

Energy Harvesting from the Cardiovascular System, or How to Get a Little Help from Yourself

ALOIS PFENNIGER, 1,2,3 MAGNUS JONSSON, ADRIAN ZURBUCHEN, 1,3 VOLKER M. KOCH, and ROLF VOGEL 1,4

¹ARTORG Center for Biomedical Engineering Research, University of Bern, Murtenstrasse 50, 3010 Bern, Switzerland; ²Engineering and Information Technology, Bern University of Applied Sciences, Biel, Switzerland; ³Graduate School for Cellular and Biomedical Sciences, University of Bern, Bern, Switzerland; and ⁴Department of Cardiology, Solothurn Hospitals, Solothurn, Switzerland

(Received 25 March 2013; accepted 5 August 2013; published online 15 August 2013)

Associate Editor Peter E. McHugh oversaw the review of this article.

Abstract—Human energy harvesting is envisioned as a remedy to the weight, the size, and the poor energy density of primary batteries in medical implants. The first implant to have necessarily raised the idea of a biological power supply was the pacemaker in the early 1960s. So far, review articles on human energy harvesting have been rather unspecific and no tribute has been given to the early role of the pacemaker and the cardiovascular system in triggering research in the field. The purpose of the present article is to provide an upto-date review of research efforts targeting the cardiovascular system as an alternative energy source for active medical implants. To this end, a chronological survey of the last 14 most influential publications is proposed. They include experimental and/or theoretical studies based on electromagnetic, piezoelectric, or electrostatic transducers harnessing various forms of energy, such as heart motion, pressure gradients, and blood flow. Technical feasibility does not imply clinical applicability: although most of the reported devices were shown to harvest an interesting amount of energy from a physiological environment, none of them were tested in vivo for a longer period of time.

Keywords—Heart motion, Blood flow, Blood pressure, Artery, Piezoelectric, Electromagnetic, Electrostatic.

INTRODUCTION

The year 2010 marked the 50th anniversary of the first pacemaker implantation in the USA.⁶ Behind the scene was the electrical engineer Wilson Greatbatch, who would play a major role in the early developments of pacemaker technology.²³ The poor energy density of primary batteries was among the core issues of the first pacemaker generations. Mercury cells used in the early

Address correspondence to Rolf Vogel, ARTORG Center for Biomedical Engineering Research, University of Bern, Murtenstrasse 50, 3010 Bern, Switzerland. Electronic mail: rolf.vogel@spital.so.ch

1960s lasted for about 2 years only. ⁴² In a desperate search for a long-lasting supply, nuclear power (Plutonium-238) was introduced, but quickly abandoned due to obvious security concerns and the advent of more promising solutions. ⁴² The real breakthrough came with the lithium battery in the 1970s: its high energy density allowed for the uninterrupted operation of a pacemaker up to 10 years. ⁴² However, the surgical replacement of pacemakers signalling an "elective replacement indicator" remains a frequent procedure to this day.

A pacemaker triggers something that is inherently much more powerful than the stimulus itself. In principle, a tiny fraction of the energy released during cardiac contraction could be reused as pulse energy, turning the patient into his own supplier. How long did it last until the idea of a human-powered pacemaker rose among the community?

First experiments on a dog were reported by Parsonnet et al.⁵² as early as 1963, emphasizing that pacemaker autonomy was a serious problem from the very beginning. Their device featured a series of piezoelectric bimorph beams wrapped around the aorta, rigidly connected on the one end and free to move with the systolic/diastolic deformation of the aorta on the other end. The alternating electric voltage obtained from the cyclic straining of the piezoelectric material was rectified and passed to a pacemaker. An improved version with a clamp geometry made from only two beams was presented a few years later. 40 The generator was reported to produce enough power to operate a cardiac pacemaker, but it was not clear how energy production would be affected by long-term foreign body reactions. Generally speaking, this first decade (1960s) was characterized by three distinct energy harvesting approaches³⁶: piezoelectric transducers (driven by body motion)^{34,40,52}; fuel cells (reduction/oxidation of body reactants)^{10,13}; galvanic batteries (potentials between different body fluids acting as electrolytes),^{35,37} which have been later abandoned.

The pacemaker did not remain the only medical implant that could benefit from a biological power supply. In his early survey of *in vivo* energy sources, Konikoff³⁶ put it almost poetically: "Long term implants of electronic gadgetry have also become relatively commonplace in the biomedical community...". That was back in 1967.

Today, human energy harvesting has become a global quest. The advances in ultralow-power electronics¹² have lowered the demand of medical implants to a level where the offer of intracorporeal energy harvesters becomes attractive, fostering research in this field. Certain classes of active implants still need an excessive amount of power (e.g., hearing aids with secondary batteries or retinal stimulators); here, harvesting energy from the subject's body could improve his quality of life by extending the time between two battery charges. The advancing age of the population further motivates the development of self-supplying implants, because repeated battery replacement during a patient's life-time must be avoided. Finally, even if life-lasting implants may seem less profitable to sell, their strongly innovative character enables companies to strengthen their position as market leaders. This intense activity is evidenced by a large spectrum of review articles: human energy in general, 63,67,68 and, more specifically but not necessarily limited to human energy, kinetic energy, ^{7,30,43} thermal energy, ⁷³ biological fuel cells, ^{8,29} piezoelectric transducers, ² nanoscale transducers.41

It is the purpose of this article to provide an up-todate review of research efforts specifically targeting the human cardiovascular system as energy source. What forms of energy can be considered in the cardiovascular system? Which theoretical and/or experimental achievements were reported in the recent years? How do they compare?

THE CARDIOVASCULAR SYSTEM AS ENERGY SOURCE

The heart is the driving force behind the cardiovascular system. Acting as a pump, it supports the pulmonary and the systemic circulation by doing work on blood during systole. Although originating in the myocardium, heart activity can be exploited indirectly at different locations.

The product of mean aortic pressure p_{mean} and cardiac output CO gives the mean hydraulic power

output of the heart. It amounts to ≈1.4 W in a healthy subject $(p_{\rm mean} \approx 100 \ {\rm mmHg} \ {\rm and} \ CO \approx$ 6.3 L min⁻¹).³⁸ Approximately 25% should be added to this value when taking pulsatility into account. ⁷⁶ To what extent can we tap this power source without substantially influencing the cardiovascular system? A sound answer can only be formulated on the basis of (currently lacking) long-term in vivo trials. Nonetheless, we believe that 1 mW of continuous electric power, which is less than 1% of the above estimated power output of the heart, is still a conservative estimate. The mechanical efficiency of the myocardium, defined as the ratio of useful energy produced (i.e., stroke work) to oxygen consumed, amounts to $\approx 25\%$ under normal conditions.³³ For the idealistic engineer, this conversion efficiency is surprisingly low. However, the endurance of this organ is amazing: at an assumed constant pulse rate of 1 Hz, the heart of a 65-year-old subject contracted over 2 billions times.

The following forms of energy resulting from heart activity are of particular interest.

Heart Motion

The cyclic contraction of the heart results in a mechanical motion of the myocardium at a frequency of 1-3 Hz.³⁸ Besides a longitudinal component characterized by a fractional shortening of the distance between the apex and the aortic valve of $\approx 20\%$, 71 this motion features complex twisting patterns as observed in magnetic resonance imaging tagging or echocardiography. 48 This suggests that generators working both on linear and/or rotational principles should be considered. By attaching a device to the heart, energy can be harvested from its motion. 4,16,22,26,28,69,78 Such a device could be accommodated on the endocardial side of the apex or in accessory cavities like the atrial appendages. If delivered by a minimally invasive catheter-based approach, the device should come as a cylindrical structure with maximal diameter and length of 8 and 14 mm, respectively (assuming an adult patient). For an epicardial placement, i.e., into the pericardial space, the preferred geometry is flat (<3 mm) but can be larger ($16 \times 16 \text{ mm}^2$). In order not to disturb cardiac contraction, the device should typically not weight more than 1-2% of heart mass, i.e., 3-6 g. 38

Pressure Gradients

In a healthy subject, the arterial blood pressure varies between 80–85 mmHg at diastole and 120–125 mmHg at systole.³⁸ During ventricular contraction, high pressure gradients are found between the ventricles and the atria. In the left heart, the atrioventricular gradient easily reaches 100 mmHg at peak



systole.³⁹ During diastole, the pressure is higher in the atrium to support ventricular filling (in the left heart, $\Delta p_{\rm max} \approx 12$ mmHg). High pressure gradients can also be obtained by shunting the arterial and the venous sides of the systemic circulation (central venous pressure: ≈5 mmHg).³⁸ Whether a function of time and/or space, pressure gradients can be used to drive a generator. 17,20,21,45,57,60–62,65 Most efforts to develop blood pressure harvesters have so far concentrated on technological aspects irrespective of a specific implantation site. As will appear later, pressure-loaded piezoelectric diaphragms have received the greatest deal of attention. They require exposure to blood on one side of the diaphragm only, suggesting an implantation along the endocardium or along the endothelium of larger arteries to minimize the impact on blood flow. This configuration would restrict the maximal area of the diaphragm to $\approx 5 \text{ cm}^2$.

Blood Flow

The kinetic energy of flowing blood depends on the velocity and the vessel size. In the aorta, peak flow velocity can reach up to 1.6 m s⁻¹. However, the aorta is hardly a realistic target as implantation site because any defect of the device would result in a major adverse event. Of particular interest are small and non-vital vessels, like the left and right internal thoracic arteries. With approximately 20 cm length, a luminal diameter of 2.0–3.0 mm⁷² and an average flow rate of 40 mL min⁻¹, typical flow velocity is of the order of 10–20 cm s⁻¹. The ability to remodel their diameter in response to flow requirements⁶⁴ and the very low incidence of atheromatous plaque formation¹ are two interesting qualities of these vessels. Also conceivable is an arterio-venous shunt offering a lowflow high-pressure environment. Several patents disclosing ideas to harvest energy from blood flow were found. 18,19,24,66

Although this energy source may be obvious, researchers in the field did not investigate its potential until very recently.⁷⁴ It appears that four decades of accumulated experience in implanting foreign bodies such as stents, valves, or cardiac assist devices into the human cardiovascular system have convinced some that it is time to seriously consider the idea of an endovascular generator, despite the known complexity of the biological interaction.

Arterial Compliance

Due to the compliant nature of arteries, the pressure change between diastole and systole is accompanied by a volume change of the lumen. This (visco-)elastic

buffering capability of arteries, often compared to a capacitor in electrical engineering, contributes to smoothen the pulsatile nature of blood flow. This is essential to ensure optimal exchange at the capillary level. As example, the increase in diameter between diastole and systole in carotid arteries reaches $\approx 10\%$. 9,15 This pulsating motion of the arterial wall can in turn be coupled to a generator. 3,11,47,53,54,58,59 The perivascular nature of this approach limits the risks of occluding or hampering blood flow and the risks of infections or blood clotting.⁵⁹ Because a deformation of reasonable amplitude is needed, only mid- to large-sized arteries are appropriate. For a 10 mm-wide artery, a surrounding circular structure of up to 2 mm thickness seems acceptable. In a first approximation, the output power of the generator scales linearly with its length. However, the presence of side branches will make it difficult to find a "clean" arterial segment of more than 20 mm. The proximity of functional implant and generator is essential to avoid excessive wiring: for example, an artificial urinary sphincter could be powered from the iliac arteries, a drug delivery pump from the abdominal aorta and a deep brain stimulator from the subclavian arteries.

ENERGY HARVESTING FROM THE CARDIOVASCULAR SYSTEM: STATE OF THE ART

This chapter surveys a selection of 14 contributions pertinent to the topic of interest in the last 15 years. The articles are grouped according to the classification introduced in the previous chapter and they appear in a chronological order within each section.

Heart Motion

Feasibility of Using the Automatic Generating System for Quartz Watches as a Leadless Pacemaker Power Source, Goto et al., 1999

Among the well-known issues of pacemakers are the risks of lead fracture and the complications associated with the surgical replacement of depleted batteries. Still a dream 10 years ago, the leadless and human powered pacemaker is currently a hot topic and almost advertised as a *fait accompli* by several research groups.

Although a similar idea—likely inspired from automatic wristwatches—had been patented already in 1969,⁴ it is only 30 years later that the principle of an eccentric wheel driven not anymore by arm but by heart motion and coupled to a tiny electro-magnetic generator was first experimented by Goto *et al.*²² The



mechano-electric transducer of a Seiko automatic quartz watch (Fig. 1) was encapsulated in a polyvinyl casing and sutured to the right atrioventricular wall of an anaesthetised dog. A home-made pulse generator served as pacemaker. Harvesting (200 bpm) and pacing (140 bpm) were conducted in two separate experiments. In average, 13 μJ were harvested per heartbeat, whereas $50 \mu J$ were consumed per pulse (pulse energy + pacemaker consumption). Closed-loop operation of the device could therefore not be demonstrated. However, with later developments in lowpower electronics, as illustrated by a pacemaker consuming as little as 8 μ W, 77 this prototype would have already delivered sufficient power.

Development of an Electrostatic Generator for a Cardiac Pacemaker that Harnesses the Ventricular Wall Motion, Tashiro et al., 2002

The next attempt to exploit heart motion was by Tashiro et al., 69 who built an electrostatic generator based on a motion-driven variable capacitor (VC). A VC undergoes a decrease in capacitance due to an external force while maintaining its electric charge, which results in an increase of the voltage and thus of the stored electrostatic energy. This approach was chosen because of the direct dependency of energy density on the surface area of the capacitor's electrodes and on the spacing between them—an optimization and miniaturisation task easily addressed with MEMS. A cyclic change of capacitance could be obtained from the relative motion between the heart and the chest wall. This would however require the device to be fixed to both sides and could obstruct cardiac contraction. Instead, the authors advocated an oscillator design,

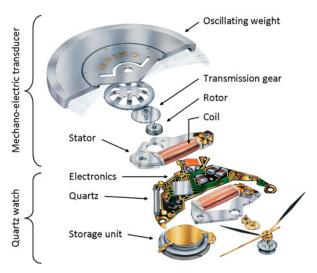


FIGURE 1. Exploded view of Seiko Kinetic watch mechanism (courtesy of Seiko Watch Corporation).

which only needs attachment to the left ventricular free wall. To this end, the handmade honeycomb-type VC was mounted between two endplates and subsequently turned into an oscillator by suspending one endplate by springs and adding a weight to it. The prototype, which could not be miniaturised sufficiently to be implanted into the thoracic cavity, was installed on a vibrating table mimicking heart movements thanks to a tiny 3-axis accelerometer placed on the left ventricular wall of an anesthetised dog. To close the loop, the output power of the generator was supplied to a homemade pacemaker with two myocardial electrodes in the dog's right atrium. A mean power of $36~\mu W$ was obtained at a pacing rate of $180~\rm bpm$, which was sufficient to ensure a continuous operation.

Energy Harvesting System for Cardiac Implant Applications, Deterre et al., 2011

Inertial energy harvester are widely spread in environments were vibrations are available. They consist of a proof mass suspended by springs to an enclosing frame, where the relative displacement of the proof mass with respect to the frame is converted to electrical energy by a piezoelectric, electrostatic of electromagnetic transducer.

Are inertial harvesters appropriate for heartbeat vibrations? The recent study by Deterre et al. 16 suggests that it is the case. The frequency spectrum of heartbeat vibrations was measured by accelerometers implanted in several heart cavities. Besides the fundamental frequency of the heartbeat, a plateau was found between 10 and 30 Hz, a range better suited for inertial harvesters. The simulated output power of a harvester tuned to a resonance/excitation frequency of 25 Hz yielded 30 μW per gram of proof mass. As pointed out by the authors, this is before any transducer is coupled to the proof mass. Hence, the conversion efficiency of the transducer (no specific choice made in the study) will eventually determine the electric output power. Assuming a 3.5 g proof mass made of Tungsten and springs microstructured in a silicon wafer, the authors concluded that a device delivering 100 µW (prior to mechano-electric conversion) could be fitted in a volume of $15 \times 7 \times 5$ mm³. It was not discussed how the performances would scale if the principal component(s) of vibrations and the degree(s) of freedom of the proof mass were poorly aligned.

Powering Pacemakers from Heartbeat Vibrations Using Linear and Nonlinear Energy Harvesters, Karami and Inman, 2012

Karami and Inman²⁸ referred to early ultrasonic vibration measurements of the intravascular septum²⁵



to determine the best resonance frequency for their piezoelectric harvester (39 Hz). A 50% decrease of standard battery size in pacemakers was targeted, yielding a maximum harvester volume of $27 \times 27 \times 6$ mm³. Because the resonance frequency of a standard cantilever beam is inversely dependent upon its length, making MEMS devices ineffective for ambient vibrations, the authors pioneered a "zigzag" geometry (Fig. 2a) featuring a low resonance frequency.²⁷ The output power of an optimized generator was simulated to $10~\mu\text{W}$, but proved highly sensitive to heart rate.

To overcome this limitation, the authors designed a nonlinear harvester by combining a bimorph beam with two magnets (Fig. 2b). The nonlinear behaviour follows from the repelling force between both magnets being a nonlinear function of their relative position. When this force is dimensioned to be larger than the elastic restoring force of the beam, a bi-stable system is obtained, which tends to respond chaotically to heartbeat excitations.

In an experiment on a mechanical shaker, the nonlinear piezoelectric harvester generated $\geq 10~\mu W$ over heart rates from 40 to 250 bpm (max: 17 μW at 52 bpm). The ability of this device to cope with such changes in heart rhythm remains unmatched to date.



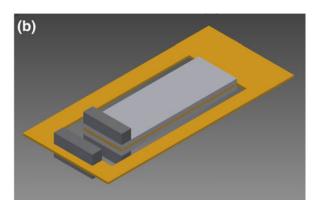


FIGURE 2. (a) Zigzag harvester tuneable to low resonance frequencies but sensitive to heart rate and (b) nonlinear design featuring a piezoelectric bimorph beam and repelling magnets (one on the beam, one on the surrounding frame) to produce a bi-stable chaotic system robust to variations in heart rate (reproduced with permission).²⁸



Energy Harvesting from the Beating Heart by a Mass Imbalance Oscillation Generator, Zurbuchen et al., 2013

Unlike previous approaches based on the frequency spectrum of heartbeats, Zurbuchen *et al.*⁷⁸ acquired MRI tagging data of a human left ventricle to identify favourable implantation sites. The heart was discretized by a point grid for motion analysis. Long trajectories were found in the basal region, mainly on the inferolateral side, with cumulated displacements per cardiac cycle up to 40.9 mm. Cyclic rotation of the heart surface was $\geq 27.3^{\circ}$ at each point.

The transducer of the automatic quartz watch used here differs slightly from the one used by Goto *et al.* (Fig. 1 vs. Fig. 9). In an *in vivo* study, the prototype (\emptyset 31 mm \times 7 mm, 16.7 g) was sutured to the mid-lateral wall of a sheep's left ventricle, generating 11.1 μ J per beat at a heart rate of 90 bpm.

For decades, watchmakers have been tuning this device to the motion spectrum of the arm. Motivated by the optimization potential with respect to heartbeat excitations, the authors proposed a mathematical model to predict the output power of the device for a given heart motion pattern and varying device parameters (e.g., mass or radius of the oscillating weight).

Pressure Gradients

Piezoelectric Energy Harvesting for Bio MEMS Applications, Ramsay and Clark, 2001

Ramsay and Clark⁶⁰ first suggested the use of a piezoelectric square membrane exposed to blood on one side and to a chamber with constant pressure on the other side to exploit blood pressure fluctuations. Although the piezoelectric strain and stress coefficients are larger for the longitudinal mode, they showed that the mechanical advantages of the transverse mode for energy conversion in such low-pressure environment should favour the latter. Output power is maximized for a membrane with maximum area and minimal thickness. For a physiological arterial pressure variation of 40 mmHg at a rate of 1 Hz, the power density of the envisioned 9 μ m thick PZT-5A plate was estimated to 2.3 μ W cm⁻² (PZT: lead zirconate titanate).

An Investigation on Piezoelectric Energy Harvesting for MEMS Power Sources, Sohn et al., 2005

Sohn *et al.*⁶⁵ compared the performances of a square vs. a circular piezoelectric membrane on the basis of both a finite element (FE) simulation and a verbatim repetition of Ramsay and Clark's theoretical formulation of power. Polyvinylidene fluoride (PVDF) was chosen in this analysis. The output power of the

circular membrane was found to be 30% higher than the square one, which is attributed to an advantageous stress distribution and a larger stress magnitude with a circular geometry. A pneumatic compressor and two solenoid valves were used to apply the desired pressure pulse onto the piezoelectric membrane. The test conditions were identical to those described by Ramsay and Clark. FE and experiment were in excellent agreement: for an area of 1 cm² and a thickness of 28 μ m, the circular membrane yielded 0.37 μ W (FE) vs. 0.33 μ W (exp), whereas the square one yielded 0.27 μ W (FE) vs. 0.25 μ W (exp).

The results with a square membrane are almost one order of magnitude smaller than the value predicted by Ramsay and Clark (0.25 μ W vs. 2.3 μ W). This may be explained by the different material (PVDF vs. PZT-5A) and the thicker membrane (28 μ W vs. 9 μ W) used in this study.

Harvesting the Energy of Cardiac Motion to Power a Pacemaker, Roberts et al., 2008

In December 2006, the Self-Energizing Implantable Medical Microsystem (SIMM) project was initiated in the UK.⁶¹ The generator, a catheter-mounted device placed on a conventional pacemaker or defibrillator lead, consists of a pacemaker electrode incorporating a coaxially mounted device with two pressure responsive bladders that utilise cardiac pressure to drive a linear generator.⁶² The two bladders, one in the right ventricle and one in the right atrium, are linked together by a conduit and filled with a fluid. An electromagnetic generator is coupled to the fluid motion in the conduit (Fig. 3). During ventricular diastole, the atrioventricular pressure gradient points towards the atrium; during ventricular systole, the pressure gradient is reversed. Thus, during one cardiac cycle, the generator is driven once forth and back.

In 2008, Roberts *et al.*⁶² reported about the first successful animal trial. The device was implanted in an anesthetised pig. At a heart rate of 80 bpm and systolic/diastolic blood pressures of 100/60 mmHg, the mean energy gained per heartbeat was 4.3 μ J, which is already halfway fulfilling a modern pacemaker's needs.

Experimental Validation of Energy Harvesting Performance for Pressure-Loaded Piezoelectric Circular Diaphragms, Mo et al., 2010

Mo et al.⁴⁵ built on Ramsay and Clark's early analysis of membranes and on an intermediate study by Kim et al.,^{31,32} who showed that "due to an inversion of sign in the strain in the piezoelectric layer as one traces it from the center to the outer edge of the diaphragm, the maximum amount of energy can be harvested when the electrode is divided at the line of

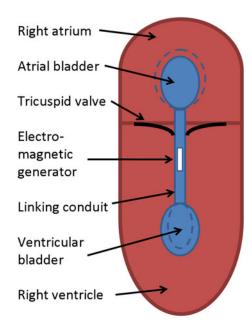


FIGURE 3. Working principle of SIMM generator: a fluid is pumped back and forth between two bladders as a function of the atrioventricular pressure gradient; a generator converts the fluid motion into electrical energy.

charge inversion so that the inverse charges can be added instead of canceling each other."⁴⁵

Mo et al.⁴⁴ subsequently found that for unimorph diaphragms, there is an optimal ratio between the radius of the supporting substrate and the radius of the piezoelectric layer coverage for given parameters (working pressure, materials and thicknesses of substrate and piezoelectric layer) (Fig. 4). The authors also showed that thinner substrates increase strain in the piezoelectric layer and thus yield more power, up to a point where the neutral axis passes through the piezoelectric layer, diminishing the net charge production.

Experiments with a PZT-5H wafer (thickness: $127 \mu m$; radius: 1.27 cm) epoxy-bonded to an aluminium substrate (thickness: $254 \mu m$; radius: 2.12 cm) yielded up to $128 \mu J$ per loading cycle ($\Delta p = 40 \text{ mmHg}$). Because of open-loop measurements, the energy was computed as the product of output voltage squared and capacitance. The authors acknowledged that the useful power in a matched load could be overestimated by up to 80% due to coupling effects. 56

An Active Piezoelectric Energy Extraction Method for Pressure Energy Harvesting, Deterre et al., 2012

Efforts in extracting energy from pressure gradients by piezoelectric diaphragms had so far been concentrated on optimising the geometrical properties of substrate and piezoelectric layer. 45,60,65 Recently, Deterre *et al.* 17 investigated the impact of the electric circuitry.



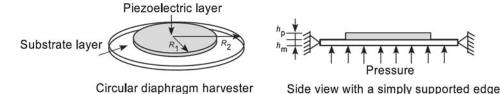


FIGURE 4. Ratios of radii and thicknesses in a unimorph circular diaphragm (reproduced with permission).⁴⁵

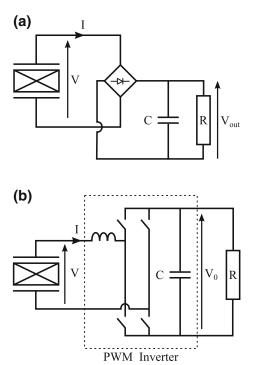


FIGURE 5. (a) Classical passive energy extraction method with a rectifier and (b) active charge extraction method with PWM inverter for square-wave control voltage (reproduced with permission).¹⁷

According to the authors, piezoelectric energy extraction strategies are classified into passive (rectifier-based), semi-active (switching-based), and active. An active extraction method supplies the piezoelectric material with a square-wave voltage in phase with the pressure variation on the diaphragm. The underlying principle is that the extraction of charges during straining of the piezoelectric material can happen at a higher voltage without affecting the current. Risks of mechanical and electrical damages of the piezoelectric material limit the magnitude of this voltage. The efficiency of the electric circuitry required to apply this voltage dictates the overall benefit.

The authors experimentally compared a passive with an active approach (Fig. 5). A cyclic pressure variation of 50 mmHg at a rate of 2 Hz was applied on a diaphragm (brass substrate: 22.5 mm radius, $100 \mu m$ thickness; PZT layer: 12.5 mm radius, $110 \mu m$

thickness). Compared to the rectifier-based approach yielding approximately ± 2 V, a forced square-wave control voltage of ± 10 V resulted in a 9-fold increase of output power (8 μ J per loading cycle). Importantly, the efficiency of the power management electronics is not reflected in this value.

Blood Flow

Electromagnetic Energy Harvesting from Vibrations Induced by Kármán Vortex Street, Wang et al., 2012

Human-induced vibrations show very low fundamental frequencies and a rapid decrease of amplitude at higher harmonics, which makes it difficult to benefit from resonance effects. To induce vibrations where they do not occur naturally, Wang *et al.*⁷⁴ submerged a bluff body in a channel (Fig. 6). The disturbance of the flow produces vortex shedding, which is seen downstream of the bluff body as a Kármán vortex street causing a pressure oscillation. The channel wall is replaced by a diaphragm at the location of maximal oscillation amplitude. Energy is harvested by coupling an electromagnetic transducer to the vibrating diaphragm.

In an experiment, a square channel (15.7 \times 15.7 \times 50 mm³) was perfused with water at a constant average velocity of 1.38 m s⁻¹. Pressure oscillations of \approx 2.3 mmHg at a frequency of 62 Hz were observed. The resulting output power in a matched 38 Ω load was 1.77 μ W.

Although the authors did not primarily aim at reproducing a physiological test scenario, the reported flow conditions were similar to those found in the human abdominal aorta at peak systole (except for water instead of blood). Blood flow was suggested as possible energy source by the authors, 55 but the risk of vortex-induced thrombi raises major concerns.

Arterial Compliance

An Arterial Cuff Energy Scavenger for Implanted Microsystems, Potkay and Brooks, 2008

Potkay and Brooks^{58,59} recently revisited the early trials by Parsonnet *et al.*⁵² and Lewin *et al.*⁴⁰ in the 1960s. They designed a self-curling cuff consisting of a



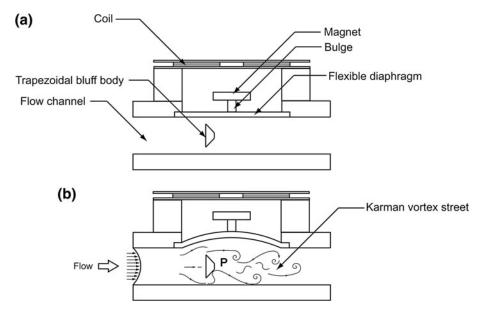


FIGURE 6. Electromagnetic energy conversion from bluff body-induced Kármán vortex street: (a) device layout and (b) Kármán vortex street causing oscillations of the flexible diaphragm (reproduced with permission).⁷⁴

PVDF piezoelectric film encapsulated in a medical-grade silicone sheet. PVDF was chosen due to its low Young's modulus (the cuff should not restrict arterial expansion/contraction) and due to the absence of toxic material. The $0.25~{\rm cm}^3$ cuff was wrapped around a latex tube (ø $12.7~{\rm mm}$) undergoing pulsatile pressure changes. For systolic/diastolic pressures of $\approx 140/60~{\rm mmHg}$ and a heart rate of $1.5~{\rm Hz}$, the device yielded an average output power of $6~{\rm nW}$. This is more than three orders of magnitude below the $8~\mu{\rm W}$ pacemaker by Wong *et al.*⁷⁷

Design and Realization of an Energy Harvester Using Pulsating Arterial Pressure, Pfenniger et al., 2013

In 1997, Nagel⁴⁷ patented the idea of winding a flexible coil around an artery. When applying an external magnetic field, the rhythmic deformation of the artery and the coil due to the pulsating blood would create an electromotive force. This approach was never realized because of a lack of elastic wires with a high conductivity.

Pfenniger et al.⁵⁴ used freely deformable coil designs as shown in Fig. 7. In an ex vivo experiment with a pig artery (Ø 10 mm × 30 mm), the 31.5 cm³ device (Ø 34 mm × 38 mm) generated an average power of 42 nW for a pressure variation of 85 mmHg at a rate of 1 Hz. Compared to the results of the 0.25 cm³ piezoelectric cuff by Potkay and Brooks, the average power of this electromagnetic generator was by a factor of seven higher. The authors also analysed their device analytically by considering its equation of motion. They concluded that it is probably not possible to significantly increase the output power unless a

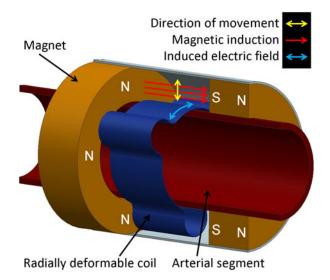


FIGURE 7. Schematic prototype design. Radial flexibility is given by the side-loops, such that the coil can move with the systolic/diastolic deformation of the artery. The induced electric field's direction obeys the right-hand rule.

revolutionary design is found that has a more flexible coil and a larger coil volume at the same time—two conflicting requirements.

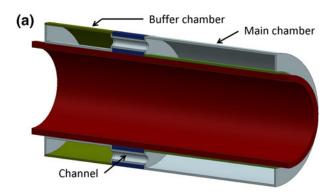
Energy Harvesting Through Arterial Wall Deformation: Design Considerations for a Magneto-Hydrodynamic Generator, Pfenniger et al., 2013

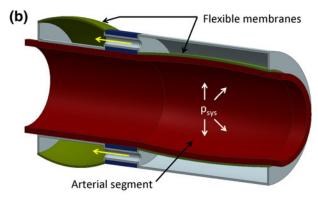
The main lesson learnt from the flexible coil prototype was that the velocity of the deforming artery ($\approx 1 \text{ mm s}^{-1}$) does not produce a meaningful rate of change of the magnetic flux in the coil. Can the slow



motion of the arterial wall be amplified to useful levels for electromagnetic energy conversion? Pfenniger *et al.*⁵³ found that an appropriate lever-arm mechanism is obtained by magneto-hydrodynamics (MHD; generalization of the electromagnetic induction theory to non-solid conductors, combining the Maxwell's with the Navier–Stokes equations).

Two compliant and oppositely-configured chambers (Fig. 8), linked by four channels and filled with Galinstan, a non-toxic liquid metal alloy, enclose an artery (Ø 10 mm). Each channel is delimited by two electrodes and two permanent magnets. The pulsatile arterial pressure causes an alternating flow through the channels, thereby inducing an alternating voltage between





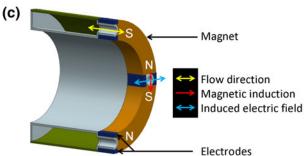


FIGURE 8. Schematic design of the envisioned MHD generator: (a) channels linking main and buffer chambers, filled with an electrically conductive fluid; (b) forward flow in the channels during systole (backward flow during diastole); and (c) section view depicting magnets and electrodes as well as the electric field induced by MHD.



the electrodes by the principle of MHD. Based on an analytical study of the device, the authors predicted an average output power between 65 and 135 μ W for a 3 cm³ circular generator. Compared to the deformable coil prototype, this represents an increase of output power by three orders of magnitude at a tenth of the volume.

DISCUSSION

A quantitative assessment of harvester effectiveness by a dimensionless figure of merit⁴³ is impossible due to the lack of systematic reporting (device size and mass, excitation pattern). Instead, the works are discussed by category for consistency with the previous chapters.

Heart Motion

The studied architectures can be categorized into two groups:

- automatic watch mechanisms based on a rotating eccentric mass;
- inertial harvesters based on the linear displacement of a proof mass.

Even if the reported devices were tested under different conditions, the achieved output power (Table 1) seems relatively independent of conversion principle, harvester architecture, and year (differences well below one order of magnitude). The only prototype that could not be tested *in vivo* because of size was the electrostatic device by Tashiro *et al.* Today the size issue has vanished, as illustrated by a MEMS version of an electrostatic harvester under development by the Heart Beat Scavenger consortium, founded in 2010.

It is worthwhile taking a closer look at the latest two studies, the nonlinear piezoelectric harvester (NPH²⁶) and the mass imbalance oscillation generator (MIOG⁷⁸; Fig. 9):

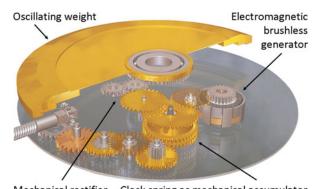
- the MIOG is approximately 25% larger in size (NPH: $2.7 \times 2.7 \times 0.6 \text{ cm}^3 = 4.4 \text{ cm}^3$; MIOG: \emptyset 3.1 cm \times 0.7 cm = 5.3 cm³);
- at the same pacing rate (90 bpm), the MIOG delivered approximately 50% more power (NPH: 11 μW²⁶; MIOG: 17 μW);
- the NPH was shown to perform well over a wide range of excitation frequencies, whereas the MIOG was evaluated at a specific heart rate only;
- the NPH had been optimized to the heartbeat spectrum, whereas the MIOG not; and
- both devices were tested under non-physiological conditions: the NPH was vibrated by a

TABLE 1. Energy harvesting from heart motion.

Source	Output power	Heart rate (bpm)	Site	Transducer	Study type
Goto et al. ²²	44 μ W	200	Mongrel dog, right atrioventricular wall	EM	In vivo
Tashiro et al.69	36 μW	180	Vibrating table	ES	Theoretical + in vitro/in vivo
Deterre et al. 16	30 μ W g ^{-1,a}	_	_	_	Theoretical
Karami <i>et al</i> .26	17 μW	52	Mechanical shaker	PE	Theoretical + in vitro
Zurbuchen et al. ⁷⁸	17 μW	90	Sheep, left ventricular mid-lateral wall	EM	Theoretical + in vivo

EM: electromagnetic; ES: electrostatic; PE: piezoelectric.

^aBefore any transducer is coupled to the oscillating proof mass.



Mechanical rectifier Clock spring as mechanical accumulator

FIGURE 9. Automatic wristwatch mechanism as used by Zurbuchen *et al.* Developed by Kinetron and found, e.g., in ETA 204 movement (courtesy of Kinetron B.V.).

mechanical shaker, yielding unrealistically good alignment of shaking direction and motion axis of proof mass; the MIOG experiment was openchest, which does not reflect true *in vivo* heart motion.

This assessment shows that none of the two devices clearly outplays the other. In this context, the one century old principle of the automatic wristwatch stands up to the latest technological developments. The MIOG gradually accumulates strain energy in an intermediate spring by mechanical coupling with the rotating mass. When this energy reaches a threshold, it is converted by a tiny electromagnetic brushless generator at optimal efficiency over a very short time. Hence, the mechano-electrical conversion efficiency is not affected by the excitation frequency/pattern, making this device ideal for low frequency and irregular motions. Further, the only damping acting on the rotating mass is due to mechanical friction in the bearings; there is no coupling with the electromagnetic damping in the generator. Finally, the MIOG is able to catch accelerations along 5 degrees of freedom (2 translations, 3 rotations), in contrast to the NPH which is limited to 2 degrees of freedom (1 translation, 1 rotation). Given the complex motion pattern of the heart, this is of significant importance. Further studies will reveal if an optimized version of the MIOG can be made sufficiently small and still powerful enough to be integrated in a pacemaker.

At an early stage of development, the technical feasibility of a given concept is of primary interest. However, the critical issue of biocompatibility must be addressed at some stage. Devices harvesting kinetic energy through their housing—like the NPH and the MIOG—are easy to package and integrate because they can be hermetically sealed as there are no moving parts interacting with the environment. ¹⁶ The challenge is rather to couple the generator to the source of movement, which means attaching a solid structure to soft tissue undergoing deformations. At the same time, this interface should maximise accelerations of the casing. Possible scenarios include suturing, clamping, or insertion in accessory cavities of the heart. The local impact on myocardial contractility and the local inflammatory response are of primary concern. Whether heart function is compromised eventually depends on the size and the weight of this parasitic item. Clearly, the success of heartbeat harvesters requires further miniaturisation of the state-of-the-art technology.

Pressure Gradients

Pressure gradients have been exploited mostly by piezoelectric diaphragms, for which a steady increase of understanding has been documented over the years: superiority of the transverse mode over the longitudinal mode in the low-pressure environment of the cardiovascular system⁶⁰; advantage of circular membranes over square ones⁶⁵; dependency of output power on the amount of piezoelectric coverage of the substrate⁴⁵; improvement of the electric extraction by applying a square-wave control voltage to the specimen.¹⁷



On the experimental side, it has not yet been proven that a piezoelectric diaphragm of reasonable dimension ($<5~\rm cm^2$) is able to power a cardiac pacemaker from a physiologic systolic/diastolic pressure difference (Table 2). However, the foreseeable fusion of the latest developments suggests that 10 μ W will be reached soon.

Pressure-loaded diaphragms are in direct contact with blood, but the simple geometry of this approach greatly reduces the problem of biocompatibility. The diaphragms could be coated with a layer of endothelial cells, making them virtually invisible and hence preventing thrombogenicity. Such techniques have been developed in tissue engineering, e.g., for printable polymers.

The SIMM device⁶² with the two bladders in the right heart can be easily integrated onto existing pacemaker leads. However, the right heart's performance is very sensitive to atrial and ventricular blood volumes and the hemodynamic consequence may prevent its clinical use. Furthermore, stable position must be guaranteed to prevent dysfunction of the tricuspid valve. On the other hand, the presence of a diseased cardiac valve may be a contraindication. The SIMM device is designed to operate under an alternating asymmetric pressure gradient. No details were disclosed about the linear electromagnetic generator used to convert the reciprocal motion of the fluid between the two bladders into electrical energy, but most of the energy is logically produced during systole, when the atrioventricular pressure gradient is highest. A decrease of the systolic pressure gradient would directly impair the performances of the device. This condition would typically be met in patients suffering from

tricuspid regurgitation (TR), e.g., as a result of the very common congestive heart failure, endocarditis, or induced by the device itself. The ability of the SIMM device to power a pacemaker in this patient population would depend on the regurgitation fraction and on the design margin. The situation is less critical if TR is induced by pulmonary arterial hypertension (PAH). Although a higher pulmonary arterial systolic pressure is associated with a progressively higher frequency of moderate to severe TR, there remains a large proportion of mild TR in patients suffering from a high pulmonary arterial systolic pressure. 46 Moreover. echocardiographic studies showed that for a high pulmonary arterial systolic pressure (≥70 mmHg), the atrioventricular systolic pressure gradient is independent of TR severity (63 mmHg; vs. ≈25 mmHg in a healthy subject). 46 Hence, it can be hypothesised that the SIMM device would perform better in patients with PAH (and TR) than in a healthy heart.

Blood Flow

The size of Table 3 testifies to the lack of enthusiasm towards blood flow so far. More efforts have been made in patenting ideas than materializing them into working prototypes. The authors are currently investigating a miniature Tesla⁷⁰ turbine to harvest energy from flowing blood in the milliwatt range.

Arterial Compliance

The combination of the pressure-driven deformation of an artery with piezoelectricity (Potkay and Brooks) or electromagnetism (Pfenniger *et al.*⁵⁴)

TABLE 2. Energy harvesting from pressure gradients.

Source	Output power or energy	Pressure difference (mmHg)	Heart rate (bpm)	Transducer	Study type
Ramsay and Clark ⁶⁰	2.3 μ W cm ⁻²	40	60	PE	Theoretical Theoretical + in vitro In vivo
Sohn <i>et al.</i> ⁶⁵	0.33 μ W cm ⁻²	40	60	PE	
Roberts <i>et al.</i> ⁶²	4.3 μ J/heartbeat	—	80	EM	
Mo <i>et al.</i> ⁴⁵	128 μJ/14.1 cm ² /loading cycle ^a	40	-	PE	Theoretical + in vitro Theoretical + in vitro
Deterre <i>et al.</i> ¹⁷	8 μJ/15.9 cm ² /loading cycle ^b	50	120	PE	

PE: piezoelectric; EM: electromagnetic.

TABLE 3. Energy harvesting from blood flow.

Source	Output power	Flow rate	Pressure drop	Transducer	Study type
Wang et al. ⁷⁴	1.77 μW	20.4 L min ⁻¹	_	EM	Theoretical + in vitro

EM: electromagnetic.



^aOverestimation of up to 80% due to missing load coupling.

bW/o losses of circuitry for control voltage.

TABLE 4. Energy harvesting through arterial compliance.

Source	Output power	(mmHg)	Heart rate (bpm)	Transducer	Study type
Potkay and Brooks ⁵⁹	6 nW	80	90	PE	Theoretical + in vitro
Pfenniger et al.54	42 nW	85 ^a	60	EM	Theoretical + ex vivo
Pfenniger et al. ⁵³	65–135 μW	40	66	MHD (EM)	Theoretical

PE: piezoelectric; EM: electromagnetic.

proved impracticable. With output powers of a few nanowatts (Table 4), several orders of magnitude separate these devices from any realistic application. Advances in ultralow power electronics will bring further down the consumption of medical implants; however, the expenditure associated with certain tasks, like the pulse energy to stimulate a cardiac contraction, will remain.

This conclusion does not apply to the novel MHD generator proposed by Pfenniger *et al.*⁵³ One can draw a parallel with the SIMM device, both relying on the displacement of a fluid in a channel between two compartments, said fluid displacement converted to electrical energy. The simulated output power is three orders of magnitude higher than previous attempts. The main challenge for transferring this concept from the *in silico* realm into a prototype is the output voltage in the submillivolt range, requiring an ultra-efficient energy converter. An experimental demonstration is not yet available.

How would the presence of the MHD generator affect the cardiovascular system? From an energetic perspective, the impact is clearly negligible: the energetic cost to produce the predicted output power from the pressure-driven deformation of a 10 mm-wide arterial segment is less than the intrinsic hysteresis loss of the undisturbed arterial segment due to its viscoelastic nature. ^{53,75} Another aspect is the compliance mismatch between the segment comprising the generator and the remaining of the artery, which may affect the propagation of the pressure wave. Because the generator and the wavelength have different length scales (cm vs. m), the amount of wave reflection should be insignificant. ^{49,53}

Taking Stock of the Present Situation

Heart motion and pressure gradients offer the best compromise between invasiveness and power: heart-beat harvesters "sit" directly on the myocardium and avoid any contact with blood; pressure-loaded diaphragms benefit from the full systolic/diastolic pressure difference and do not induce significant flow disturbances. For the past 15 years, these two energy

sources have attracted the greatest number of researchers. Today, the question is not anymore if a pacemaker can be powered from cardiac contraction, but what the final integrated design will look like: MEMS devices featuring either a piezoelectric or an electrostatic inertial harvester or a mechanism inspired from the automatic wristwatch coupled to an electromagnetic generator and optimized for the motion spectrum of the heart. An integrated harvester-pacemaker solution could be implanted directly onto or into the heart, thereby alleviating the need for pacemaker leads. To reach this goal, future research in the field should focus on the miniaturisation of the proposed harvesting technology (both the NPH and the MIOG should be reduced to $< 1 \text{ cm}^3$) as well as on the development of efficient energy conversion and storage strategies. The very fact that harvester and implant could be combined in a single device because of their proximity makes the human-powered pacemaker a highly attractive and tangible prospect. At the same time, the mutual dependency between the heart and the harvester raises safety concerns. A partial dysfunction of one of both would automatically lead to a vicious circle. Therefore, such a pacemaker must include a backup power supply to bridge the time between the occurrence of an anomaly and the proper handling of it. One approach would be to slightly overdesign the harvester capability and store the excess energy in a supercapacitor. Obviously, regulatory authorities will require clinical evidence showing that a novel humanpowered pacemaker is superior to the current pacemaker technology. Not only does this mean maintenance-free operation and biocompatibility for the intended lifetime; but also a device design not jeopardising proper heart function, a stable fixation of the device in the long-term and adequate safety mechanisms in case of insufficient energy harvesting (whatever the cause may be).

Blood flow is the most intrusive and hazardous approach, but this energy source is present throughout the body and could be exploited for any biomedical application relying on active implants. Moreover, the device could be deployed almost anywhere in the body



^aPressure required to achieve a 10% physiological diameter distension of the undisturbed arterial segment.

using the vascular pathway, which could also be used for some kind of wiring when needed, e.g., the pacemaker in its actual realisation.

Finally, generators coupled via arterial compliance gain their extravascular character at the cost of a reduced pressure variation due to vessel straining, which makes them less effective. Further, hardening of the arterial wall due to aging or other aetiologies may impact power production over time.⁵³ The fact that they are inferior to pressure-loaded diaphragms and more complex to realize logically suggests that this approach should be put aside. Instead, pressure-loaded diaphragms should receive more attention, as they are ideal candidates to power tiny implanted MEMS sensors, e.g., for long-term blood pressure monitoring. The study of pressure-loaded diaphragms has been conducted exclusively in vitro, and it is time to proceed with in vivo testing in order to determine appropriate implantation sites and methods, a task which has been neglected so far.

CLINICAL PERSPECTIVE

Drivers for Energy Harvesting Research

One of the many unwritten laws in medicine states: a treatment's complications increase—probably exponentially—with the distance between the point of administration and site of action. This is obvious for systematic drug therapy vs. local and targeted delivery. However, this applies for devices as well. The pacemaker, for instance, has two critical components that are mutually dependent: leads and batteries. Batteries run down and must be replaced; 1/4-1/3 of the implantation procedures are only replacements. Since it is not possible to re-operate on a heart repeatedly, the pacemaker is implanted in a site that is easily accessibly by surgery, at the cost of leads that deliver the therapeutic stimulus into the heart. The potential complications of this approach are: bleeding, infection, thrombosis, pneumothorax, lead fracture, and dislocation. Having a perpetual energy source, the pacemaker could be implanted once inside the heart without the need of long cables.

Energy harvesting is a beautiful and logic concept. However, the technology faces complex hurdles when it comes to medical applications and investments must be justified by clear clinical needs. There are two driving forces that keep the research going. First, energy harvesting research is pushed by approved devices in clinical use. These devices could be improved to prolong their life span and reduce their size and weight, which is also related with complications. Of course, present pacemaker technology offers very

efficient solutions for a majority of patients, i.e., the elderly in developed countries. This may not apply for other countries or places with long travelling distances to medical facilities. It is definitively not satisfactory for younger or paediatric patients who may depend on artificial pacing during 80 years or more. Other devices such as implantable defibrillators or carotid stimulators require much more power and the need to extend their life span is generally accepted. Second, energy harvesting research is pulled by future applications that depend on autonomous energy sources. Applications like body area networks may be used to treat diseases with dynamic behaviour governed by multiple factors. In the very common congestive heart failure as an example, body fluid volumes, pulmonary and arterial pressure, left ventricular filling pressure, and kidney function interact in a multifaceted way and are influenced by fluid and salt intake as well as the patient's medication and the adherence to the regimen. Any imbalance may cause cardiac decompensation and hospitalization implying intravenous diuretics or vasoactive substances. A system of autonomous sensors measuring these parameters and an actor administering diuretics would be an optimal approach to cope with such a disease.

Is Enough Today Enough Tomorrow?

Throughout this article, a 10 μ W pacemaker⁷⁷ was used as benchmark to put the various achievements into perspective. This is the typical power required for right ventricular (RV) pacing, the usual pacemaker therapy today. We concluded from Table 1 that a harvester providing enough power for RV pacing is feasible

However, it has been shown very recently that biventricular pacing can reduce mortality in patients with atrioventricular block as compared to standard RV pacing.¹⁴ We may therefore observe a shift from uni- to biventricular pacing in the near future. Biventricular pacing uses three electrodes (right atrium, right ventricle, left ventricle) to deliver an additional stimulus. A conservative estimate would have biventricular pacing consume roughly twice as much as RV pacing, i.e., 20 μ W. Would this increased power consumption prevent the human-powered pacemaker from becoming reality? Table 1 shows that 20 μ W is not an impossible target, in particular in light of the fact that some of the devices have not yet been optimised to the spectrum of heartbeat vibrations. Hence, we believe that there is sufficient room to develop heartbeat harvesters that can cope with the demand of more complex pacemakers.



Evolving Technology vs. Life-Lasting Implant

Is a life-lasting human-powered pacemaker the best solution? A young patient receiving an autonomous pacemaker today could indeed avoid repeated surgical interventions. But as technology evolves, he would not benefit from the improved functionality of next-generation pacemakers. If the prospect of better pacing schemes balances out the risks and the costs associated with surgery, a life-lasting pacemaker is not a competitive option. The fact that lots of efforts are put into developing this very device, both in academia and in industry, shows that people believe in its clinical benefit and economic potential. Furthermore, our daily business with mobile electronic equipments has taught us that a device's functionality may be expanded wirelessly in the future (this is true for software, not for hardware). A similar move could be observed with pacemaker technology, where new and better algorithms could be implemented while the device is already implanted. In other words: a life-lasting, humanpowered and updatable pacemaker.

CONCLUSION

The last decade and a half has witnessed repeated attempts to harvest energy from the cardiovascular system as a mean to overcome the limitations associated with primary batteries in medical implants. Heart motion and blood pressure gradients were the most investigated forms of energy and their ability to provide enough power to supply a cardiac pacemaker (10 μ W) has been established. The prospect of a human-powered pacemaker has never been so tangible, a good reason to pursue this endeavour more intensively. The need to prolong the life span of existing implants and the emergence of new therapies relying on interacting autonomous subsystems will keep researchers in the field busy for some more time.

REFERENCES

- ¹Abad, C., C. Santana, J. Diaz, and J. Feijoo. Arteriosclerotic histologic evaluation of the internal mammary artery in patients undergoing coronary artery bypass grafting. *Eur. J. Cardiothorac. Surg.* 9:198–201, 1995.
- ²Anton, S. R., and H. A. Sodano. A review of power harvesting using piezoelectric materials (2003–2006). *Smart Mater. Struct.* 16:R1–R21, 2007.
- ³Ariav, A. Method and apparatus for body generation of electrical energy. Patent: US7081683, 2006.
- ⁴Auphan, M. Heart-actuated, spring driven cardiac stimulator. Patent: US3486506, 1969.

- ⁵Bauman, L., C. S. Chung, M. Karamanoglu, and S. J. Kovács. The peak atrioventricular pressure gradient to transmitral flow relation: kinematic model prediction with in vivo validation. *J. Am. Soc. Echocardiogr.* 17:839–844, 2004
- ⁶Beck, H., W. E. Boden, S. Patibandla, D. Kireyev, V. Gupta, F. Campagna, M. E. Cain, and J. E. Marine. 50th anniversary of the first successful permanent pacemaker implantation in the United States: historical review and future directions. *Am. J. Cardiol.* 106:810–818, 2010.
- ⁷Beeby, S. P., M. J. Tudor, and N. M. White. Energy harvesting vibration sources for microsystems applications. *Meas. Sci. Technol.* 17:R175–R195, 2006.
- ⁸Bullen, R. A., T. C. Arnot, J. B. Lakeman, and F. C. Walsh. Biofuel cells and their development. *Biosens. Bioelectron*. 21:2015–2045, 2006.
- ⁹Bussy, C., P. Boutouyrie, P. Lacolley, P. Challande, and S. Laurent. Intrinsic stiffness of the carotid arterial wall material in essential hypertensives. *Hypertension* 35:1049–1054, 2000.
- ¹⁰Cahill, A. E., D. Nash, J. F. Neville, and W. J. van der Grinten. Program for development of an implantable fuel cell. In: Proceedings of the Biochemical Fuel Cell Session, Interagency Advanced Power Group Publications, PIC-BAT 209/5, 1962.
- ¹¹Cernasov, A. N. Apparatus and method for supplying power to subcutaneously implanted devices. Patent: US7813810, 2010.
- ¹²Chandrakasan, A. P., N. Verma, and D. C. Daly. Ultralow-power electronics for biomedical applications. *Annu. Rev. Biomed. Eng.* 10:247–274, 2008.
- ¹³Colton, C. K., and R. F. Drake. Analysis of in vivo deoxygenation of human blood: a feasibility study for an implantable biological fuel cell. *Trans. Am. Soc. Artif. Intern. Organs* 15:187–199, 1969.
- ¹⁴Curtis, A. B., S. J. Worley, P. B. Adamson, E. S. Chung, I. Niazi, L. Sherfesee, T. Shinn, and M. St. John Sutton. Biventricular pacing for atrioventricular block and systolic dysfunction. *N. Engl. J. Med.* 368:1585–1593, 2013.
- ¹⁵Dammers, R., F. Stifft, J. H. M. Tordoir, J. M. M. Hameleers, A. P. G. Hoeks, and P. J. E. H. M. Kitslaar. Shear stress depends on vascular territory: comparison between common carotid and brachial artery. *J. Appl. Physiol.* 94:485–489, 2003.
- ¹⁶Deterre, M., B. Boutaud, R. Dalmolin, S. Boisseau, J.-J. Chaillout, E. Lefeuvre, and E. Dufour-Gergam. Energy harvesting system for cardiac implant applications. In: Symposium on Design, Test, Integration and Packaging of MEMS/MOEMS (DTIP), 2011, pp. 387–391.
- ¹⁷Deterre, M., E. Lefeuvre, and E. Dufour-Gergam. An active piezoelectric energy extraction method for pressure energy harvesting. *Smart Mater. Struct.* 21:085004, 2012.
- ¹⁸Eli, U. Implantable device with miniature rotating portion for energy harvesting. Patent: US2009/0171448, 2009.
- ¹⁹Farco, J. Biomechatronic device. Patent: WO2011/119779.
 ²⁰Gelbart, D., and S. V. Lichtenstein. Self-powered leadless pacemaker. Patent: US2007/0276444.
- ²¹Gelbart, D., and S. V. Lichtenstein. Self-powered resonant leadless pacemaker. Patent: US2007/0293904.
- ²²Goto, H., T. Sugiura, Y. Harada, and T. Kazui. Feasibility of using the automatic generating system for quartz watches as a leadless pacemaker power source. *Med. Biol. Eng. Comput.* 37:377–380, 1999.
- ²³Greatbatch, W. Origins of the implantable cardiac pace-maker. *J. Cardiovasc. Nurs.* 5:80–85, 1991.



²⁴Holzer, A. Micro-generator implant. Patent: US2005/ 0256549.

- ²⁵Kanai, H., M. Sato, Y. Koiwa, and N. Chubachi. Transcutaneous measurement and spectrum analysis of heart wall vibrations. *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* 43:791–810, 1996.
- ²⁶Karami, M. A., D. J. Bradley, and D. J. Inman. Abstract 15551: Vibration powered cardiac rhythm devices. *Circulation* 126:A15551, 2012.
- ²⁷Karami, M. A., and D. J. Inman. Analytical modeling and experimental verification of the vibrations of the zigzag microstructure for energy harvesting. *J. Vib. Acoust.* 133:011002, 2010.
- ²⁸Karami, M. A., and D. J. Inman. Powering pacemakers from heartbeat vibrations using linear and nonlinear energy harvesters. *Appl. Phys. Lett.* 100:042901-1–042901-4, 2012.
- ²⁹Kerzenmacher, S., J. Ducrée, R. Zengerle, and F. von Stetten. Energy harvesting by implantable abiotically catalyzed glucose fuel cells. J. Power Sources 182:1–17, 2008.
- ³⁰Khaligh, A., P. Zeng, and C. Zheng. Kinetic energy harvesting using piezoelectric and electromagnetic technologies—state of the art. *IEEE Trans. Ind. Electron.* 57:850–860, 2010.
- ³¹Kim, S., W. W. Clark, and Q.-M. Wang. Piezoelectric energy harvesting with a clamped circular plate: analysis. *J. Intell. Mater. Syst. Struct.* 16:847–854, 2005.
- ³²Kim, S., W. W. Clark, and Q.-M. Wang. Piezoelectric energy harvesting with a clamped circular plate: experimental study. *J. Intell. Mater. Syst. Struct.* 16:855–863, 2005.
- ³³Knaapen, P., T. Germans, J. Knuuti, W. J. Paulus, P. A. Dijkmans, C. P. Allaart, A. A. Lammertsma, and F. C. Visser. Myocardial energetics and efficiency current status of the noninvasive approach. *Circulation* 115:918–927, 2007.
- ³⁴Ko, W. H. Piezoelectric energy converter for electronic implants. Patent: US3456134, 1969.
- ³⁵Konikoff, J. J. In vivo experiments with the bioelectric potentials. *Aerosp. Med.* 37:824–828, 1966.
- ³⁶Konikoff, J. J. A Survey of in Vivo Energy Sources. Washington: American Institute of Biological Sciences Bioinstrumentation Advisory Council, 1967, 22 pp.
- ³⁷Konikoff, J. J., and L. W. Reynolds. Results of some experiments in biochemical electricity. In: Proceedings of the Biochemical Fuel Cell Session, Interagency Advanced Power Group Publications, PIC-BAT 209/5, 1962.
- ³⁸Lentner, C. Geigy Scientific Table, Vol. 5, Heart and Circulation. Basel: CIBA-GEIGY Ltd, 278 pp., 1990.
- ³⁹Levy, M. N., and A. J. Pappano. Cardiovascular Physiology. Philadelphia: Mosby Elsevier, 288 pp., 2007.
- ⁴⁰Lewin, G., G. H. Myers, V. Parsonnet, and V. Raman. An improved biological power source for cardiac pacemakers. ASAIO Trans. 14:215–219, 1968.
- ⁴¹Liu, J., G. Cao, Z. Yang, D. Wang, D. Dubois, X. Zhou, G. L. Graff, L. R. Pederson, and J.-G. Zhang. Oriented nanostructures for energy conversion and storage. *ChemSusChem* 1:676–697, 2008.
- ⁴²Mallela, V. S., V. Ilankumaran, and N. S. Rao. Trends in cardiac pacemaker batteries. *Indian Pacing Electrophysiol*. *J*. 4:201–212, 2004.
- ⁴³Mitcheson, P. D., E. M. Yeatman, G. K. Rao, A. S. Holmes, and T. C. Green. Energy harvesting from human and machine motion for wireless electronic devices. *Proc. IEEE* 96:1457–1486, 2008.
- ⁴⁴Mo, C., L. J. Radziemski, and W. W. Clark. Analysis of piezoelectric circular diaphragm energy harvesters for use

- in a pressure fluctuating system. Smart Mater. Struct. 19:025016, 2010.
- ⁴⁵Mo, C., L. J. Radziemski, and W. W. Clark. Experimental validation of energy harvesting performance for pressureloaded piezoelectric circular diaphragms. *Smart Mater. Struct.* 19:075010, 2010.
- ⁴⁶Mutlak, D., D. Aronson, J. Lessick, S. A. Reisner, S. Dabbah, and Y. Agmon. Functional tricuspid regurgitation in patients with pulmonary hypertension: is pulmonary artery pressure the only determinant of regurgitation severity? *Chest* 135:115–121, 2009.
- ⁴⁷Nagel, M. Vorrichtung zur Erzeugung elektrischer Energie in lebenden Organismen. Patent: DE19535566, 1997.
- ⁴⁸Nakatani, S. Left ventricular rotation and twist: why should we learn? J. Cardiovasc. Ultrasound 19:1–6, 2011.
- ⁴⁹Nicoud, F. Hemodynamic changes induced by stenting in elastic arteries. Center for Turbulence Research, Annual Research Briefs 335–347, 2002.
- ⁵⁰Novosel, E. C., C. Kleinhans, and P. J. Kluger. Vascularization is the key challenge in tissue engineering. *Adv. Drug Deliv. Rev.* 63:300–311, 2011.
- ⁵¹Novosel, E. C., W. Meyer, N. Klechowitz, H. Krüger, M. Wegener, H. Walles, G. E. M. Tovar, T. Hirth, and P. J. Kluger. Evaluation of cell–material interactions on newly designed, printable polymers for tissue engineering applications. *Adv. Eng. Mater.* 13:B467–B475, 2011.
- ⁵²Parsonnet, V., G. H. Myers, R. Zucker, H. Lotman, and M. M. Asa. A cardiac pacemaker using biologic energy sources. *ASAIO Trans*. 9:174–177, 1963.
- ⁵³Pfenniger, A., D. Obrist, A. Stahel, V. M. Koch, and R. Vogel. Energy harvesting through arterial wall deformation: design considerations for a magneto-hydrodynamic generator. *Med. Biol. Eng. Comput.* 51:741–755, 2013.
- ⁵⁴Pfenniger, A., L. N. Wickramarathna, R. Vogel, and V. M. Koch. Design and realization of an energy harvester using pulsating arterial pressure. *Med. Eng. Phys.* 35:1256–1265, 2013.
- ⁵⁵Pham, H.-T., C.-Y. Chiu, and D.-A. Wang. An electromagnetic energy harvester based on pressure fluctuation in Kármán vortex street. In: The 1st International Symposium on Automotive & Convergence Engineering, 2011, pp. 1–4.
- ⁵⁶Platt, S. R., S. Farritor, and H. Haider. On low-frequency electric power generation with PZT ceramics. *IEEE/ASME Trans. Mechatron.* 10:240–252, 2005.
- ⁵⁷Pless, B. D. Device for energy harvesting within a vessel. Patent: US8283793, 2012.
- ⁵⁸Potkay, J. A. In situ energy harvesting systems for implanted medical devices. Patent: US2010/0298720.
- ⁵⁹Potkay, J. A., and K. Brooks. An arterial cuff energy scavenger for implanted microsystems. In: The 2nd International Conference on Bioinformatics and Biomedical Engineering, 2008, pp. 1580–1583.
- ⁶⁰Ramsay, M. J., and W. W. Clark. Piezoelectric energy harvesting for bio MEMS applications. *Proc. SPIE* 4332:429–438, 2001.
- ⁶¹Roberts, S., R. Freeland, G. Stanley, K. D. Dawkins, J. M. Morgan, and P. R. Roberts. Energy harvester for an implant device. Patent: US8135469, 2012.
- ⁶²Roberts, P., G. Stanley, and J. M. Morgan. Abstract 2165: Harvesting the energy of cardiac motion to power a pace-maker. *Circulation* 118:679–680, 2008.
- ⁶³Romero, E., R. O. Warrington, and M. R. Neuman. Energy scavenging sources for biomedical sensors. *Physiol. Meas.* 30:R35–R62, 2009.



- ⁶⁴Shimokawa, T., S. Manabe, T. Fukui, and S. Takanashi. Remodeling of reconstructed left anterior descending coronary arteries with internal thoracic artery grafts. *Ann. Thorac. Surg.* 88:54–57, 2009.
- ⁶⁵Sohn, J. W., S. B. Choi, and D. Y. Lee. An investigation on piezoelectric energy harvesting for MEMS power sources. *Proc. IMechE C* 219:429–436, 2005.
- ⁶⁶Sood, A. K., and S. Ghosh. Carbon nanotube flow sensor device and method. Patent: US6718834, 2004.
- ⁶⁷Starner, T. Human-powered wearable computing. *IBM Syst. J.* 35:618–629, 1996.
- ⁶⁸Starner, T., and J. A. Paradiso. Human-generated power for mobile electronics. In: Low-Power Electronics Design, edited by C. Piguet. Boca Raton: CRC Press, 2004, pp. 45-1–45-35.
- ⁶⁹Tashiro, R., N. Kabei, K. Katayama, E. Tsuboi, and K. Tsuchiya. Development of an electrostatic generator for a cardiac pacemaker that harnesses the ventricular wall motion. *J. Artif. Organs* 5:239–245, 2002.

⁷⁰Tesla, N. Turbine. Patent: US1061206, 1913.

⁷¹Thüring, C., O. M. Hess, T. Murakami, N. H. Goebel, J. Grimm, and H. P. Krayenbühl. Normalwerte der linksventrikulären Funktion. Biplane Angiokardiographie, unter Berücksichtigung geschlechtsspezifischer Unterschiede. *Fortschr. Röntgenstr.* 150:562–568, 1989.

- ⁷²Tortora, G. J., and B. H. Derrickson. Principles of Anatomy and Physiology. Hoboken: John Wiley & Sons, 1174 pp., 2009.
- ⁷³Vullers, R. J. M., R. van Schaijk, I. Doms, C. Van Hoof, and R. Mertens. Micropower energy harvesting. *Solid-State Electron*. 53:684–693, 2009.
- ⁷⁴Wang, D.-A., C.-Y. Chiu, and H.-T. Pham. Electromagnetic energy harvesting from vibrations induced by Kármán vortex street. *Mechatronics* 22:746–756, 2012.
- ⁷⁵Warriner, R. K., K. W. Johnston, and R. S. C. Cobbold. A viscoelastic model of arterial wall motion in pulsatile flow: implications for Doppler ultrasound clutter assessment. *Physiol. Meas.* 29:157–179, 2008.
- Westerhof, N., N. Stergiopulos, and M. I. M. Noble. Snapshots of Hemodynamics—An Aid for Clinical Research and Graduate Education. Boston: Springer, 192 pp., 2005.
- ⁷⁷Wong, L. S. Y., S. Hossain, A. Ta, J. Edvinsson, D. H. Rivas, and H. Naas. A very low-power CMOS mixed-signal IC for implantable pacemaker applications. *IEEE J. Solid-State Circuits* 39:2446–2456, 2004.
- ⁷⁸Zurbuchen, A., A. Pfenniger, A. Stahel, C. T. Stoeck, S. Vandenberghe, V. M. Koch, and R. Vogel. Energy harvesting from the beating heart by a mass imbalance oscillation generator. *Ann. Biomed. Eng.* 41:131–141, 2013.

