Implantable Cardiac Pacemakers – 50 Years from the First Implantation

Vsadljivi srčni spodbujevalniki – 50-letnica prve vsaditve

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Izvleček

Izhodišča: Okoli 4 milijone ljudi na svetu živi z vsajenimi srčnimi napravami. Sodobni spodbujevalniki so majhne in lahke medicinske naprave, ki jih vsadimo v lokalni anesteziji, omogočajo pa zdravljenje široke palete bolezni srca. So izjemno varni, zanesljivi in uporabni dolgo časa. Članek pregledno predstavi razvoj teh naprav s tehničnega zornega kota.

Pregled: Razvoj vsadljivih srčnih spodbujevalnikov je omogočil pomemben izum silikonskega tranzistorja. Čeprav je bila iznajdba primernih litijevih celic za zagotavljanje energije osnovnega pomena za podaljšanje življenjske dobe baterije in za večjo zanesljivost spodbujevalnikov, so pomembni številni drugi izumi v sodobni elektroniki: od tranzistorjev, ki omogočajo majhnost in nizko porabo energije, hibridnih vgrajenih elementov, ki omogočajo programiranje, do mikroprocesorjev, ki odpirajo nove možnosti programiranja, diagnostike, telemetrije in informacijsko-komunikacijske tehnologije; ta zagotovlja spremljanje bolnikov na daljavo in nadzorovanje že vsajenih naprav.

Zaključki: Vsadljivi srčni spodbujevalniki so zanesljive naprave, ki se uporabljajo pri raznovrstnih motnjah srčnega ritma in pri odpovedi srca. Še vedno je veliko stvari, ki se jih je treba naučiti o delovanju zdravega in popuščajočega srca. Sodobni spodbujevalniki zagotavljajo zdravnikom pomembne podatke iz svojega spomina po vgrajenem telemetrijskem sistemu. Te informacije jim pomagajo bolje razumeti bolezenske procese v srcu in s tem prispevajo k razvoju novih zamisli za zdravljenje bolezni srca in za natančno prilagajanje zdravljenja bolnikovim potrebam. Čeprav so vsadljivi srčni spodbujevalniki dosegli raven zrele tehnologije, se bodo še izpopolnjevali in bodo tako omogočili boljše načine diagnosticiranja in zdravljenja, s tem pa izboljšali bolnikovo kakovost življenja.

Abstract

Background: There are over 4 million people around the world living with implanted cardiac devices. Modern pacemakers are small and light medical devices, which are implanted under local anaesthesia and provide therapy for a broad range of cardiac diseases. They are extremely safe, reliable and long lasting. The aim of this paper is to present review of the development of implantable pacemakers from an engineering point of view since the first implanted device in October 1958 till today.

Overview: Development of implantable cardiac pacemaker was enabled by another important invention, the silicon transistor.

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Though the invention of suitable lithium cells as appropriate power supply was essential for prolongation of battery life cycle and for increased reliability of pacemakers, main milestones in the development were associated with technological breakthroughs in electronics: from transistors, which introduced such features as small size and low power consumption, to hybrid and integrated circuits, which enabled programmability, microprocessors, which added more options in programming (multiprogrammability), diagnostics and telemetry, and the ICT (information communication technology) that enabled physicians remote access to patients and interrogation of their implantable devices.

Conclusions: Implantable pacemakers are reliable devices indicated for a wide range of different therapies of cardiac rhythm disorders and heart failure. There is still a lot to learn about the physiology of a normal heart and even more about the failing heart. Modern pacemakers provide physicians valuable information from pacemakers' memory via the built-in telemetry system. These information help physicians to better understand pathologic processes within the heart, thus contributing to the development of new ideas for treatment of diseases and for precise tailoring of the therapy to the patient's needs. Although implantable pacemakers have reached the level of mature technology, they will continue to develop with therapies and diagnostics to facilitate a higher quality of life.

Introduction

Cardiac pacemaker has been the first electronic device ever implanted into a human body. Implantable cardiac pacemakers are considered to be the most successful therapeutic devices ever produced for saving human life and improving the patient's quality of life.

The first implantable cardiac pacemaker was implanted in October 1958. It was designed and produced by Dr. Rune Elmqvist, an electrical engineer from Elema – Schönander. It was a hockey puck size device, powered by rechargeable batteries and it had only one silicon transistor. Dr. Ake Senning implanted it to Mr. Arne Larsson, a patient who had been in bed for several months due to severe Gerbezius-Adam's–Stokes attacks. The first implanted pacemaker worked properly for only a few hours and it had to be replaced the same day by a second pacemaker of the same type, the only "backup" device Elmqvist and Senning had. Fortunately enough, the second pacemaker worked successfully for several months and Mr. Larsson survived. Moreover, until his death in 2001, he underwent more than 25 pacemaker reimplantations.[1]

Fig. 1: a) Early General Electric pacemaker model from 1967 in plastic housing. (8x6,5x2,2cm; 200g). b) X-ray of the pacemaker. Six pieces of zinc-mercury batteries and discrete electronic components can be recognized.

Fig. 2: Cordis implantable pacemaker, model Ectocor from 1975. The batteries and electronic circuits are sealed in epoxy resin (6,8x5,8x2,3cm; 140g)

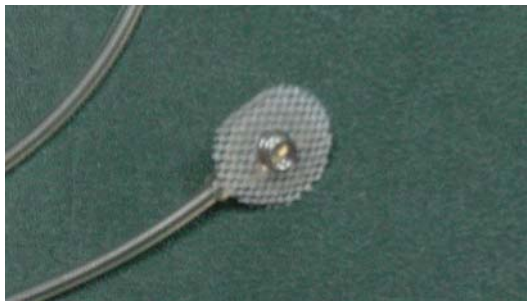
During this last 50 years since its first implantation, the implantable cardiac pacemaker has transformed from a simple electronic device that generated short electrical pulses at a fixed frequency into a sophisticated, automated device consisting of a computer with computational power of a contemporary personal computer, peripheries that sense signals from the patient's body and its environment, communication circuits that enable exchange of information between the implanted pacemaker and medical staff, and an output amplifier that generates pulses to stimulate the heart. All these functional subunits added new functionalities to the simple pacemaker – pulse generator only, in order to control heart in the best, most physiological way.

The aim of this paper is to present a review of major technical achievements and innovations related to the development of implantable cardiac pacemakers from a biomedical engineering point of view and to give an insight into possible ways that engineering research will take in order to make pacemakers even better devices than they are today.

The first human implanted pacemaker

Electrical excitability of the heart muscle tissue enables application of electrical pulses for cardiac therapy. John Hopps, a Canadian electrical engineer, constructed an external pacemaker in 1950 and tested it on himself.[2] Successful ventricular pacing in ten patients with an external pacemaker was reported in 1952 by P. Zoll who used subcutaneous needle electrodes in his clinical study.[3] Cardiac pacing was gradually introduced as a temporary cardiac therapy which stayed in clinical use until today.[4,5] Early commercial pacemakers were devices designed with electronic tubes, which rendered them large and heavy. The invention (in 1947) and industrialization of silicon transistor in mid twentieth century made it possible to design, produce and introduce into clinical practice a number of new biomedical devices, much smaller in size and weight and therefore more practical for use by medical staff and patients. Among those medical devices, transistorized portable external pacemakers were used in therapy for patients with severe heart diseases. Earl Bakken, a co-founder of Medtronic Inc., designed such a battery-powered model in the late fifties.[6] Patients could walk around carrying the pacemaker attached to a belt, but they had an incision in their skin allowing the wires (cable) to reach the electrodes attached to the heart. Such a therapy was associated with many complications, mainly due to infections, but also due to technology, such as breaking of wires and displacement of electrodes.

At the same time, a number of physicians and biomedical engineers became aware of the advantages that transistors brought into the designing of medical devices and started to develop implantable cardiac pacemakers. The first implantable prototypes had been tested on animals before the human implantations began. It was only a question of time when the first implantable pacemaker was going to be implanted into a human. However, a concurrence of events led to the first implantation. Mr. Arne Larsson, 43 at the time, suffering from high grade AV block and severe syncope attacks for years, was not able to



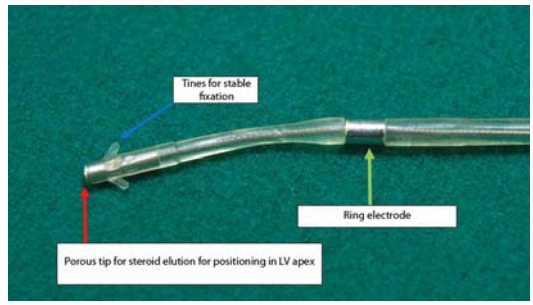


Fig. 3: a) Endocardial electrode is screwed into the myocardial muscle. b) Tip of a pacemaker endocardial bipolar lead which is introduced into the heart through a vein and positioned in the apex of the right ventricle.

move from his bed due to this condition and was willing to try any new therapy in order to improve the quality of his life. No known medication or therapy was successful and his case was considered hopeless. Åke Senning, a surgeon from Karolinska Hospital in Stockholm, Sweden, studied during his visit to USA the implantations of the pacing electrodes for the external pacemaker performed by C. W. Lillehei and was aware of patients' complications. He thought that the time for a better, permanent solution came. Rune Elmqvist, a research engineer from Electromedical Division of Elema Schönander, designed and produced two prototypes of an implantable pacemaker. Since Larsson's health condition was rapidly deteriorating, the decision was made and the pacemaker was implanted to Mr. Larsson on October 8, 1958 at Karolinska Hospital .

The first pacemaker implant was not operational for a long time: only for three hours after the implantation. It failed most probably due to the damage in insulation that occurred during the implantation and the device had to be replaced on the following day with the second alias of the prototype. However, the second pacemaker did not work properly for a long time, this time due to a malfunction in connection wiring. The pacemaker was left implanted with intention to be re-activated after a better solution for connecting the pacemaker and the electrodes was found. Mr. Larsson survived long enough to get a more reliable pacemaker system implanted and lived until 2001 when he died from a cause not related to his heart disease. In his lifetime, he has undergone 26 re-implantations of a new model of pacemaker due to a variety of reasons. From today's point of view, when implantable pacemakers are expected to work properly for up to 15 years, Larsson's story may not appear as a success. But for a person whose life was prolonged for 43 years, i.e. whose lifetime literary doubled from the moment he received the first device, it is completely the opposite. No matter how interesting the authors find the case study of Mr. Larsson, we used it just in order to introduce all those challenges that early pacing researchers and inventors had to face. The complete case history with details regarding re-implantations of pacemakers to Mr. Larsson may be found elsewhere.[7]

The pacemaker Elmqvist designed was a very simple electronic device, delivering 2 V amplitude pulses having duration of 1.5 ms at a fixed frequency of 50 pulses per minute. It was powered by two rechargeable nickel-cadmium batteries, which had been charged inductively. The energy transfer was wireless by means of two antennas: one attached to the transmitter oscillator working at 150 kHz was positioned above the implant, and the other antenna loop was within the pacemaker attached to a rectifier and the batteries.

It seems that Elmqvist and Senning did not realize what kind of a breakthrough for cardiac patients they made by showing that human implantation of a pacemaker is feasible. They reported the first implantation at the Second International Congress on Biomedical Electronics in Paris, France in 1959,[1] but none of them has submitted a patent application.

Wilson Greatbatch, an American electrical engineer, designed an implantable pacemaker powered by zinc-mercury batteries, which did not require recharging while ensuring operation of the pacemaker for at least 15 months. In 1960, he submitted a patent application assigned to Medical Cardiac Pacemaker[8] in the USA and became the first owner of intellectual property for an implantable pacemaker. Greatbatch was collaborating with William Chardack, the head of the

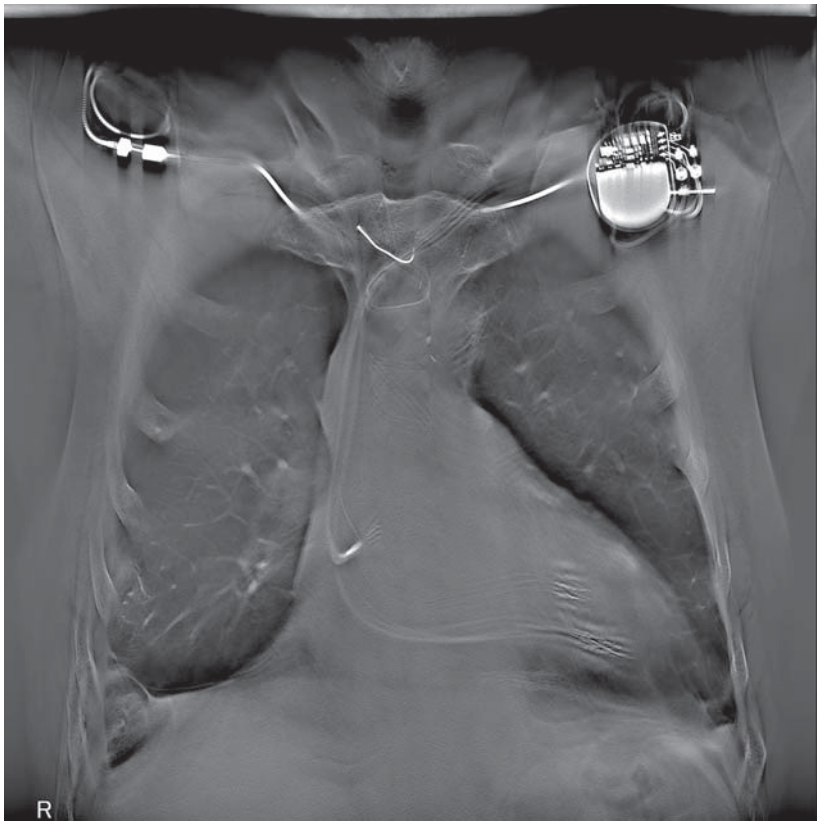


Fig. 4: Image of a modern biventricular pacemaker implanted subclavicularly into a patient obtained by tomosynthesis.

Department of Surgery at the VA Hospital in Buffalo. The first commercial pacemakers are thus often referred to as Chardack-Greatbach pacemakers.

Challenges of the Early Pacemaker Design

Experience with the early pacemaker implantations clearly showed that the electronic circuitry itself was not the actual cause of limited functionality of implantable devices. Most problems were associated with mechanical parts such as lead wires, encapsulation, tissue-electrode interface or the pacemaker power source. First pacemakers were produced as single compact systems, since the pulse generator and the lead were permanently connected and nondetachable. With the increasing number of implantations, it became obvious that producing the pulse generator separately from the leads turned out to be more efficient and less traumatic for the patient since only the particular part which had a malfunction could be replaced without replacing the functional components. In addition, the surgical procedure for the implantation was invasive and required an open chest surgery.[9] All these facts called for new solutions, both in terms of implantation procedure and in terms of device technology.

Pacemaker Power Sources

Rechargeable batteries used in early pacemakers left the responsibility for recharging with the patients, which is considered unsafe and is avoided in modern medical practice except in non life supporting devices such as neural stimulators. Additionally, the need for recharging and the whole procedure rendered the patients feel insecure. Therefore, rechargeable batteries were replaced in the earliest pacemaker models with primary cells, mainly with zinc-mercury batteries as proposed by Greatbatch. These batteries had high energy density and still small size, and one could assume that they would power the pacemaker for two years. However, there were two main concerns related to these types of batteries: the extended internal self-discharge due to constant operation at body temperature and the generation of hydrogen, a by-product of the chemical reaction within the zinc-mercury batteries (Figs. 1 and 2). The batteries could not be hermetically sealed when implanted into the body in order to allow the generated gas to exit from the pacemaker housing.[10]

Some research groups were investigating possible ways of powering implantable devices at the same time, without the need to implant any kind of a battery into the patient. William Glenn from the Yale University Medical School introduced in 1958 a radio frequency pacing system in which only a passive receiver circuit was implanted to a patient and attached to a myocardial lead. The transmitter was small and easy to fix on a patient's chest over the implanted receiver. The physicians were able to adapt the heart stimulation parameters at the transmitter, and batteries could be replaced from the outside. The RF principle was improved by a surgeon Leonardo Cammilli and engineer Renato Pozzi from Florence, Italy, who in 1959 developed a receiver that was attached directly to the epicardial surface, thus reduc-

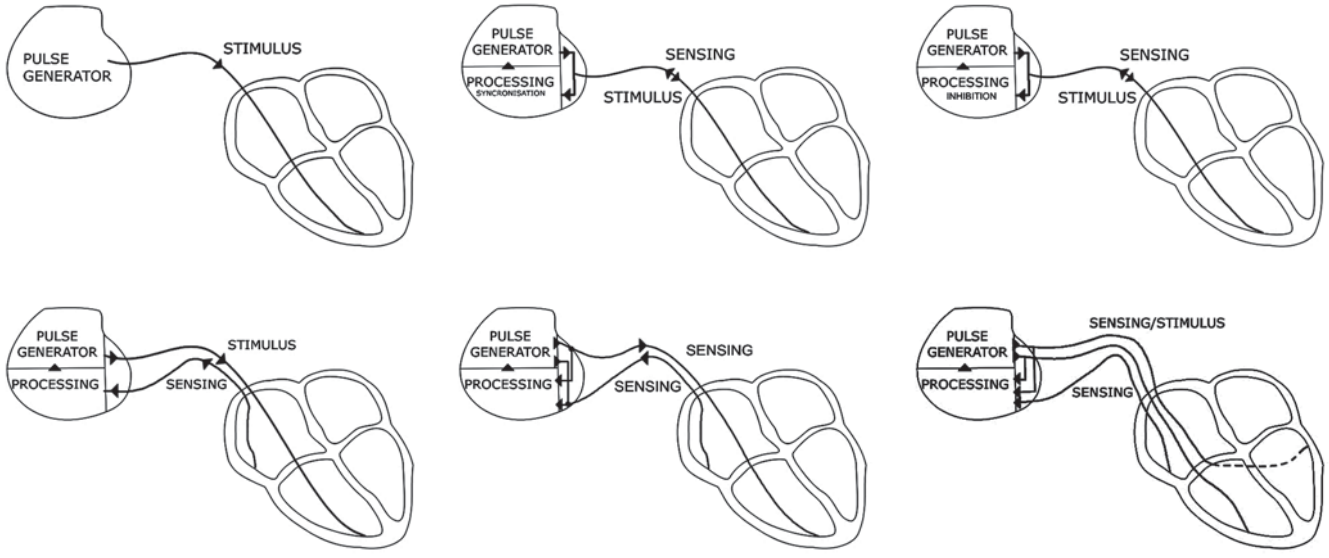


Fig. 5: Different modalities of cardiac pacing
a) asynchronous
b) R-wave synchronous
c) R-wave inhibited
d) P-wave synchronous
e) multiprogrammable DDD pacemaker
and f) bi-ventricular pacemaker

ing the probability of lead malfunction during permanent pacing. The implanted part of the pacemaker developed by a group led by surgeon L.D. Abrams from the Birmingham University, UK, consisted only of a multiturn coil which was attached to the epicardial wall. The external part of the pacemaker, the pulse generator, was carried by the patient over the implanted receiver coil and in case a normal sinus rhythm was restored, the patient could even switch the pacemaker off. The advantage of such a design was not only the power supply but also the control of the stimulation parameters that could be kept under the supervision of the physician. Still, these models were not accepted by the patients and never made it to the mass production and clinical use.

The need to find the power supply for pacemakers brought Victor Parsonnet to the idea to propose the developing of a nuclear power source for pacemakers.[11] The US Atomic Energy Commission approved the idea and in 1969, a nuclear power supply prototype was available. The power source used an alpha emitter, plutonium 238, as a heat source and the thermal energy was converted into electrical energy by a number of thermocouples connected into a series. Though power sources based on plutonium 238 showed longevity of 10 years (which was a large improvement compared to batteries) and high reliability, pacemakers with nuclear power source were abandoned by medical profession owing to the toxicity of plutonium and stayed as an option for implantation in clinical practice for 10 years only. Since plutonium 238 has an extremely long half life (87 years), agencies required of manufacturers and hospitals that implanted pacemakers with atomic power sources extensive administrative work, tracking patients with such pacemakers and taking care of explanted devices. It is interesting to mention that today the idea of supplying power by nuclear power sources is being considered again, but for implantable cardioverter-defibrillators, which need much more power than implantable pacemakers and currently have a lifetime of approximately 7 years.

A stable solution for longevity of batteries for implantable pacemakers (and most of active implantable devices invented later than pacemakers) was found by introducing lithium/iodine battery in the early seventies. It was Wilson Greatbatch again who was successful in his research for appropriate power source for pacemakers and who designed lithium (lithium / iodine-polyvinylpyridine) batteries that have major advantages compared to other cells: high energy density (J/cm^3), high specific energy (J/g), produce no gas, low self-discharge rate and a voltage characteristic that allows easy determination of battery end-of-life point. Lithium batteries were applied to implantable pacemakers in the early seventies and since then the characteristics of batteries aimed for implantable

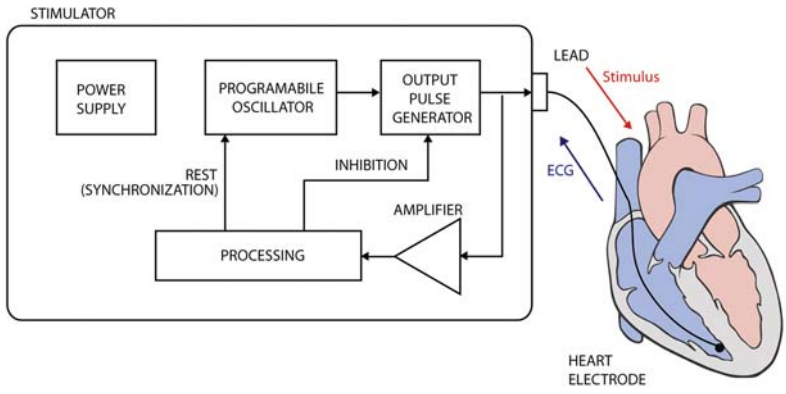


Fig. 6:. Block diagram of an early R-wave synchronous pacemaker.

devices have been steadily improving so that life expectancy of modern lithium battery powered pacemakers increased up to twenty years. Nevertheless, many new features increasing the battery current drain could be implemented in order to produce clinically more efficient devices, however, having end-of-life cycle of approximately 10 years.

Pacemaker Leads and Electrodes

In early days of permanent cardiac pacing, fractures of wires leading from the pacemaker to the electrode occurred very often, thus being the major cause of reoperation. Once the wires were positioned within the body, they were under strain due to rhythmical heartbeats and there was always one point on the wire under the highest strain and therefore at the highest risk of fracture. A simple calculation shows that the heart of a person having average heart rate 70/min, contracts more than 100.000 times per day or more than 36.000.000 times a year. A major improvement was the introduction of coil conductors in the early sixties, since the level of fatigue of leads due to frequent flexing decreased drastically as a result of the coil design. New materials, more resistant to fatigue and corrosion were introduced. Stainless steel based wires were replaced in the sixties by multi-component alloys (such as Elgiloy or MP35N).

Mechanical problems of nearly the same nature were encountered with the lead insulation in order to make it resistant to lead body flexions. Moreover, since the insulation is in contact with body fluids, it had to be biocompatible. First insulating materials were Teflon and polyethylene, which were later replaced with silicone rubber. In the late seventies, polyether polyurethane was introduced and stayed in use up to the present day along with silicone rubber.

Many engineers and physicians were trying to improve the cardiac pacing therapy, finding the best possible technology for different parts of a pacing system. However, that was not sufficient since the surgical interventions were invasive and therefore not appropriate for many elderly patients and for those in advanced stage of disease. A less invasive procedure was found in conjunction with intravenous introduction of catheters, which were used for right ventricular pacing with an external pacemaker since 1960 by Lillehei and his colleagues (Fig. 3). In such a procedure, a small incision was made in the upper chest under the collarbone, in order to reach a vein. The lead was introduced through the vein and after reaching the apex of the right ventricle the pacemaker was tested and finally inserted between the layers of subcutaneous tissue and the muscles in the vicinity of the incision in the upper thorax (Fig 4). In the described procedure, which lasted usually less than one hour, the patient was under local anaesthesia and remained awake. The possibility of introducing the leads into the heart intravenously contributed to increasing the number of medical institutions and physicians implanting pacemakers. There was no need for open chest surgery any more and patients could leave the hospital much earlier than after an invasive chest surgery. The number of (potential) receivers of pacemaker increased as many elderly and weak patients could now become recipients due to greater acceptability of surgery. In many institutions, thoracic surgeon in the role of implanting physician was replaced by a cardiologist, who could implant the intravenous lead and the pacemaker in a catheterization laboratory.

This new type of lead has also had an impact on changes in the shape and materials used for its production. The first implanted leads were only wires inserted and fixed into myocardium, while the Hunter-Roth electrode represented a more advanced model,

Fig. 7: Omnicor Programmer model 166B, Cordis, 1975, used for programming of early programmable pacemaker series. One of the switches was used to set the pacemaker model, and the other two for setting the amplitude and the stimulus rate. The pacemaker was (re-) programmed through the skin of the patient after implantation.

which consisted of two stainless steel pin electrodes on a rubber base. The pins were advanced into the myocardium and sutured in the place.

Introducing Different Modes of Cardiac Pacing

From the very beginning of pacemaker development, it was obvious that the device could effectively replace "the clock" in patients with total heart block, but for all those patients who had different kinds of arrhythmia, there was a concern whether fixed rate pacemakers could satisfy demands for their therapy. The fixed rate pacemakers had a pulse generator that generated an output pulse with fixed period of pulses, no matter what kind of underlying cardiac rhythm was present. Fixed rate pacemakers are also called "asynchronous pacemakers" since there is no relation between the device and the patient's intrinsic rhythm.

Fig. 8: CyberLith I model of implantable pacemaker, Intermedics, 1981, one of the first pacemaker models with telemetry (4,5x5,4x1cm; 60g).

One of the concerns was whether an electrical pulse from a fixed rate pacemaker, which falls into the vulnerable zone of a normally conducted heartbeat could induce ventricular fibrillation. Also, some of the patients with episodes of normal heart rhythm felt discomfort when paced by fixed rate pacemakers. It was obvious that some kind of synchronization between the heart and the device should be applied (Fig. 5).

Firstly, the potential danger of a pacemaker pulse falling into the vulnerable zone was excluded by introducing "R-wave synchronous" pacing mode. Such a pacemaker had an additional sensing amplifier, which was sensing the cardiac activity (intracardial electrogram–IEGM) and could detect the onset of ventricular depolarization. If an R-wave was present, the pulse generator would generate an output pulse exactly after a preset period of time after the R-wave was recognized.

However, since there was a spontaneous heartbeat, the energy spent by the output pulse generator was spent for nothing. Therefore another concept was soon developed to solve the problem of two pulse sources competing: the "R-wave inhibited" pacing mode or "on demand" pacemaker mode (Fig 6). In this mode, the occurrence of an R-wave would block the output stage of the pacemaker, i.e. the energy would stay preserved and the battery of a demand pacemaker could last much longer than in the asynchronous or R-wave synchronous mode. The concept was introduced by B.V. Berkovits in 1963 and became the main mode of operation of cardiac pacemakers in the late sixties.[12] Generally, "on demand" pacemakers were produced in such a way that they had a preset fixed rate of output pulses (e.g. 60 pulses/min), but in case the heart rate was faster than the preset value, the pacemaker would not generate the pulses and the heart would beat according to its natural rhythm.

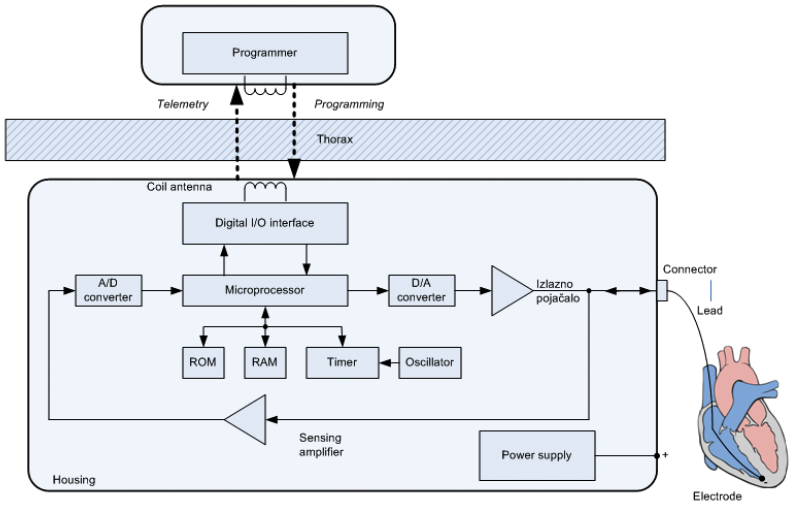


Fig. 9: Block diagram of a multiprogrammable pacemaker. All functions are controlled by a microprocessor. Communication through the chest is bi-directional. The programmer enables changes in the settings of the pacemaker and telemetric reading of the data from the pacemaker.

Programmable Pacemakers

In the early seventies, pacemaker was already a reliable device. Main obstacles caused by mechanical imperfection were solved as well as the problem of a stable and long-lasting power source. The stage was open for new ideas and a lot of start-up companies entered the market. Physicians started introducing new indications for pacing, such as sick sinus syndrome, while the engineers introduced new technology, hybrid and integrated circuits.

Longevity of pacemakers enabled by lithium batteries required that pacemakers adapt to the needs of aging patients and changes in their health status. Integrated circuits enabled the required flexibility. The programmable pacemaker was developed and entered the market in the mid-seventies.

The main feature that the programmable pacemakers had to fulfil was to change pacing parameters non-invasively. Cordis introduced a new model of programmable asynchronous pacemaker, the Omnicor: physicians could choose six pacing rates and four stimulus amplitudes. A handheld pacemaker programmer, held over the implanted pacemaker could re-program the pacemaker by sending magnetic pulses which were detected by the implanted circuitry and changed the output parameters of the pacemaker to a new value. The main value of reprogramming was that the amplitude of the output pulses could be adapted to the changes of stimulation threshold of the cardiac tissue. In addition, the use of lower energy pulses for a longer period saved the battery and extended its life. Later in the seventies, a third programmable parameter was added, a pulse duration (Fig 7).

The next step in pacemaker technology development was the introduction of a two way communication: the CyberLith pacemaker model from Intermedics could be programmed, but it was also able to send data on the status of the implanted device, the patient's heart and the battery (Fig 8). In the same way the programmer was programming the implanted pacemaker, it had a possibility to interrogate the circuitry in the pacemaker to send the collected data to the programmer. This feature is called telemetry, and there is no need to penetrate the skin in order to receive information from the pacemaker. In the late seventies, such models with telemetry options were called multiprogrammable communicational pacemakers (Fig 9 and 10).

In many cases, the electrical activity of the sinus – atrial (SA) node is not affected by the disease. It is considered that the natural pulse (rhythm) produced by the SA node is optimal for the heart and the patient. Therefore, for all those patients who had normal activity of the SA node and a block in the conduction system on the atrio-ventricular level, the most natural ventricular contraction achieved by artificial pacing would be if it were synchronized with the SA node activity. Again, a new concept was developed: P-wave synchronized ventricular pacing, dual chamber pacemakers having a sensing electrode within the right atrium and an amplifier for sensing its electrical activity thereby triggering the pacing of the right ventricle after atrial sensing and predefined A-V delay. Dual chamber pacemaker was invented in the late sixties, but owing to the complexity of introducing two leads to the heart, one to the atrium and another to the ventricle, the interest for dual chamber pacemakers actually started in the early eighties when technological development allowed downsizing of the devices.

With dual chamber pacemakers, the complexity of pacemaker design has increased and the designers gradually changed the basic concept from specialized hybrid elec-

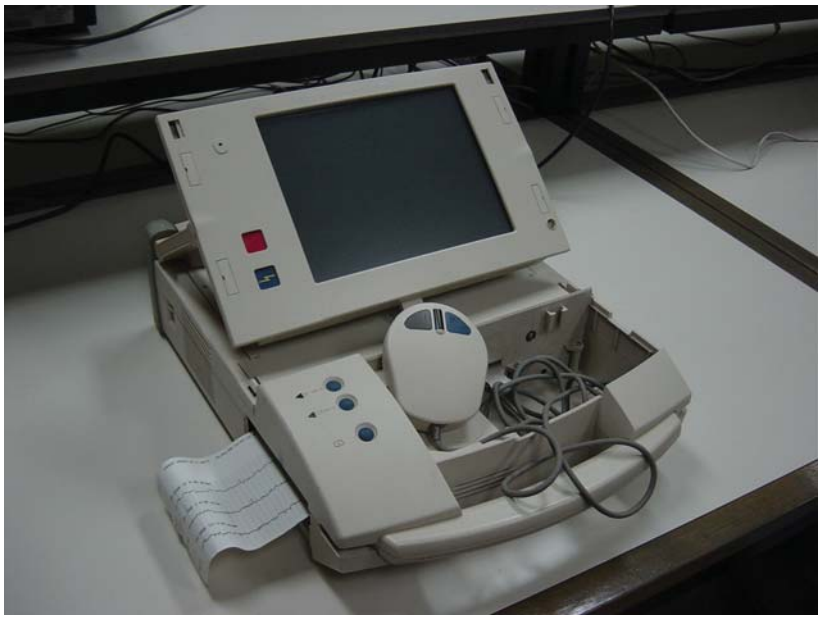


Fig. 10: Modern programmers look very much like computers and their structure indeed is very similar. The device looking like the computer mouse is the programming head to be placed over the implanted pacemaker for programming and telemetry.

tronics to microprocessor-based circuits which allowed even more software programmability. By the end of the eighties most pacemaker companies offered DDD (dual chamber sensed, dual chamber paced, dual chamber programmable) pacemakers, but the physicians still preferred the VVI (ventricle sensed, ventricle paced, inhibited mode) models.

Still, in the late eighties, pacemakers embedded software options for cardiac electrotherapy decisions, most of which were made automatically after the implantation and made them more independent from physicians' decisions. Pacemakers became automatic, nearly autonomous devices with only limited need for external programming.[13] Embedded software (different algorithms) continuously monitored patients' heart functions and if necessary, adapted pacemaker pulse parameters or mode of operation.

Rate Responsiveness

Many patients suffer from irregular rhythm caused by the atrial fibrillation being therefore chronotropically incompetent. At the time when the research on dual chamber pacemakers began, engineers and physicians started research on whether the paced cardiac function could be improved by adding the pacing algorithms implemented in pacemaker software in response to additional information from sensors embedded into the pacemaker.[14] These sensors could monitor the physical activity of the patients and adapt the pacing rate to the needs of the activity of the patient. They would replace the spontaneous regulation of the heart rhythm by the nervous system through (processed information based) regulation by the pacemaker processor. Accordingly, the first rate-responsive pacemaker used QT interval, physiologic parameter dependent on circulatory catecholamines, to determine the pacing rate. In 1981, the first pacemakers with piezoelectric activity sensor were implanted and these new, "rate adaptive" pacemakers became new concept in pacing. Activity sensor monitored vibrations and sounds produced by the bodily activity, but in the years to follow, different types of sensors were investigated in order to find the most physiologic solution for adapting the pacemaker rate to physiological needs of an active patient.[15,16] It is practically impossible to enumerate all sensor modalities which were considered for implementation in cardiac pacemakers: from accelerometers as physical activity sensors; to microphones and bioimpedence measurements of breathing rate; temperature sensors measuring blood temperature also as a measure of body activity, measurement of the oxygen saturation in the blood, advanced signal processing of intracardial ECG[17,18]… Implanting these physiological sensors into pacemakers made it possible for the physicians to individually optimize pacing parameters for each patient. Pacemakers can also have two sensors monitoring different physiological quantities and an embedded sensors cross-checking and blending algorithms to optimize their performance.

Implantable cardioverter-defibrillators

One of the developments of cardiac electrotherapy that also started in the eighties was the implantable cardioverter-defibrillator (ICD). These implantable devices manage life-threatening arrhythmias such as ventricular tachycardia (VT) and ventricular fibrillation (VF). Pathologic VT usually compromises the patient's hemodynamic stability often progressing to VF being a fast unsyn-

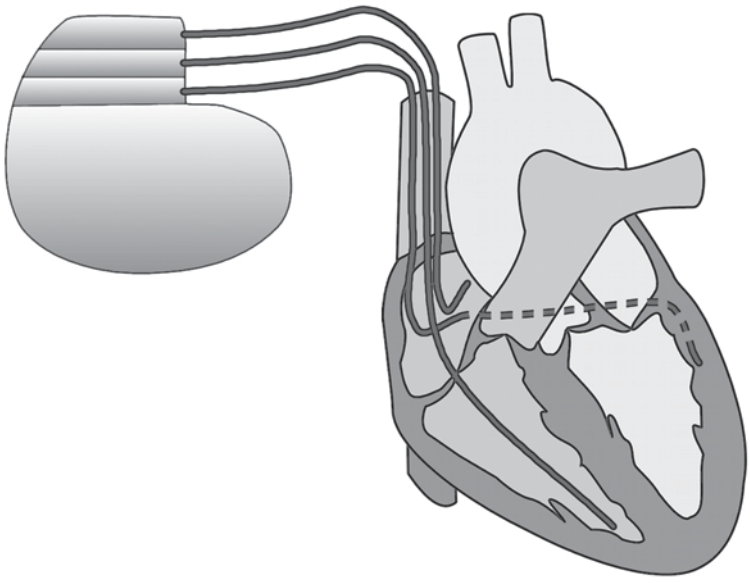


Fig. 11: Position of leads of a biventricular r pacemaker with atrial sensing shown on a cross-section of the heart.

chronized activity which leads to death if not treated in due time.[19] In their early development, the ICDs had a completely different function than pacemakers, but today all ICDs have a pacing option embedded as well. The description of the art of ICD functioning and the differences in technical details between the ICDs and pacemakers exceeds the scope of this paper. Nevertheless, a contemporary ICD is a complex device for arrhythmia management and patient follow-up delivering variety of tiered therapies and comprising sophisticated telemetry, thus yielding numerous diagnostic data. However, it has to be emphasized that most of modern implantable devices – various stimulators and pumps have gained from the development of the technology primarily developed for cardiac pacemakers.

Cardiac Resynchronization Therapy

Many patients suffer from advanced congestive heart failure characterized by desynchronization in activity between the right and the left heart. Cardiac Resynchronization Therapy (CRT) is a mode of cardiac electrotherapy where the pacemaker can also pace the left ventricle. In such a mode of cardiac pacing, it is possible to achieve synchronization of the contractions of right and left ventricles, thereby improving the cardiac output.[20] In addition to a lead implanted within the right ventricle, the additional lead has to be inserted through the coronary venous system to enable pacing of the left ventricle. Implantation of the pacing lead through the coronary vein system is a rather difficult task so companies developed new tools, introducers and a large variety of leads in order to increase the procedure success. Patients with normal sinus rhythm also have a sensing lead implanted into the right atrium, to synchronize the pacing with atrial activity (Fig. 11). The leads for CRT devices may be even multipolar in order to enable programming of the optimal pacing site. Therefore the connector of the CRT has to accommodate more leads and occupies much more space compared to a "regular" pacemakers (Fig. 12). One of the critical parameters to be programmed are the periods from atrial activity to ventricular stimulation and the delay between stimulation of the left and the right side of the heart.[21] Memory capacity of CRT's processors is large in order to memorize events which are characteristic for heart failure follow-up and need interpretation after transferring into a programmer. Pacemakers used in CRT applications are also called biventricular pacemakers. Patients treated with CRT have improved ventricular function.[22,23]

Safety of Implanted Cardiac Pacemakers

The development of the technology of active implantable devices in the last 50 years enabled pacemakers to obtain a status of a safe and reliable device. The regulations in health care require from the industry to prove that each new model complies with medical device safety standards, which are very strict for implantable devices.[24] Modern pacemakers have a large diversity of programming parameters and though it makes them individually adaptable to each patient needs, it also opens a possibility of their suboptimal programming. Some producers complain that physicians tend to leave the initial settings of the devices after implantation and do not use all the features of the implantable de-

Fig. 12: Model of a biventricularar pacemaker InSync III, Medtronic, 1988 (5,9x5,1x0,8 cm; 30g).

vices. In individual cases, adverse reactions or infections may occur after the implantation.[25] Also, after leaving the hospital, patients are advised not to intentionally come into the vicinity of apparatus producing electromagnetic interference which might jeopardize the function of the pacemakers: radars, microwave sources, power stations, etc.[26] Medical personnel shall also take care of pacemaker patients during procedures in clinical institutions during MR based imaging or electrosurgical procedures.[27]

Future Trends in Cardiac Pacing

Development of technology enabled widening of the implantable pacemaker applications from life-saving devices to devices that cure cardiac diseases and improve the quality of life.[28,29] New pacemakers will contribute to improved management of patients with arrhythmias, especially those with tachycardia.[30] It has to be expected that research will result in new, more adequate and applicable sensors for rate adaptive pacemakers.[31] However, the adaptation to the physiological needs of patients may in the future also be achieved by means of bio-engineered pacemakers.[25,32] The computational power of microprocessors embedded into pacemakers will increase and allow more sophisticated algorithms to be implemented for intracardiac ECG processing and processing of information gained from the patients' environment.[33] Also, these algorithms will enable more personalized programming of pacemakers. The memory capacity and new algorithms will enable better monitoring of the patient and tracking of cardiac events. Monitoring of patients and their pacemakers function as well as re-programming through communication networks will be improved, and become more user friendly.[34]

Conclusion

In fifty years from the first implantation, cardiac pacemakers have become safe and reliable medical devices with a large diversity of models and functionalities. Implanted pacemakers generate life-saving pulses when necessary, but also monitor the patient, measure physiological parameters and make decisions that influence life style and the quality of patients' life. These decisions are supported by a powerful embedded computer with computational power of an average personal computer. In most cases, long-lasting power supply enables patient's periods of more than ten years without replacement of the pacemaker, and build-in telemetry system allows communication with the physician without going to a clinical setting.

The state of art of implantable cardiac pacemakers shows a success story of long-lasting collaboration between physicians and engineers, which continues by developing new concepts for therapy of cardiac diseases and new devices. The newest developments in the field are bio-engineered pacemakers, i.e. myocardial implants of exogenous cells that sustain pacemaking activity once connected to the myocardium. Biologically engineered pacemakers, once they reach maturity for clinical application, would overcome potential biocompatibility and wiring problems of electronic devices. However, the performance and reliability of current electronic implantable pacemakers, makes it difficult for researchers of any competing technology to achieve the same success.

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