Original Article

PULSED FIELD ABLATION: A NOVEL TREATMENT FOR ATRIAL FIBRILLATION

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Abstract

Atrial Fibrillation (AF) is most common sustained cardiac arrhythmia. Catheter ablation is a therapy, which can be used in symptomatic patients refractory to antiarrhythmic treatment.Any ablation treatment still relies on Pulmonary vein isolation (PVI), which is fundamental. Even when the PVI is carried out in highly skilled institutions, PVI reconnection was observed in roughly 20% of patients, which highlights a significant shortcoming of existing catheter ablation methods. Therefore, better technology is required to enhance ablation lesions. One of the novel treatment is Pulsed Field Ablation (PFA), a non-thermal energy that uses trains of high-voltage, very-short-duration pulses to kill the cells. The mechanism of action of this energy consists of creating pores in the myocardiocyte cell membrane in a highly selective and tissue-specific way; this leads to death of the target cells reducing the risk of damage to surrounding non-cardiac tissues. It has been demonstrated that PFA does not harm esophageal tissue when administered directly to the esophagus or when administered inadvertently via ablation in the left atrium. The aim of this review is to report the confirming its safety and efficacy towards Atrial Fibrillation.

Introduction

Heart is a hollow, muscular organ, about the size of a closed fist.The heart beats about 100,000 times a day and 2.5 billion times during a typical lifetime.[1] The heart contains four chambers, two atria and two ventricles. The atria are upper chambers that receive returning venous blood. The ventricles are located below the atria and pump blood from the heart into the arteries. The normal heart rhythm is called sinus rhythm. [2]

The **electrocardiogram (ECG)** is one of the simplest and oldest cardiac investigations available, yet it can provide a wealth of useful information and remains an essential part of the assessment of arrhythmia.[3]

Cardiac arrhythmia is the condition in which the heart's normal rhythm is disrupted.Arrhythmias are widely varied in their clinical presentations, they possess shared electrophysiologicproperties at the cellular level. The 3 main mechanisms responsible for cardiac arrhythmias are automaticity, triggered activity, and reentry.[4]

Atrial Fibrillation (AF) is a complex arrhythmia characterized by an extremely rapid atrial rate (350 to 600 beats per minute). The atria experience numerous wave fronts during AF. The atria can't contract in a coordinated manner when there are many wave fronts present during Atrial Fibrillation.

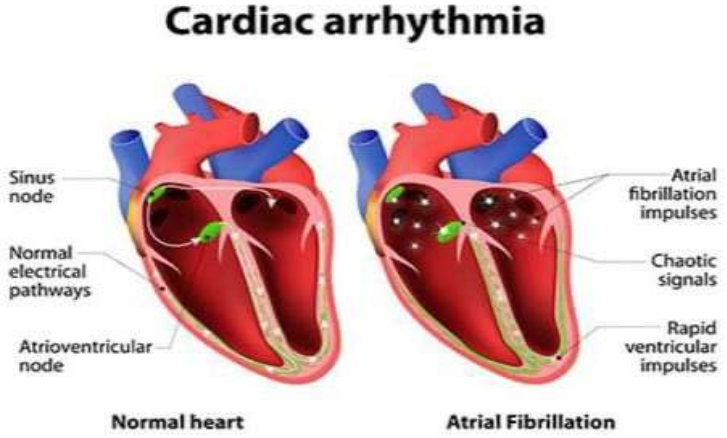

Figure: 2 Comparison of normal heart and Atrial Fibrillation[6]

Atrial Fibrillation can lead to other cardiac problems, including an increased and more irregular ventricular rate along with a significantly increased risk of stroke, which can result from blood stasis in the atria that promotes the development of clots. Electrophysiological alterations brought on by brief atrial fibrillation episodes seem to make the condition more frequent and persistent over time.

The European guidelines recommend catheter ablation of AF in symptomatic patients refractory to drugs or with heart failure. Regardless of the patient's features, pulmonary vein isolation (PVI) continues to be the cornerstone of all ablation procedures. Thus **Pulse Field Ablation** (PFA) becomes novel and most convenient method for the patients suffering from Atrial Fibrillation.

Let us now study in detail how Pulse Field Ablation treats Atrial Fibrillation.

Pulse Field Ablation: A Novel treatment History

The conventional approach used by cardiac electrophysiologists to perform AF ablation isradiofrequency (RF) energy.Power, tissue impedance and temperature, ablation time, and contact force are just a few of the key variables to take into account when deciding on the ideal lesion size and depth following RF ablation.In the clinical practice, other technologies are actually used to perform catheter ablation as cryoenergy and laser energies, and many multicentric trials have shown no differences in efficacy between all technologies.[1]

However, it's crucial to acknowledge a significant drawback of the most recent catheter ablation techniques.PVI reconnection was observed in roughly 20% of patients, even when the PVI is carried out in highly skilled institutions.Additionally, these technologies have been linked to lesions in the tissues close to the heart, specifically the esophagus and phrenic nerve. [1]

Therefore, to improve ablation lesions and treat AF, more reliable and secure technology is required. One of the novelties in recent years is pulsed filed ablation (PFA), a non-thermal energy that uses trains of high-voltage, very-short-duration pulses to kill the cells. [1]

The mechanism of action of this energy consists of creating pores in the myocardiocyte cell membrane in a highly selective and tissue-specific way; this leads to death of the target cells, reducing the risk of damage to surrounding non-cardiac tissues such as the esophagus, nerves, and vessels. [5]

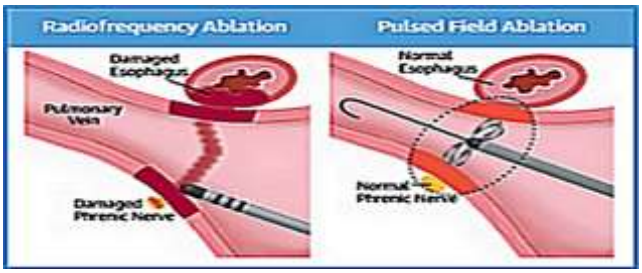

Figure : Pictorial demonstration of PFA mechanism[7]

Heart: It's Anatomy and Physiology

Before knowing what Pulse Field ablation is, we first need to know the anatomy and physiology of heart.

The heart is a hollow, muscular, roughly cone-shaped organ. Its size is comparable to the owner's fist and is approximately 10 cm long.[8]

Position

The mediastinum of the thoracic cavity, between the lungs, is where the heart is located.It has an apex below and a base above where it lies obliquely, slightly more to the left than the right.A little below the nipple and a bit closer to the midline, the apex is located at the level of the fifth intercostal space, approximately 9 cm to the left of the midline.The base approaches the second rib's level.[8]

Figure: position of heart[9]

Structure

The heart is made up of three tissue layers: the pericardium, myocardium, and endocardium.[8]

- **Pericardium**: The pericardium is outer most layer which splits into two sacs. The outer sac is made of fibrous tissue, whereas the interior sac is made of a continuous double layer of serous membrane.

The fibrous sac is lined with the *parietal pericardium*, which is the outer layer of the serous membrane. The inner layer, *the visceral pericardium*, or epicardium, which is continuous with the parietal pericardium, is attached to the heart muscle.[8]

- **Myocardium**: The myocardium is the middle layer of heart wall made up of specialized cardiac muscle found solely in the heart.

The apex of the myocardium is the thickest, and it thins off towards the base. This represents how much work each chamber contributes to blood pumping. The left ventricle has the most thickness.[8]

- **Endocardium**: The endocardium is what makes up the lining of the myocardium and the heart valves. It is a thin, silky, gleaming membrane that allows blood to flow freely inside the heart. It is made up of flattened epithelial cells that are connected to the endothelium that coats the blood vessels.[8]

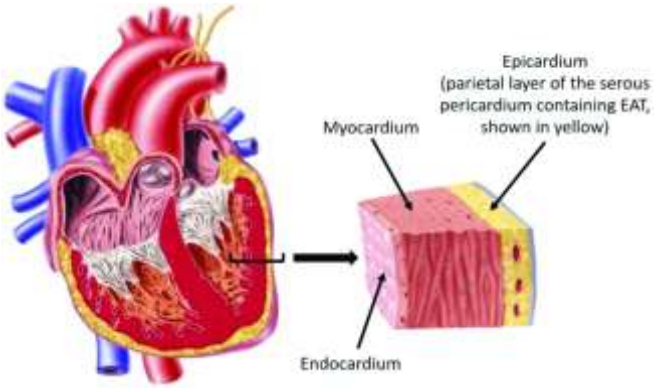

Figure : Layers of heart[10]

Flow of blood:

The right atrium receives the contents of the body's two biggest veins, the superior and inferior venaecavae. This blood is pumped into the pulmonary artery or trunk by the right atrioventricular valve after passing through the right ventricle.[8]

The pulmonary valve, which is made up of three semilunar cusps, protects the opening of thepulmonary artery. In the case that the ventricular muscle relaxes, this valve stops blood from flowing back into the right ventricle.[8]

The pulmonary artery splits into the left and right pulmonary arteries after leaving the heart,which then convey the venous blood to the lungs where gas exchange occurs: carbon dioxide is exhaled and oxygen is taken in.[8]

Each lung contains two pulmonary veins that return oxygenated blood to the left atrium.The leftventricle receives the blood once it has passed through the left atrioventricular valve, and the

blood then flows into the aorta, the first artery of the general circulation.The aortic valve, which is made up of three semilunar cusps, protects the entrance of the aorta.[8]

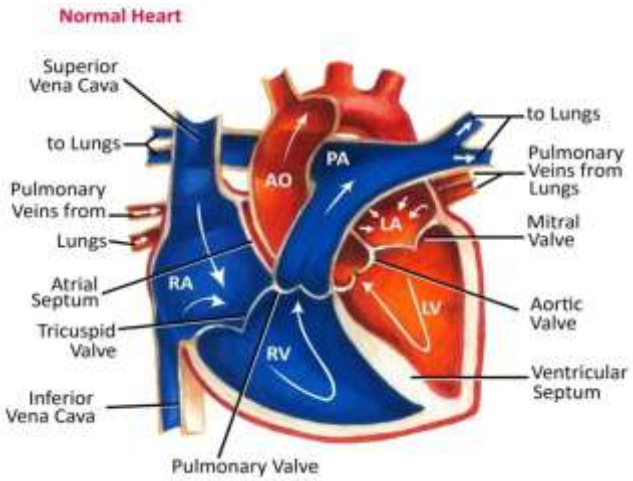

Figure : Blood flow in heart[11]

The cardiac cycle

The purpose of the heart is to keep the blood flowing continuously through the body. The cardiac cycle is a succession of events that make up the heart's activity as a pump.[8]

The heart contracts and then relaxes during each cardiac cycle, or heartbeat. Systole is the period of contraction and diastole is the phase of relaxation.[8]

Stages of cardiac cycle

Cardiovascular cycles per minute typically range from 60 to 80.[8]Using 74 as an example, each cycle lasts approximately 0.8 second and consists of:

- atrial systole — contraction of the atria[8]
- ventricular systole — contraction of the ventricles[8]
- complete cardiac diastole — relaxation of the atria and ventricles.[8]

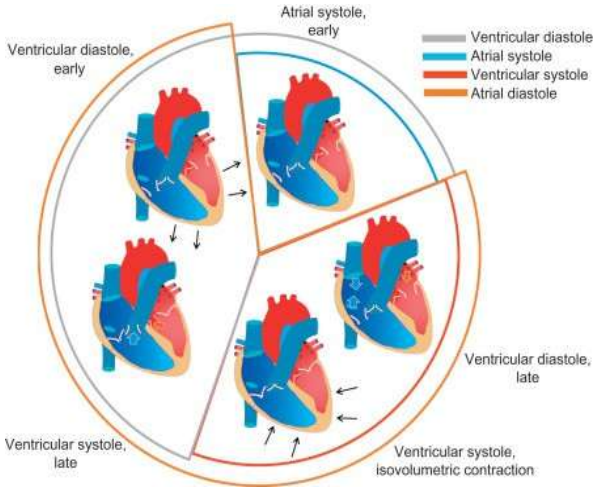

Figure : Stages of cardiac cycle[12]

Electrical changes in heart

By attaching electrodes to the body's surface, electrical activity within the heart can be monitored because body fluids and tissues are effective conductors of electricity. The electrical activity pattern can be seen on the screen of an oscilloscope or sketched on paper. Electrocardiograms (ECGs) are produced using an electrocardiograph as the tool.[8]
An ECG is simply a representation of the electrical activity of the heart muscle as it changes with time, usually printed on paper for easier analysis. Like other muscles, cardiac muscle contracts in response to electrical depolarisation of the muscle cells. It is the sum of this electrical activity, when amplified and recorded for just a few seconds that we know as an ECG.[4]

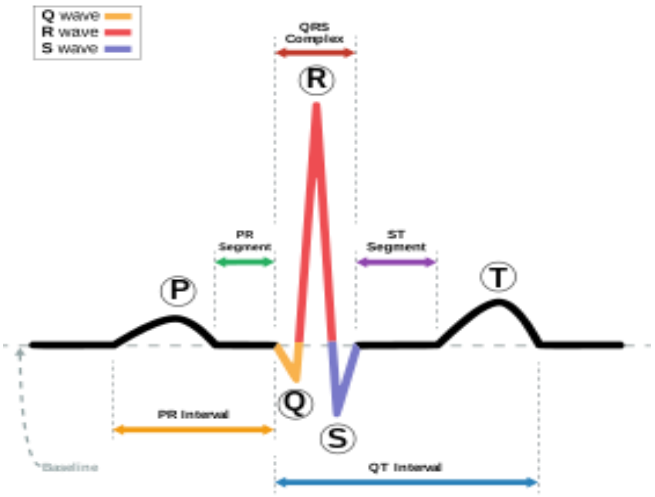

Figure: Electrocardiogram[13]

Five waves can be seen on a standard ECG trace and have been given the names P, Q, R, S, and T. [8]
The impulse from the SA node crosses the atria, causing the P wave to occur.[8]
The Purkinje fibers and AV bundle, as well as the electrical activity of the ventricular muscle, are all represented by the QRS complex, which is the very rapid spread of the impulse from the AV node.[8]
The T wave is an indication of the ventricular muscle relaxing.[8]
Sinus rhythm is the term used to describe the above-mentioned ECG, which comes from the SA node. Sinus rhythm occurs between 60 and 100 times per minute. Bradycardia is a slower heart rate while tachycardia is a faster heart rate.[8]
Information on the condition of the myocardium and the cardiac conduction system can be discovered by analyzing the wave pattern, the time interval between cycles, and individual cycles.[8]

Arrhythmia: A Cardiac disorder What is arrhythmia?

A disorder termed **cardiac arrhythmia** occurs when the heart's regular beat is altered.[6]

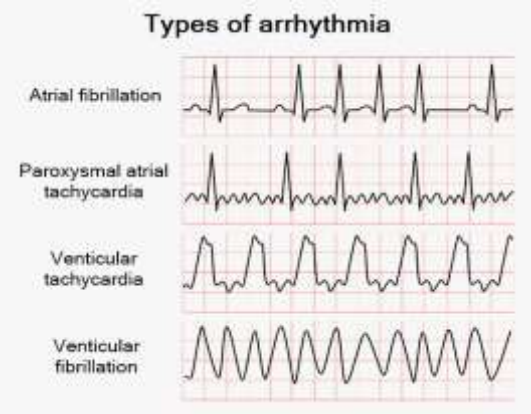

Figure : Types of arrhythmia[15]

Pulse Field Ablation is used to treat Atrial Fibrillation. Atrial Fibrillation

Atrial fibrillation (AF) is a complex arrhythmia characterized by an extremely rapid atrial rate (350 to 600 beats per minute). Like ventricular fibrillation, during AF multiple wavefronts are present in the atria and compromise the ability of the atria to contract in a coordinated fashion. However, because the atria serve primarily as filling chambers, their contraction is not as necessary for cardiac function, and for this reason AF is not immediately life-threatening. Nevertheless, AF can lead to other cardiac problems, including an increased and more irregular ventricular rate along with a significantly increased risk of stroke, which can result from blood stasis in the atria that promotes the development of clots. Like atrial flutter, AF can be paroxysmal or persistent. It also has been documented that even short bouts of atrial fibrillation lead to electrophysiological changes that over time tend to make atrial fibrillation more frequent and longer-lasting (Wijffels et al., 1995). AF can be treated by direct cardioversion but morefrequently is treated with antiarrhythmic and/or anti-coagulation drug therapy.[12]

Pulse Field Ablation

Pulsed field ablation (PFA), a non-thermal energy that kills cells using trains of high-voltage, extremely brief pulses, is one of the novelties of recent years. This energy works by selectively and tissue-specifically opening pores in the myocardiocyte cell membrane, which causes the target cells to die and lowers the chance of harm to nearby non-cardiac tissues such the esophagus, nerves, and veins.

Methods

The PULSED AF study, also known as the Pulsed Field Ablation to Irreversibly Electroporate Tissue and Treat AF was a research conducted worldwide. It involved centers. Followed a nonrandomized approach, with paired single arm design. The study focused on patients suffering from n=150) or persistent (n=150) atrial fibrillation (AF) that did not respond to class I or III antiarrhythmic drugs. These patients were treated using pulsed field ablation. Throughout the study patients were closely monitored for a year using symptomatic monitoring, ECGs at 3 months, 6 months and 12 months intervals, as well as 24 hour Holter monitoring at 6 months and 12 months. The primary measure of effectiveness was determined by evaluating freedom from failure arrhythmia recurrence or escalation of antiarrhythmic medications within a year after the procedure.

A blanking period of 3 months was excluded to allow recovery time. As for safety assessment freedom, from events related to the procedure or device was considered. The primary end points were evaluated using Kaplan Meier methods.[12]

Pulsed Field Ablation: Animal Studies review

Several laboratory studies showed a rational foundation for pulsed field ablation application in the clinical situation.Animal and human cell investigations were used to evaluate the safe and efficient PFA delivery.Animal and human cell investigations were used to evaluate the safe and efficient PFA delivery.PFA was carried out on myocardial cell H9C2 and smooth muscle cellA7r5 using two in vitro ablation models of single-cell systems and monolayer cell systems.[16]
Three Bamaminipigs were used to verify the in vivo ablation effect of PFA. In the monolayer cell system, H9C2 was significantly sensitive to PFA compared with A7r5. Bidirectional PFA performed on Bamaminipigs was able to effectively obtain PVI without stenosis; furthermore, bidirectional PFA was able to significantly ablate myocardial cells, maintain cell–cell connection,and reduce muscle contraction. [17]One of the severe complications of PVI using thermal ablation is esophageal damages, in particular, atrio-esophageal fistula. In 84 New Zealand rabbits, nonthermal irreversible electroporation was directly applied to their esophagi. After 16 weeks from ablation, no lumen stenosis, epithelial erythema, erosion, ulcer, or fistula were reported[18]

Pulsed Field Ablation: Clinical Studies review

Initial experience of PFA ablation was performed in 22 patients with symptomatic paroxysmal AF, using a monophasic waveform, either with an endocardial or epicardial ablation catheter, but no safety or efficacy follow-up data are available [36]. In particular, this study was performed at two centers and reported data regarding 15 endocardial and 7 epicardial AF ablations. PVI was obtained in 100% of patients and surgical box lesions in 86% of patients.[19]

Conclusion

Pulse field ablation is an innovative technique that appears to be effective and safe in the treatment of AF patients. PFA appears to be a viable tool for electrical PVI and myocardial ablation, resulting in high lesion durability and safety, according to all investigations. Numerous experimental cardiac and non-cardiac studies show that the majority of the adverse effects and difficulties associated with thermal catheter ablation do not exist with electroporation ablation. In the middle of enormous electroporation lesions, blood vessels, the esophagus, and nerves are spared, and ablations deep inside the PV do not cause PV stenosis.

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