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EDITORIAL

Brief History of Cardiac Arrhythmias in Facts and Photos

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Cardiac arrhythmias, as well as their diagnosis and treatment, have a long history. The ancient Chinese pulse theory laid the foundations for the study of arrhythmias in the 5th century BC. Complex theories recognized pulse beats as a diagnosis and prognosis of pathologies, and there may be harmony or dissonance[1-4].

In the *Papyrus scrolls*, the oldest and best preserved medical document from Egyptian culture (1550 BC), descriptions of the correlation between the peripheral pulse and the heartbeat were already observed (Fig. 1). Furthermore, the studies carried out by the famous Roman physician Claudius Galen (129-199 AD) and by the British anatomist William Harvey (1578-1657), although at different times, were fundamental for the advancement of understanding about the functioning of the cardiovascular system, since there was the formation of basic theories about the human pulse by Galen and the discovery of the importance of cardiac pumping by Harvey, among other findings. The most important advances took place in the 20th century, because of the better understanding of topics such as electrophysiology and pharmacology and the increasing clinical relevance of cardiac rhythm disorders.[1,2]

Figure 1. (a) Pulse theory, derived from ancient Chinese studies, the pulse divided into parts, reflecting some organs; (b) Claudius Galen, Galen's pulse theory, 129 BC, established different types of pulse and related them to different pathologies; (c) William Harvey described blood circulation; (d) Harvey's circulatory theory[1-4].

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In most cases, the diagnosis of arrhythmia depends on non-invasive tests. The basic tool in this area is the electrocardiogram. The first human electrocardiogram was performed by Augustus Desiré Waller (1856-1922) in 1887, but Waller, interestingly, did not recognize the clinical significance of the test. Willem Einthoven (1860-1927), Dutch physician, having performed his first electrocardiogram (ECG) in 1892, introduced the bipolar ECG system, which was named in his honor, having received the Nobel Prize in 1924 for his work with electrocardiography and the galvanometer (Fig. 2). He designated the letters still known today for ECG tracings as P, Q, R, S and T. Holter monitoring, with a prolonged assessment of cardiac activity, was another great advance, created by Norman Holter (1914-1983) and released for commercial production in 1962[1,2].

The first known treatments for arrhythmia are described in the *Ebers Papyrus*, from 1550 BC, and are based on the use of sea onion (*Urginea scilla maritima*). Today, it is known that the healing properties present in this plant are due to the presence of cardiac glycosides. Another prominent medicinal plant was foxglove (*Digitalis purpurea*), first pointed out in the 13th century in Wales and again in 1542 by Leonhart Fuchs (1501-1566) (Fig. 3)[1-4].

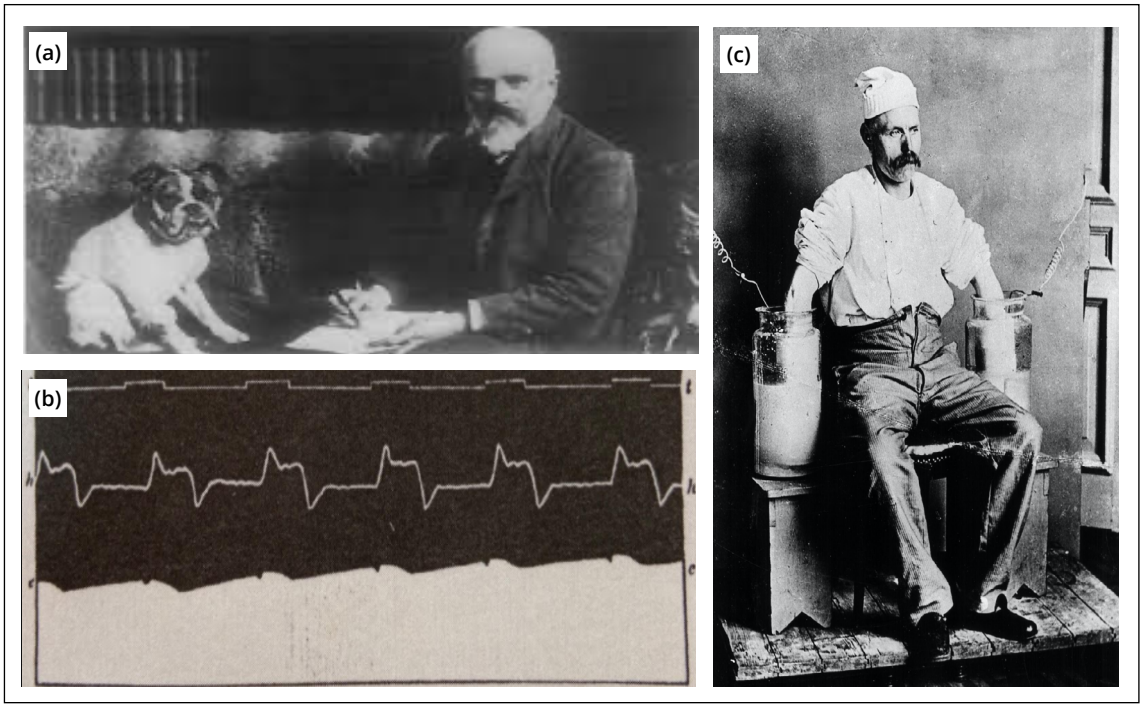

Figure 2. (a) Augustus Desiré Waller and (b) his first human electrocardiographic recording; (c) in 1905, in the laboratory of Willem Einthoven, performing an electrocardiogram in the D1 derivation[1-4].

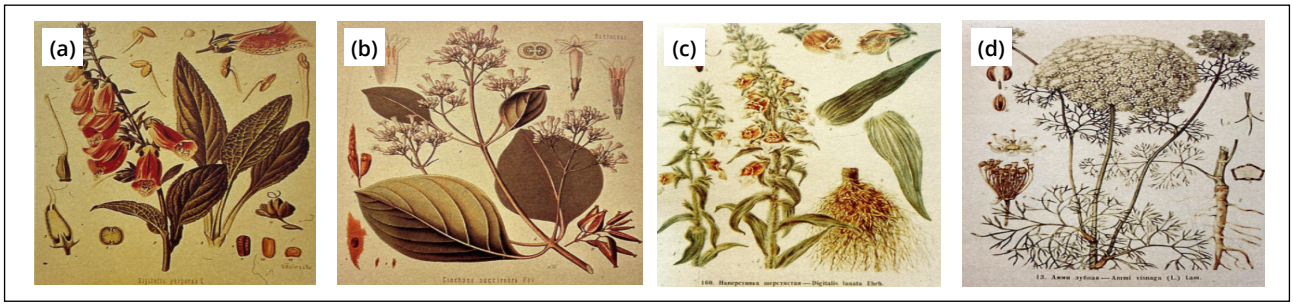

Figure 3. (a) *Digitalis purpurea* and (b) *Digitalis lanata*,described by Leonhart Fuchs in his herbal book and by William Withering for their diuretic effects in patients with anasarca, it being Withering who actually initiated digitalis therapy. (c) *Cinchona succirubra* plant, which gave rise to quinidine and (d) *Ammi visnaga*, an original Mediterranean plant, which gave rise to amiodarone[1-4].

The first antiarrhythmic drug was quinine, the effect of which was first detailed in 1914 by Karel F. Wenckebach (1864-1940), who reported ridding a patient of tachycardia with 1 gram of quinine. Wenckebach also described a patient with malaria, treated with quinine, who had his atrial fibrillation controlled. Lidocaine was first synthesized in 1943, approved

for use in the United States and Sweden in 1948, and first used to prevent ventricular tachycardia in 1950. Amiodarone, the prototype class III antiarrhythmics, was discovered as a result of an accidental observation by GV Anrep in 1946, after improvement of an angina in an assistant, being completely synthesized in 1961, used at first as an anti-ischemic and only latter as an anti-arrhythmic (Fig. 3)[1-4].

Wenckebach also published "Arrhythmia as an expression of a particular cardiac dysfunction" in 1903 and in 1914 "Irregular cardiac activity and its clinical significance", legendary works in the study of cardiac arrhythmias. He described internodal bundles, 2nd degree blocks, and antiarrhythmic therapies. Great physiologists and anatomists contributed to the description of the sinus node, the atrioventricular (AV) node, the cardiac conduction bundles, and the accessory bundles.(Figs. 4-6)[1-4].

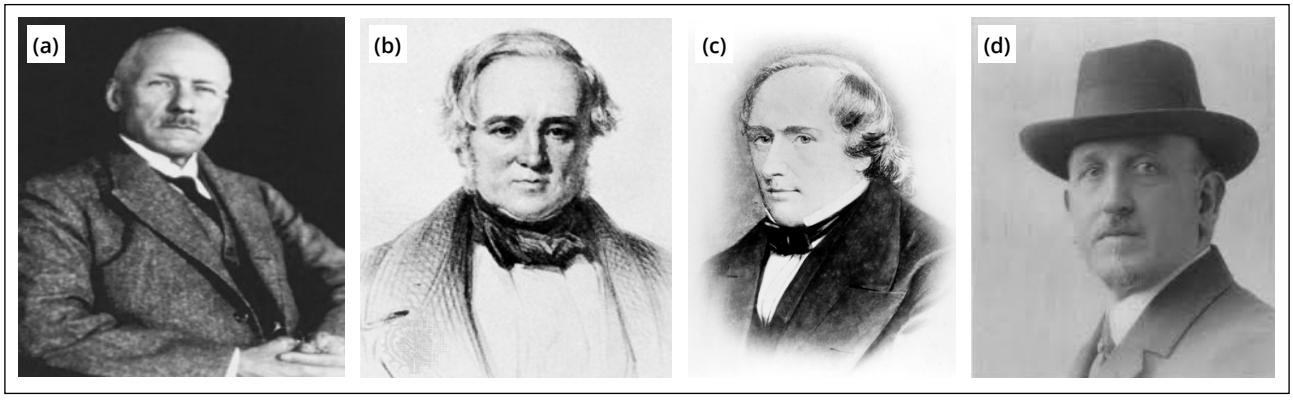

Figure 4. (a) Karel F. Wenckebach (1864-1940), considered the author of the diagnosis of atrioventricular blocks and a pioneer in the treatment of cardiac arrhythmias with quinidine; (b) Robert Adams (1791-1875), Irish surgeon, and (c) William Stokes (1804-1878), famous Irish physician with over 100 publications, described the Morgagni-Adams-Stokes syndrome, chronologically correct. (d) Louis Benedict Gallavardin (1875-1957), Frenchman from Lyon, published studies on the various forms of paroxysmal supraventricular tachycardias and was the founder of French cardiology[1-4].

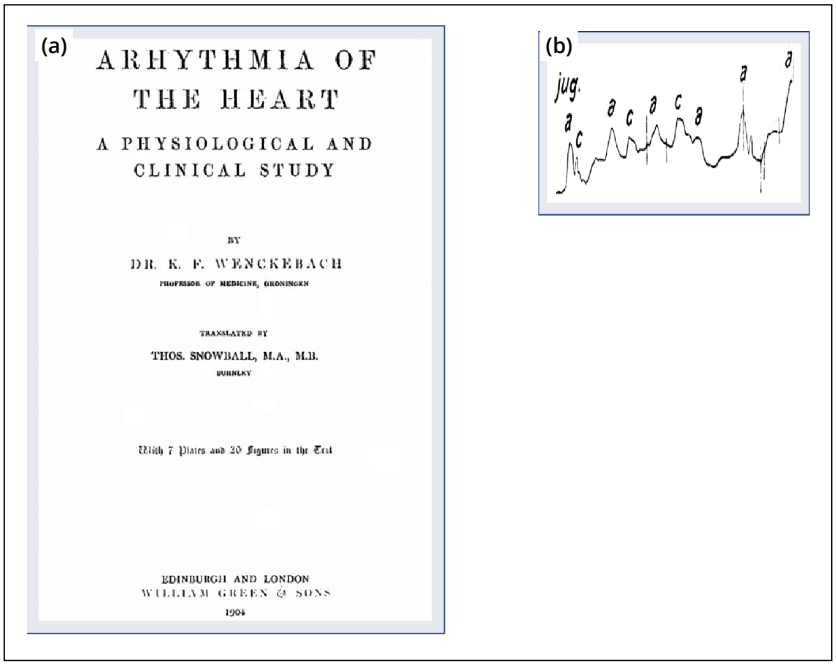

Figure 5. (a) Wenckebach's original treatise on cardiac arrhythmias;
(b) type I second-degree atrioventricular block diagnosed by jugular venous pulse1-4.

The first report of electrotherapy dates from antiquity, from the year 46 AD, when Scribonius Largus used electric fish discharges (Torpedo ocellata) to treat rheumatism and headache. Electric fish was also used during the first centuries of the Christian era. Electrotherapy for arrhythmic disorders dates back to the 16th century.[3,4]

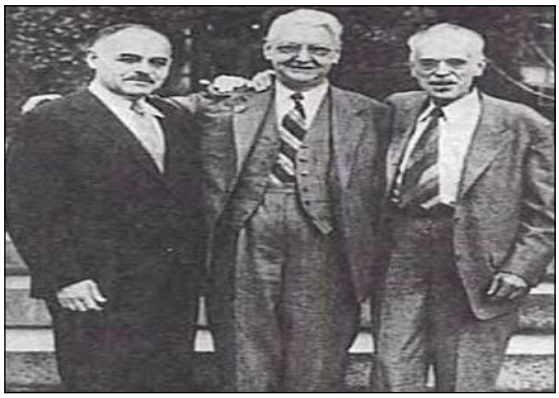

Figure 6. (left) Louis Wolff (1898-1972), American assistant to Paul White at the hospital in Boston; (center) John Parkinson (1885-1976), Englishman, known to White, was interested in gathering 11 cases of the syndrome and publishing them; and (right) Paul Dudley White (1886-1973), an American who studied and worked at Harvard, was a co-founder of the American Heart Association, author of numerous articles and books, and cardiologist emeritus of several institutions and countries.[1]

Jeronimus Mercurialis (1530-1606), an Italian humanist of the Renaissance, had already formulated the concept of syncope and demonstrated its connection with the weak pulse in the year 1580. He was the precursor of the differentiation between cardiac syncope and loss of consciousness from neurological cause[1].

The first description of external cardiac stimulation of the heart was in 1774, in the records of the Royal Humane Society, London, England. Luigi Galvani (1737-1798) published his findings on electrical phenomena in frog muscles and hearts in 1791, which was an essential contribution to the beginnings of modern electrophysiology and to the development of the study of batteries and electricity. During the French Revolution, experiments were described in decapitated humans, in which the heart could be stimulated with an electrical current.[1] (Figs. 7 e 8).

Figure 7. (a) Bernard Low was born in Lithuania and studied in the United States, describing sinus node disease and performing experiments with alternating and direct currents for reversal of atrial arrhythmias, experiments that helped in cardiac defibrillation therapies; (b) Arthur Keith (1866-1955), Scottish anatomist who described the sinus node; (c) Ludwig Aschoff (1866-1942), German pathologist who described the atrioventricular node and rheumatic nodules in cardiac muscle; (d) Wilhelm His Jr. (1863-1934), Swiss physician, studied and described the bundle of His; (e) Johannes Evangelista Purkinje (1787-1869), anatomist and physiologist, considered the greatest physiologist of the 19th century, developed studies in several areas, particularly vision, cartilage, nerves and heart[1-4].

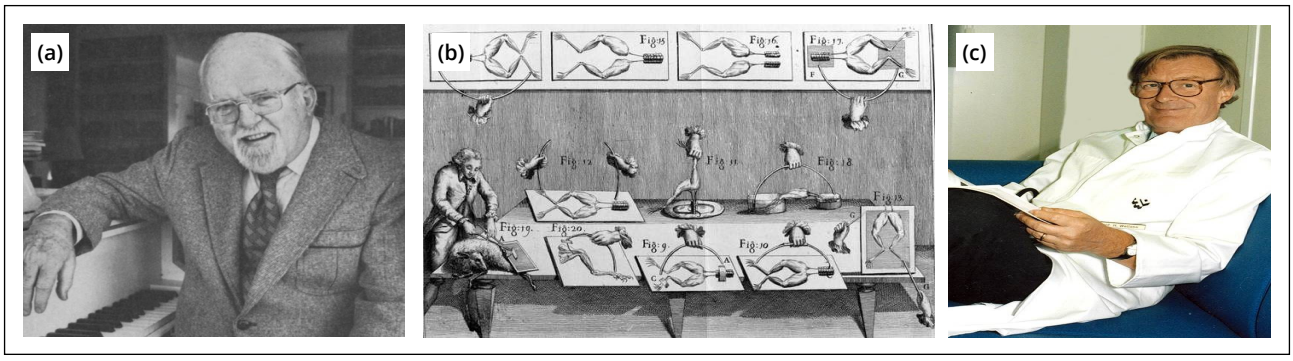

Figure 8. (a)Norman Jefferis Holter designed the 24-hour ambulatory monitoring system, one of the greatest advances in the diagnosis of cardiac arrhythmias. After Einthoven transmitted electrocardiographic signals over wires in 1906, Holter, in 1949, developed the principles of bioelectrical telemetry signals. Luigi Galvani published important contributions to modern electrophysiology, (b) through his electrical experiments on frog muscles and hearts. (c) Hein Wellens (1935-2020) introduced programmed cardiac pacing, allowing for invasive electrophysiological studies[1-4].

The experiments of Hugo von Ziemssen (1829-1902) on the patient Catharina Serafin, in 1882, using cardiac stimulation by Faraday and galvanic currents, entered the annals of physiology and cardiac stimulation. His experiment images are shown in Fig. 9[2,3].

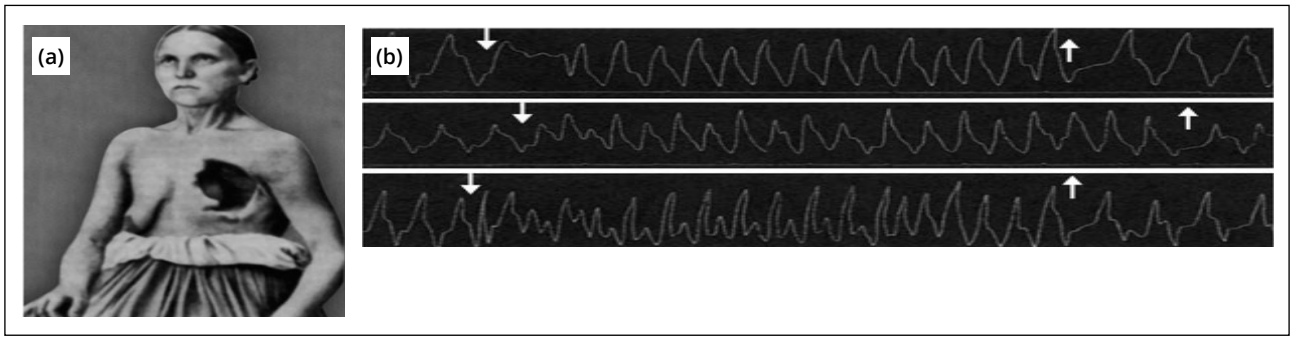

Figure 9. Historical experiment in patient Catharina Serafin, operated on for a thoracic tumor, leaving her heart exposed after surgery, separated only by a thin layer of skin. This situation allowed her doctor, Hugo von Ziemssen, in 1882, in Prussia, to perform direct external cardiac stimulation, changing the heart rate.[1-4].

After years of research, Albert Hyman (1893-1972), a physiologist from New York, reported for the first time, in 1932, the successful application of an external pacemaker in animals and humans, thus inventing the device named artificial pacemaker, at the time a generator with mechanism used in clockwork (Fig. 10). In Sweden, on October 8, 1958, the first complete pacemaker was implanted in a patient with Stokes-Adams syndrome.[3,4] (Fig. 10).

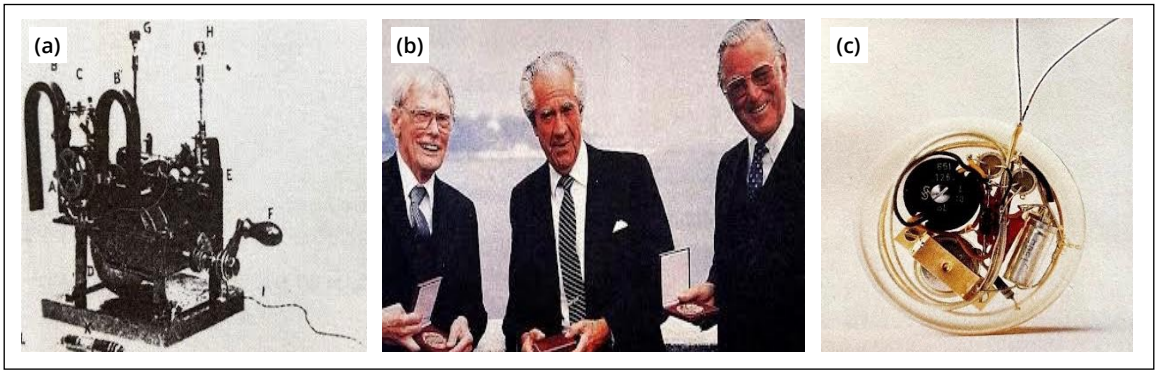

Figure 10. (a) Albert Hyman's first external pacemaker with clockwork mechanism. (b) Elmquist, Senning and Larsson, respectively, inventor, surgeon, and patient of the first human implant in 1958, together after receiving honorary medals at the 1986 Pacemaker Congress in Monaco. The device needed to be recharged every week. The patient had Stokes-Adams syndrome. (c) The first implantable pacemaker, made by Elmquist and Senning, in 1958[1].

The first use of cardiac defibrillation was in 1947, in Cleveland, by Claude S. Beck (1894-1971), successfully defibrillating the open heart of a 14-year-old boy. After the experiments of Bernard Lown (1921-2021), in 1952, and of Paul M. Zoll (1911-1999), in 1956, the principles of therapy with external electrodes in the chest for defibrillation were discovered. Only in 1963, Nathan and Center performed the first implantation of an atrioventricular pacemaker and, in the same year, Lagergreen, Johannson, Siddons and Davies performed an implant in the current models, with a subcutaneous generator and with a transvenous implant, and no longer by thoracotomy[1,5].

Automated internal cardiac defibrillators represented an important step in the treatment of potentially lethal cardiac arrhythmias. Its first concepts were started with Michel Mirowski (1924-1990) in 1970 and his co-worker, Morton Mower (1933-). The first human implant took place in 1980, beginning the era of sudden cardiac death prevention.[5] (Fig. 11).

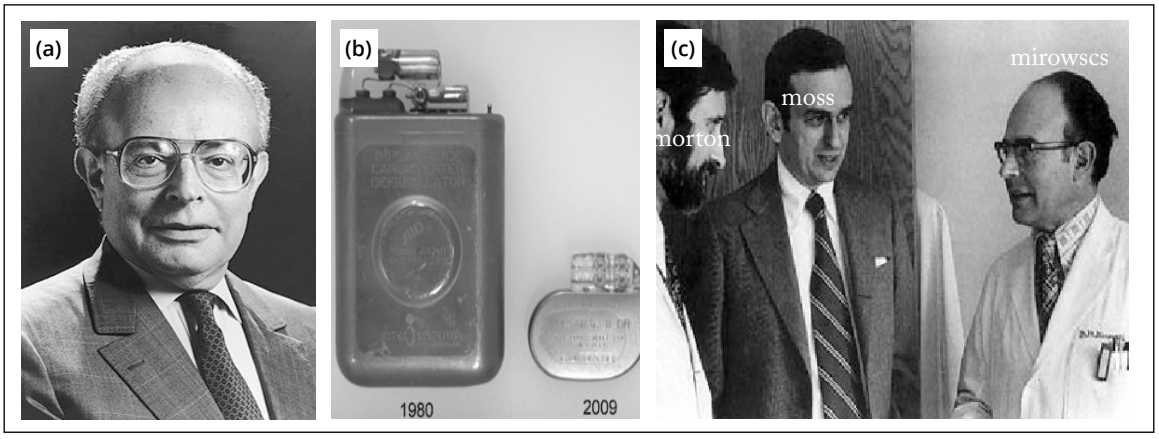

Figure 11. (a) Mieczyslaw "Michel" Mirowski, responsible for the creation of implantable internal cardiac defibrillators (ICD), with the first implantation in humans taking place in 1980, a decade after research and experiments with animals. (b) First defibrillators (1980), with a weight of 280 g and a volume of 150 mL and, more recently, a weight of 70 g and a volume of 31 mL. (c) Meeting between Morton Mower (left), Mirowski (right) and Arthur Moss (center); Morton worked directly with Mirowski in the creation of ICDs and Arthur Moss, author of several studies with ICD, including the classic MADIT studies[5].

Programmed cardiac pacing was first introduced as a cardiac diagnostic tool in 1967. Gallagher and Scheinman performed the first ablation of the His bundle in humans in 1982, initially with energy from external defibrillators (direct current), which caused clotting and local necrosis, with greater risks to the patient's health.

In 1983, Weber and Schmitz reported the first ablation in a patient with Wolff-Parkinson-White syndrome, and in 1986 modern radiofrequency ablation techniques with controlled energy and time (up to 50 W and time generally between 10 and 90 seconds in applications), the effects being well localized and with less risk. Three-dimensional electroanatomical mapping is a system that allows the geometric reconstruction of the entire heart and pulmonary veins in three dimensions (3D), increasing the accuracy of arrhythmia localization and decreasing radiation exposure. This system was a recent technological advance in the ablation of cardiac arrhythmias.[2-4]

Pacemakers have been made available for use as a therapeutic option for congestive heart failure (CHF). A new era was beginning. Patients with CHF, severe left ventricular dysfunction and left bundle branch block could be treated with a pacemaker with three leads, one in the right atrium, another in the right ventricle and another in the left ventricle, initially by thoracotomy and, subsequently, via coronary sinus, promoting a more synchronous and physiological stimulation. Cardiac pacing evolved from the treatment of bradycardias to the treatment of CHF. The concept of intra and interventricular cardiac dyssynchrony was established[6-8].

Some images of these historical and relevant moments of cardiac arrhythmias are shown below. This story was built over many years, through the ingenious observation of great characters, which allowed us to have modern and safe techniques for the diagnosis and treatment are shown in these work.

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Writing – Reviewing & Editing: Gondim DSP, Rocha MEQA, Rocha EAQA.

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