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# Introductory Chapter: From Basic Foundations to Future Developments

Mart Min

## 1. Early pacemakers

Dr. Rune Elmqvist (1906–1996), a physician working for the Swedish company Elema-Schönander (later a part of Siemens) as an engineer, developed the first implantable pacemaker. Dr. Elmqvist developed the device in cooperation with Åke Senning (1915–2000), a senior physician and cardiac surgeon at the Hospital of Karolinska Institute in Solna near Stockholm [1]. Their first patient, Arne Larsson (1915–2001), underwent secret emergency surgery to implant his first pacemaker on October 8, 1958, just in the middle of his lifetime. The role of his wife Else-Marie was important. She persuaded the scientists to make the surgery, though they strongly refused, initially. Finally, it was an officially unacceptable prank, made under the pressure of female power! Later Arne Larsson went on to receive more than 20 pacemakers in the 43 years following the first implantation.

The pacemaker contained a single transistor-based blocking pulse oscillator which delivered pacing impulses at an amplitude of 2 V and a pulse width of 1.5 ms through a transistor buffer. The frequency of pulse sequence was set to have a constant rate pacing of 70 beats per minute. The energy utilized by a totally two-transistor electronic circuit from a nickel-cadmium battery was minimal since Elmqvist managed to obtain a few of the first silicon transistors produced by Texas Instruments, USA. Recharging of the battery once a week for 12 h was accomplished inductively by a 150 kHz radio frequency current generated externally.

Dr. Elmqvist produced two of such handmade units encapsulated in a new epoxy resin (Araldite), which had excellent biocompatibility. He used a shoe polish can from Kiwi with a diameter 55 mm and thickness of 16 mm as a mold.

After being a young trainee of Dr. Åke Senning in Sweden, Dr. Orestes Fiandra (later founder of the company CCC del Uruguay, now Integer) implanted a pacemaker designed by Dr. Rune Elmqvist and produced by Elema-Schönander (Sweden), in Uruguay on February 2, 1960, together with Dr. Roberto Rubio.

In parallel, Earl E. Bakken (1914–2018), an electrical engineer and co-founder of the company Medtronic in 1949 in Minneapolis, USA, made a transistor-based blocking oscillator for the first battery-operated wearable pacemaker (1957). Famous doctor C. Walton Lillehei (1918–1999) from the University of Minnesota, “the father of open chest surgery,” took the device into medical use in 1958. This pacemaker became known as the Medtronic Cardiac Pacemaker 5800 (produced in 1958). The chosen pacemaker output was a 2 ms square wave, variable in amplitude from 1 to 20 mA into a 1000  $\Omega$  load, which gives from 1 to 20 V. The pacing rate was variable from 60 to 180 pulses per minute. Meanwhile, Dr. Lillehei and his co-workers developed the myocardial wire (1957) for the implanting of pacemakers:

a braided stainless steel wire in a Teflon sleeve implemented directly into the myocardium, while the other end was connected to the pacemaker via stab incision. To close the electrical circuit, a common (neutral) large area electrode was buried under the skin. As a result, only 1.5 V is needed for effective pacing. Meanwhile (1958), a transvenous catheter electrode was introduced fluoroscopically via the basilic vein into the right ventricle. Medtronic Inc. continues production of the cardiac rhythm devices being nowadays the largest medical technology company in the world.

At about the same time, in 1958, Mr. Wilson Greatbatch (1919–2011) was working on the recording of tachycardias. He recognized that the low-level electrical current could power the implantable pacemaker and drive a human heart. Mr. Greatbatch asked Dr. William Chardack (1915–2006), chief of surgery at Buffalo's Veterans Hospital, and surgeon Dr. Andrew Gage to test a mercury battery-powered implantable pacemaker at the hospital's animal lab. The design was proven to work.

In 1960, Dr. Chardack successfully implanted the device in a 77-year-old man, who lived for 2 years before dying of unrelated causes. Later Medtronic Inc. owned the Chardack-Greatbatch pacemaker [2]. Mr. Greatbatch invented also the lithium battery for pacemakers [3] and formed a company Wilson Greatbatch Ltd. for the production of these batteries. The company continues to save the lives of patients worldwide as a part of Integer Holdings Corporation. Modern batteries can work 10–12 years continuously in nowadays pacemakers.

## **2. Demand pacemaker**

The next big step was invention of the demand pacemaker by Barouh V. Berkovits [4]. The early pacemakers generated pacing pulses continuously at a preset constant frequency/rate regardless of any spontaneous activity of the heart, that is, whether the natural pacemaker in the heart beats or not. The competition of two pacing sources took place, and, as a result, arrhythmias and/or ventricular fibrillation provoked making normal heart work impossible. The demand pacemaker has sensing electronics for the detecting of natural pacing. The artificial pacing switched off when the natural one works. The demand pacemaker contains the first implantable cardiac monitor inside.

## **3. Physiological pacing**

One more step leads us to physiological pacing introduced with implementation of the dual-chamber pacemaker having the electrodes for synchronized pacing and exact timing in both the right atrium and right ventricle. This pacemaker senses the natural activity of atrium and ventricle separately. The aim is to define, whether, and in which compartment – in atrium, ventricle or in both – the artificial pacing is required at certain moments to achieve the best mimicking of natural heart work, see the US Patent by Berkovits [5]. However, the latest investigation shows that achieving adequate physiological pacing still remains problematic even nowadays, 50 years later.

Attempts to achieve left ventricle (LV) pacing are introduced for getting more exact physiological pacing. There is still no way to move the pacing electrodes directly into the left ventricle because of too high blood pressure delivered there. Therefore, different indirect pacing ways were introduced. First, left ventricle septal pacing shows to be promising in restoring the pumping performance. Then, endocardial and epicardial LV pacing modes are introduced, where endocardial stimulation appears to be more physiological and less problematic than epicardial activation.

Cardiac resynchronization therapy (CRT) using biventricular (BIV) pacing has proved its effectiveness to correct myocardial asynchrony [6] and improve clinical status of patients with severe congestive heart failure (CHF). Multipolar LV leads for multisite pacing have recently become available for biventricular pacing [7].

## **4. Rate-responsive pacing**

While earlier pacemakers have a predetermined pacing rate, set to fixed “optimal” value, rate-responsive adaptive pacemakers speed up or slow down your heart rate depending on metabolic demand of your body. Modern rate-responsive pacemakers are capable of adapting to a wide range of sensors information relating to physiological needs depending on physical activity of the patient. The first proposal to introduce the adaption of pacing rate to respiratory parameters was made in 1967 already [8], but real implementation of rate-responsive pacing began in the early 1980s [9].

Rate-responsive pacemakers use a physiologic sensor in the cardiac monitor embedded into the pacemaker to adjust the pacing rate according to the physiologic needs of the patient, which is proportional to his/her metabolic demand. The latter is the response to an oxygen debt.

It should ideally operate in a closed-loop system, making rate-adaptive pacing insensitive to not heart-related inputs. Finally, dedicated sensors should avoid undesirable over pacing. Safety operation needs reliable electronics and complex programming.

### **4.1 Sensing and monitoring**

Different parameters have been investigated for the regulating of pacing rate: oxygen saturation, venous pH, QT interval, body motion, respiratory rate, stroke volume, central venous temperature, minute ventilation, peak endocardial acceleration, and changes of the right ventricular impedance during the cardiac cycle (closed-loop stimulation). Clinical studies have outlined advantages and limitations of the different sensed parameters; only some of these are still used in sensor technology.

Only some of these sensing principles are in practical use; nowadays, all of which are unable to recognize the oxygen debt directly.

Activity sensors are older and more widely used. The principle of work of these sensors bases on the relationship between the physical activity and the corresponding heart rate. Activity may be acknowledged either (1) by a piezoelectric crystal, which recognizes the muscular pressure waves, or (2) by an accelerometer that identifies the postural changes and the body movements related to physical activity. Both types of sensors are housed inside the pacemaker's case.

Unfortunately, these sensors respond to artifacts not related to body movements like laughing and coughing, but some of the relevant efforts, as isometric or slow but tiresome exercise, mental stress, and metabolic inadequacy, remain not registered. The possible mismatch between exercise intensity and the required heart rate increase represents the main limitations of activity sensors.

The sensors based on QT interval and minute ventilation (MV) provide pacing rates more closely and specifically related to physical and mental stress requirements [10].

Minute ventilation, the product of respiratory rate and tidal volume, is a physiological indicator that correlates well with metabolic demand [11]. This parameter, which also correlates linearly with heart rate, can be derived from variations in



transthoracic and intracardiac impedance signals [12]. The voltage is measured as a response to the current injected between the proximal ventricular or atrial electrode and the pacemaker casing [13].

No single sensor can reproduce all the activities of daily life. Combining different sensors might more closely mimic intrinsic heart rate. For example, the combination of an activity sensor for getting a rapid response and a bioimpedance-based minute ventilation (MV) sensor, providing delayed but close to metabolic demand response, could be a solution [14].

## **4.2 Bioimpedance-based sensing**

The most trustworthy sensing methods for the monitoring and control of pacing rate rely on measurement of electrical impedance, implementations of which are developed by Estonian scientists in collaboration with St. Jude Medical (USA/Sweden) during the period of 1999–2006. The variations of thorax impedance, measured between the tip of the pacing lead in the right ventricle and the case of pacemaker, give us lung impedance containing information about both the respiration rate and tidal volume. Using some soft computing method, e.g., fuzzy logic, we can evaluate the metabolic demand of the body and obtain a satisfactory pacing rate [15]. Implantable impedance measurement units were developed [16, 17]. Moreover, stroke volume and cardiac output are retrieved when measuring the impedance inside the right ventricle [18–20]. Finally, the balance condition between energy supply and consumption of myocardium has been calculated, and the maximal pacing rate was found to avoid over pacing [21]. Dangerously low pacing rate limit was also defined from the impedance measurements. A closed-loop control of the pacing rate by sensing of cardiac output has been discussed [22].

Both technology and clinical treatment methods have changed since the first cardiac devices developed during the twenty-first century. Diversity of cardiac pacing modes is available nowadays [23] for helping patients [24, 25]; some newest of these are considered in the next four chapters of the present book.

## **5. Novel indications and solutions presented in this book**

Chapter 2 [26] presents the indications for cardiac devices, including pacemakers, cardiac resynchronization therapy (CRT) devices, and implantable cardioverter defibrillators (ICD). Contraindications due to different health conditions of patients are considered [24–27]. Pacemaker therapy is the treatment of bradycardia. An aging population increases the use of permanent pacemakers. Leadless pacing is a new landmark in the development of pacemaker technology but still limited to pacing in the right ventricle, only. The aim of CRT is to improve synchrony in the heart's contraction and avoid ventricular fibrillation (VF) by delivering a shock during the myocardial refractory period of cardiac cycle. The CRT devices are recommended for the treatment of atrial arrhythmias and ventricular tachycardia (VT). Around 30% of patients suffer from chronic heart failure (HF). Avoidance of sudden cardiac death (SCD) possibility in heart failure (HF) cases is also a task of CRT devices. The CRT with the ability to work as a cardiac defibrillator is termed as CRT-D, whereas the term CRT-P designates solely a pacing function. One major cause of death worldwide is sudden cardiac death SCD, which can be prevented most effectively by the aid of a specific device—the implantable cardiac defibrillator (ICD).

The subcutaneous ICD (S-ICD) is introduced in Chapter 3 [28]. This important advancement in defibrillation therapy obviates the need for a transvenous lead, the most frequent complication maker with transvenous devices. Unfortunately, the

S-ICD is appropriate for patients who require only rescue defibrillation. It cannot be used when the pacing against bradycardia or tachycardia is needed. Lead failure is the most frequent source of complication requiring surgical revision. Extraction of leads may cause devastating complications, including death.

Chapter 4 [29] deals with leadless or transcatheter pacemakers [30, 31] that have been introduced to the market some years ago with important benefits and some limitations. These devices are entirely implantable within the right ventricle. Thus, the transvenous pacing leads and pacemaker pockets are not needed anymore. This reduces the risk of infections and lead-related problems. Unfortunately, only the pacing in the right ventricle is available. Atrial sensing, anti-tachycardia pacing, and A/V synchrony are not possible, but the rate response by the aid of programmable accelerometer works.

Chapter 5 [32] explains that underdiagnosed atrial fibrillation (AF) may be potentially life-threatening arrhythmia, the appearance of which is episodic. Therefore, long-term day-and-night monitoring is required. Though the implantable cardiac monitors are in use for years already [25], the surgery is not reasonable in many cases. The chapter introduces a new user-friendly device that allows for frequent self-monitoring of the heart rhythm. This thumb ECG wearable device is a small format, patient-friendly device that can be used to monitor their heart rhythm regularly and continuously. Clinicians monitor the results by accessing a secure portal via an ordinary laptop computer. Bluetooth and mobile phone communication are available.

## 6. Summary

The present chapter reviews the developments of the implantable heart rhythm management from its dawn to mature technology. The book as a whole provides information about today's achievements in the field of cardiac pacing and monitoring with a view to the future.

## Conflict of interest

The author has received financial and technical support in frames of the research agreements with St. Jude Medical and Guidant/Boston Scientific in 1999–2006.


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