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The Evolution and Advancement of Pacemaker Technology

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ABSTRACT:
Arrhythmia is one of the major cardiovascular diseases that affect a large number of population globally. Certain cases of arrhythmias such as severe tachycardia or bradycardia require implantation of ICD and pacemaker respectively to correct the rhythm artificially. Report from leading health care organizations, such as WHO has predicted to increase CVDs cases in coming future. Therefore, demand of the implantation devices such as pacemakers and ICDs are also expected to increase rapidly. Due to the above reasons a lot of research and development activities are happening and expected to happen in this domain. Advancements in all other domains such as, VLSI, SoC, Signal Processing etc. has improved all of the design metric parameters related to these devices. The present article also aims to provide a detailed overview of all technological developments in field of such a medical implantation device called pacemaker. The article briefly reviews various pacing methods, types of pacemakers, pacing modes and codes, electronic circuitry and techniques used in pacemakers, and battery technology etc. A systematic literature related to pacemaker technology, major developments, emerging technologies, and issues is provided in the article. A brief discussion related to the areas where future work is expected is also provided for future research work. Overall this article provides a basic understanding of pacemaker technology, starting from Hymen's artificial pacemaker to most recent Nano-stim pacemaker, and some novel methods of artificial pacing such as biological pacing and ANN based pacing are also discussed.
Keywords**:** Pacemaker, Cardiovascular disease, Battery technology, Leadless pacemaker, Cardiac resynchronization therapy, Arrhythmia, System on Chip.

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I. INTRODUCTION

Nowadays pacemakers are the active implantable devices which are being used abundantly. Since the first artificial pacemaker was introduced in 1932 [1], much has changed and will continue to change in future. The complexity and reliability in modern pacemakers has increased drastically mainly due to developments in integrated circuit and batteries. This is the article on the history of the development of artificial pacemakers with the evolution of the various power sources needed for the designing of the pacemaker. Pacemakers play a crucial role to help in the control for heart rhythms [2] . In all animals the stimulation of heart muscle which causes the contraction of heart is actuated by electrical signals known as action potentials and the rate at which this action potential is generated is called the heart rate. The generation of this rhythmic impulses or sinus rhythm is due to the cells present in the Sinoatrial (SA) node of heart are called pacemaker cells. These pacemaker cells construct the cardiac pacemaker or natural pacemaker of the heart [3] . The rhythmic contraction of heart is responsible for the pumping of the oxygenated blood to the body and deoxygenated blood to the lungs. The total capacity of the blood pumping of the heart per beat is known as cardiac output which must vary in response to the need of the cell's oxygen and nutrient requirements in varying conditions. The SA node or natural pacemaker is responsible for maintaining the rhythmic pumping of heart in appropriate manner so that flow of the blood throughout the body can be maintained as per need of the body activity and the metabolism is controlled by the nervous systems, endocrine system and other factors [4].

An external device can be used to replenish the rhythmic pumping of heart at the instances of failure of proper functioning of the body's natural pacemaker. This external electronic device which is known as artificial pacemaker is implanted via operative methods to help the heart to function properly. Pacemakers produce an artificial electrical pulse and provide it to the heart in order to prompt the heart beat at a normal rate. The prime role of the pacemaker is to help in some of the arrhythmias and their fatal consequences using external electrical pulsing. In some arrhythmias the heart beat rate, heart pulsing and beating mechanism are irregular and improper. Arrhythmias (or dysrhythmias) occur due to cardiac problems producing abnormal heart rhythm [5]. In general arrhythmias reduce hemodynamic performance, including situations where the heart's natural pacemaker develops an abnormal rate or rhythm or when normal conduction pathways are interrupted and a different part of the heart takes over control of the rhythm. An arrhythmia can involve an abnormal rhythm increase (tachycardia; >100 bpm) or decrease (bradycardia; <60 bpm), or may be characterized by an irregular cardiac rhythm, e.g. due to asynchrony of the cardiac chambers. An "artificial pacemaker" can restore synchrony between the atria and ventricles. The heart beat can go either too fast or too slow than the required rate [2]. When it beats too fast then it is termed as tachycardia and when it beats to slow then it is termed as bradycardia. When there is an irregular heartbeat, the heart is unable to pump the sufficient blood throughout the body leading to fatigue, shortness of breath and even fainting. Some arrhythmias symptoms such as fatigue and fainting can be relieved by pacemaker and it also help a person who has abnormal heart rhythms to resumes a more active lifestyle [2].

II. METHODS OF PACING

Several methods exist to artificially pace the heart as per requirement in different situations and can be categorized in several ways which will generally depend on the aim, pacing area, heart chambers, sensing and response of pacemaker etc. The description of terminology of methods for pacing employed in general sense is as follows:

2.1 Percussive pacing

This pacing method is common and ancient procedure used in saving lives. In this method the heart is pumped externally by applying pressure on the lower edge of left side of sternum over the right ventricle in the vena cava using closed fist as shown in Figure 1.1 which in turn stimulates the ventricle. This method is also known as transthoracic mechanical pacing. This method must be applied to produce ventricular pressure of 10 – 15 mmHg to generate electrical impulse as per the information provided in the British Journal of Anesthesia. [6]

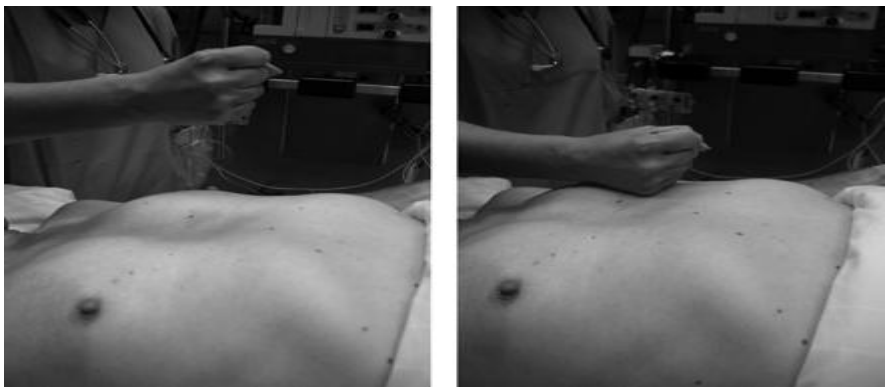


Figure 1: Percussive Pacing Method [7]

2.2 Transcutaneous pacing

This method of pacing is confided for the initial stabilization of almost all hemodynamically major bradycardias, but there are also few hemodynamically conditions like cardiac arrest with a flat line ECG where this pacing technique is not effective. It is also known as external pacing. The course is executed when two pacing pads are placed on the chest of the patient, either in the anterior/posterior position or anterior/lateral position. The pacing rate is chosen by the rescuer and the pacing current (measured in mA) is gradually increased until electrical capture (characterized by a wide QRS complex with a tall, broad T wave on the ECG is attained, with a corresponding pulse. The artifact on the ECG due to pacing and severe jerking of muscle may make this resolution difficult. This pacing could not depend upon for a long span of time. It is a zero hour process that acts as a way until transvenous pacing or other therapies or cures can be applied [8].

The main issue with this pacing method is uncomfortable procedure; for which a pre drug therapy for sedation is required. Also it may cause severe burns on chest skin therefore in cases where transcutaneous pacing is required for more than 30 minutes periodic inspection is highly prescribed [8].

2.3 Epicardial pacing

This method is a temporary pacing method which is used while performing open heart surgery. Some surgical cardiac procedure may create a blockage between the atrium and ventricle. This procedure is performed by placing the electrodes in contact with the epicardium of the ventricle to keep up the required cardiac output until an interim transvenous electrode has been inserted.

Since pacing wires are in direct contact with epicardium number 1 priority should be given to prevention from condition such as micro shock which has potential to produce lethal rhythms. This is due the presence of unattached pacing wires which has possibility to provide a direct path for flow of electrical current through heart. Different studies to this context reveals that a small amount of current (in range of 0.1 mA) can also cause ventricular fibrillation and hence various safety precautions at patient's bedside are required [9].

2.4 Transvenous pacing

Transvenous pacing, when used for temporary pacing, is an alternative to transcutaneous pacing. It is also called endocardial pacing, in this pacing method a pacemaker wire is inserted and placed inside a vein using electrographic and fluoroscopic guidance, under infertile conditions, and then passed into either the right ventricle or right atrium [10], there is an external pacemaker outside the body which is then connected to the pacing wire. Transvenous pacing is mostly used as a way to placement of a permanent pacemaker. As it is a temporary pacing, it can be placed till a permanent pacemaker is implanted or there is no requirement and then it is removed. Moreover, X-ray is always required after the procedure to confirm the proper placement of pacing electrode [11].

Transvenous pacing is useful in treatment of profound Bradycardia, but major advantage of this pacing is treatment of Symptomatic Bradycardia where other methods such as transcutaneous pacing and drug therapy do not show signs of enough improvement [10].

2.5 Endocardial pacing

This is a permanent pacing with a pacemaker implantation which involves transvenous placement of one or more pacing electrodes within a chamber, or chambers, of the heart, while the pacemaker is implanted inside the skin under the clavicle as its name defines. The procedure is performed by incising a capable vein into which the electrode lead will be inserted and passed along the vein, through the valve of the heart, until placed properly in the chamber [12]. The procedure is eased by fluoroscopy so that the physician can watch the passage of the electrode. When the electrode is placed in the suitable position the placement is confirmed and then the opposite end of the electrode lead is connected to the generator of the pacemaker. A post procedure X-ray may be required in order to confirm the proper placement of pacing electrodes [13].

2.6 Biventricular pacing

This method consist in pacing both the septal and lateral walls of the left ventricle for patients with asynchronous contraction in the left ventricle and between left and right ventricle, that is seen in approximately 25–50% of heart failure patients. Biventricular stimulation or CRT (cardiac resynchronization therapy) restores synchronicity and improves contractility and prognosis [14].

CRT devices have minimum two leads, one passing through the vena cava and the right atrium into the right ventricle to stimulate the septum, and another passing through the vena cava and the right atrium and inserted through the coronary sinus to pace the epicardial wall of the left ventricle. Often, for patients in normal sinus rhythm, there is also a lead in the right atrium to facilitate synchrony with the atrial contraction. Thus, timing between the atrial and ventricular contractions, as well as between the septal and lateral walls of the left ventricle can be adjusted to achieve optimal cardiac function [15].

CRT devices have been shown potential to reduce mortality and improve quality of life in patients with heart failure symptoms; a LV ejection fraction (It is measure of percentage of blood pumped from filled ventricle with each heartbeat and it normally measured in left ventricle)less than or equal to 35% and QRS duration on EKG of 120 ms or greater [16]

Biventricular pacing alone is known as CRT-P denoting P for the word pacing. Few patients at risk of arrhythmias are chosen in whom the CRT-D pacing can be implemented. The CRT-D method is nothing but the combination of CRT with an implantable cardioverter-defibrillator (ICD) as per its name the D denotes the word defibrillation. This ICD also provides efficacious ammunition upon life risking arrhythmias [17].

III. PACING MODE AND CODES

The North American Society of Pacing and Electrophysiology (NASPE) and British Pacing and Electrophysiology Group (BPEG) regularized the standard pacemaker code and modes known as NBG coding system which make the globally accepted standard for the pacemaker functioning. In revised NBG code in 2002, there are five positions which refer to pacemaker function. In the NBG code sensing is stand for the detection of

spontaneous cardiac depolarization by the device. Table 1 is showing the position category and letters used for the different modes of pacing [18].

Table 1: Revised NASPE/BPEG Generic Code (2002) [19]

The NASPE/BPEG Generic code (NBG Code)					
Position Category	**I Chamber(s) Paced**	**II Chamber(s) sensed**	**III Response to sensing**	**IV Rate Modulation**	**V Multisite Pacing**
Letters used	**O**- None **A**-Atrium **V**-Ventricle **D**-Dual (A+V)	**O**- None **A**-Atrium **V**-Ventricle **D**-Dual (A+V)	**O**- None **R** – Rate Modulation	**O**- None **P**-Simple Programmable **M**-Multi Programmable **C**-Communicating **R**-Rate Modulation	**O**- None **A**-Atrium **V**-Ventricle **D**-Dual (A+V)

Position I - This position denotes to the chamber which is going to be paced. If it is 'A' then it is Atrium and 'V' refers to Ventricle. If there are provision for pacing of both chamber then 'D' dual is used.
Position II – This position denotes to chamber that are sensed by the pulse generator of pacemaker. It is similar to Position I and letter 'O' stands for none or asynchronous pacing.
Position III – This position presents the device response to a sensed event. In this there are four letters in which one is choose according to pacemaker response to sensed event. Letter 'O' indicates that there is no response to sensed event, letter 'I' indicates the inhibited pacing impulse by pacemaker in response to sensed event, while letter 'T' refers to triggered impulse in response to sensed event. The letters 'D' is for the dual chamber system and provide both triggered and inhibited function.
Position IV – Position IV is generally for indication of presence or absence of rate responsive or rate modulating pacing and the information of single programmable or multi programmable or it is communicating. If letter 'R' is used it means pacemaker is integrated with some other sensors which sense the physiological conditions like activity, vibration of acceleration to adjust the heart rate as per need of hemodialysis of body but it does not describe the type of sensors and letter 'O' stands for no any rate modulation program.
Position V – This position provide the information about multisite pacing is present in the device or not. Letter 'O' means there is in none of cardiac chamber. Letter 'A' means multisite pacing is present one or both atria and 'V' stands for one or both ventricle. Letter 'D' is used for both atria and ventricle pacing. [19]
As per these positions, several modes can be resembled like single chambered mode AAO, AAI, VOO, VVI, and double chamber modes like DDD, DDDR, VDD, DDI, DOO, rate responsive mode like AAIR, DDIR, VVIR, etc. Some common used modes are detailed below.
VVI or VVIR – It is common mode and generally used in most of patients. This mode of pacing is used for the ventricular bradycardia and generally used in patients who suffering from atrial fibrillation and slow ventricular response. This code denotes that sensed and paced chamber is ventricular and inhibited impulse is provided with demand rate of pacing [18].
AAI or AAIR - This type of pacing mode is used for the pacing of the atrial chamber by inhibited impulse while sensing events comes from atrial chamber. It is atrial demand pacing. This mode is useful for the patient who suffering from sinus node dysfunction but have proper AV nodal function. This mode also can be used in patients having dual chamber system to address the ventricular pacing with an algorithm that can switch the mode from AAI to DDD or DDD to AAI as per demand depending on sensed AV nodal conduction.
DDD or DDDR: - It is dual chamber pacing mode and it is most commonly used mode. It has ability to sense and pace both chamber and it is used in those patients who have the combined sinus node dysfunction and AV nodal dysfunction. It may resemble the AAI, VAT, VDD, DVI mode [18].

Four distinct patterns can be observed with DDD pacing
1. Sensing the atrium and sensing the ventricle
2. Pacing in the atrium and sensing in the ventricle
3. Sensing in the atrium and pacing in the Ventricle (P wave tracking)
4. Pacing in the atrium and pacing in the ventricle

Asynchronous modes, VOO or DOO: - In the asynchronous modes the pacing is in fixed rate without any sensing capability. In this mode pacemaker is not in rhythm of natural heart rate and continuously deliver the impulses to heart [18].

IV. CLASSIFICATION OF PACEMAKERS:

There are several types of pacemakers which are different from each other on basis of design, sensors, types of signals, number of modes, pacing rate, pacing chamber, number of leads and algorithms etc. Selection of a particular type of pacemaker for a particular patient is done by an expert cardiologist on the basis of patient's physiological need, type of arrhythmias, reliability and availability of device. Hence, certain areas may be explored where classification may be considered in general way are as follows:

4.1 Classification based on placement of pulse generator:

The pacemaker device can be classified on the basis of its pulse generator placement like external placed, internal or implanted inside body [20]. In beginning of the pacemaker technology evolution, the first pacemaker device was external type of device and used only in open heart condition to pace heart temporarily for life saving treatment but after some years, advancement in pacemaker technology provides a small sized device which can be implanted inside the body and provides permanent solution for the bradycardia. So it is termed as permanent pacemaker. On this basis there are two type of pacemaker one is External (Temporary) and second is Implantable pacemaker (Permanent).

- **External pacemaker (Temporary):** These types of pacemakers are used to treat the critical condition of bradyarrhythmia (Second or third degree atrioventricular block (AVB) or severe symptomatic bradycardia in emergency situation of patients who are thermodynamically unstable. In this type of pacemaker, the pace generator is placed outside the body and pacing electrodes are introduced inside the heart using proper protocols [11].
- **Implantable Pacemaker (Permanent):** According to definition of implantable internal pacemaker, an internal pacemaker is one in which electrodes are placed into heart; and the electronic circuitry and power supply are implanted within the body [21] [22]. Implantable permanent pacemakers may function continuously to contract the heart or on demand of heart when natural pacemaker fails to stimulate the heart with or without physiological need of body which depends on selection of pacemaker among fixed rate, demand type or rate responsive pacemaker. First implantable pacemaker was invented by Wilson Greatbatch in 1958 while he was working on circuitry of oscillator to record of heart sound and mistakenly he put the wrong value register and it started to give electric pulse in regular intervals. Later this circuit was improved and used with the corrosion free lithium battery as first implanted pacemaker [23].
- **Implanted cardiac defibrillators (ICD):** Pacemaker is a device used to treat the bradycardia that is the situation when heart rate is too slow (less than 60 bpm) [24]. However, with known, sustained ventricular tachycardia or fibrillation type of arrhythmia where pacemaker are not useful implanted cardiac defibrillators particularly known as ICD is used [25]. An ICD is battery powered device having two leads which implanted in pocket under collarbone. The electrode lead is introduced through blood veins into heart chamber that transmit the electric impulse from pulse generator to heart in case of life-threatening ventricular tachycardia and prevent to sudden death of patient due to heart attack [26]. Current generation device is available with functioning capability of both pacemaker and ICD.

4.2 Classification based on need of pacing

The classification can also be done on the basis of rate of pacing available in pacemaker device either it may be fixed rate or variable rate. So there are two types of pacemaker, one is fixed rate pacemaker and second is variable rate pacemaker.

- **Fixed-rate pacemaker (Asynchronous pacemaker):** As per definition of fixed rate pacemaker, it is the device which delivers electric stimulus at a constant frequency/rate regardless of heart's rhythm [27]. It is also called asynchronous pacemaker due to non-synchronization with any atrial or ventricle activities and provide impulses at fixed rate. This type of pacemaker does not use sensing element to pick up the heart rhythm. Their pacing rate is generally set 60-70 beats per second in adults and 80-100 beats in children. Their pulse generator circuitry is simple in construction because of non-requirement of feedback path but due to continuous operation, battery power drainage is high. Other disadvantage of this type of pacemaker is emergence of competition between natural pacing of heart and device pacing due to interference by any spontaneous electric activity occurring within the heart [5] [28] and it also increase the risk of atrial fibrillation and perforating the thin heart wall. Fixed rate pacemaker provides three types of pacing modes AOO for atrial pacing, VOO for ventricle pacing and DOO for dual pacing.

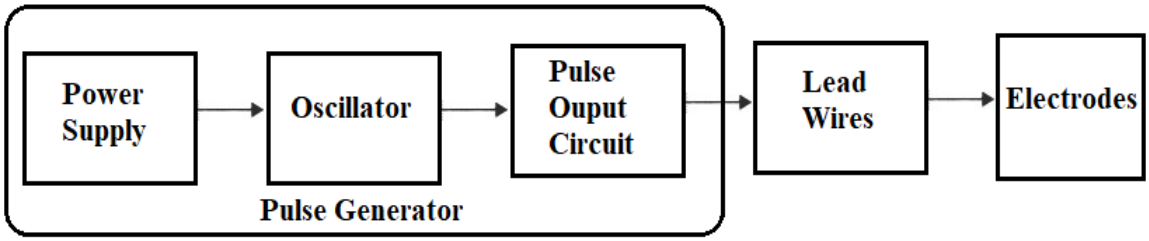


Figure 2: Block Diagram of asynchronous pacemaker [29]

- **Variable rate pacemaker:** In this type of pacemaker pacing rate can be varied according to either setting of the specific pacing mode or activity of body. This type of pacemaker equipped with the sensor which detects the heart pulse and feedback to actuator of pulse generator. The variable rate pacemaker can be further categorized in two types one is demand type pacemaker or synchronous pacemaker and second is rate responsive pacemaker.

i) **Demand pacemaker (Synchronous):** This type of pacemaker provides electrical stimulation to the heart when it senses indication of inadequate spontaneous pacing of natural pacemaker of heart due to any arrhythmic severity. It's also known as triggered circuit [28]. Most of the time this type of pacemaker's pulse generator remains in standby mode in condition of accurate functioning of heart that is sensed by the sensors integrated in feedback path of the circuit. If sensor detects any absence of heart pulse, it activates the actuator of pulse generator and an electrical impulse is transmitted to heart chamber through the electrodes.

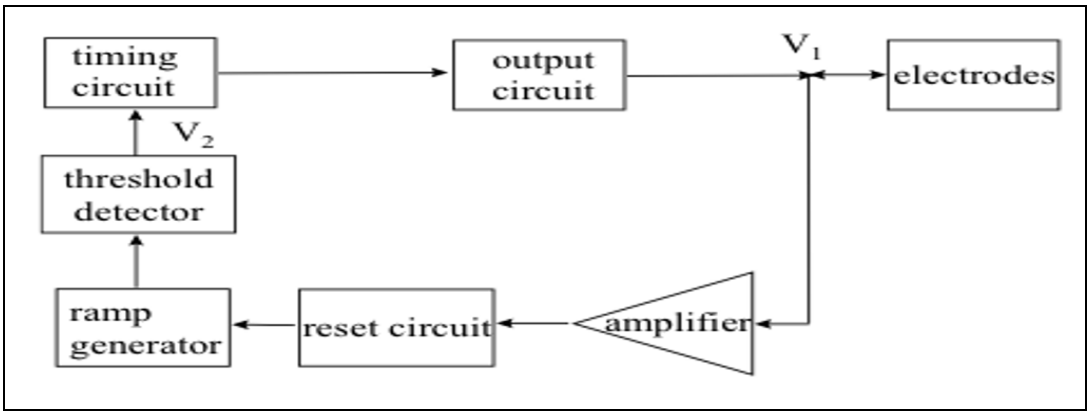


Figure 3: Block diagram of the demand type pacemaker synchronous pacemaker [29].

It provides the pulse on demand of heart so it is called demand type pacemaker and also it avoids the competition between the pacemaker's stimulation and natural pacing of heart and maintain the synchronization with intrinsic cardiac rhythm so it is also called the synchronous pacemaker. Figure 3 is showing the block diagram of the demand type synchronous pacemaker. There are three types of synchronous pacemaker (a) atrial synchronous pacemaker, (b) ventricular synchronous pacemaker and (c) ventricular inhibited pacemaker

a) Atrial synchronous pacemaker: It's triggers action and triggered rate is dependent on the sensing of the atrial contraction voltage (Sense of P wave) and if it is less than threshold voltage (in case of absence of atrial contraction or P wave) then after a predefine time intervals which is simulated by P-R interval (SA to AV node 120ms), it emits the ventricular stimulus [28]. A monostable multivibrator circuit is used to provide delay about 500 ms between the current stimulation and next stimulation if subsequent natural atrial stimulation is skipped by heart to simulate the refractory time of natural heart rhythm. This type of pacemaker consists the two electrodes one for atrial sensing and second for ventricular pacing. If the atrial stimulation is permanently lost by any means then this pacemaker is programmed in such a way that it functions as asynchronous mode with 60-70 beats per second pacing rate.

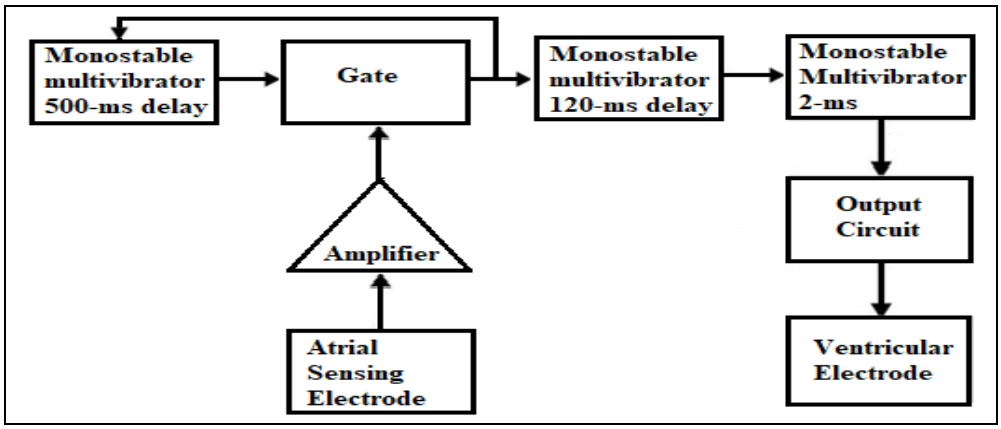


Figure 4: Block diagram of atrial synchronous demand type pacemaker [29]

b) Ventricular synchronous pacemaker: This type of pacemaker senses the ventricular stimulation (QRS peak or R wave) employing electrodes and in absence of ventricular depolarization**,** it triggers the pulse generator to stimulate the ventricular muscles of heart by same electrode. It utilizes single electrode for both sensing and stimulation that is placed in the myocardium of ventricle wall. It has less trigger sensitivity but quite fast trigger response. It provides 400 msec delay equivalent to refractory time from QRS to next P wave using monostable multivibrator [28].

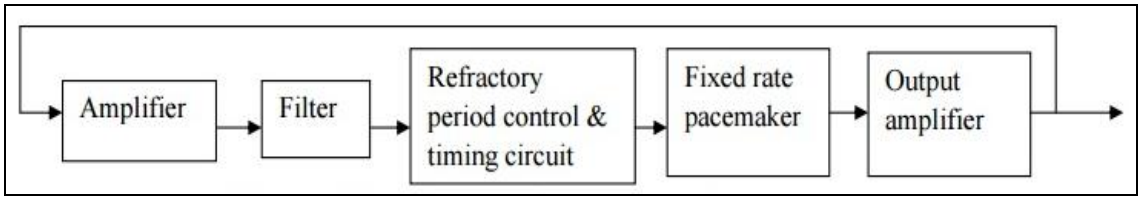


Figure 5: Block diagram of Ventricular Synchronous Pacemaker

c) Ventricular Inhibited Pulse generator: This type of pulse generator provides the ventricular stimulation asynchronously if the natural ventricular activity is absent or below the threshold level otherwise it remains in noncompetitive mode and holds its impulse in response to natural ventricular depolarization. It continuously monitor the heart rate, if this is found below the (60-70 beats per second) then it stimulates the heart in fixed rate and if it is above the threshold rate it suppress the stimulus output. The refractory time (75-325msec) is kept low to early response to activity. The Figure 5 is showing the general block diagram of the ventricular inhibited pulse generator. In the circuit block diagram, pacing rate of the pulse generator is determined by the comparator and pulse width circuit determines the duration of stimulating pulses. Comparator is disabled by the rate limiting circuit for short time and limits the rate. Sensing circuit and reversion circuit with refractory circuit is given in feedback path in which spontaneous R-wave is detected by the sensing circuit and it also resets the oscillator timing capacitor and reversion circuit helps to detect low level continuous wave interference. Voltage monitor circuit control the energy compensation circuit and rate slow down circuit to increase the battery usage [30].

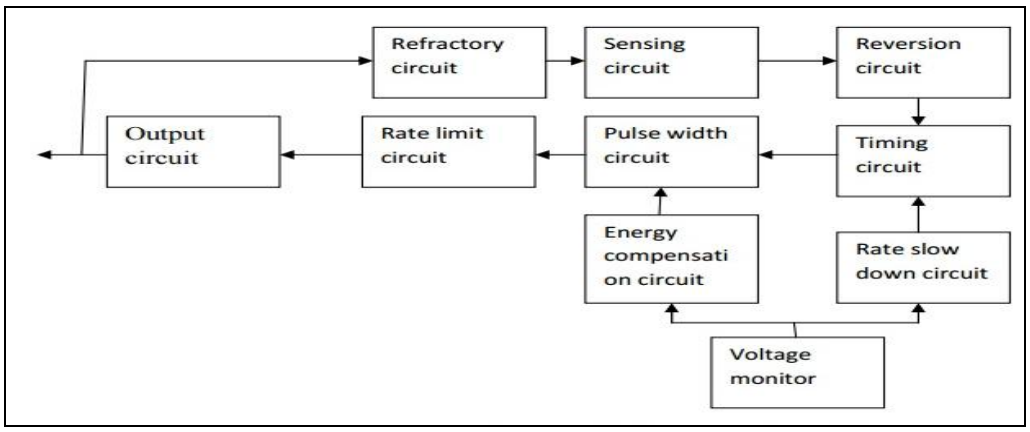


Figure 6: Block diagram of Ventricular Inhibited Pulse generator

ii) **Rate Responsive Pacemaker:** Rate responsive or rate adaptive pacemaker provides the pacing rate as per hemodynamic need of heart. During exercise or any physiological activity, there is requirement of increased heart rate to provide the high volume of cardiac output to fulfill the metabolic need of body [31]. It's integrated with some physiology activity sensor which continuously monitors and paced the heart analogous to variation in activity of body. The selection of algorithm and sensor principle determines the hemodynamic efficiency of the rate adaptive pacemaker [32] [33]. Actually it provides effective pacing due to assessment of hemodynamic performance of heart and establishment of a physiological correlation between inotropic and chronotropic cardiac function [34]. Inotropic cardiac function is related to heart contraction and chronotropic cardiac function affects the heart rate. There are various physiological parameters which affect the variation of heart rate so efficiency of rate adaptive pacemaker depends on number of sensor, different parameters being considered, sensing technology and adaptive algorithms. The list of few physiological variables and their corresponding sensors is shown in Table 2. Figure 7 shows the basic block diagram of rate responsive pacemaker [29].

iii)

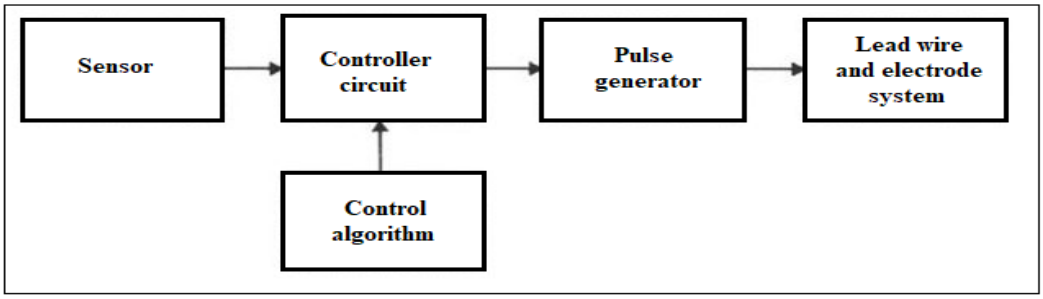


Figure 7: Block diagram of Rate responsive pacemaker [29]

Table 2: Possible physiological variables and corresponding sensor which may include in rate responsive pacemaker

Physiological Variables	Sensor
Blood Temperature (in right Ventricle)	Thermistor
Stimulus to T wave interval (in ECG)	ECG electrodes
R wave area (in ECG)	ECG electrodes
Blood pH	Electrochemical pH electrode
Rate of pressure change (of right ventricle)	Semiconductor strain gauge
Blood oxygen saturation	Optical oximeter
Intracardiac volume changes	Impedance plythysmography
Respiratory rate and /or volume	Impedance plythysmography
Body vibration	Accelerometer

4.3 Classification based on stimulation of chamber or number of leads

The pacemaker device may be categorized on the basis of number of chambers of heart to which pacing is provided and number of electrode lead also depends on and generally equal to the number of chamber for which electrical stimulation is available. There are three types of pacemaker available depending on the number of stimulated chamber or number of lead basis:

- **Single chamber/ One lead pacemaker**: This pacemaker has one single lead implanted in heart either in the atrium or ventricle but most probably in the right ventricle.
- **Dual chamber / Two lead pacemaker**: In this type of pacemaker pacing wire is placed in two chamber, one in atrium and second in ventricle. This type of pacemaker tries to resemble the natural heart rhythm by pacing atrium and ventricle in proper coordination.
- **Biventricular / Three lead pacemaker:** This type of pacemaker has three lead system and functioning of this pacemaker is also called the cardiac resynchronization therapy (CRT). CRT is used in the patients who are suffering from ventricle dyssynchrony, a condition in which the left and right ventricles do not contract

simultaneously [35]. Biventricular pacemaker is used to stimulate both the septal and lateral walls of the left ventricle to resynchronize the ventricular contraction. One lead of this pacemaker placed in the right ventricle to pace the septum through the vena cava and right atrium, second lead is inserted in to the epicardial wall of the left ventricle through the vena cava, right atrium and coronary sinus and third lead inserted in the right atrium to maintain the synchrony with atrial contraction generally for the patient of normal sinus rhythm [20].

V. BRIEF HISTORY OF PACEMAKER

The first acquisition of knowledge about importance of cardiac pacing and heart pulse with relation to healthy life of human being was studied long back say approximately 460 BC before [1]. Some great ancient philosopher like Hippocrates and Aristotle showed initial signs for the knowledge of heart pacing as necessity of life. In China, Wang Shu-he, an ancient philosopher, wrote ten books on the heart and its pulse. The study of pulse is called "shygmology" and pulse as "shygmos" by Greeks scientists. In 1580, Geronimo Mercuriale derived the concept of syncope and illustrated its connection with a slow pulse rate [1].

. In 1775, first time electrodes were used on the sides of hen's chest and defibrillation of heart undertaken by Danish physicist Nickolev Abildgaard. In 1791, electric activity was found in frog muscles and heart by an Italian physician and natural scientist, and his published experimental finding was contribution to modern cardiac electrophysiology. . "Action currents" of the heart was derived by Rudolph Albert von Kollicker in 1855. In 1982, first time in history of cardiac therapy, a human heart (a 46 year old female "Catherina Serafin") was stimulated using electric current and her hate rate was controlled as required [1].

In 1889, A English doctor John Mac William, published his experiments in the *British Medical Journal* (BMJ) which described the application of electric impulses at rate of 60-70 per minute across the chest that provoke the ventricular contractions with heart rhythm of 60-70 bpm [36].

The next step of advancement in recording of cardiac pacing was the invention of extremity bipolar electrode system by F.N. Wilson wherein he introduced the unipolar chest wall electrodes in 1933. In 1942, augmented (Unipolar amplified) extremity lead was invented by E. Goldberger which completed the formation of 12 lead electrocardiogram systems [37].

First Artificial Pacemaker:

The credit of development of first pacemaker goes to two doctors: Mark Lidwill from Australia and Albert Hyman from America but they work independently unknown and distant to each other. In 1926, Mark C Lidwill who was working in Royal Prince Alfred Hospital of Sydney used the two pole electrodes in which one was applied to a skin pad soaked in saline solution and other was a needle that is pinned into the appropriate cardiac chamber. He used the ac supply to run this portable device later on known as the pacemaker. The rate of pacing of this device was 80 to 120 pulses per minute with input supply voltage variation from 1.5 to 120 volts. [38].

In the early 20^{th} century, Albert Hyman designed the first experimental heart pacemaker which was spring wound hand cranked motor named as 'artificial Pacemaker' [1] [39]. The generator of this pacemaker was capable of providing pulses for 6 minutes without rewinding [38]. In this pacemaker, the supply current is provided by the magneto-generator (A) to interrupter disc on surface contact when a spring motor (D) is powered by hand crank (F) rotation. The interrupter disc is rotated by rotations of spring motor at desired speed set by part E and H. The magnetic pieces B′ and B″ are used to provide necessary flux to magneto generator. The periodic pacing is provided by electrode needle (L) at 30, 60 or 120 bpm, generated by interrupted disc and regulated by the impulse controller (G). At condition of any hindrance in generation of stimulus a neon bulb is glowed. In Figure 8 (a) a real set up and functional diagram of Hyman's pacemaker is and Figure 8 (b) is showing the block diagram of first artificial pacemaker. [38].

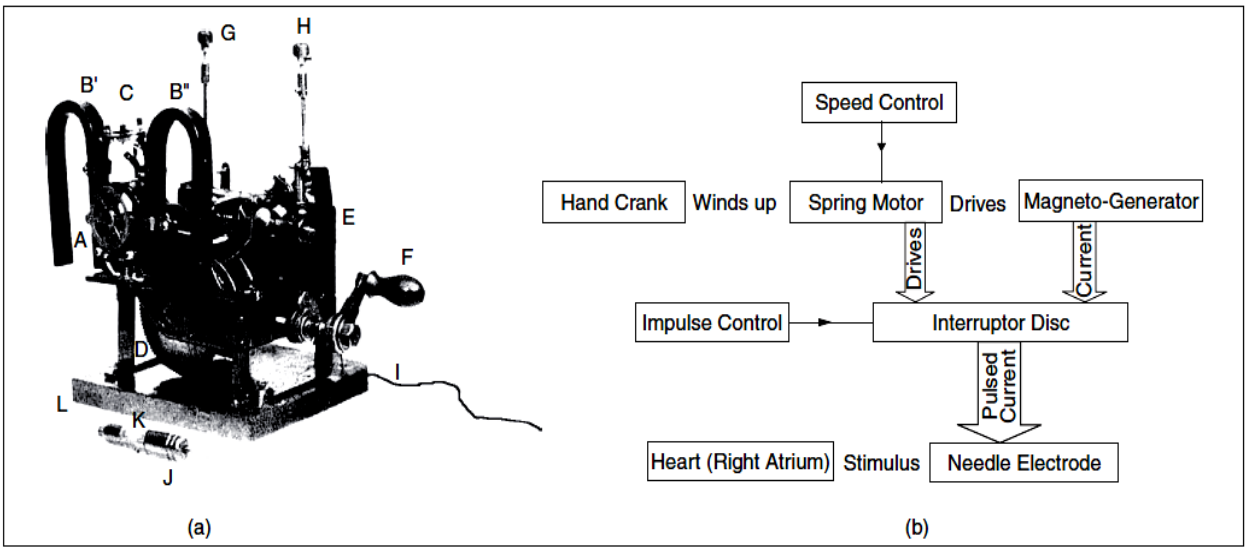
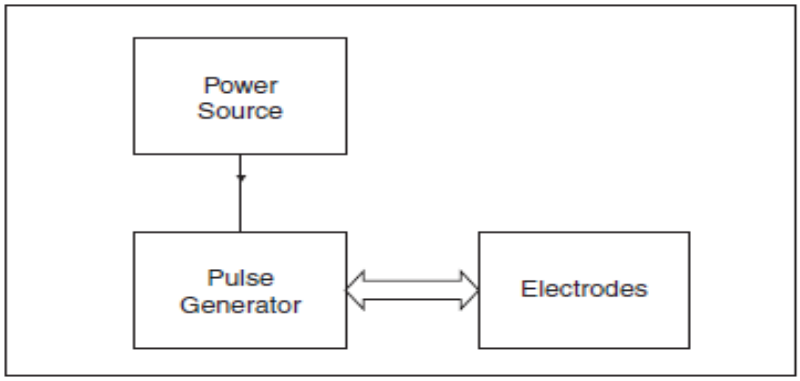


Figure 8: (a) The real time set up of Hymen's artificial pacemaker and (b) Block diagram of working of Hyman's pacemaker [39]



1.

Figure 9: Block diagram of first artificial pacemaker [40].

Electric supply based external Pacemaker

In 1950, first electronic device developed as cardiac pacemaker was invented by a researcher John Hopp who was working at National Research Council of Canada. His results were based on some observation of experiment done on dog by Wilfred Bieglow and John Callaghan in Toronto, Canada in 1949. John Hopp's pacemaker was vacuum tube based external device having bipolar catheter as electrode to transfer the electrical signals to atria without uncomfortable chest wall [20].

VI. KEY INVENTION IN THE FIELD OF PACEMAKER TECHNOLOGY IN THE PREVIOUS DECADES

Presently pacemakers and ICD (Implantable Cardioverter-Defibrillators) are available in several variations, with enhanced capability and longevity. However, their designs and operating procedures are rule based and executed using microcontroller based circuitry. They also support reprogrammable capability to allow doctors to reprogram several of their criterions to better suit the needs of the patients. This has led to reprogrammable and adaptive rate-responsive pacemakers which dynamically evolve to pace alongside the relevant physical conditions of the patient. Recent advances have also been made into specific pacemakers which deals with a singular type of cardiac problem. Given below are some evaluations of the different innovation filed in the previous decades to generalize the advancements made in pacemaker technology over the years.

- **Counter Controlled Variable Rate Pacemaker**

The technology of this type pacemaker has been patented by an American inventor Michael Lopin in 1972 [41]**.** In this design flip-flops were arranged in a counter configuration, which are cycled by monostable magnetic read switch that provide proper rate of operation pulsed by applying an external magnetic field near the patient chest. This technology provides the mechanical switching and it does not require the maintaining of the charging current once established improveing the overall reliability of the system [41].

- **Cardiac implantable demand pacemaker**

This technology invented by Greatbatch Wilson and assigned by Medtronic Inc published on 18th November 1969. This technology includes the semiconductor pulse generator enveloped by moisture proof and body reaction free enclosure with plurality of electrodes which provide the artificial pulse on demand of heart itself. It claimed the sensing of cardiac arrest and subsequently delivers timed electrical pulses to heart to help it restore the normal rhythm [42].

Prior to this technology, same inventor patented the technology on 9th October , 1962 assigned by Wilson Greatbatch Inc titled "Medical cardiac pacemaker". This technology pledged to advancement of prior pacemaker art in sense of discomfort and incapacitation of patients, infection and other danger which might accompany a permanent or semi-permanent penetration of the human body shell by a foreign object. The inventions claimed the less battery consumptions, improved cardiac pacing if it is inadequate due to conduction defects in the auricular ventricular bundle and employing materials which are adoptable by body environments [40] .

- **Rate-responsive pacemaker with automatic mode switching and/or variable hysteresis rate**

This technqiue introduced the hysteresis in a rate responsive pacemaker which allows the natural AV synchrony. When SA node signal is not present then heart is stimulated by pacemaker according to physiological needs after gaining natural rhythm of heart, the hysteresis is applied to extend the escape interval by prefixed value that is analogous to sensed physiological requirement. It avoids the possible completion between normal activity and paced stimulations. It introduced automatic switching from dual chamber mode to single chamber mode in case of higher heart (90 bpm or more) rate such as VVI. This technology was invented by Jason A. Sholder, Brian M. Mann and Joseph J. Florio assigned by Siemens-Pacesetter, Inc.; published on 8th October, 1987 [43].

- **Microprocessor controlled rate-responsive pacemaker having automatic rate response threshold adjustment**

This is the conventional pacemaker that includes the programmable pulse generator and sensors which detect the physiological activity and a demand pulse is generated based on activity of body or otherwise as per programming of pacemaker. Pulse generation programming is controlled by processor automatically that are based on the output from the physiological sensors. The processor has the predefined number of function sets which establish the relation between the pacing rate as output and rate of pacing requirement based on which any one of function(s) is selected by processor as per need of heart. The rate of pacing requirement is defined by physiological sensors. The selection or switching of one function threshold to another function according to need of pacing rate is done by this pacemaker automatically. This technology was published on 10th July 1990 by Brian M. Mann and John W. Poore as inventor and assigned by Siemens-Pacesetter, Inc. [44].

- **Rate stabilization pacemaker**

This pacemaker technology invented by Mr. Rahul Mehra assigned by Medtronic, Inc. published on 17th July 1990. This technology equipped with control mode of pacing that tracks natural heart beat and responds to premature ventricular contractions. The escape interval is calculated by the analysis of immediately preceding escape interval after natural contraction or stimulated beat by pacemaker, and it increases with each cycle until lower threshold is reached. This technology claimed to reduce the likelihood of onset of an episode of tachycardia [45].

The another method of pacemaker technology with same title mentioned above is also patented by Michael R. S. Hill assigned by Medtronic Inc. published on 29th September 1998. This technology determined the prematurity of most recent sensed depolarization relative to preceding depolarization which is the function of underlying heart rate, by comparing the cycle ending in the most recently sensed depolarization with the previous cycle. This helps the pacemaker to vary the increment of pacing rate analogous to the depolarization cycle length and it avoids the short long interval pattern associated with onset of tachycardia [46].

- **Hemodynamically rate responsive pacemaker and method of automatically adjusting the escape and A-V intervals**

This technology provides the method to control the pacing rate and A-V interval as per physiological need of heart that are feedback by the activity sensors. It triggers the stimulation circuitry according to optimum value of cardiac output and adjust the A-V interval until hemodynamics are optimized and so it decreases the stimulation rate and save the battery power. It provides the automatic adjustment of pacing rate by changing its programming parameters according to physiological demand. For controlling cardiac rate, a variety of sensors are incorporated to determine the state of body. This technical art was published on 18th June 1991 by James R. Thacker, Siemens-Pacesetter. Inc. [47].

- **A metabolic demand driven rate-responsive pacemaker**

This technology claimed the improvement in the dual chamber pacing which automatically determines the cardiac pacing rate output and high atrial rate driven by the sinus node. It gives the rate adaptive or demand type method of operation of pacemaker that are based on atrial synchronous pacing driven by sinus node and physiological sensors which sense the metabolic demands. This pacemaker calculates the metabolic indicator rate (MIR) using the metabolic sensor parameters which further determine the rate of pacing response and chamber of the pacing either single chamber and dual chamber. This technology was introduced by the Matthew J. Gani, John R. Hamilton et al. Telectronics N.V, published on the 18th March , 1998 [48].

- **Rate response Pacemaker with circuitry for processing multiple sensor inputs:**

The inventor of this technology provides the solution for multiple sensor interfacing with pacemaker circuitry so that decision on pacing rate can be taken appropriately and as per various parameter such as respiration rate, respiratory minute volume, blood oxygen level, blood and/or body temperature, blood pressure, the length of the Q-T interval, the length of the P-R interval, etc. In this art, input from two sensors (in which one is activity sensor and second is respiratory sensor), combined together in an optimum way to produce signals which control the rate of response of pulse generator. The circuitry of this pacemaker provides the solution of interfacing more than two sensors. This technology was published by Anders Dr. Lekholm on 9th July, 1997 [31].

- **Dual Chamber Rate responsive pacemaker with automatic mode switching**

This technology presents the dual chamber rate responsive pacemaker having the facility of automatic mode switching among DDD mode, VVIR mode and DDIR mode and switching will be directed on the difference between the average sensor rate and average atrial rate. Basic mode of this pacemaker is DDD mode in the case when the difference between average sensor rate and average atrial rate is not high but in the condition of tachyarrhythmia or atrial over-sensing the average atrial rate exceeds the average sensor rate. When this difference is greater than programmable function of two rates, the VVIR mode is selected to avoid tracking high atrial rate. In case of atrial under sensing or atrial chronotropic incompetence then the average sensor rate exceeds the average atrial rate and if this difference is increased more than second programmable function of two rates then pacemaker switched to DDIR mode to secure AV synchrony. The said invention published on 2nd May 1997 by Walter H. Olson [49].

- **Multi sensor rate-response pacemaker**

In this technology, Inventor John W. Poore and Roy B. Medlin included multiple sensors interfaced with the pacemaker which senses the various physiological parameters and regulates the pacemaker to select the pacing rate on demand. It also provides the selection circuitry and methodology for selecting a particular sensor parameter or combination of parameters that will be used as sensor indicating rate signal to control the pacing rate at a given time interval [50].

- **Minute volume rate responsive pacemaker using dual unipolar leads**

This technology was published in October, 1996 by Bruce Steinhaus, Albert Dawson and Richard Lu, that provides the automatic adjustment of pacing rate in response to changes in patient's minute volume. This pacemaker is equipped with pulse generator and two unipolar leads in which one is used as reference point. The pulse generator applies a current between electrode and reference lead by measuring impedance across lung of patients. The impedance is the measure of the plural pressure and it represents the minute volume [51].

- **Pacemaker with vasovagal syncope detection**

The inbuilt technique of vasovagal syncope detection in a pacemaker was invented by Mark.E.Erickson and H.Toby Markowitz and its grated by US in April, 2006. This invention presents the pacemaker having the improved detection of presence of vasovagal syncope episodes. Vasovagal syncope episode is the condition in which there is occurring of sudden drop of heart rate and blood pressure. So this pacemaker detects the heart rate when it drops below the threshold. Rate of pacing of this pacemaker is fallback from increased to lower rate alternatively. One sequence detects the stable rate below a threshold rate and another sequence detects the top rate as highest persistent rate and compares the difference between it [52].

- **Regularization of ventricular rate during atrial tachyarrhythmia**

The functionality of this pacemaker is to control the ventricular rate during atrial tachyarrhythmia using ventricular rate regularization function (VVR) along with the mode switching function. In nominal situation, pacemaker works in DDD or DDDR pacing mode which is atrial synchronized pacing mode but at the detection of atrial fibrillation it switches into a ventricular rate regularization pacing mode, e.g. DDIR or VDIR pacing mode with VRR function working continuously [53].

- **Pacemaker having adaptive arrhythmia detection windows**

This technology renders the device implemented software which adjusts the arrhythmia detection window and controls the Pacing AV (PAV) to address the arrhythmia. The detection window length is determined and if detection window length is shorter than required, intervals are adjusted for a specific pacing rate. Actually the

high pacing rate (PAV) have the short window length for detecting arrhythmia and to detecting arrhythmia properly, pacing rate (PAV) is forced to slow down to maintain long window [54].

VII. BATTERY TECHNOLOGY

Batteries used in Implantable cardiac pacemaker require high level of safety, reliability and longevity [51]. Technological advancement in leads/electrodes along with microelectronics reduces energy requirement by two orders and sharply reduces internal current drain which leads to decrease in size and increase in functionality, reliability and longevity [52]. A cardiac pacemaker uses half of its battery power for cardiac simulation and other half for monitoring and data logging.

During 1958-1959 rechargeable (secondary batteries) nickel-cadmium batteries were used in pacemaker implants in human beings. They were inductively recharged by the transmission of energy to the implanted receiver. The cell voltage was 1.25 V and the capacity was 190 mAh. The major problems were two fold; the first being too short life time and the second was to place the responsibility for recharging in the hands of patients, which is not a good medical practice. It was well known that primary or non-rechargeable batteries would give longer lifetime compared to secondary batteries, and patient anxiety regarding frequent recharging. Second type of batteries that were used for implanted cardiac pacemaker were "mercury-zinc" batteries [55].

The zinc-mercury oxide batteries came with the potential advantages of a high energy density and the discharge characteristics of maintaining a constant closed-circuit potential difference when operated within the prescribed current densities. Depending on the electrode design, these batteries had a long life span (up to 3 years). These batteries, however, had the disadvantage of evolving hydrogen in case residual anode (zinc oxide) was left after cathode depletion. Also, electrolyte leak from the battery destroyed the adjacent circuit elements and prevented hermetic sealing. With all these handicaps and the appearance of better power sources, these batteries appeared in 1960s and were done away after being used for about one and a half decade [55].

Next types of batteries in line were "biological batteries [56]" based on using power from human body itself but it failed experimentally for practical use. The basic principle in these batteries was to convert the body heat in to electrical energy for this purpose a large no of thermoelectric generators are built into an implantable chip. These generators exploit the well-known thermoelectric effect in which a small voltage is generated when the junctions between two dissimilar materials are kept at different temperatures, since it was seen too difficult to generate 100 uW at 3 V using a temperature difference of 1 degree Celsius, and hence this led the failure of this technology [56].

Nuclear batteries were also tried successfully for some period. Practical nuclear batteries use plutonium (238Pu). It has a half-life of 87 years so the output degrades only by 11% in 10 years [57]. However, it is highly toxic and 1μg in the blood stream could be fatal. Early pacemakers used metallic plutonium whereas later ones used ceramic plutonium oxide. The plutonium emits alpha particles, which impact upon the container and generate heat. Thermopiles of dissimilar p- or n-doped bismuth telluride generate the electricity for the pacemaker circuits. Though these nuclear power sources had long life, they were large and created problems when travelling between states and countries due to the presence of their radioactive fuel [58]. The need for it to be removed at the time of death and returned for proper disposal made them highly unfit for usage. Nuclear powered pacemakers are no longer sold. After the development of lithium batteries, nuclear batteries were completely banned. The requirements of implantable medical batteries include high energy density, reliable performance, and a long service lifetime. These requirements have typically been satisfied by lithium primary cells. Lithium-ion secondary cells are a suitable choice for many applications by virtue of their high energy and power density, low self-discharge, long service lifetimes, excellent safety characteristics. The lithium iodine batteries are the power source of most of the implanted pacemakers but the new models frequently use lithium carbon monofluoride or lithium silver vanadium oxide hybrid batteries. These chemistries have two main advantages: they have much less output impedance, which is quite important to be able to use higher currents temporarily, and they have a higher density of energy per unit of volume and per unit of mass. Lithium iodine batteries have output impedance that varies from some hundreds of Ohms at the beginning of life to more than 10 kOhms at end of life. The alternative batteries have output impedance so low as 10 Ohms at beginning of life and lower than 100 Ohms at end of life. The longevity of a pacemaker varies depending on its use. Modern pacemakers' lifespans are in the range of 6 to 10 years, for nominal settings [59].

Recent batteries are "lithium batteries" and it has three types: first type is liquid cathode system, second type is solid cathode system and third type is solid electrolyte system. Among these three systems "solid electrolyte system" or "solid electrolyte lithium cells" are used in cardiac pacemaker. This lithium electrolyte cell's cathode is a complex of iodine and poly-2 vinyl pyridine (P2VP). Since either of these components conducts electricity but when this complex is mixed heated at high temperature (i.e. 149ºC) for 3 days the black viscous paste that is formed conducts electricity. Further, this molten paste is poured into the battery which cools to form solid. During this process when the paste contacts metallic lithium a monomolecular layer of crystalline lithium iodine

forms which is a molecular semiconductor that passes lithium ions and hence flow of current occurs restricting the flow of iodine molecules [55].

VIII. RECENT INNOVATION, EMERGING TECHNOLOGY AND FUTURE ADVANCES

The past and current generation technology is facing some limitation to serve the huge population encountered by cardiovascular diseases. A survey was done by authors Udo EO, Zuithoff NP et al. which concludes that one of eight patients has early complications related to subcutaneous pacemaker lead [60]. An another research done by authors Korkeila P, Nyman K et al. deduce some late complications related to tricuspid valve insufficiency or central vein obstruction [61]. Lead failure due to insulation defects, needs the operating methods to extract the lead from heart and it is complex procedure that has potential risk of death [62]. Similarly, other limitation in sense of physiological and technological constraint can be counted in cardiac resynchronization therapy (CRT). According to study, about one third of patients are non-responder to CRT due to the anatomic limitation of coronary sinus and its venous branches which lead to wrong placement of left ventricle (LV) lead resulting in LV activation delay and lack of hemodynamic improvement. Another limitation in CRT devices is ineffective optimization which limits it to clinical usefulness [63].

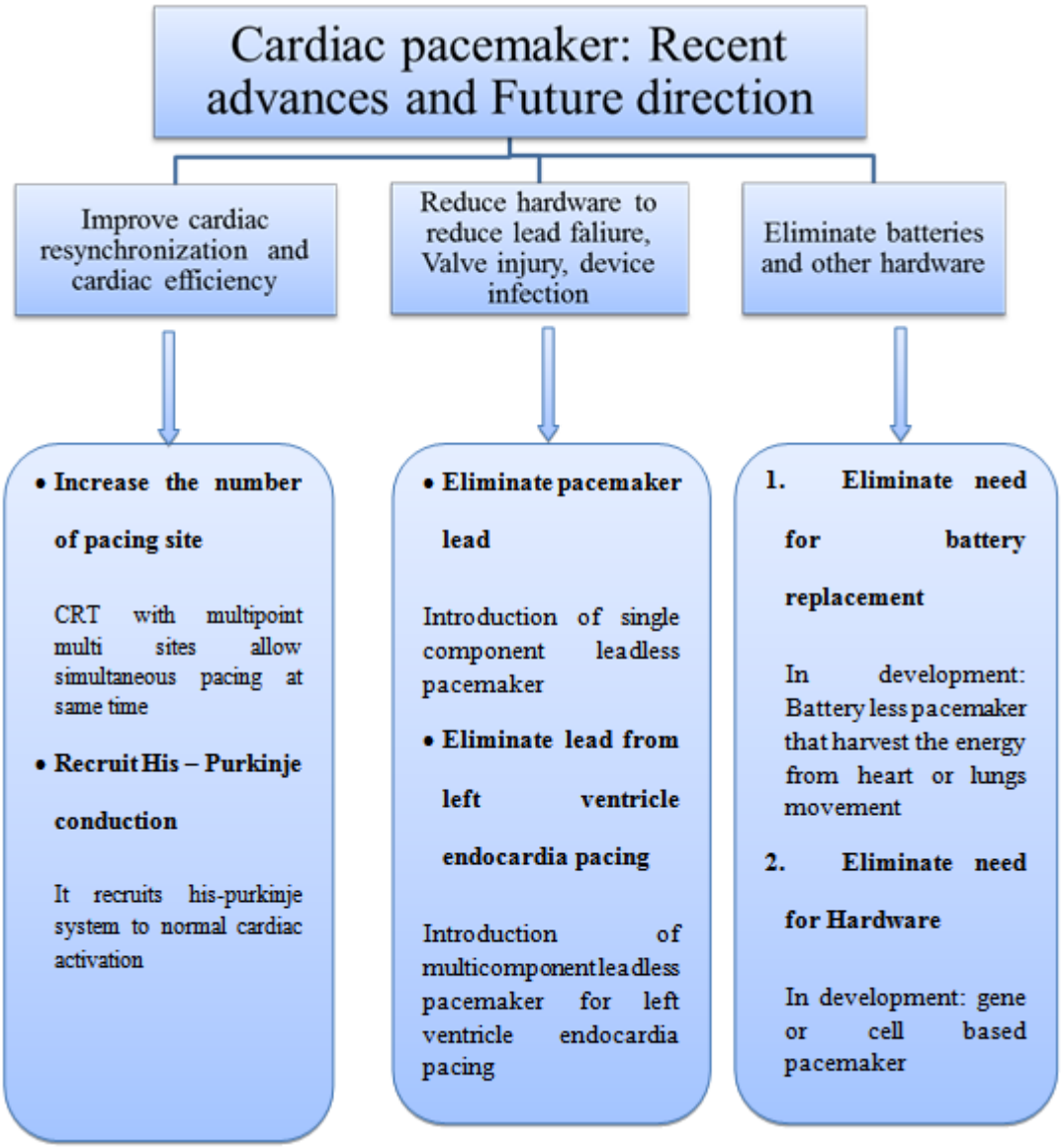


Figure 10: Future direction in cardiac pacing: Need for innovation and technology

The cardiac pacing and pacemaker technology is emerging in the direction where these complication can be addressed and lessen the limitation of current generation of pacemaker. Other than mitigation of complications of past developed technology, there are some areas like battery technology, low power circuit design, size,

shape, improved catheter design and innovative algorithm design where future advancement of technology would focus. As per need of improvement in pacemaker technology, the ongoing research and future innovation may be broadly classified in three areas, first is area of cardiac resynchronization therapy, second is size of hardware and lead less technology and third is elimination of batteries and other hardware as shown in Figure 10. Along with these areas some new advances in field of pacemaker monitoring, mode selection algorithms and software developments is in progression.

In recent advancement of pacemaker, use of engineering advancement, material design and improving the computing power were added. Use of VLSI technology in circuit design, decreased the size of circuit (< 65 nm) and improve the power consumption. New emerging technologies in circuit fabrication like SoC has decreased the semiconductor node sizes (14nm) and higher version of processor will be the integral part of future pacemaker. In addition fabrication of high impedance and small tip diameter lead which will enable to lower the current drain and maximize the current density [64]. Study shows that use of high impedance leads consume the low power and improves the battery life [65] [66] [67] [68] but device longevity is not satisfactory [69] . In battery technology lithium/Iodine batteries used in last decades has been replaced by light weighted lithium/carbon monofluoride batteries that have the higher current density provided to support onboard microprocessor [70]. Today's generation pacemakers are equipped with MRI conditional technology which provides the minimum electromagnetic interference during MRI. [71]. Last decade has seen the new advanced algorithms for arrhythmia detection and in near future the key changing technology artificial intelligence will be used in pacemaker which provides the capability to device for making suitable decision for selection of pacing mode according to physiological condition of the patient. Authors of this communication are now working on a similar project that utilizes the features of emerging artificial intelligence technology. Further, there are some technical discussions about above marked area of emerging technology and future direction of pacemaker.

Cardiac Resynchronization therapy and device:

Cardiac resynchronization therapy (CRT) is used to treat the ventricle delayed segment that is helpful to improve ventricular function, cardiac output, cellular remodeling, stroke volume, LV contractility, ejection fraction etc. with lower heart failure and lower mortality [15]. Due to left bundle branch block (LBBB), when left ventricle contract with marked delay, heart fail to produce adequate stroke volume and cardiac output, this is known as dyssynchrony. CRT helps to improve synchrony by pacing of heart and it is done by the implanted cardiac resynchronization device which sends the electrical impulse to heart muscles which resynchronizes the contraction of heart ventricles. CRT defibrillator or CRT-D is also used to apply additional function to quick address the abnormal fast life threatening heart rhythm [72]. CRT is an effective method to treat the prolonged QRS duration named as dyssynchrony in heart patients [73].

Leadless Pacemaker

After first implantation of transvenous permanent pacemaker in 1958, its technology has been continuously updating upto current generation in result of improved battery life, device performance, programing and lead reliability [74] [75] but still facing some challenges such as device infection, extraction and replacement of lead after failure and secondary tricuspid regurgitation. Most of challenges due to failure of lead or complication related to lead so for mitigating of these limitations, recently the innovators from Europe come with solution in form of leadless pacemaker [76]. Single component leadless pacemaker has been approved for commercial use in Europe and under clinical trial in USA while multicomponent leadless pacemaker is under clinical trial both in Europe and USA[68].

Single component Leadless Pacemaker

The Nanostim LCP shown in 12 (a) is single component leadless pacemaker developed by St. Jude Medical, Inc. St. Paul, MN having capability of single chamber VVIR pacing with blood temperature based rate modulation. It is having size of 42 mm length, 5.99 mm width with 2 g weight and 1 cc volume. It was introduced and implanted in right ventricle using 18 Fr venous catheter system by screw in helix mechanism. It is so designed that it can be easily extracted within 3 minutes after months of implantation [77]. Its first clinical trial was done in sheep and device successfully retrieved after 5 months of implantation and further trial was done in 300 patients implanted for 6 months. Trial was successful as it shown similar results as by traditional permanent pacemaker and over 93% patients were reported free from device side effect like infections etc. during 6 months periods [78].

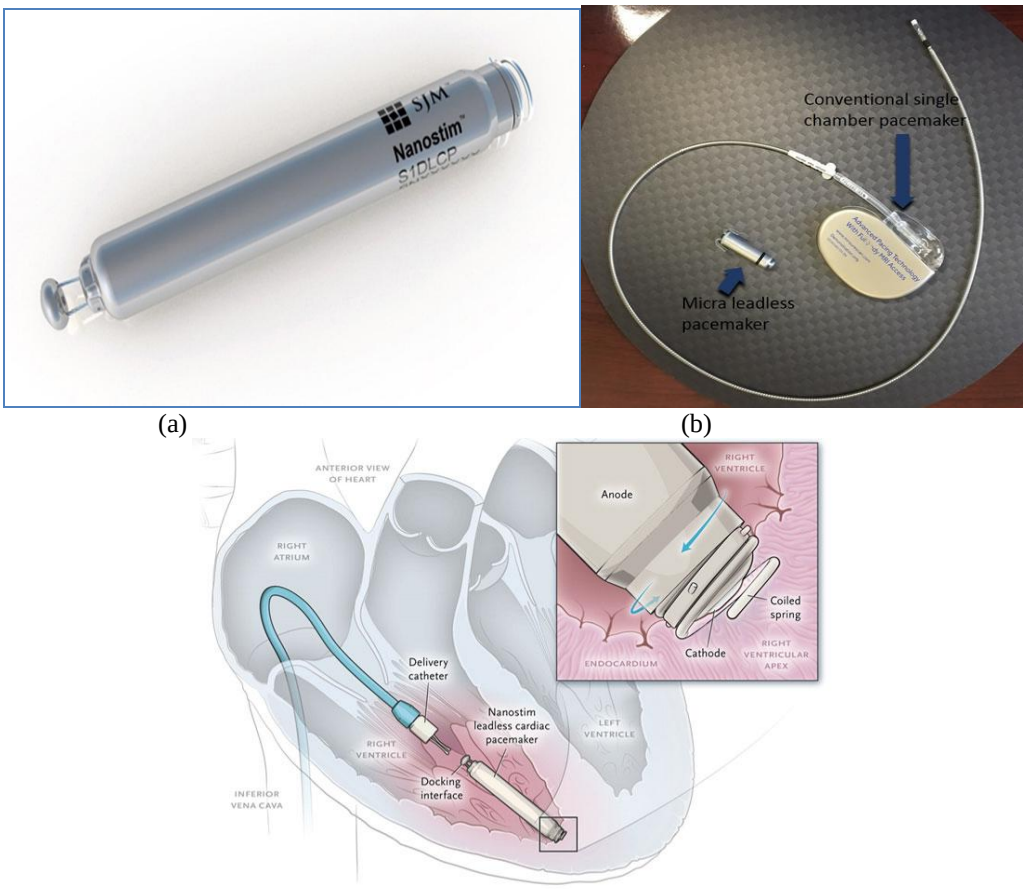


Figure11: Leadless pacemaker (a) Nanostim LCP (b) Micra Transcatheter Pacing system (c) Placement of Nanostim LCP [78]

Another device shown in Figure 11 (b) developed by Medtronic Inc., Minneapolis, MN is named as Micra Transcatheter Pacing System that provides the VVIR pacing mode and under trail in both Europe and USA. Its rate modulation is based on three axis accelerometer that makes capable the device to change the rate analogues to activities. Its size is 25.9 mm length and 6.7 mm width with 2 g weight and 0.8 cc volume. This device was implanted in 725 patients in whom 719 (99.2%) implantation was successful and that were analyzed for 4 months. The study shows that 96% among them were not counted for any complications related to implantation procedure.

The major limitation of single component leadless pacemaker is that it provides only single chamber pacing and not useful for majority of patients who need dual chamber pacing and also not be able to provide cardiac resynchronization therapy. Although clinical trial have not reported any development of arrhythmia due to device but some experts doubt that leadless pacemaker may increase risk of arrhythmia if employed for longer time period due to larger point of contact with the ventricles [80].

Leadless pacemaker		Micra		Nanostim
Device features				
Volume (cm^3)		0.8		1.0
Length (mm)		26		42
Diameter (mm)		6.7		5.99
Weight (gr)		2		2
Introducer (Fr)		24		18
Fixation		Self-expanding nitinol tines		Helical wire screw (+nylon tines)
Pacing mode		VVI(R)		VVI(R)
Periprocedural data				
Number of patients		725		526
Successful implantation		99.2%		95.8%

Final device position (%)	Apex Septum Mid-septum Outflow tract	65. 23.8 7.8 0.6	Apex Apical septum Outflow/septum / other Missing data	38.1 19.0 42.7 0.2
Procedure duration (min)		34.8±24.1		46.5±25.3
Fluoroscopy duration (min)		8.9±16.6		13.9±9.1
Major complications (%)		4.0		6.5
Device dislodgement (%)		0		1.1

Multicomponent leadless pacemaker

The multicomponent leadless pacemaker named WiCS® LV system was designed and developed by the EBR system INC., Sunnyvale, CA that is based on ultrasound technology and capable to CRT. In this the pulse generator and battery system is integrated with small transmitter and receiver electrodes. Receiver electrode is introduced into left ventricle endocardium while pulse generator is implanted into subcutaneous tissue of lateral thorax and transmitter is fixed in such a manner that it project towards the receiver. The acoustic energy from transmitter at ultrasonic frequency is transmitted to receiver where it is converted into electrical pulse. Beam intensity and duration of pulse is used for modulation of pulse width and voltage. This system can be implemented along with all existing pacemaker and it can stimulate left ventricle based on sensed right ventricle signal from existing system. This system implantation trial was done for 17 patients out of which 13 patients showed successful implantation, 3 patients had severe pericardial effusions with one patient death and one show the rapid discharging of battery [80] . The above study represents that leadless pacemaker technology is emerging widely and would have huge scope in near future. Presently, there are some limitations in both single component and multi component leadless pacemaker technology. Single component leadless pacemaker system is designed and capable only for RV pacing but it is more reliable, safe and effective while multi components leadless pacing is designed for delivery of CRT. Future progression of leadless pacing technology may be in area of biventricular pacing with reliability, safety and efficacy [11].

As with any evolving technology, the leadless pacing also have some important issues that needs to be investigated, such as clinical trials of both leadless pacing methods are required to be done in sufficient number of patients to compare and confirm the claims, also a proper method of monitoring can be added to these pacemakers using the features of wireless sensor networks so that rare complications like death as reported in clinical trials can be avoided [81], [82], [83].

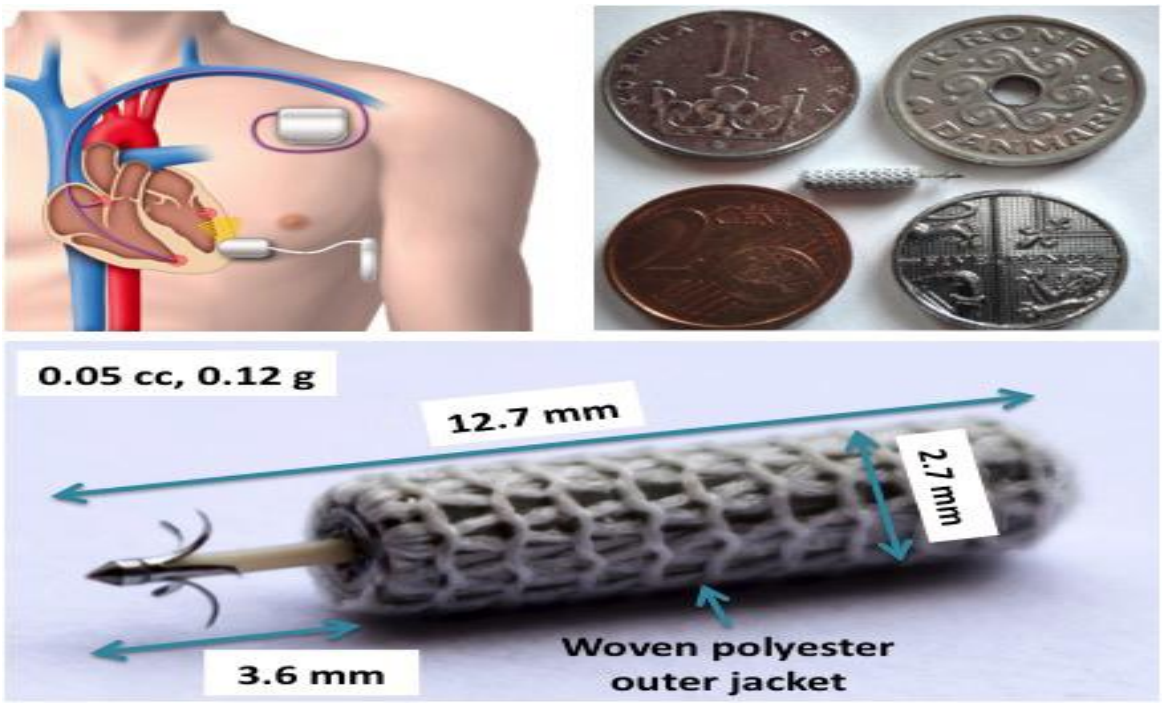


Figure 12: Overview of the system for LV endocardial lead less pacing (WiCS-LV System), Ultrasonic Receiver (Upper right corner and lower photo)

Neural network based pacemaker

While the pacemaker does aid in functioning of the heart, the present day pacemakers have a chance of putting the patient at greater risks. The programmable pacemakers have a couple of modes in which it can exist: DDD (triggered), DVI, DDDR, DDIR (non-triggered) and so on. The mode is assigned depending on the condition of the patient. If the condition of the patient changes then for reassignment the patient will have to visit the hospital again which at times could compromise their safety and cause inconvenience to them. Moreover, at most times the patient is unaware of the requirement to visit the hospital and ignores such signs. Hence, the correct solution is an artificial neural network based pacemaker which senses the patient's condition using sensor network and reacts accordingly. One major advantage of this method is the use of brain model in processing of data which results in a better prediction and control compared to other existing methods like statistical and adaptive methods.

The neural network will be trained to detect various abnormalities of the heart such as:

1. Irregular rhythms
2. Improper functioning of the SA node
3. Loss of Compressibility of the heart
4. Rapid rise/fall of BP/ hypertension which is also a major cause of death in several cases of Cardio Vascular Disease (CVD).

Based on the physiological condition of the patient, the neural network will initiate the appropriate corrective action via the pacemaker functionality. This type of pacemaker would be connected to external server or cloud server via wireless methods and provide two way communications of information and command. Presently, this is new area of research which is being focused upon by our research team.

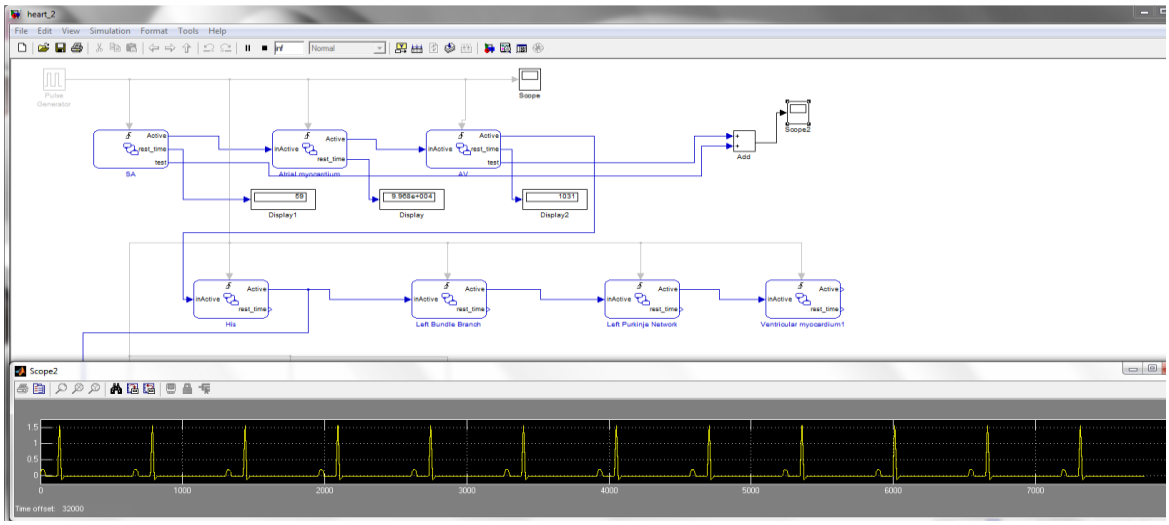


Figure 13: Simulink based model of pacemaker using neural network approach implemented by Research group

Biological Pacing

As electronic pacemaker has been lifesaving solution for more than past 5-6 decades for bradycardia and other heart arrhythmias related to conduction system but still the maturity of this traditional pacemaker technology has not been achieved. There are several issues with an electronic pacemaker such as less accurate autonomic modulation, need for repetitive lead repositioning and battery replacement procedures etc. [20]. The ideal solution for heart conduction system which mimics the natural pacemaker of heart is now seeking more research in the gene therapy and cells implantation methods and research has shown bit of success with this technology. As gene therapy and cell therapy is in progression from last 20 years and now it is well known reliable method to approach development of an ideal natural pacemaker. In cellular therapy, embryonic stem cells or induced pluripotent stem cells are used to develop a biological pacemaker. However, still there are many issues unresolved with biological pacemakers which need more investigation and validation in order to compete with existing electronic pacemakers, the major ones are bio safety and duration effect.

IX. CONCLUSION

A brief review about history, development and advancement of pacemakers is presented in this article. The starting section provides the information related to the anatomy and working of cardiovascular system along with study of cardiac abnormalities in order to create a base for understanding rest of the content. Study of the

article indicate that technology of pacemaker is continuously evolving at a very fast pace, size of modern electronic pacemakers is made quite small so that they can be implanted successfully without any discomfort, even the existence of leadless pacemakers make have been made possible. Battery life of pacemakers has been increased enough that the often battery replacement have become rare. Application of many advanced control mechanism have made the pacemakers aware about when they required to pace, presence of relatively small sensors in modern pacemakers have provided them the capability of measuring various necessary signals of interest. Recently the use of new and promising technologies like ANN and Machine Learning in electronic equipment's have opened a new era of making them smart enough to take decisions and artificial pacemakers are strong candidate to have such capability, hence a lot of future work in this area is expected, also since these technologies will be using a lot more data therefore the challenges will be going to be arises in the various aspects of pacemakers like sensing capability, power requirements in transmission and reception of data etc. Other hand attempts to provide necessary pacing using biological principles of gene therapy and cell implementation have also shown great potential but still a lot more to do in this domain and this demands a great amount of future attention. Except all these point the highest priority should be given to safety of patients and one also need to be concerned about that while working on any of the above advised topic. Moreover at this point of time we can conclude that the pacemaker technology has been travelled a lot but destination is still to come.

Competing interests

There is no conflict of interest for publishing this manuscript in your journal

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