were performed on one male pig and three female pigs, with an average weight of 250.7 lbs. Pigs were first sedated via Telazol (4–8 mg kg−1 IM) and xylazine (1–2.2 mg kg−1 IM), and endotracheal intubated and maintained on 0.5–3% isoflurane. The animal was placed on a surgical table in dorsal recumbency. Amiodarone (10–12 mg kg−1 IV) and lidocaine (2–4 mg kg−1 IV) were used to prevent ventricular fibrillation in the procedure. Following anesthesia, a micromparator pressure sensor was inserted into descending thoracic aorta under fluoroscopic guidance to monitor arterial pulse pressure, which is an indicator of the cardiac contractility through the animal studies. A commercial pressure transducer catheter was fed into porcine heart to monitor the RV blood pressure as a reference for sensing tests. Dobutamine (2–5 mg kg−1 min−1) was injected to increase contractility during the procedure. The electrical energy generated by the energy harvesters was measured using a data acquisition system. Real-time electrocardiogram, arterial pulse pressure, and right ventricular pressure were measured through-out the in vivo experiments. Following data collection, the pacemaker lead and pressure transducer catheter were removed from the porcine hearts.

Cell Culture and Cytotoxicity Test: The L929s cells (a mouse fibroblast cell line, ATCC) were cultured with Dulbecco’s Modified Eagle’s Medium (D5671), 10% bovine calf serum, l-glutamine solution (200 mM × 10−3 M), and 1% minimal essential medium (MEM) nonessential amino acids (100x), and supplemented with 1% penicillin–streptomycin solution in a 75 cm2 flask. The flask was placed in a humidified atmosphere with 5% CO2 at 37 °C. After 3 days, L929s cells were detached by Trypsin EDTA solution (1×) and resuspended in a fresh culture medium. The L929 cells were then seeded in 12-well plates and the PDMS encapsulated EH devices were attached to the substrate of each well plate for the control and experimental group, respectively. At least three replicates were taken in each trial. The plates were placed in an incubator (37 °C, 5% CO2) for 24, 48, and 72 h. At the end of each testing period, 10 µL of CCK-8 solution was added into each well of the control and experimental groups and incubated for 3 h. Using a UV–vis plate reader (TECAN, Spark 10M), the absorbance of the groups at 450 nm was measured. The survival rate of cells was determined given the formula of survival rate = (Asample − Ablank)/(Acontrol − Ablank) × 100%, where Acontrol, Ablank, and Asample are the absorbance of sample, control, and blank groups, respectively.

Cell Immunofluorescent Staining: The morphology of cells in both control and experimental groups was examined at 24, 48, and 72 h. 4’,6-diamidino-2-phenylindole (DAPI) and rhodamine phalloidin (both were purchased from Thermo Fisher Scientific) were utilized to stain nucleus and cytoskeleton of the cells, respectively. Cell morphology was observed under a bright-field microscope before immunostaining. The cell culture medium was removed, and the cells were rinsed with 1× DPBS (0.01 m, pH 7.2–7.4). Then, the cells were fixed by 4% paraformaldehyde (in PBS) for 15 min at 37 °C, followed by permeabilization with 0.5% Triton X-100 diluted in PBS. 1% bovine serum albumin solution (in PBS) was used to block the samples for 2 h at 37 °C. A staining solution of rhodamine phalloidin (1:40 of stock solution and dissolved in 1.5 mL methanol) and 4’,6-diamidino-2-phenylindole (DAPI 2 µg/mL) was added to the samples, which were left at room temperature in darkness for 1 h. Excessive staining solution in the samples was washed away by 1× DPBS. Immunofluorescent images were obtained by using the microscope.

Supporting Information
Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

blood pressure sensing, cardiac energy harvesting, implantable medical devices, porous P(VDF-TrFE)


