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Catheter ablation for Atrial Fibrillation: Techniques and Exiting Devices

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Introduction:

Atrial fibrillation is the most common sustained heart abnormality and play a crucial role in the prevalenceof morbidity and mortality. AF is related proportionally with aging and structural heart diseases such as hypertension, valvular heart disease or coronary artery disease. According to the World Health Organization (W.H.O), around 2% of people with age less than 65 have experienced the AF before, while the ratio increases sharply to reach 9% of people older than 65 years. For example,in United States of America the estimation shows that between (2.7 to 6) million people have atrial fibrillation. A study published in 2014 by Chugh and his team focused on the global distribution ratio of atrial fibrillation, showed that about 0.5 % of population around the world producing more than 33.5 million people around the world suffering from atrial fibrillation, the study predicted that in 2050 the number of person in USA who are suffering from atrial fibrillation will increase rapidly to reach 8 million[1].

Atrial fibrillation characterized by supraventricular tachyarrhythmia with nonorganized and ineffective atrial contraction leading blood flow from atria to ventricles to be irregular and chaotic. Electrocardiogram (ECG) shows the deficiency of p-wave and irregular ventricular contraction (QRS) which can aggregate some blood in atria without pumping into the ventricles due to faulty electrical signal suddenly start firing at the sinoatrial (SA) node being at another part of atria or beside the pulmonary veins, as a result atrioventricular (AV) node flooded with these electrical pulses can't send them to ventricles as fast as they arrive, producing the atria and ventricles to beat more fast than normal but in unsynchronized way.Therefor loss of atrial activity can significantly reduce the cardiac output and increase the filling pressure[2]. Consequently, AF can be classified based on episodes' duration**;** Paroxysmal AF starts suddenly without any indications and terminate spontaneously or with intervention in less than week,while Persistent AF and Longstanding persistent AF can be reoccurred for more than one week up to 12 months, but in case of permanent AF continuesrenewingdespite the treatment and intervention

Researches and studies have identified various risk factors associated to atrial fibrillation. Structural remodeling is the most noticeable change occur into atrial tissues properties such as fibrosis and atrial size, these changes in atrial structure may refer to myocardial cell stretch, neurohumoral activity and oxidative stress [3].These types of changes promote the abnormality of atria structure leading to defects in electrical conduction predominantly contributing to reentry and rotor formation.Also, electrical remodeling shows a significant profile to generate atrial fibrillation by changing ionic current, variation of Ca^{2+} can develop AF, studies such as (Shan et al.2012) have demonstrated the relation of altered Ca^{2+} controlling and delay after depolarizations which influence the formation of electrical impulses disorder [4]. While increasedK^{+} current alert resting potential producing reduction in atrial refraction and wavelength, this mechanism has supported by in vitro research achieved by (Pandit et al. 2005) and his team [5]. On the other hand, genetics and mutation play a role to influence the incidence of atrial fibrillation, where the independent risk of AF in the offspring was significantly increased for parents who had at least one of them with previous AF[6]. Mutation leading to increase channels activity including potassium and accessory proteins channels are linking to AF which may reduce the duration of action potential and refractoriness in the atria leading to early after depolarization[7]. Currently, management of atrial fibrillation include the use of anticoagulant medications, cardiac catheterization and ablation as well as surgical interventions.

Cardiac catheterization and ablation principles:

Cardiac catheterization is an invasive medical procedure for diagnoses and treatment of heart problems. Typically, cardiac catheterization take place under local anesthetic, while Cardiologists insert long, thin and flexible wire or tube called catheter through artery or vein at patient's arm, neck orgroin to reach the heart under the guide of fluoroscopic X-rayin combined with injected of certain type dye known as contrast medium enabling the visibility of blood stream into the blood vessels to detect any narrowing or blocking. Cardiac catheterization is useful to correct hear diseases; coronary heart disease can be treated by placing a stent guided by the catheter and tiny balloon, which prevent obstructive or narrowing of the artery and support blood flow, heart valves can be replaced or repairedby catheterization. Also, cardiac catheterization as diagnoses procedure can provide a significant medical information about the heart including internal pressure measurement and oxygen concentration, check the pumping efficacy of heart, take biopsy and diagnoses of congenital heart defects[8].

On the other hand, treatment of heart arrhythmia including atrial fibrillation achieves by a medical technique known as catheter ablation which is based on the fact that each arrhythmia related to critical anatomic area generate or propagate nonorganized impulses required to sustain and initiate the arrhythmia. Selective destruction of desired region of myocardial tissue using local heating or freezing such as radiofrequency energy, cold laser or nitrous oxidecan be applied through catheter tip inserted and threaded into a groin or neck to cardiac tissue, sometimes irregular electrical impulses originated at pulmonary vein causing atrial fibrillation. Cardiac ablation mechanism can reroute or reorganized irregular electrical impulses or ablate certain region of heart tissue or pulmonary vein generating abnormal cardiac rhythm. Catheter ablation technique for the treatment of atrial fibrillation can be categorized regarding the technology and principles of operation.

Radiofrequency ablation can be described as an electrical current at frequency ranged from (300-1000) kHz generate a heat at catheter tip used to ablate certain area of heart tissues or isolate the pulmonary vein. The magnitude of heating energy is proportional to power density into cardiac tissue which inversely depend on the radius of catheter tip, therefore small area of heart tissue heated directly by the catheter tip while the reaming tissue heated by conduction. Unipolar radiofrequency catheter has a wild rang of available probes used during the cardiac ablation for different area of heat tissue, but it was observed that the available resulting is less efficient and produce more thrombogenic behavior in the creation of scar tissue with heat and is often irrigated to provide a more even distribution of heat and prevent charring[9]. Bipolar radiofrequency ablation use a jaw clamping tip provide an impedance measurement of cardiac tissue to support real time assessment during heating cardiac tissue until irreversible protein denaturation occur. The outcomes of using bipolar radiofrequency technique for atrial ablation demonstrate that is safe, more efficient and doesn't develop collateral destroy to surrounding tissue, also has better

results in performing transmurally with shorter procedural time[10].Many studies and researches have investigated the factors affect cardiac ablation, experimental studies explained the association of catheter tip with higher temperature and larger radius works more effectively and developed larger lesion size. Other research achieved by Sunil Nath and coworkers demonstrated the effect of temperature into myocardial tissues, the electrode temperature above $50C^0$ is necessary for irreversible cardiac injury, while the $100C^0$ temperature promotes coagulation of tissue and increase the electrical impedance, therefore it is essential to adjust the radiofrequency to certain value of power developing temperature less than $100C^0$[11]. In addition to that, duration time of radiofrequency energy is significant for lesion formation and should be applied for 45 s at least. Pulsed delivery energy may show more advantages because of surface cooling by convention at catheter tip point is faster than conduction with tissue, thus 100C may be reached at 3 mm without boiling happened at the contact point between tip and tissue[12]. Many limitations may appear in conflict differences between the recorded temperature and the true value at the tip to cardiac tissue due to non-close contact at the targeted site, or in other cases the electrode tip become parallel to targeted tissue rather than perpendicular causing accessory pathway ablation through trans septal approaches and reducing the ablation efficiency. Therefore, the continuous temperature monitoring via thermistor ablation catheter will promote safety, effectiveness and allow operator to evaluate tissue heating and catheter stability. Increasing the size of electrode or catheter tip will directly affect the temperature distribution at the tip, creating a phenomenon known as edge effects where the temperature at the edge exceed the core electrode[13]. Furthermore, radiofrequency ablation catheter develops relatively small size lesion due the fact that the lesion size increases until reaches a particular plague. *In vivo* experimental have demonstrated that in radiofrequency ablation, lesion size increases within the first 30 seconds, but the rate of enlargement sharply reduced with continuous power delivery[14].

Cryoablation is unique invasive treatment procedure for cardiac arrhythmia by freezing targeted area of heart tissue generating defective electrical impulses, during cardiac cryoablation nitrous oxide or halocarbon gas refrigerated at high pressure delivered from a special tank toward the catheter tip, when it sprayed at the tip it starts to evaporate and absorb heat from targeted tissue, after that the warmed gas is vacuumed back through coaxial tube attached to the catheter tip. One benefit of cryoablation is that enabling ice mapping to evaluate aim tissue at temperature between $-28C^0$ to $-32C^0$ before performing irreversible phase, tissue destruction process start at $-60C^0$ for at least two minutes' duration. *In vitro* and *in vivo* investigation showed that heart tissues are more sensitive to enhance cell death by freezing rather than other type of human tissues[15]. Weimer et al 2007 used a cryoablation at $-20C^0$ to freeze heart tissue and the outcomes of his work was confirmed when applied for longer duration. Freezing rate is an important factor for cell destruction including slow rate which lead to develop extracellular ice harming closely packed cells, attached tissue to cryoablation catheter tip freezing rapidly while the cooling rate at adjacent tissue slows as the volume of frozen tissue enlarged, blood flow can perform heat exchange equilibrium in 10 to 15 min [16]. A significant reason for enhanced cell death by repeating freezing procedure is the increment of freezing rate at the second cooling stage occurred by pre-freezing surrounding tissue decreased heat associated to first cooled tissue, leading to more extensive intracellular ice crystallization [17]. Over time the lesion become sharply noticeable from adjacent tissue and replaced by fibrosis and fatty tissue which is main indication for a cut cell death. The lesion of cryoablation showed less thrombogenic behavior compared with radio frequency ablation as a result of the preservation of endothelial cells and tissue ultrastructure[18].

Furthermore, high intensity focused ultrasound (HIFU) is a new ablation technique based on a high frequency acoustic wave propagates across tissue, the ultrasound wave develops a mechanical vibration of participles within tissue medium which absorbing the energy of the waves and coverts it as dissipated heat causing thermal injury for targeted tissue. Further tissue destruction occurred due to the acoustic cavitation developing microbubbles by propagated ultrasound waves. Microbubbles improve the effect of HIFU by generating non-absorbable medium which increase the acoustic impedance[19]. Ultrasound energy can be focused at narrow beam using acoustical or electrical focusing technique producing rapid increment of temperature up to 80 C^0 within 60 seconds creating thermal damage into limited volume without direct interaction between probe and tissue [20]. Clinical investigations have performed *in vitro* and *in vivo* to show the successful results of using HIFU for treatment of atrial fibrillation.

Ninet et al. 2005 and his team achieved a multicenter study including 5 heart center in Europe, follow up patients with paroxysmal AF and had treated by HIFU, found that 85% of the patient were free from atrial fibrillation after six months [21]. Other studies declared that the lesion size is dose dependent and proportionally related to the duration time and the power of ultrasound wave. The lesion deep may be reached up to (11 mm) and demarked with normal surrounding tissue [22]. The therapeutic application of HIFU for atrial fibrillation is considerably limited due to critical complications such as pulmonary embolism, phrenic nerve damage and even mortality compared with radiofrequency and cryoablation [23].

Therapeutic Approaches for Atrial Fibrillation:

Recently the management of atrial fibrillation includes the use of rate and rhythm control strategies in parallel with surgical interventions. treatment strategies dileverd to pathophysiological mechanism developing structural changes essential to prevent occurrence and reoccurrence of atrial fibrillation.

Rate control:

It is useful approach in older patients above 65 years of age with chronic situation, suffering from limited symptoms as they control cardiac ventricular rate by targeting the atrioventricular node (AVN) which is responsible to transmits electrical signals from the atria to the ventricles including β-adrenergic receptor blockers, calcium channel blockers and digitalis glycosides. Therapies for rate control included adjusted doses of beta-blockers with digitalis to achieve the targeted heart ratewhich prolong AVN refractoriness (reduce conduction velocity) by eventually reducing sympathetic tone or voidingCa^{2+} overload to slow ventricular rate at relax and during exercise without converting the heart to a regular rhythm[24]. Combinatorial uses of β blocker or calcium channel blockers have established beneficial for rate control. Consequently, controlling ventricular rate in AF not only minimize the risk of tachycardia related indications and cardiomyopathy associated with a rapid heart rate but can also relieve heart failure symptoms by lengthening diastole [25].However, some complications related to control drugs can slow the heart beat too muchdeveloping sinus bradycardia and heart block. Patients experienced these symptoms may needsurgical interventions such as implantation of pacemaker or ablation for AV node to reorganized ventricular rate [26].

Rhythm control:

Rhythm control approach seek to find cardioversion by converting the heart inti sinus rhythm through antiarrhythmic medication in combined with direct electric current. Clinical evaluation proved it is favorable strategy for patients intolerant to rate control or younger patients with limited heart disease complications. Direct current cardioversion is essentially used to restore sinus rhythm, especially for rapid tachycardia and hemodynamic instability. Patients suffering of atrial fibrillation treated with anticoagulant therapies are subjected to electrical currents (monophasic or biphasic waveforms) via metal pads or patches that are synchronized with the R wave to depolarize the atrial tissue that initiate the reentrant circuits. Consequently, the circuits no longer generate or propagate because the atria essentially become refractory.Clinical researches have demonstrated the advantages of biphasic cardioversion, low-energy, current flows in both directions producing greater efficiency shock with less energy compared with monophasic[27].Furthermore, rhythm control can be performed by invasive ablation procedures, especially for patients who are intolerant to conventional rhythm control approaches or when medication show ineffective or toxic.

Commercial catheter ablation devices:

Several commercial systems and devices are available to support and treat patients suffering from atrial fibrillation. Stryker corporation have a radiofrequency generator called MultiGen which have the ability to support 4 lesion simultaneously with independent control which can significantly reduce the overall procedure time, also it can support monopolar and bipolar catheter at the same time. Medtronic as a leader company develop Cool Tip RF Ablation which is a unique radiofrequency system based on internallycirculatedchilled water into the catheter tip to cool the surrounding tissue around the target area, this allow to decrease treatment time where 6 lesion can be

performed into 16 min. The RF source contain exclusive feedback algorithm to monitor tissue impedance and automatically adjust out deliver power through a thermocouple at the catheter tip which can measure tissue temperature. Switching controller allow to use threeelectrodes at the same time with different power setting[28]. Furthermore, RF 3000™ Radiofrequency Generator manufactured by Boston scientific company to support 4 different type of catheters, Chilli cardiac RF catheter with closed loop cooling system prevent fluid infusion to the patient, thus will not cause any saline clouds interference. While Blazer II XP temperature ablation catheter has unique clinical results with outstanding safety profile, simplicity using and temperature control. In addition to that, IntellaTip MiFi XP uses MiFi sensor based on new technology of high resolution catheter for ablation. It is designed to support highly localized electricity of unsurpassed clarity to make clinical see the critical information in real time[29].

Cryoconsole is cardiac ablation system found by Medtronic corporation stores and controls the delivery of the liquid (N_2O) through the coaxial tube to the catheter, recovers the refrigerant vapor from the catheter under constant vacuum, and disposes of the refrigerant through the hospital scavenging system. While the AtriCur medical company have a cryoICE BOX V6intuitive and reliable cryosurgical treatment of cardiac arrhythmias supported a wild range of cryoablation catheters. Boston Scientific and AtriCor have signed an agreement to improve and develop a CryoCor console to deliver cryo energy to Boston Scientific's proprietary cryo catheter and balloon[30].

St. Jude Medical developed HIFU systems; UltraCinch enables creation of a uniform, continuous, linear lesion during cardiac ablation. It can be placed securely around the patient’s atrium while transducers apply HIFU energy safely and precisely through the targeted tissue. The UltraCinch device is offered in seven sizes to accommodate varying patient anatomies. Also, the UltraWand handheld ablation device using the same transducer technology as in the UltraCinch device, the UltraWand allows complimentary linear lesions to be created during cardiac ablation procedures. This provides physicians with the flexibility to create the lesion set that is most appropriate for each patient.The Epicor Positioning and Sizing (PAS) System is dual-purpose designed to indicate the proper UltraCinch device size and act as a guide for simple, accurate placement of that device. It is designed to track smoothly through the cardiac anatomy, and to facilitate less invasive approaches. The tourniquets ensure secure placement of devices on the patient’s heart[31].

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