L.I.Anatychuk acad. National Academy of sciences of Ukraine^{1,2}, R.R. Kobylianskyi cand. phys.– math. sciences^{1,2}, Dzhal S.A.^{1,2}

¹Institute of Thermoelectricity of the NAS and MES of Ukraine, 1, Nauky str., Chernivtsi, 58029, Ukraine; *e-mail: anatych@gmail.com*²Yu.Fedkovych Chernivtsi National University, Chernivtsi, 58012, Ukraine

ON THE USE OF THERMOELECTRIC MICROGENERATORS FOR POWERING CARDIAC PACEMAKERS

The paper describes the design and operation of modern pacemakers, as well as their classification by the mechanism of work and power supplies. A comparative analysis of power supplies is given and prospects for the use of thermoelectric microgenerators for powering pacemakers are determined. Bibl. 66, Fig. 15, Tabl. 8.

Key words: cardiac pacemaker, power supply, thermoelectric microgenerator, cardiovascular diseases.

Introduction

General characterization of the problem. According to the World Health Organization (WHO), cardiovascular diseases (hypertension, coronary heart disease, circulatory disorders, heart failure, and other heart defects) account for one-third of deaths worldwide. It is reported that in 2017 there were more than 400 million people suffering from cardiovascular diseases in the world. Each year, they take more than 17 million lives, and experts predict that by 2030 this number will increase to 23 million people [1].

In the European Region, cardiovascular diseases account for half of all deaths. 80% of cardiovascular diseases are reported in low- and middle-income countries. According to UNIAN, cardiovascular diseases are the leading cause of death in Ukraine, especially among men. Cardiovascular diseases include ischemic heart disease (heart attacks), stroke, high blood pressure (hypertension), peripheral artery disease, rheumatic heart disease, congenital heart disease and heart failure [2].

Ukraine ranks first in Europe in mortality from cardiovascular diseases. According to the WHO, in 2015, 440 thousand Ukrainians died from cardiovascular diseases, and this figure is increasing annually. Mortality from cardiovascular diseases in Ukraine is 66.3% of the total. Among the diseases of the adult population, cardiovascular diseases lead in the form of hypertension – 41 %, coronary heart disease – 28 %, cerebrovascular diseases – 16 %, etc. [3, 4].

However, the implantation of cardiac pacemakers, artificial heart rhythm drivers, makes it possible to reduce the mortality rate from cardiovascular diseases. About 600,000 cardiac pacemakers are implanted annually worldwide [11], which allows prolonging the life of patients with severe cardiac impairment. Currently, there are various types of cardiac pacemakers (single-chamber, two-

chamber, three-chamber and rate-responsive, etc.), the electric power consumption of which varies greatly and ranges from 10 μ W to 300 mW. To power such pacemakers, electrochemical galvanic batteries, radioisotope thermoelectric generators, as well as thermoelectric and piezoelectric microgenerators can be used. It should be noted that the most common power supplies for cardiac pacemakers are electrochemical galvanic batteries, whose lifetime is about 10 years, following which it is necessary to replace the electrochemical battery, i.e. perform a second operation. Therefore, the urgent problem is the replacement of galvanic batteries by alternative power sources with a long life [5].

The purpose of this work is to conduct a comparative analysis of power supplies for cardiac pacemakers and to determine the feasibility of using thermoelectric microgenerators.

The structure and operating principle of a cardiac pacemaker

Cardiac pacemaker is an electronic device that performs the function of an artificial heart rhythm driver, which is set for a person in order to restore and normalize heart rhythm disturbances. Cardiac pacemaker is equipped with a special circuit for generating electrical pulses. Most commonly, a cardiac pacemaker is set for bradycardia, atrioventricular blockade, sinus node weakness syndrome [12].

Currently, there are the following basic types of cardiac pacemakers in medical practice: temporary, external and implanted. A modern temporary pacemaker (Fig. 1, 2) is a device that is set when it is necessary to quickly adjust the heart rate (for example, in acute myocardial infarction, as well as some types of bradycardia and tachyarrhythmia). Also, such a pacemaker is used in the pre-operative period with the subsequent implantation of a permanent instrument that replaces the temporary external pacemaker.

Each external pacemaker belongs to the group of temporary pacemakers and is widely used to correct heart rate by various indicators. The design of the external pacemaker provides for the presence of sufficiently large-size electrodes, which are superimposed in the region of the heart on the chest and on the area between the spine and the left shoulder blade (cardiac projection). Modern external pacemakers are in demand in the diagnosis, prevention and urgent restoration of the normal rhythm of heart contractions without surgical intervention [20].



Fig.1. Temporary cardiac pacemaker [12]



Fig.2. External cardiac pacemaker [12]

However, the subject of this work is precisely implanted cardiac pacemakers, so we will consider them in more detail.

In turn, implanted cardiac pacemakers are divided into single-chamber, two-chamber, threechamber and rate-responsive (intracardiac). The type of device needed for each clinical case is determined by doctor individually, based on the results of diagnostic studies [19-29].

A single-chamber pacemaker has only one active electrode and stimulates only one heart chamber (ventricle or atrium). Such a pacemaker is a simple and inexpensive device that does not have the ability to simulate physiological (natural) contraction of the heart muscle (Fig. 3). To date, such a cardiac pacemaker is accepted to use only with a constant form of pleural arrhythmia, with the electrode installed in the right ventricle.

A two-chamber cardiac pacemaker is connected via electrodes to the atrium and ventricle at the same time (Fig. 4). In the event of a need for stimulation, the generated pulse is sequentially fed first to the atrium, and then to the ventricle. This mode corresponds to the physiological contraction of the myocardium, normalizes cardiac output, ensures the coordinated work of the atrium and ventricle, and also improves the patient's adaptation to physical activity. Additional functions of modern two-chamber cardiac pacemakers make it possible to choose the optimal mode for each patient.

A three-chamber pacemaker (cardiosynchronization) is able to stimulate three chambers of the heart in a certain sequence: the right and left ventricle, as well as the right atrium (Fig. 5). Such cardiac pacemakers ensure the normal functioning of the heart and physiological intracardiac hemodynamics. These cardiosynchronization devices can be used to eliminate desynchronization of the heart chambers in severe forms of bradyarrhythmia or bradycardia. Such devices are implanted in patients with a dangerous form of arrhythmia - ventricular tachycardia and ventricular fibrillation or for the prevention of sudden cardiac death.

A rate-responsive cardiac pacemaker is a tiny device that is implanted completely inside the heart (Fig. 6). Such a pacemaker is equipped with sensors that can record changes in nervous system activity, respiratory rate and body temperature. Cardiac pacemakers of this type are used for cardiac pacing with rigid sinus rhythm, which is provoked by significant heart failure. Such pacemakers can much more accurately determine changes in physical activity and heart rate of the patient than the above two- and three-chamber.



Fig.3. Implanted single-chamber cardiac pacemaker [31]



Fig.4. Implanted two-chamber cardiac pacemaker [31]



Fig.5.Implanted three-chamber cardiac pacemaker [31]



Fig.6. Implanted rate-responsive (intracardiac) pacemaker [31]

An implanted cardiac pacemaker consists of a set of endocardial electrodes, a connector block, a microprocessor, a housing, and a battery (Fig. 7). The electrodes are flexible and durable spiral conductors that are fixed in the chambers of the heart and transmit pulses emitted by the device to the heart and also transmit information about the activity of the heart to the microprocessor. The number of endocardial electrodes depends on the state of the disease and the need to stimulate various parts of the heart.

The connector block is designed to connect the pacemaker housing to the endocardial electrodes. The housing of the device is made of titanium or other alloys that do not interact with the human body. Inside the housing there is a microprocessor, which works offline and is a special device for monitoring and adjusting the settings of the pacemaker. Using highly sensitive sensors, the processor also carries out Holter monitoring and observation of the human heartbeat, interfering with the work of the heart in case of violations.

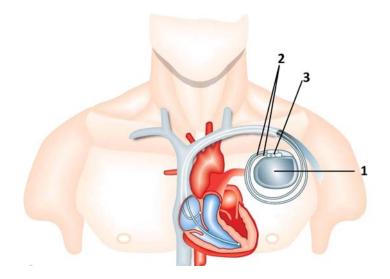


Fig. 7. Design of implanted cardiac pacemaker: 1 – cardiac pacemaker, 2 – endocardial electrodes, 3 – connector block

The main elements of a cardiac pacemaker are endocardial electrodes, used for stimulation, resynchronization or defibrillation of the heart. They consist of several common components, including electrodes, conductors, insulators, locking mechanisms, and connector pins (Fig. 8). Defibrillation openings also include shock coils for delivering high voltage electrical discharges to stop ventricular fibrillation. The number of electrodes depends on the condition of the disease and the need for stimulation of the heart [15]

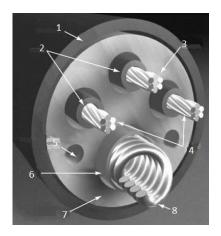


Fig. 8. Design of endocardial electrode [15]:
1 – urethane protective coating, 2 – ETFE (coating), 3 – sensor, 4 – defibrillator, 5 – squeezed clearance, 6 – PTFE(coating), 7 – HP silicone, 8 – electrode

The operating principle of a cardiac pacemaker is to control the heart rate (stimulation or inhibition) and defibrillation of the heart if it stops, by artificially contracting the heart muscles with the help of electrical pulses. Cardiac pacemaker stimulates the human heart by transmitting electrical pulses from the processor through the endocardial electrodes to the heart muscles [16, 17].

The microprocessor of a cardiac pacemaker constantly analyzes the pulses generated by the heart, conducts pulses to the wall of the heart and controls their synchronization. The endocardial electrodes transmit the pulse generated by the pacemaker to the heart chamber and transmit information about the activity of the heart back to the microprocessor. At the end of each endocardial electrode there is a metal nozzle, which provides contact of the electrode with the corresponding part of the heart, and also "reads" information about the electrical activity of the heart and, if necessary, transmits electrical pulses.

With a small number of heart contractions or their complete absence, the cardiac pacemaker switches to the mode of constant stimulation and transmits pulses to the heart with a frequency that was set during implantation of the device. During normal heart function, a cardiac pacemaker starts to work in standby mode and functions only in the absence of independent heart contractions. In modern cardiac pacemaker models, the control of work settings is carried out by a microprocessor, is programmed during implantation and can be changed remotely and without surgical intervention [18].

General requirements for pacemaker power supplies

Over the past 50 years, there has been a rapid evolution of the technology of manufacturing cardiac pacemakers (Fig. 9). The overall dimensions and power consumption of modern cardiac

pacemakers have significantly decreased with the simultaneous increase of their functionality. Currently, the most common are single-, two-, and three-chamber cardiac pacemakers implanted in the subcutaneous pocket near the heart, followed by electrode insertion into the heart chambers, and rate-responsive cardiac pacemakers implanted directly inside the heart. The above-mentioned types of cardiac pacemakers are powered by electrochemical galvanic batteries. The power requirements of these cardiac pacemakers are different. A comparative analysis of technical specifications of power supplies for cardiac pacemakers is shown in Table 1.



Fig. 9. Evolution of the technology of manufacturing cardiac pacemakers Evolution of implanted cardiac pacemakers. 1958 Weight 74.4 g

<u>Table 1</u>

Technical specifications of power supplies for cardiac pacemakers [34,43-46,]

Parameter	Single-, two- and three-chamber cardiac pacemekers	Rate-responsive (intracardiac) cardiac pacemeakers
Dimensions	49 mm x 46 mm x 6 mm	length 42 mm, diameter 5.99 mm
Mass	20-30 g	2-5 g
Operating voltage	1.5-4.7 V	1.5-2 V
Electric power	0.1-370 mW	0.070 mW
Battery capacity	2000 mA	120-248 mA (novel)
Service life	9-10 years	4.7-14.7 years

Table 1 shows that the overall dimensions of electrochemical galvanic power supplies for implanted single-, dual- and three-chamber pacemakers are within 49 mm x 46 mm x 6 mm, and for implanted rate-responsive pacemakers - 42 mm, with a maximum diameter of 5.99 mm. The weight of such power supplies does not exceed 20-30 g and 2-5 g, respectively. The minimum operating

voltage is 1.5 V for both types of pacemakers. The electric power consumption of one-, two- and three-chamber cardiac pacemakers is 0.1-370 mW, which significantly exceeds the power consumption of rate-responsive pacemakers, is 0.070 mW. These power supplies provide the necessary electrical power and voltage for 9-10 years for various types of pacemakers. However, the main disadvantage of such power supplies for cardiac pacemakers is the need for their periodic replacement after the end of life (re-operation) and their toxicity. However, the developers predict that in the event of a depleted power supply, the cardiac pacemaker switches to power-saving mode, limiting most of the additional functions in order to save the vital options. In this mode, the cardiac pacemaker can work up to 3 months [10 - 14].

Operating principle and technical specifications of power supplies for cardiac pacemakers

Implanted cardiac pacemakers can have the following power supplies: electrochemical galvanic battery, radioisotope thermoelectric generator, piezoelectric and thermoelectric microgenerators, as well as pendulum actuated [40, 49, 39].

Cardiac pacemakers with electrochemical galvanic battery

Lithium-ion batteries for cardiac pacemakers are tiny power supplies (the weight of a cardiac pacemaker without electrodes, but with a battery is 26-28 grams), the charge of which is enough for about 10 years of continuous operation [34-42]. In practice, there are different types of pacemakers weighing from 20 to 50 grams, and a service life of up to 10 years [21, 22]. The appearance and technical specifications of the pacemakers with electrochemical galvanic battery are shown in Fig. 10 and Table 2.

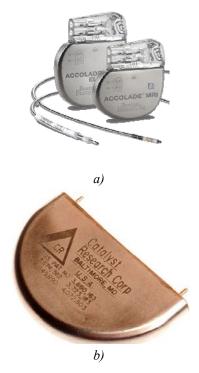


Fig.10. Cardiac pacemaker with electrochemical galvanic battery [44]:
a) cardiac pacemakers Boston Scientific Accolade on lithium-ion batteries,
b) lithium-ion battery of diameter 30 mm.

Power supply	Operating voltage	Power	Average dimensions	Manufacturers
Lithium-ion battery	2.2 ÷ 2.8 V	25-30 mW	49 mm × 46 mm × 6 mm	Saint Jude medical, Boston Scientific, Medtronic, Vitatron

Technical specifications of cardiac pacemakers with electrochemical galvanic battery

Usually, regular visits to the doctor will assess the condition of the power supply to determine the time during which it will still work. If the battery is depleted, the doctor recommends a procedure for the replacement of the cardiac pacemaker. During this procedure, not only the battery but also the entire pacemaker is replaced. Therefore, the operation is very similar to that performed at the first implantation of the device.

Battery life depends on the manufacturer. Modern pacemakers often use more energy because the battery not only sends pulses to the heart, but also regulates pacemakers, stores heart rate information and performs other functions. If the pacemaker is rarely activated, the battery can run for a long time. The batteries in the cardiac pacemaker are depleted quickly if the device has to be regularly activated to support the heart. This is one reason why doctors cannot accurately predict the life of a device. In each case, the battery charge will deplete at different speeds, so each patient's case is individual [28,39-40, 43].

There are also rare cases of implanting a device with a battery that has certain disadvantages. The cardiac pacemaker power supply is carefully tested before implanting the device, however sometimes testing does not reveal an existing problem, and the battery charge decreases abnormally quickly. Another cause of rapid battery depletion may be microprocessor defects or other components of the cardiac pacemaker. This is one of the reasons why the patient needs to visit the doctor repeatedly for several weeks immediately after implanting the device, and to make sure that the device is working properly.

Lithium-ion battery is the cheapest and most compact power supply for cardiac pacemakers, but its main disadvantage is short life.

It should be noted that in 2013, the American startup Nanostim Micra implemented a fundamentally new type of cardiac pacemaker without endocardial electrodes, it was notable for its tiny size and implantation feature (although the patent for a utility model dates back to 1976 [51], a serial advanced model was released only in 2013 [48]). Such cardiac pacemaker is set without surgical intervention - via transvenous access (through the femoral vein) into the chambers of the heart. Experts say that this technological novelty is a grand stride forward, and although it is quite new, it is actively developing [43-49]. The appearance and technical specifications of the rate-responsive cardiac pacemaker are shown in Fig. 11 and Table 3.



Fig.11. Rate-responsive (intracardiac) pacemaker [43-49,52]

Technical specifications of the rate-responsive cardiac pacemaker

Power supply	Operating voltage	Power	Dimensions	Manufacturers
 Electrochemical galvanic battery based on: Lithium-carbon monofloride Lithium-argentum- vanadium oxide 	1.5-2 V	70 μW	Length: 13.5-42 mm, diameter: 2.6-5.99 mm	Medtronic, Sant Jude Medical (Nanostim), EBR Systems (CambridgeConsul- tants)

An incision is made on the patient's skin to set a standard pacemaker, and then the doctor passes the endocardial electrodes through the lateral vein into the heart. The device itself is placed in a special subcutaneous pocket near the chest. Such a system is far from perfect through the great risks of infection of the subcutaneous pocket, and the presence of a conventional pacemaker limits the patient's mobility and life. In contrast, the Nanostim Micra pacemaker is set by insertion into the femoral vein via a small incision in the groin area, and then transported to the patient's heart by a catheter. The wireless device is equipped with a tiny battery and can operate from 8 to 10 years. The absence of endocardial electrodes and the necessary subcutaneous pocket reduces the possibility of infection and, moreover, patients are not limited in their activity.

A positive perception of intracardiac pacemaker by the human body and a productive life were observed in 280 of 300 patients (93.3 %). After 6 months, serious side effects associated with the device were observed in 6.7 % of patients; cases included device overload during surgical removal (1.7 %), cardiac perforation (1.3 %), which required removal and replacement of the device (1.3 %) [47].

The latest pacemaker models of this type are already equipped with an inductive battery charging system. Animal tests were successful, which gave impetus to the further improvement and implantation of this type of pacemakers. In addition, recharging is fast enough. For example, a battery with a capacity of 1050 mA from 50 to 100 % can be charged in 56 minutes by placing the transmitter

at a distance of 10 mm from the patient's chest at a frequency of 13.56 MHz. There are no similar analogues in the market of artificial pacemakers, which makes this type of device the "flagship" of pacing [37, 38].

Cardiac pacemaker with a radioisotope thermoelectric generator

This cardiac pacemaker uses as a power supply a thermoelectric generator with a radioactive isotope heat source. The pacemaker consists of a housing which accommodates a thermoelectric generator and a lead capsule with radioactive uranium or plutonium, as well as a microprocessor, is connected to a set of endocardial electrodes using a connector block. The operating principle of the RITEG is to convert the heat generated from the radioactive decay of uranium into electrical energy using a thermoelectric generator. Unlike lithium-ion battery, the RITEG is more durable (service life is up to 30 years), but it is more large-format [41 - 42]. The appearance and technical specifications of a cardiac pacemaker with a radioisotope thermoelectric generator are shown in Fig. 12 and in Table 4.

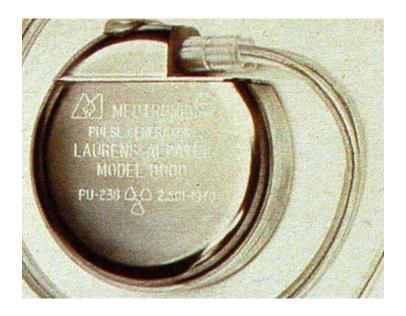


Fig. 12. Cardiac pacemaker with a radioisotope thermoelectric generator [53]

Table 4

Technical specifications of a cardiac pacemaker with a radioisotope thermoleectric generator

Power supply	Operating voltage	Power	Dimensions	Manufacturers
Radioisotope thermoelectric generator (RITEG)	4-4.7 V	300-370 mW	$30 \times 60 \times 40$ mm	Medtronic CCC ArcoMedical American Opticals

RITEG were first introduced in the 1970s in order to extend the life of cardiac pacemakers. At that time, such a pacemaker was a good substitute for mercury-zinc batteries, which, in addition to their unreliability, had a very short service life - less than three years. From this standpoint, RITEG, which provided patients with the opportunity to have only one cardiac pacemaker for life, was a good alternative. The first implantation of such a pacemaker, manufactured by Medtronic together with Alcatel, took place in 1970 in Paris [41].

However, in the early 1980s, such batteries slowly began to be displaced by lithium-ion. In those days, the service life of lithium-ion batteries was about 5-10 years. Therefore, the doctors decided that it is better to do the operation at intervals of one decade and to change the device to a newer one, than to walk with an outdated overall device for a lifetime. Therefore, the implantation of cardiac pacemaker with RITEG was discontinued between 1985 and 1990. As of 2003, approximately 100 people lived in the United States who had been implanted cardiac pacemakers with RITEG [42]. Patient status information as of 2019 was not found.

And yet, it should be noted that despite its size, the main drawback of RITEG is toxicity. Patients and their entourage, despite the isolation and protective housing of the cardiac maker, are adversely affected by radioactive radiation [48].

Cardiac pacemaker with a piezoelectric generator

The power supply for such a pacemaker is a piezoelectric element consisting of a housing containing a membrane, quartz plates and electrical terminals through which the generated electricity is transmitted to an electronic amplifier housed inside the pacemaker [59-62]. Z-section quartz crystalline elements (along the axis of symmetry) of a piezoelectric element are cropped quartz plates covered by several protective layers - a layer of chromium and Cr-Au gold, a photoresistive layer and a layer of galvanic copper.

Stimulation of the human heart by such a pacemaker is carried out by transmitting electrical pulses from the processor through the endocardial electrodes to the heart muscles [60]. The power supply of such a pacemaker is provided by a piezoelectric element. The principle of its work is to convert the mechanical energy of deformation created by the human breath into electrical energy. Due to the compression of the quartz plates of the piezoelectric element along one of the three symmetry axes, one side of the plate is charged positively and the other negatively.

When the plate restores equilibrium, the phenomenon of the inverse piezoelectric effect is observed: the positively charged side becomes negatively charged, the negatively charged side – vice versa. The magnitude of the electric charge is directly proportional to the magnitude of the pressure on the quartz plates. In this case, longitudinal compression is used, as a result of which compression of the quartz plate on one side leads to charging of this plate on the opposite side. Thus, the power supply of the pacemaker is as follows: the compression of the housing is converted by the membrane into an effort, causing the compression of quartz plates (for example, with a diameter of 5 mm and a thickness of 1 mm). The electric charge generated at the electrical terminals is transmitted to the electronic amplifier and stabilized by means of a voltage stabilizer to the level of $1.5 \div 2$ V. The appearance and technical specifications of a pacemaker with a kinetic (piezoelectric) generator are shown in Fig. 13 and Table 5.



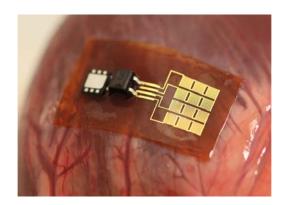


Fig. 13. Piezoelectric generator for cardiac pacemakers [62]

Technical specifications of cardiac pacemakers with a kinetic (piezoelectric) generator

Power supply	Operating voltage	Power density and current strength	Dimensions
 Piezoelectric generator with crystals	1.5-2 V	7 mW/cm ³	0.1-20 × 0.1-20 × 0.0001
(nanolegs) based on: Zinc oxide (ZnO); Barium titanate (BaTiO₃); Plumbum zirkonititanate (PZT).		0,19 μA/cm ²	mm

Pacemakers with piezoelectric generators have also been developed that are capable of converting into electricity even the compression energy generated by the motions of the lungs, blood flow, palpitation and vascular contraction. Such piezoelectric generators consist of zinc oxide (ZnO) or barium titanate (BaTiO₃) nanolegs. In a generator about 2 mm² in size, there are over 1 million nanolegs. The nanowire array is coated with a silicon electrode with a zigzag platinum coating, which is used to increase the electrode conductivity. When chemically grown legs located at the end of the electrode bend are subject to vibration, the ions in them shift. This imbalance creates an electric field that produces electricity and can be used as a potential source of energy. The efficiency of such a piezoelectric generator is 17-30%.

In 2010, scientists at Arizona State University developed miniature piezoelectric generators that can convert heart muscle energy into electrical energy. The research team was able to successfully implant polymer-based piezoelectric generators. The current generated by the generators is enough for powering low-power medical devices, as well as for charging the battery of the set cardiac pacemaker. Experiments have been conducted to show that, at periodic deformation of the device, the voltage at the terminals is from 1 to 2 V and the current is about 100 nA [60] Initial tests on rabbit hearts showed voltages and currents of about 1 mV and 0.2 mA, respectively. Output power is much less than what is needed for the existing pacemakers. However, novel thin-film generators on the basis of barium titanate and plumbum zirkonititanate are much more efficient [60]. The BaTiO₃ ferroelectric solid films were deposited by radio frequency magnetron sputtering on a Pt/Ti/SiO₂ /(100) Si substrate and subjected to an electric field of 100 kV /cm. Metal insulators (BaTiO₃)-metal-structured tapes were

transferred to a flexible substrate and connected by electrodes. During the periodic deformation stage, a flexible BaTiO₃-based nanogenerator generates an output voltage of up to 1.0 V. This nanogenerator produces an output current density of 0.19 μ A/cm² and a power of ~ 7 mW/cm³. According to scientists, the piezoelectric generator used in this study is able to produce enough electricity to meet all the needs of the cardiac pacemakers [60].

Another option is a piezoelectric nanogenerator based on the legs of plumbum zirconititanate (PZT), which uses a soft polymer silicon substrate. Such a piezoelectric nanogenerator, with a diameter of approximately 60 nm, is capable of generating an output voltage of 1.63 V and an electrical power of 0.03 μ W with periodic compression of the soft polymer [61]. The use of such piezoelectric nanogenerators with an extended service life or the complete rejection of batteries in implanted medical devices (cardiac pacemakers) will protect patients from repeated operations and from the risk of postoperative complications (infection, rejection of the implant by the body, etc.).

It has been found experimentally that a piezoelectric generator produces ten times more power than a cardiac pacemaker needs, and its size is about half that of a battery of such implants. In addition, such a piezoelectric generator works regardless of the heart rate - it produces sufficient electric power with a pulse of 20 to 600 beats per minute. The developers also claim that its work is not affected by mobile phones, microwave ovens and other similar devices [61]. It should be noted that piezoelectric generators are promising for powering cardiac pacemakers, but they still do not have wide practical application, since they require a large number of further medical and clinical trials. The service life of the piezoelectric generator is difficult to evaluate, since it depends on the location, voltage, etc., although there is a generator that has been operating since 1982 [63].

Cardiac pacemakers without electrodes, battery-free and mechanically controlled by heart

Swedish scientists Dr. Adrian Zurbuchen, Andreas Heberlin and Lucas Beroiter of the University of Bern in Switzerland in 2016 developed a fundamentally new approach to pacemaker technology. The power source of such a pacemaker is a winding mechanism, which works on the principle of a wristwatch. This device does not have a power supply that must be periodically changed, as well as endocardial electrodes, i.e. it is placed directly on the heart, which does not limit the patient's movement, and is better perceived by the body due to its small size.

The power supply is a mechanism based on the ETA $204 \setminus ETA$ SA winding, Grenchen Switzerland. The weight of 12 g was achieved by skeletonization of the body.

The main structural elements are the oscillation weight (pendulum), which is made of platinum alloy (7.5 g), which turns the heartbeat into circular rotation of the pendulum, a mechanical rectifier that allows you to convert energy from the oscillations of the pendulum in both directions, a spiral spring, which is temporarily stores energy in a mechanical form and an electric microgenerator (MG205, Kinetron BV, Netherlands), which converts the energy of rotational motion into an electrical signal. When the torque of the coil spring is equalized with the torque needed to operate the generator, the coil is released and powers the electric micro-generator. The resulting pulse includes about 80 μ J at a load resistance of 1 k Ω [64].

The power supply and electronics of the cardiac pacemaker are combined in a special polymer housing. Two electrodes with a diameter of 0.5 mm and a length of 3 mm are placed at the bottom of the housing and pierce the myocardium. The housing has a diameter of 27 mm and a thickness of 8.3 mm.



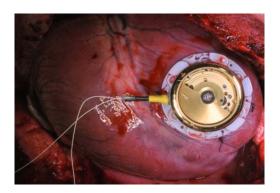


Fig. 14. Cardiac pacemaker mechanically controlled by heart [66]

Power supply	Operating voltage	Power	Dimensions
Self-winding mechanism (similar to wristwatches)	~3 V	82-90 μW	Diameter 27mm Height 8.3mm

Technical specifications of cardiac pacemakers without electrodes, battery-free and mechanically controlled by heart

The experimental results showed high output power, especially when placed on the left side of the heart. When placing the device in this position, constant power values of $82 \pm 4\mu$ W and $90.1 \pm 0.7\mu$ W were taken, which are reasonably good parameters for power supply. Also, the pacemaker is equipped with a 47μ F capacitor, which absorbs excess energy and, in the event of a lack of energy, can supply the pacemaker for a minute [64]. This development is conceptual and requires further improvements, such as increasing the capacity of capacitor, reducing the weight of the pendulum and increasing the power. But despite this, the development is promising.

Cardiac pacemaker with a thermoelectric microgenerator

Such a pacemaker contains a set of endocardial electrodes, a connector block, a thermoelectric microgenerator (TEG), a microprocessor, a capacitor, a voltage stabilizer, and a housing (Fig. 15) [6, 8, 55 – 58]. The thermoelectric microgenerator is a multi-element thermocouple thermoelectric micromodule with two ceramic plates and electrical terminals. The thermoelectric micromodule consists of a set of semiconductor thermocouple elements connected in a series circuit, the gaps between which are filled with an insulating epoxy compound, and two ceramic plates that are tightly in contact with the upper and lower faces of the thermocouple elements, as well as two electrical terminals. Such a thermoelectric micromodule is made on the basis of modern high-performance thermoelectric materials based on *Bi-Te*. The manufacturing technique of such micromodules provides a packing density of up to 5000 legs of *n*- and *p*-type thermoelectric material per 1 cm² of micromodule area [8]. For example, a typical thermopile with a total surface area of 1.5 cm² generates a voltage of 1.5 V and provides a power of 100 μ W at a temperature difference of 1 ° C. The technical specifications of a cardiac pacemaker with a thermoelectric microgenerator are shown in Table 7.

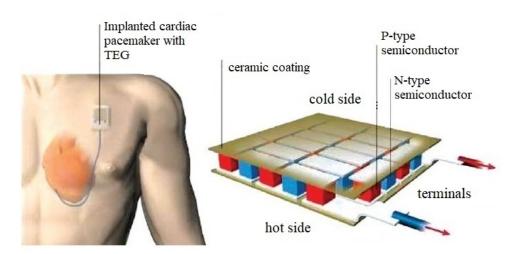


Fig.15. Schematic of implanted cardiac pacemaker with TEG [49,55]

TT 1 · 1	· ^ , ·	C 1.	1	• 1 1	1	• ,
Lochnical	cnocifications	of cardiac	r nacomakore	1 λ η th η	mooloctric	microgonorator
rechnicui	SDECINCULOUS	u	παιεπακειδ	wiin a men	noelectric r	nicroseneraior
	~p		r			nicrogenerator

Power supply	Operating voltage	Power	Dimensions
Thermoelectric microgenerator	1.5-2 V (at temperature difference 1 °C)	100 μW	$10 \times 15 \times 2 \text{ mm}$

In order to obtain the necessary voltage and power using a thermoelectric micromodule for powering cardiac pacemaker, a temperature difference between its faces should be arranged. To ensure the heat flux through the thermoelectric micromodule, it is necessary to place the thermoelectric converter inside the human body between internal organs having different temperatures, for example, near a vessel through which blood circulates at a temperature of $37 \,^{\circ}$ C. It should be noted that the temperature differences between the internal organs of a person reach 0.5-1 $^{\circ}$ C, which is quite enough to generate the necessary electrical power for a cardiac pacemaker. In the design of the device, a capacitor can also be used to accumulate the electric charge necessary for the operation of a cardiac pacemaker, and a voltage stabilizer of the thermoelectric micromodule to the level of 1.5-2 V.

The main advantage of cardiac pacemakers with thermoelectric microgenerators is the ability to work for 30-50 years, which significantly reduces the number of medical procedures required to replace implants during the patient's life, and this, in turn, reduces the likelihood of possible complications and costs. The lifetime of such pacemakers is 5 times longer compared to the most common pacemakers with an electrochemical galvanic battery. At the same time, the negative influence of radioactive radiation inherent in pacemakers with a radioisotope thermoelectric generator is completely absent.

Comparative analysis of power supplies for cardiac pacemakers

Table 8

Comparative analysis of power supplies
for cardiac pacemakers

Parameter	Electrochemi cal galvanic battery for single-, two- and three- chamber cardiac pacemakers	Electrochemic al galvanic battery for intracardiac pacemakers	RITEG	Piezoelectric generator	Winding mechanism for cardiac pacema- kers	Thermo- electric microgene- rator
Mass	20-30 g	2-5 g	20-50 g	10-14 g	12 g	2-5 g
Operating voltage	1.5-2.8 V	1.5-2.0 V	4-4.7 V	1.5-2 V	~3 V	1.5-2 V
Electric power	25 mW	0.070 mW	370 mW	7 mW	0.082- 0.09 mW	0.1 mW
Battery capacity	2000 mA	140 mA	_	_	_	-
Service life	8-10 years	15 years	\geq 30 years	≥30 years	≥30 years	\geq 30-50 years
Dimensions	$49 \times 46 \times 6$ mm	Ø6x42 mm	30 × 60 × 40 mm	$\begin{array}{ccc} 20\times 20\times & 1\\ 0^{-4} \ mm \end{array}$	27 mm - 8.3 mm	5-20 mm
Toxicity	Yes	Yes	Yes	No	No	No
The degree of readiness for use	Serial production	Serial production	Out of productio n	Under development	Under developme nt	Under development

From the comparative analysis it follows that the use of thermoelectric sources of electric energy for powering cardiac pacemakers holds much promise. Such sources are not toxic, have almost unlimited service life and, therefore, do not require replacement or charging. It is estimated that they can be much cheaper that chemical sources, and in terms of usage and principle of operation they are more reliable than other sources of electric energy.

Conclusions

- A comparative analysis of the structures, the principle of operation and technical specifications of lithium-ion, radioisotope, piezoelectric, mechanical and thermoelectric power supplies for cardiac pacemakers is performed. From a comparative analysis it follows that the use of thermoelectric sources of electric energy for powering cardiac pacemakers holds much promise. Such sources are not toxic, have almost unlimited service life and, therefore, do not require replacement or charging. It is estimated that they can be much cheaper than chemical sources, and in terms of usage and principle of operation they are more reliable than other sources of electric energy.
- 2. It has been found that thermoelectric microgenerators implanted in the human body make it possible to generate 1.5-2 volts of electrical voltage and 100 μ W of electrical power at a temperature difference of 1 °C, which is quite sufficient for powering modern pacemakers.

References

- Benjamin Emelia J., Virani Salim S., Callaway Clifton W., et al. (2018). Heart disease and stroke statistics—2018 update: a report from the American Heart Association. *Circulation*, 137: e67– e492.
- 2. Terenda N.O. (2015). Smertnist vid sertsevo-sudynnykh zakhvoriuvan yak derzhavna problema [Mortality from cardiovascular diseases as a state problem]. *Visnyk naukovykh doslidzhen-Herald of Scientific Research*, 4, 1-13 [in Ukrainian].
- 3. Handziuk V.A. (2014). Analiz zakhvoriuvanosti na ishemichnu khvorobu sertsia v Ukraini [Analysis of the incidence of coronary heart disease in Ukraine]. *Ukrainian Journal of Cardiology*, 3, 45-52.
- 4. Chepelevska L.A., Liubinets O.V. (2009). Prohnozni tendentsii smertnosti naselennia Ukrainy [Predictive tendencies of mortality of the population of Ukraine]. *Visnyk sotsialnoi hihieny ta okhorony zdorovia Ukrainy Bulletin of Social Hygiene and Health Care Organization of Ukraine*, 3,10–15 [in Ukrainian].
- Strutinskaya L.T. (2008). Termoelektricheskiie mikrogeneratory. Sovremennoie sostoianiie i perspektivy ispolzovaniia [Thermoelectric microgenerators. Curent status and prospects of use]. *Tekhnologiia i konstruirovaniie v elektronnoi apparature – Technology and Design in Electronic Equipment*, 4, 5-13 [in Russian].
- 6. Anatychuk L.I. (1979). Termoelementy i termoelektricheskiie ustroistva: Spravochnik [Thermoelements and thermoelectric devices: Handbook]. Kyiv: Naukova dumka [in Russian].
- 7. Anatychuk L.I. (2003). *Termoelektrichestvo. T.2. Termoelektricheskiie preobrazovateli energii* [*Thermoelectricity. Vol.2. Thermoelectric power converters*]. Kyiv, Chernivtsi: Institute of Thermoelectricity [in Russian].
- 8. Application for utility model № u 2017 11815 (2017). Anatychuk L.I., Kobylianskyi R.R., Dzhal S.A. Cardiac pacemaker with a thermoelectric power supply [in Ukrainian].
- 9. Application for utility model № u 2017 11818 (2017). Anatychuk L.I., Kobylianskyi R.R., Dzhal S.A. Cardiac pacemaker with a combined power supply [in Ukrainian].
- 10. Ludwig A, Zong X, Hofmann F, Biel M. (1999). Structure and function of cardiac pacemaker channels. *Cell Physiol Biochem*, 4-5:179-86.PMCID: 10575196
- 11. https://www.futurity.org/tiny-pacemaker-1049422/
- 12. http://www.kardiodom.ru/articles/572.html.
- 13. Skundin A.M, Fateev S.A, Kulova T.L. Battery for cardiac pacemaker: an alternative to lithium iodine system. Moscow: Institute of Electrochemistry of RAS.

- 14. Julien C., Mauger A., Vijh A., et al. (2016). Lithium batteries. *Science and Technology*, 15. ISBN: 978-3-319-19107-2.
- 15. https://clinicalgate.com/engineering-and-construction-of-pacemaker-and-icd-leads-2/
- 16. Tracy C.M., Epstein A.E., Darbar D., et al. (2012) ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J. Am. Coll. Cardiol., Dec 12.
- Potpara Tatjana S., Lip Gregory Y.H., Larsen Torben B., et al. (2016). Stroke prevention strategies in patients with atrial fibrillation and heart valve abnormalities: perceptions of 'valvular' atrial fibrillation: results of the European Heart Rhythm Association Survey. *Europace*, 18, 1593–1598.
- Bongiorni Maria Gracia, Blomstrom-Lundqvist Carina, Pison Laurent, et al. (2014). Management of malfunctioning and recalled pacemaker and defibrillator leads: results of the European Heart Rhythm Association survey. *Europace*, 16, 674–1678.
- Livenson A.R. (1981). Elektromeditsinskaia apparatura. [Electromedical equipment]. 5th ed. [in Russian].
- 20. http://www.eurolab.ua/encyclopedia/ambulance/48886/
- 21. Patent US 3057356A. (1962). Greatbatch Wilson. Medical cardiac pacemaker.
- 22. Patent US 5562715A. (1996). John J. Czura, Randolph H. Kricke. Cardiac pulse generator.
- 23. Aizawa Y, Kunitomi A, Nakajima K, Kashimura S, Katsumata Y, Nishiyama T, Kimura T, Nishiyama N, Tanimoto Y, Kohsaka S, Takatsuki S, Fukuda K. (2015). Risk factors for early replacement of cardiovascular implantable electronic devices. *Int. J. Cardiol*, 178, 99–101.
- 24. https://link.springer.com/chapter/10.1007%2F978-3-642-50209-5_11
- 25. Patent US 4056105. (1977). Richard J. Ravas. Pulse generator.
- 26. Patent US 3835864. (1974). Ned S.Rasor. Intra-cardiac stimulator.
- 27. Brignole Michele, Auricchio Angelo, Baron-Esquivias Gonzalo. (2013). ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. *European Heart Journal*, 34, 2281–2329.
- 28. Benkemoun H., Sacrez J., Lagrange P., et al. (2012). Optimizing pacemaker longevity with pacing mode and settings programming: results from a pacemaker multicenter registry. *Pacing Clin Electrophysiology*, 35(4), 403-8.
- 29. Hernandez Antonio, Lewalter Thorsten, Proclemer Alessandro (2014). Remote monitoring of cardiac implantable electronic devices in Europe: results of the European Heart Rhythm Association survey. *Europace*, 16, 129–132.
- 30. Maltsev Victor A., Yaniv Yael, Maltsev Anna V., et al. (2014). Modern perspectives on numerical modeling of cardiac pacemaker cell. *Pharmacol Science Journal*, 125(1), 6–38.
- 31. http://www.kardiodom.ru/hirurgia/375.html
- Bock David C., Marschilok Amy C., Takeuchi Kenneth J., Tekeuchi Esther S. (2012). Batteries used to power implantable biomedical devices. *Electrochim Acta*. Published online 2012 Mar 23. PMCID: PMC3811938.
- Abdulianov I.V., Vagizov I.I. (2013). Modern approaches to constant pacing. *Practical Medicine*, 3(71).
- 34. Sarma Mallela Venkateswara, Ilankumaran V., Srinivasa Rao N. (2004). Trends in cardiac pacemaker batteries. *Indian Pacing Electrophysiol J.*, 4(4), 201–212. Published online 2004 Oct 1.PMCID: PMC1502062.

- 35. Todd Derick, Proclemer Alessandro, Bongiorni Maria Grazia, et al. (2015). How are arrhythmias detected by implanted cardiac devices managed in Europe? Results of the European Heart Rhythm Association Survey. *Europace*, 17, 1449–1453.
- 36. Lenarczyk Radoslaw, Potpara Tatjana S., Hauga Kristina H., et al. (2016). The use of wearable cardioverter-defibrillators in Europe: results of the European Heart Rhythm Association survey. *Europace*, 18, 146–150.
- 37. Abiri Parinaz, Abiri Ahmad, Sevag Packard Rene R., et al. (2017). Inductively powered wireless pacing via a miniature pacemaker and remote stimulation control system. *Scientific reports* 7, Article number:6180 (2017)
- 38. Patel, J. (2018). Wireless charging of implantable pacemaker's battery. Journal of Biosensors and *Bioelectronics*, 9, 3 DOI: 10.4172/2155-6210.1000258
- 39. Amar Achraf Ben, Kouki Ammar B. and Cao Hung (2015). Power approaches for implantable medical devices. *Sensors*, 15, 28889–28914.
- Badranova G.U., Gotovtsev P.M., Shapovalova A.A. (2014). Ustroistva elektrosnabzheniia dlia meditsinskikh implantov i materialy dlia ikh konstruktsii [Power supply devices for medical implants and materials for their construction]. Vestnik biotekhnologii i fiziko-kmicheskoi biologii imeni Yu.A.Ovchinnikova – Bulletin of Biotechnology and physico-chemical biology named after Yu.A.Ovchinnikov, 10, 4, 54-66 [in Russian].
- 41. www.prutchi.com/pdf/implantable/nuclear_pacemakers.pdf
- 42. https://www.orau.org/ptp/collection/Miscellaneous/pacemaker.htm Henry Sutanto (2017). Leadless cardiac pacemaker as a novel intervention modality for atrioventricular conduction disturbance in hypertopic c ardiomyopathy. *Journal of Advanced Therapies and Medical Innovation Sciences*, 2.
- 43. https://newatlas.com/nanostim-leadless-pacemaker/29443
- 44. https://www.medscape.com/viewarticle/827034
- 45. *Leadless pacemaker devices*. Prepared for the February 18, 2016 meeting of the Circulatory System Devices Advisory Panel Gaithersburg Hilton; Gaithersburg, MD.
- 46. Vivek Y. Reddy, M.D., Derek V. Exner, M.D., et al. (2015). Implantation of an entirely intracardiac leadless pacemaker. *The New England Journal of Medicine*. Published online on August 30, 2015 DOI: 10.1056/NEJMoa1507192.
- 47. *Patent US20110208260A1*. (2017). Peter M. Jacobson. Rate responsive leadless cardiac pacemaker.
- 48. http://www.implantable-device.com/2011/12/24/nanostims-leadless-pacemaker/
- 49. Bhatia Dinesh, Bairagi Sweeti, Goel Sanat, Jangra Manoj, et al. (2010). Pacemakers charging using body energy. *Journal of Pharmacy and Bioallied Sciences*, 2(1), 51–54. PMCID: PMC3146093.
- 50. Patent US 3943936 (1976). Ned S.Rasor. Self powered pacers and stimulators.
- 51. Sutanto Henry. (2017). Leadlesss cardiac pacemaker as a novel intervention modality for atrioventricular conduction disturbance in hypertrophic cardiomyopathy. *Journal of Advanced Therapies and Medical Innovation Sciences*, 2.
- 52. Norman John C., Molokhia Farouk A., Harmison Lowell T., et al. An implantable nuclear-fueled circulatory support system. *Annsurgery*, 0260-0062. 492-502.
- 53. Albert, H. M, Glass B. A., Pittman. B. (1969). Plutonium for pacemakers e. *British Medical Journal*, 22.11, 447.
- 54. Huffman Fred N., Migliore Joseph J., Robinson William J., Norman John C. (1974).

Radioisotope powered cardiac pacemakers. *Cardiovascular Diseases* (now published as *Texas Heart Institute Journal*), ISSN 0093-3546), 1(1), 52-60.

- 55. Patent US 20100257871. (2010). Rama Venkatasubramanian. Thin film thermoelectric devices for power conversion and cooling.
- 56. Patent US 6470212 (2002). Koen J. Weijand. Body heat powered implantable medical device.
- 57. Patent US 4002497 (1977). Harol Brown. Thermoelectric batteries.
- Kwi-Il Park, Sheng Xu, Ying Liu, et al. (2010). Piezoelectric BaTiO3 thin film nanogenerator on plastic substrates. *American Chemical Society, Nano Lett.*, 2010, 10 (12), 4939–4943; DOI: 10.1021/nl102959k.
- 59. Dagdevirena Canan, Yanga Byung Duk, Su Yewang, et al. (2013). Conformal piezoelectric energy harvesting and storage from motions of the heart, lung, and diaphragm. *Proceedings of the National Academy of Sciences of the United States, December 16, 2013*, doi: 10.1073/pnas.1317233111.
- 60. Xi Chen, Xu Shiyou, Nan Yao and Yong Shi (2010). 1.6 V nanogenerator for mechanical energy harvesting using PZT nanofibers. *American Chemical Society, May 25, 2010, Nano Lett.*, 10 (6), 2133–2137 DOI: 10.1021/nl100812k.
- 61. https://inhabitat.com/wild-new-nanoribbon-implant-uses-heartbeats-to-power-pacemakers/?variation=d
- 62. http://www.piezo.com/tech3faq.html#app7
- Zurbuchen Adrian, Haeberlin Andreas, Bereuter Lukas (2010). The swiss approach for a hertbetdriven lead – and batteryless pacemaker. Heart Rhythm, My 25, 2010, *Nano Lett.*, 10 (6), 2133– 2137 DOI: 10.1021/nl100812k.
- 64. https://www.powerelectronics.com/energy-harvesting/energy-harvesting-poised-eliminate-pacemaker-battery
- 65. https://newatlas.com/wristwatch-pacemaker/33624/
- 66. Hannan Mahammad A., Mutashar Saad, Samad Salina A. (2014). Energy harvesting for the implantable biomedical devices: issues and challenges. *Hannan et al. BioMedical Engineering OnLine*, 4, 13:79, 1-23.

Submitted 07.11.2019

Анатичук Л.І. ак. НАН України,^{1,2} Кобилянський Р.Р. канд. фіз.-мат. наук^{1,2}, Джал С.А.^{1,2}

¹Інститут термоелектрики НАН та МОН України, Чернівці, Україна e-mail: anatych@gmail.com; ²Чернівецький національний університет ім. Ю. Федьковича, Чернівці, Україна

ПРО ВИКОРИСТАННЯ ТЕРМОЕЛЕКТРИЧНИХ МІКРОГЕНЕРАТОРІВ ДЛЯ ЖИВЛЕННЯ ЕЛЕКТРОКАРДІОСТИМУЛЯТОРІВ

У роботі наведено конструкцію та принцип роботи сучасних електрокардіостимуляторів, а також їх класифікацію за механізмом роботи та джерелами живлення. Наведено порівняльний аналіз джерел живлення та визначено перспективи застосування термоелектричних мікрогенераторів для живлення електрокардіостимуляторів. Бібл. 66, рис.15, табл. 8.

Ключові слова: електрокардіостимулятор, джерело живлення, термоелектричний мікрогенератор, серцево-судинні захворювання.

Анатичук Л.І. ак. НАН України,^{1,2} Кобилянський Р.Р. канд. фіз.-мат. наук^{1,2}, Джал С.А.^{1,2}

¹Институт термоэлектричества НАН и МОН Украины, Черновцы, Украина *e-mail: anatych@gmail.com* ²Черновицкий национальный университет им. Ю. Федьковича, Черновцы, Украина

ОБ ИСПОЛЬЗОВАНИИ ТЕРМОЭЛЕКТРИЧЕСКИХ МИКРОГЕНЕРАТОРОВ ДЛЯ ПИТАНИЯ ЭЛЕКТРОКАРДИОСТИМУЛЯТОРОВ

В работе описаны конструкции и принципы работы современных электрокардиостимуляторов, а также их классификация по механизму действия и источникам питания. Приведен сравнительный анализ источников питания и определены перспективы использования термоэлектрических микрогенераторов для питания электрокардиостимуляторов. Библ. 66, рис. 15, табл. 8.

Ключевые слова: электрокардиостимулятор, источник питания, термоэлектрический микрогенератор, болезни кровообращения.

References

- Benjamin Emelia J., Virani Salim S., Callaway Clifton W., et al. (2018). Heart disease and stroke statistics—2018 update: a report from the American Heart Association. *Circulation*, 137: e67– e492.
- 2. Terenda N.O. (2015). Smertnist vid sertsevo-sudynnykh zakhvoriuvan yak derzhavna problema [Mortality from cardiovascular diseases as a state problem]. *Visnyk naukovykh doslidzhen-Herald of Scientific Research*, 4, 1-13 [in Ukrainian].

- 3. Handziuk V.A. (2014). Analiz zakhvoriuvanosti na ishemichnu khvorobu sertsia v Ukraini [Analysis of the incidence of coronary heart disease in Ukraine]. *Ukrainian Journal of Cardiology*, 3, 45-52.
- 4. Chepelevska L.A., Liubinets O.V. (2009). Prohnozni tendentsii smertnosti naselennia Ukrainy [Predictive tendencies of mortality of the population of Ukraine]. *Visnyk sotsialnoi hihieny ta okhorony zdorovia Ukrainy Bulletin of Social Hygiene and Health Care Organization of Ukraine*, 3,10–15 [in Ukrainian].
- Strutinskaya L.T. (2008). Termoelektricheskiie mikrogeneratory. Sovremennoie sostoianiie i perspektivy ispolzovaniia [Thermoelectric microgenerators. Curent status and prospects of use]. *Tekhnologiia i konstruirovaniie v elektronnoi apparature – Technology and Design in Electronic Equipment*, 4, 5-13 [in Russian].
- 6. Anatychuk L.I. (1979). Termoelementy i termoelektricheskiie ustroistva: Spravochnik [Thermoelements and thermoelectric devices: Handbook]. Kyiv: Naukova dumka [in Russian].
- 7. Anatychuk L.I. (2003). Termoelektrichestvo. T.2. Termoelektricheskiie preobrazovateli energii [Thermoelectricity. Vol.2. Thermoelectric power converters]. Kyiv, Chernivtsi: Institute of Thermoelectricity [in Russian].
- 8. Application for utility model № u 2017 11815 (2017). Anatychuk L.I., Kobylianskyi R.R., Dzhal S.A. Cardiac pacemaker with a thermoelectric power supply [in Ukrainian].
- 9. Application for utility model № u 2017 11818 (2017). Anatychuk L.I., Kobylianskyi R.R., Dzhal S.A. Cardiac pacemaker with a combined power supply [in Ukrainian].
- 10. Ludwig A, Zong X, Hofmann F, Biel M. (1999). Structure and function of cardiac pacemaker channels. *Cell Physiol Biochem*, 4-5:179-86.PMCID: 10575196
- 11. https://www.futurity.org/tiny-pacemaker-1049422/
- 12. http://www.kardiodom.ru/articles/572.html.
- 13. Skundin A.M, Fateev S.A, Kulova T.L. Battery for cardiac pacemaker: an alternative to lithium iodine system. Moscow: Institute of Electrochemistry of RAS.
- 14. Julien C., Mauger A., Vijh A., et al. (2016). Lithium batteries. *Science and Technology*, 15. ISBN: 978-3-319-19107-2.
- 15. https://clinicalgate.com/engineering-and-construction-of-pacemaker-and-icd-leads-2/
- 16. Tracy C.M., Epstein A.E., Darbar D., et al. (2012) ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J. Am. Coll. Cardiol., Dec 12.
- Potpara Tatjana S., Lip Gregory Y.H., Larsen Torben B., et al. (2016). Stroke prevention strategies in patients with atrial fibrillation and heart valve abnormalities: perceptions of 'valvular' atrial fibrillation: results of the European Heart Rhythm Association Survey. *Europace*, 18, 1593–1598.
- Bongiorni Maria Gracia, Blomstrom-Lundqvist Carina, Pison Laurent, et al. (2014). Management of malfunctioning and recalled pacemaker and defibrillator leads: results of the European Heart Rhythm Association survey. *Europace*, 16, 674–1678.
- Livenson A.R. (1981). Elektromeditsinskaia apparatura. [Electromedical equipment]. 5th ed. [in Russian].
- 20. http://www.eurolab.ua/encyclopedia/ambulance/48886/
- 21. Patent US 3057356A. (1962). Greatbatch Wilson. Medical cardiac pacemaker.

- 22. Patent US 5562715A. (1996). John J. Czura, Randolph H. Kricke. Cardiac pulse generator.
- 23. Aizawa Y, Kunitomi A, Nakajima K, Kashimura S, Katsumata Y, Nishiyama T, Kimura T, Nishiyama N, Tanimoto Y, Kohsaka S, Takatsuki S, Fukuda K. (2015). Risk factors for early replacement of cardiovascular implantable electronic devices. *Int. J. Cardiol*, 178, 99–101.
- 24. https://link.springer.com/chapter/10.1007%2F978-3-642-50209-5_11
- 25. Patent US 4056105. (1977). Richard J. Ravas. Pulse generator.
- 26. Patent US 3835864. (1974). Ned S.Rasor. Intra-cardiac stimulator.
- 27. Brignole Michele, Auricchio Angelo, Baron-Esquivias Gonzalo. (2013). ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. *European Heart Journal*, 34, 2281–2329.
- 28. Benkemoun H., Sacrez J., Lagrange P., et al. (2012). Optimizing pacemaker longevity with pacing mode and settings programming: results from a pacemaker multicenter registry. *Pacing Clin Electrophysiology*, 35(4), 403-8.
- 29. Hernandez Antonio, Lewalter Thorsten, Proclemer Alessandro (2014). Remote monitoring of cardiac implantable electronic devices in Europe: results of the European Heart Rhythm Association survey. *Europace*, 16, 129–132.
- 30. Maltsev Victor A., Yaniv Yael, Maltsev Anna V., et al. (2014). Modern perspectives on numerical modeling of cardiac pacemaker cell. *Pharmacol Science Journal*, 125(1), 6–38.
- 31. http://www.kardiodom.ru/hirurgia/375.html
- Bock David C., Marschilok Amy C., Takeuchi Kenneth J., Tekeuchi Esther S. (2012). Batteries used to power implantable biomedical devices. *Electrochim Acta*. Published online 2012 Mar 23. PMCID: PMC3811938.
- 33. Abdulianov I.V., Vagizov I.I. (2013). Modern approaches to constant pacing. *Practical Medicine*, 3(71).
- Sarma Mallela Venkateswara, Ilankumaran V., Srinivasa Rao N. (2004). Trends in cardiac pacemaker batteries. *Indian Pacing Electrophysiol J.*, 4(4), 201–212. Published online 2004 Oct 1.PMCID: PMC1502062.
- 35. Todd Derick, Proclemer Alessandro, Bongiorni Maria Grazia, et al. (2015). How are arrhythmias detected by implanted cardiac devices managed in Europe? Results of the European Heart Rhythm Association Survey. *Europace*, 17, 1449–1453.
- 36. Lenarczyk Radoslaw, Potpara Tatjana S., Hauga Kristina H., et al. (2016). The use of wearable cardioverter-defibrillators in Europe: results of the European Heart Rhythm Association survey. *Europace*, 18, 146–150.
- 37. Abiri Parinaz, Abiri Ahmad, Sevag Packard Rene R., et al. (2017). Inductively powered wireless pacing via a miniature pacemaker and remote stimulation control system. *Scientific reports* 7, Article number:6180 (2017)
- 38. Patel, J. (2018). Wireless charging of implantable pacemaker's battery. Journal of Biosensors and *Bioelectronics*, 9, 3 DOI: 10.4172/2155-6210.1000258
- 39. Amar Achraf Ben, Kouki Ammar B. and Cao Hung (2015). Power approaches for implantable medical devices. *Sensors*, 15, 28889–28914.
- Badranova G.U., Gotovtsev P.M., Shapovalova A.A. (2014). Ustroistva elektrosnabzheniia dlia meditsinskikh implantov i materialy dlia ikh konstruktsii [Power supply devices for medical implants and materials for their construction]. Vestnik biotekhnologii i fiziko-kmicheskoi biologii imeni Yu.A.Ovchinnikova – Bulletin of Biotechnology and physico-chemical biology named after Yu.A.Ovchinnikov, 10, 4, 54-66 [in Russian].
- 41. www.prutchi.com/pdf/implantable/nuclear_pacemakers.pdf

- 42. https://www.orau.org/ptp/collection/Miscellaneous/pacemaker.htm Henry Sutanto (2017). Leadless cardiac pacemaker as a novel intervention modality for atrioventricular conduction disturbance in hypertopic c ardiomyopathy. *Journal of Advanced Therapies and Medical Innovation Sciences*, 2.
- 43. https://newatlas.com/nanostim-leadless-pacemaker/29443
- 44. https://www.medscape.com/viewarticle/827034
- 45. *Leadless pacemaker devices*. Prepared for the February 18, 2016 meeting of the Circulatory System Devices Advisory Panel Gaithersburg Hilton; Gaithersburg, MD.
- 46. Vivek Y. Reddy, M.D., Derek V. Exner, M.D., et al. (2015). Implantation of an entirely intracardiac leadless pacemaker. *The New England Journal of Medicine*. Published online on August 30, 2015 DOI: 10.1056/NEJMoa1507192.
- 47. *Patent US20110208260A1*. (2017). Peter M. Jacobson. Rate responsive leadless cardiac pacemaker.
- 48. http://www.implantable-device.com/2011/12/24/nanostims-leadless-pacemaker/
- 49. Bhatia Dinesh, Bairagi Sweeti, Goel Sanat, Jangra Manoj, et al. (2010). Pacemakers charging using body energy. *Journal of Pharmacy and Bioallied Sciences*, 2(1), 51–54. PMCID: PMC3146093.
- 50. Patent US 3943936 (1976). Ned S.Rasor. Self powered pacers and stimulators.
- 51. Sutanto Henry. (2017). Leadlesss cardiac pacemaker as a novel intervention modality for atrioventricular conduction disturbance in hypertrophic cardiomyopathy. *Journal of Advanced Therapies and Medical Innovation Sciences*, 2.
- 52. Norman John C., Molokhia Farouk A., Harmison Lowell T., et al. An implantable nuclear-fueled circulatory support system. *Annsurgery*, 0260-0062. 492-502.
- 53. Albert, H. M, Glass B. A., Pittman. B. (1969). Plutonium for pacemakers e. *British Medical Journal*, 22.11, 447.
- Huffman Fred N., Migliore Joseph J., Robinson William J., Norman John C. (1974). Radioisotope powered cardiac pacemakers. *Cardiovascular Diseases* (now published as *Texas Heart Institute Journal*), ISSN 0093-3546), 1(1), 52-60.
- 55. Patent US 20100257871. (2010). Rama Venkatasubramanian. Thin film thermoelectric devices for power conversion and cooling.
- 56. Patent US 6470212 (2002). Koen J. Weijand. Body heat powered implantable medical device.
- 57. Patent US 4002497 (1977). Harol Brown. Thermoelectric batteries.
- Kwi-Il Park, Sheng Xu, Ying Liu, et al. (2010). Piezoelectric BaTiO3 thin film nanogenerator on plastic substrates. *American Chemical Society, Nano Lett.*, 2010, 10 (12), 4939–4943; DOI: 10.1021/nl102959k.
- 59. Dagdevirena Canan, Yanga Byung Duk, Su Yewang, et al. (2013). Conformal piezoelectric energy harvesting and storage from motions of the heart, lung, and diaphragm. *Proceedings of the National Academy of Sciences of the United States, December 16, 2013*, doi: 10.1073/pnas.1317233111.
- Xi Chen, Xu Shiyou, Nan Yao and Yong Shi (2010). 1.6 V nanogenerator for mechanical energy harvesting using PZT nanofibers. *American Chemical Society, May 25, 2010, Nano Lett.*, 10 (6), 2133–2137 DOI: 10.1021/nl100812k.
- 61. https://inhabitat.com/wild-new-nanoribbon-implant-uses-heartbeats-to-power-pacemakers/?variation=d
- 62. http://www.piezo.com/tech3faq.html#app7

- 63. Zurbuchen Adrian, Haeberlin Andreas, Bereuter Lukas (2010). The swiss approach for a hertbetdriven lead – and batteryless pacemaker. Heart Rhythm, My 25, 2010, *Nano Lett.*, 10 (6), 2133– 2137 DOI: 10.1021/nl100812k.
- 64. https://www.powerelectronics.com/energy-harvesting/energy-harvesting-poised-eliminate-pacemaker-battery
- 65. https://newatlas.com/wristwatch-pacemaker/33624/
- 66. Hannan Mahammad A., Mutashar Saad, Samad Salina A. (2014). Energy harvesting for the implantable biomedical devices: issues and challenges. *Hannan et al. BioMedical Engineering OnLine*, 4, 13:79, 1-23.

Submitted 07.11.2019