INTRODUCTION

With expanding indications for device therapies for management of cardiovascular diseases, the number of patients receiving pacemaker implantations is increasing every year ***(Lakshmanadoss et al., 2011)***.

In an environment where we are being increasingly surrounded by developing technology, pacemaker patients are questioning the possible effects of the increasing associated environmental and electromagnetic "noise" on their implants ***(American Radio Relay League, 2013)***.

Electromagnetic interference (EMI) by radiofrequency (RF) waves with medical devices is an important issue for the medical safety of patients who are using life-supporting medical devices ***(Pashazadeh et al., 2013)***.

It should be stated quite clearly that, despite the increased prevalence of interference, clinically significant problems remain uncommon and that the continual improvement in pacemaker protection circuitry design evident in the industry, should keep the incidence low ***(American Radio Relay League, 2013)***.

The transmission signal generated from a cellular base station (BS) is different from that of mobile radio

units. In second-generation Mobile system, such as the personal digital cellular (PDC) telecommunication system and the global system for mobile (GSM) communication, the transmission signal of a cellular BS is multicarrier because a BS must handle many mobile radio units simultaneously ***(Tarusawa et al., 2005).***

In the third-generation Mobile system, the wideband code-division multiple access (W-CDMA) mobile system, the transmission signal of the BS has a multicode signal that includes a large number of traffic channels because a BS must handle many mobile radio units simultaneously ***(Onoe et al., 2001).*** Waveforms of multicarrier or multicode signals are different from those of a single-carrier or single-code signal. Multicarrier or multicode signals increase the peak-to-average power ratio of the signals ***Narahashi et al., 1995).***

In general, electronic device EMI depends on the peak-to-average power ratio of the transmission signal exciting the electromagnetic field (EMF), although the average power is the same. For mobile radio units, different types of pacemakers were tested using a single-carrier or single-code EMI estimation protocol ***(Irnich et al., 1996, Hayes et al., 1996)***

This situation raises questions concerning the difference between multicarrier and single-carrier

transmission, and between multicode and single-code transmission. Consequently, a study on implantable cardiac pacemaker EMI based on multicarrier or multicode transmission signals is needed ***(Tarusawa et al., 2005)***.

AIM OF THE WORK

The aim of the present work is to study the effect of exposure to radiofrequency waves with different power density generated from mobile base stations over implanted pacemakers.

Chapter1

CARDIAC PACEMAKERS

History of Pacemakers:

In 1899, McWilliam reported in the British Medical Journal his experiments in which application of an electrical impulse to the human heart in asystole caused a ventricular contraction and that a heart rhythm of 60-70 beats per minute could be evoked by impulses applied at spacing equal to 60–70/minute ***(McWilliam, 1899)***.

In 1926, Lidwell of the Royal Prince Alfred Hospital of Sydney, supported by physicist Booth of the University of Sydney, devised a portable apparatus which "plugged into a lighting point" and in which "One pole was applied to a skin pad soaked in strong salt solution" while the other pole "consisted of a needle insulated except at its point, and was plunged into the appropriate cardiac chamber". "The pacemaker rate was variable from about 80 to 120 pulses per minute, and likewise the voltage variable from 1.5 to 120 volts". In 1928, the apparatus was used to revive a stillborn infant at Crown Street Women's Hospital, Sydney whose heart continued "to beat on its own accord", "at the end of 10 minutes" of stimulation ***(Lidwell, 1929).***

In 1932, American physiologist Hyman, working independently, described an electro-mechanical instrument of his own, powered by a spring-wound hand-cranked motor. Hyman himself referred to his invention as an "artificial pacemaker" **(Figure 1)**, the term continuing in use to this day ***(Furman et al., 2005)***.

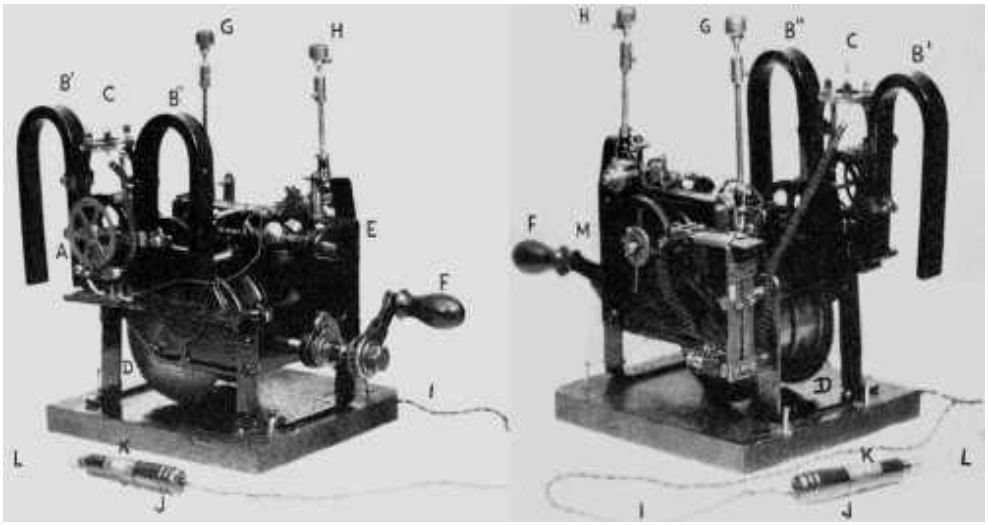

Figure (1): Albert Hyman's "artificial pacemaker": from a 1932 photograph.

A = magnetogenerator; B' and B' = companion magnet pieces; C = neon lamps; D = spring motor; E = ballistic governor; F = handle; G = impulse control; H = speed control; / = flexible electric cord; J = insulated handle; K = handle switch; L = electrode needle **(*Quoted from Aquilina, 2006).***

An apparent hiatus in publication of research conducted between the early 1930s and World War II may be attributed to the public perception of interfering with nature by 'reviving the dead'. For example, "Hyman did not publish data on the use of his pacemaker in humans because of adverse publicity, both among his

fellow physicians, and due to newspaper reporting at the time. Lidwell may have been aware of this and did not proceed with his experiments in humans" ***(Mond et al., 1982)***.

An external pacemaker was designed and built by the Canadian electrical engineer John Hopps in 1950 based upon observations by cardio-thoracic surgeon Wilfred Gordon Bigelow at Toronto General Hospital. A substantial external device using vacuum tube technology to provide transcutaneous pacing, it was somewhat crude and painful to the patient in use and, being powered from an Alternating Current (AC) wall socket, carried a potential hazard of electrocution of the patient by inducing ventricular fibrillation. A number of innovators, including Paul Zoll, made smaller but still bulky transcutaneous pacing devices in the following years using a large rechargeable battery as the power supply ***(Zoll, 1973)***.

In 1957, Weirich published the results of research performed at the University of Minnesota. These studies demonstrated the restoration of heart rate, cardiac output and mean aortic pressures in animal subjects with complete heart block through the use of a myocardial electrode ***(Weirich et al., 1957)***.

In 1958, Colombian doctor Laverde and Colombian electrical engineer Pombo constructed an external pacemaker, similar to those of Hopps and Zoll, weighing 45kg and

powered by a 12 volt auto battery, but connected to electrodes attached to the heart. This apparatus was successfully used to sustain a 70 year old priest, Gerardo Florez **(Figure 2),** ***(Greatbatch and Holmes, 1991)***.

Figure (2): Early external electronic pacemaker ***(Quoted from Aquilina, 2006).***

The Development of Implantable Pacemakers:

The development of the silicon transistor and its first commercial availability in 1956 was the pivotal event which led to rapid development of practical cardiac pacemaking. In 1957, engineer Earl Bakken of Minnesota, produced the first wearable external pacemaker for a patient of Dr. Lillehei. This transistorised pacemaker,

housed in a small plastic box, had controls to permit adjustment of pacing heart rate and output voltage and was connected to electrode leads which passed through the skin of the patient to terminate in electrodes attached to the surface of the myocardium of the heart **(Figure 3 and Figure 4)** ***(Senning, 1959)***.

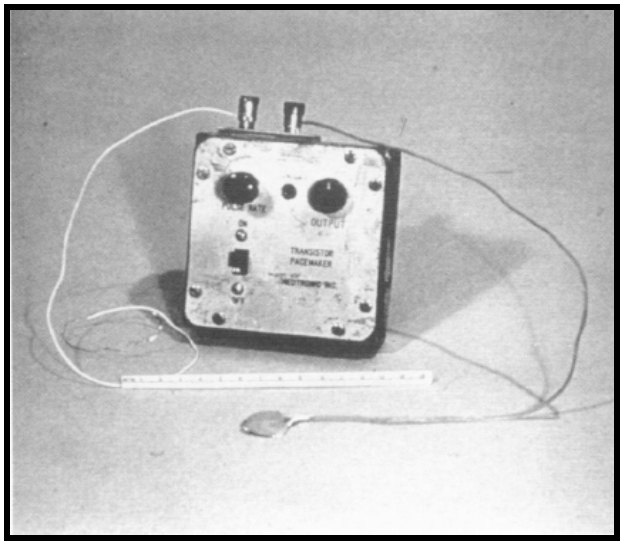

Figure (3): (Medtronic's 1st pacemaker built in 1957 by Earl Bakken for use by Dr. Lillehei of the University of Minnesota Hospitals. About the size of a large bar of soap, it was the world's lst transistorized, battery-powered, wearable pacemaker ***(Quoted from: Furman and Escher, 1970)***.

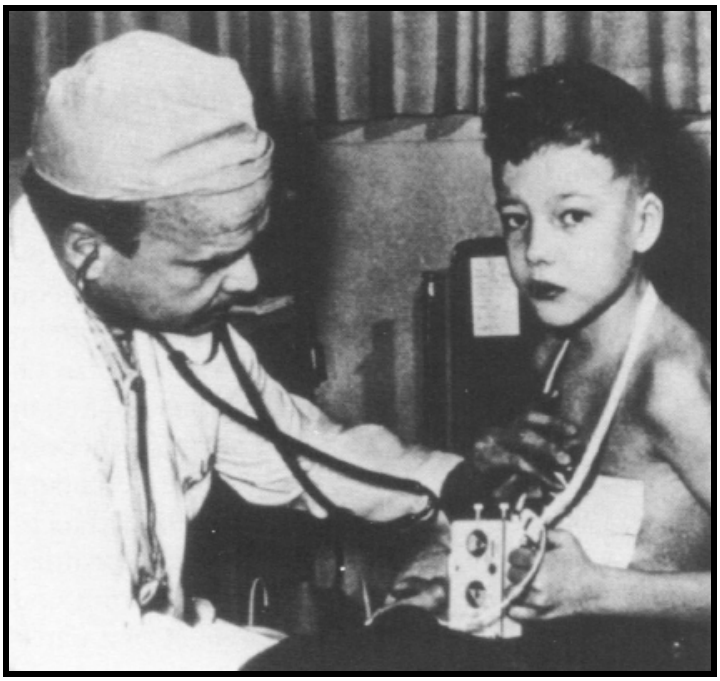

Figure (4): Dr. Lillehei examines a young patient who is wearing an external pacemaker of the type invented by Earl Bakken ***(Quoted from: Furman and Escher, 1970).***

The first clinical implantation into a human of a fully implantable pacemaker was in 1958 at the Karolinska Institute in Sweden, using a pacemaker designed by Elmqvist and Senning, connected to electrodes attached to the myocardium of the heart by thoracotomy. The device failed after three hours. A second device was then implanted which lasted for two days ***(Elmqvist et al., 1963)***.

The world's first implantable pacemaker patient, Arne Larsson, went on to receive 26 different pacemakers during his lifetime. He died in 2001, at the age of 86, outliving the inventor as well as the surgeon ***(Aquilina, 2006)***.

In 1959, temporary transvenous pacing was first demonstrated by Furman in which the catheter electrode was inserted via the patient's basilic vein **(Figure 5)**, ***(Furman and Schwedel, 1959)***.

Figure (5): The 1st patient paced with a long-term transvenous lead, which was developed by Dr. Seymour Furman. Pacing was maintained for 96 days in 1958, at Montefiore Hospital in New York City. A 50-ft extension cord enabled ambulation ***(Quoted from: Furman and Escher, 1970)***.

In February 1960, an improved version of the Swedish Elmqvist design was implanted in Uruguay, in the Casmu Hospital by Doctors Fiandra and Rubio. That

device lasted until the patient died of other ailments, 9 months later. The early Swedish-designed devices used rechargeable batteries, which were charged by an induction coil from the outside ***(Greatbatch and Holmes, 1991)***.

Implantable pacemakers constructed by engineer Wilson Greatbatch entered use in humans from April 1960 following extensive animal testing. The Greatbatch innovation varied from the earlier Swedish devices in using primary cells (mercury battery) as the energy source. The first patient lived for a further 18 months ***(Greatbatch and Holmes, 1991)***.

The first use of transvenous pacing in conjunction with an implanted pacemaker was by Parsonnet in the USA ***(Parsonnet et al., 1962 a and 1962 b)*** and Lagergren in Sweden ***(Lagergren and Johansson, 1963)*** in 1962-63. The transvenous, or pervenous, procedure involved incision of a vein into which was inserted the catheter electrode lead under fluoroscopic guidance, until it was lodged within the trabeculae of the right ventricle. This method was to become the method of choice by the mid-1960s ***(Lagergren, 1978)***.

In the late 1960s, several companies, including ARCO in the USA, developed isotope powered pacemakers, but this development was overtaken by the development in 1971 of the lithium-iodide cell by Wilson Greatbatch. Lithium-iodide or

lithium anode cells became the standard for future pacemaker designs **(Figure 6)** ***(Greatbatch and Holmes, 1991)***.

The preceding implantable devices all suffered from the unreliability and short lifetime of the available primary cell technology which was mainly that of the mercury battery ***(Aquilina, 2006)***.

Figure (6): Devices of the 60's **(*Quoted from Aquilina, 2006)*.**

A further impediment to reliability of the early devices was the diffusion of water vapour from the body fluids through the epoxy resin encapsulation affecting the electronic circuitry. This phenomenon was overcome by encasing the pacemaker generator in an hermetically sealed metal case, initially by Telectronics of Australia in 1969 followed by Cardiac Pacemakers Inc of Minneapolis in 1972. This technology, using titanium as

the encasing metal, became the standard by the mid-1970s ***(Parsonnet, 1978)***.

Subsequent Improvements:

Pacemaker and lead technology continued to develop rapidly to make these devices reliable, automatic and flexible in the therapy they provide. The therapeutic end-point shifted from saving life to enhancing its quality and simplifying follow-up. Electrotherapy has become socially accepted and its indications are extending also to non-cardiac pathology: Parkinson's Disease, pain-control, drug delivery ***(Aquilina, 2006)***.

Lead design improved: “tined” for passive fixation and “screw-in” for active fixation. The lithium-iodine battery was developed to replace the mercury oxide-zinc battery that had been used till then. This resulted in greatly increased pacemaker longevity **(Figure 7)**, ***(Aquilina, 2006)***.

Figure (7): Devices of the 70's ***(Quoted from Aquilina, 2006)*.**

Nuclear pacemakers with projected longevity in the 1970s:

In 1978, an American-made radioisotope pacemaker was implanted by Parsonnet and colleagues. These nuclear pacemakers had an expected life of 20 years but went out of fashion mainly due to the need for extensive regulatory paperwork ***(Parsonnet et al., 1978)***.

Titanium casing was developed to enclose the battery and circuitry. This replaced the epoxy resin and silicone rubber that was previously utilised to encase the