Current Surgical Options for Treatment of Atrial Fibrillation

ATRİYAL FİBRİLASYON TEDAVİSİNDE GÜNCEL CERRAHİ SEÇENEKLERİ

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Abstract

Atrial fibrillation remains an unsteady hurdle toward the cure of supraventricular arrhythmias. Despite its high prevalence, a definitive treatment for atrial fibrillation has not been shown. Surgical ablation, which originated with the favorable results of the Maze procedure developed by Cox, has an important role in the cure of atrial fibrillation associated with heart disease patients who require cardiac surgery. Although this procedure cures atrial fibrillation in the majority of patients, it has not had widespread application due to its complexity. The development of new operations that use alternate resources and simplified left atrial lesions have demonstrated acceptable results. Alternative sources enable surgeons to create lesions more rapidly with a decreased postoperative risk profile. Additionally, these sources can be applied on a beating heart allowing for minimally invasive and totally endoscopic approaches in surgical ablation of atrial fibrillation. The purpose of this review is to update the rationale for surgical ablation of this common pathology.

Key Words: Atrial fibrillation, catheter ablation, cryosurgery

Özet

Atriyal fibrilasyon, supraventriküler aritmilerin tedavisinde halen bir engel olarak karşımıza çıkmaktadır. Yaygın olarak görülmesine rağmen, kesin bir tedavisi gösterilememiştir. Cox tarafından geliştirilmiş olan Maze prosedürünün nispet sonuçlarından kaynaklanan cerrahi ablasyon kardiyak cerrahi gereken hastalarda atriyal fibrilasyonun tedavisinde önemli bir role sahiptir. Bu prosedür çoğu hastada tedavi sağlayabilmesine rağmen kompleks olduğu için yaygın olarak kullanılmamaktadır. Alternatif kaynaklar sayesinde, düşük postoperatif risk ile hızlıca lezyonlar oluşturulabilir. Bu kaynaklar atan kalpte uygulanabilirliği ile minimal invaziv ve total endoskopik yaklaşımlar ile tedavi sağlayabilmektedir. Bu derlemenin amacı bu sık görülen patolojinin cerrahi ablasyon temelini güncellemektir.

Anahtar Kelimeler: Atriyal fibrilasyon, katater ablasyon, kriocerrahi

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Atrial fibrillation (AF) along with its treatment and consequences are protagonists in a never-ending story. An estimated 2.2 million people in the United States have AF and the number is growing by 160.000 new cases annually.[1] AF is an epidemiologically significant problem among persons over age 65 with an incidence of 5 to 10%.[2] Patients have high morbidity and eventually increased mortality rates because of tachycardia-induced cardiomyopathy, hemodynamic compromise, and thromboembolism with a five to sevenfold increase in the risk of stroke, causing serious health concern and financial costs.[2,3]

Despite the astonishing advances that have been made in AF prophylaxis and treatment over the past 40 years, a definite therapeutical goal has not yet been reached. Pharmacologic therapy is characterized by many recurrences of the arrhythmia and non-pharmacologic therapies are still a "work in progress".[4] The prevalence of AF, given the limitations of pharmacological therapy for the maintenance of sinus rhythm, has led to the development of alternative, non pharmacological approaches to the management of this disorder. Surgery and surgical ablations have shown promising

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results. Yet, percutaneous catheter based approaches are still affected by several risks of complications and by an unsatisfactory success rate, particularly in patients with permanent AF and associated cardiac disease.

The surgical treatment of drug-refractory AF was performed by Seally for the first time in 1981 who used cryo-ablation to interrupt the His bundle.[5] After a year, closed catheter ablation of the His bundle became a widely used treatment for drug-refractory AF which resulted in life-long artificial pacemaker dependancy due to the interruption of atrioventricular synchrony. Later, other surgical options were developed, including the left atrial isolation procedure by Williams, the Corridor procedure by Guiraudon, and the Maze procedure improved by Cox.[6-8]

The Cox Maze III procedure is a precisely defined pattern of bi-atrial incisions, used to eliminate AF. This procedure aims to interrupt the multiple wavelet macro reentry circuits, which perpetuate AF.[9] The complexity of the "cut and sew" Cox-Maze technique is considered a major drawback. Therefore, this procedure is not universially accepted as a standard practice for the surgical treatment of AF. Therefore, alternative sources of energy, such as cryoablation, radiofrequency, microwave, laser and focused ultrasound have recently been introduced into surgical practice to simplify the traditional Maze procedure for the treatment of AF.[10] Still, the efficacy of the alternative energy sources is debated, because the benefits of the creation of transmural atrial lesions, which act as an electrophysiological conduction block, are considered to be doubtful.

The objective of this article is to outline the contemporary and emerging surgical approaches to AF and to give an overview of new and evolving techniques.

Pathophysiology of Atrial Fibrillation and Relationship to Surgical Technique

AF is a complicated arrhytmia and its pathogenesis is not completely understood. AF is believed to arise from enhanced automaticity at one or more rapidly depolarizing foci or result from reentry involving one or more circuits.[11] Ectopic foci, single circuit re-entry, and multiple circuit reentry have been reported as initiating and maintaining AF. The focal origins of AF have been demonstrated to localize predominantly in the pulmonary veins, which appear to be more important in particular patients presenting paroxysmal AF.[12] In some circumstances (6%), foci may exist in the right atrium, the superior vean cava, or the coronary sinus.[13] Moe and colleagues presented a re-entrant phenomenon using a computer simulation showing that multiple wandering wavelets are present during AF.[14,15] They propose that fractionation of wave fronts while depolarization propagates through the atria, results in self-perpetuating continous wavelets and depends on local differences in the refractory period, mass, and conduction velocity within atria. These changes explain AF occurrences in the presence of underlying structural heart disease. "Domestication" of the arrhythmia followed by a cycle of electrophysiological and structural changes- in which AF causes electrical modeling that favors maintenance of itself - was observed by Allesie and co-workers.[16] Therefore, prolonged AF effects the choice and success of therapy.

With regards to persistent and permanent AF, endocardial electrophysiological mapping data demonstrate that the pulmonary veins and posterior left atrium are the critical anatomic sites with isolated AF.[17] Regular and repetitive activation can be observed in these areas.[18,19] These observations support developing procedures to ablate persistent AF, which mainly originates on the left atrium and pulmonary veins.

Goals of AF Treatment

Ferguson and Cox defined five goals to treat AF.[20] 1) Elimination of atrial fibrillation 2) restoration of sinus rhythm 3) reestablishment of atrioventricular synchrony 4) restoration of atrial transport function 5) prevention of the risk of thromboembolism. Based on the understanding of the mechanisms of AF, several procedures have accomplished these goals to varying degrees.

The Cox-Maze Procedure

Classical Cox-Maze III procedure has been considered a gold standard therapy with proven long-term efficacy in curing AF.[21-25] The Maze operation involves multiple full-thickness cuts and sutures within the atrial wall that disrupt abnormal reentry pathways.[3] Initially, the surgical Maze procedure was performed as an isolated cardiac operation but as its use increased, it has been performed concomitantly with other cardiac procedures. Reports of the Cox-Maze operation have demonstrated a long-term elimination of AF in 84% to 98% of cases.[21,22,26,27] After Maze, restoration of biatrial transport has been demonstrated in greater than 80% of patients,[28] and the incidence of stroke is markedly reduced.[29] Pacemaker implantation is required post-operatively in 5-10% of patients.[30] Yet, the Maze procedure is not widely applied due to operative complexity of the procedure, prolonged cardiopulmonary bypass, and risk of bleeding.[10-27]

The role of emerging knowledge of the pulmonary vein- left atrial junction relationship, combined with the low adoption rate of the Maze procedure in the surgical community, led several groups to evaluate novel strategies based on the following changes: The use of alternate energy sources replacing cutting and sewing to create the lines of block, and the simplification of the lesion pattern consisting of the omission of some of the Maze-III incisions for epicardial rather than endocardial applications.

Alternative Energy Sources

The majority of energy sources create lesions via hyperthermic injury. In the case of atrial injury, the goal with hyperthermic ablation is the electrophysiological disruption obtained with a tissue temperature of 50°C. In order to avoid cavitation and/or tissue disruption tissue temperature must not exceed the boiling point of water (100°C). Experimental data demonstrate that heating atrial tissue for approximately 1 minute at 70°C to 80°C produces lesions 3 to 6 mm deep, usually sufficient to create a transmural line of conduction block.[1] The cellular mechanism for hyperthermic ablation is not entirely understood but is likely related to injury of the sarcoplasmic reticulum with resulting influx of calcium into the cytosol. Histological preparations of ablated myocardium show a well-demarcated area of thermal injury characterized by necrotic myocardium at the center, a borderline area of edema and intramural hemorrhage, and surrounding normal tissue. Long-term lesions at 6 months show dense scar tissue that is sharply demarcated from normal tissue.[3]

Data regarding the mechanism of cryoablation suggest that the tissue should achieve a temperature of -55°C for at least 2 minutes.[31] Newer sources, which include different gases, obtain much lower temperatures and time duration less than 2 min. The mechanism of cryoablation is divided into three phases. The first involves mitochondrial and organelle dysfunction that may be due to intracellular ice crystal formation. The second involves edema and subsequent necrosis. The third is the remodeling phase in which the lesion is replaced with fibrous scar tissue.

Microwaves produce a field that causes oscillation of dipoles producing kinetic energy and eventually heat generation through dielectric effects and a component of conductive heating. Ultrasound waves are emitted from the transducer and the resulting wave travels through the tissue causing compression, refraction, and particle movement, resulting in kinetic energy and heat. Laser energy induces a harmonic oscillating in water molecules with resulting kinetic energy and heat generation.

Radiofrequency

Radiofrequency (RF) current is an alternating electrical current whose frequency is in the radio band. Electrical current passes between a catheter and a pad placed on the patient's back without affecting the body's structures because most of the energy is dissipated at the contact surface between the catheter and the myocardial tissue. Energy is dissipated in the form of heat and in subsequent ablation there is coagulation resulting from the vibration of molecules created by electrical interaction. Heat propagation is based on resistive and passive mechanisms. Myocardial tissue is heated up to 50 to 60 °C with consequent coagulation and irreversible destruction of cell and collagen structures in the immediate proximity of the probe (2-3 mm). Further away from the probe, the resistance offered by the tissue decreases exponentially and the heat rapidly decreases. Over a long period of time, irreversible damage occurs within the peripheral portion of the lesion with passive heat. Tissue lesions are similar in depth and width since both the resistive and the passive heat runs in all of the directions. Fisher et al. showed formation of scar tissue with similar width and depth up to 8 to 10 mm after a few weeks following RF application in a canine model.[3,32]

Several different radiofrequency catheter systems are available for surgical application. They include long flexible probes, rigid probes, pencil like probes with a cooled tip, and a probe that is configured as a bipolar clamp. While there are multiple modifications of RF, there are three general methods: unipolar, bipolar, and irrigated. Unipolar RF ablation relies on grounding pads to act as the other pole and is the simplest way to apply energy. In unipolar ablation, the energy is focused at the ablating surface (highest current density) and disperses throughout the body to exit through the ground. This is the slowest and most inefficient of the RF modalities, but is also the most controlled method.[33] To enhance the penetration of heat, devices with cold saline irrigation have been developed which creates less endocardial damage and a 1 to 2 mm increase in depth.[34] The cooling effect on the surface of the tissue also prevents the accumulation of burns on the ablating surface as can occur with standard unipolar ablation.

The interface between the probe and the tissue may be the most important factor when using RF energy because the resistance determines the propagation of heat offered by the tissue. The optimal temperature for RF is not entirely clear. Temperatures greater than 50 °C are normally required for reliable and effective endocardial ablation. However, since there is greater variability in atrial tissue characteristics particularly due to associated pathologies, some suggest using 80 °C.[33] Multiple shock applications have been shown to be more effective.[34] It is also important to note that the hottest temperature should never be set up more than 95 °C to avoid potential tissue disruption. Ablations must be performed for at least 60 seconds to achieve a steady state, which is not achieved until after 40-50 seconds.

Bipolar RF is another RF modality, which has the ability to make very fast and discrete lesions. This modality simply relies on having a pole on each side of the tissue to be ablated. This focuses all of the energy between the two poles and lesions can be made in less than 10 seconds. The currently available bipolar products also have impedance sensors that detect when transmural ablation has occurred, though clinical experience has shown this algorithm to be flawed, with the requirement for repeated applications of the ablation instrument. In the case of repeated ablations needed to achieve electrophysiologically effective lesions, these can be created fast as well. Majority of these new devices are applied epicardially. Epicardial placement permits beating heart and off-pump AF ablation. These lesions are predominantly created from the epicardium, provided the lesion is in an area of the heart that can be opposed to itself or one of the poles can be inserted into the heart. Since both poles must be perfectly opposed to each other, they have poor flexibility.[33] The major limitations of this procedure are the difficulty of achieving transmurality in all the lesions, poor outcomes when the atria are larger than 5 cm, and if epicardial fat is thick and covers the atria.[32,33]

The risk of overheating and perforation is minimal when RF energy is used since the energy transmission is self-limiting. Nonetheless, there have been adverse events related to the use of RF. Thromboembolism and burning of the endocardial surface have been reported despite the use of heparin, especially when using coil-tip catheters. The coil-tip catheters cause wide lesions and produce a raw surface area. Pulmonary vein stenosis has also been reported during the percutaneous approach with RF, which would not be expected with surgical intervention.[3] Damage to the circumflex artery and catastrophic atrioesophageal fistula have also been implicated though these complications are exceedingly rare.[35,36] Finally, many patients need post-operative pacemaker implantation.[9]

The outcomes of RF have shown positive results. Several reports, which used irrigated tip monopolar RF catheters, demonstrated that actuarial freedom from AF was 80% and 70% at mid and long-term outcomes.[37-39] In reports using different types of RF ablations sinus rhythm has been achieved in 42 to 92% of patients with only a 0 to 10% post-operative pacemaker implantation rate.[9]

Cryoablation

Cryoablation has the longest history of procedures used in surgical ablation and is an important component of Cox-maze procedures.[33] The most common source of cryothermal energy applied in cardiac surgery is by internally expanding nitrous oxide. This type of cryothermal energy is delivered to the biological tissue through a cryo-probe normally consisting of a hollow shaft, a closed electrode tip, and and integrated thermo couple used for distal temperature recording. Traditional cryoablation systems have difficulties due to the warming effect they can have on endocardial blood. This led to the development of newer argon and helium-based systems allowing for much colder temperatures that help to decrease the ablation time.

Cryoablation with argon or helium-based systems begin with fluid being passed into the tip maintained under vacuum. Then a liquid-gas phase change occurs, provoking a rapid cooling of the temperature (-60^{o}C). The gas is then aspirated by vacuum through a separate return lumen to the console. The application of the cryoprobe to the tissue surface results in a well-demarcated block or line of frozen tissue. Cells in the center of frozen tissue are irreversibly damaged early in the freezing process, ultimately resulting in the histological end point of scar tissue formation.

The effect of cryothermal energy on the biological substrate can be divided into 3 phases. 1) The freeze/thaw phase: Both intracellular and extracellular ice crystals are formed. Their size, shape, and position depend on the proximity of the tissue to the cryoprobe, the local microcirculation, and the duration of each cryothermal application. The microscopic effect is due mainly to the mechanical compression and distortion exerted by the crystals on the adjacent cell membranes and cytoplasmic organelles. Extensive irreversible lesions are evident within 2 hours after the application. 2) The inflammatory/hemorrhagic phase: It usually begins approximately 48 hours after the cryothermal application; the development of hemorrhage, edema, and inflammation becomes predominant. 3) Fibrosis phase: After 1 week of thaw, peripheral infiltration of inflammatory cells and strands of fibrin with capillary in-growth initiate the third phase of fibrosis replacement. By 12 weeks after cryothermal application, small, fibrotic homogeneous lesions appear. These lesions cross the full thickness of the atrial wall, surrounded by several small and large blood vessels. In summary, the cryothermal lesion is characterized by extensive local cell disruption, but at the same time, maintatins the preservation of the basic tissue architecture with minimal thrombus formation.[3]

The final cryolesions show extremely low myocardial potentials, whereas the tissue adjacent to the lesion has normal electrical activity. Cryoablation has an excellent clinical safety record, though its use in AF surgery has typically been reserved for creating spot lesions over the tricuspid and mitral valve annuli. Due to its generally safe record and arrhythmia-specific indication and introduction of new cold gas sources, promising results are also obtained in epicardial use.[33,40] In addition, cryoablation seems to be less thrombogenic and easier to use because it is a less demanding technique with respect to contact area and time of exposition (normally 90 seconds). Most importantly, the lesion formation can be constantly monitored during the surgery by direct vision. Furthermore, the creation of a new variable length and flexible probe has helped to facilitate its epicardial use.

There are only a few reported complications with the use of cryoablation; specifically during cases of coronary artery stenosis.[41] Smaller series of cases using left atrial ablation patterns during cryosurgery have shown acceptable sinus rhythm conversions with rates between 59-84%.[9,40,42]

Microwave Energy

Microwaves are electromagnetic waves delivered at a very high frequency (2.45 GHz) that provoke the induction of vibration/rotation of dipoles (such as water molecules) and the generation of heat. For medical use, microwave ablation can be performed at either 915 MHz or 2450 MHz. Not all of the ablation occurs through dielectric effects and there is a component of conductive heating. A microwave catheter normally includes: 1) an antenna, of either monopolar or helico-coil type, mounted on a plastic shaft designed to direct the waves to the targeted site to protect the surrounding tissue, 2) a thermocouple for monitoring the temperature of the device and 3) a generator system.

Microwave energy has the advantage of creating deeper lesions than RF lesions while still being done in a similar amount of time. The mechanism of tissue injury is heat-based just as it is for RF energy. At temperatures above 50^{o}C, myocyte injury is already detectable within a few seconds of application. A well-demarcated area of thermal injury, a borderline area of edema and intramural hemorrhage, and surrounding normal tissue are features of histological examination after microwave energy use. Very few thrombi are seen on the coagulated endocardial surface, although craters without bleeding or perforation are sometimes seen at the site of antenna insertion. Long-term lesions after 6 months show dense scar tissue that is sharply demarcated from normal tissue. Thermal profiles of these lesions demonstrate efficient and uniform penetration depth without areas of overheating and no char formation.[3,33] Due to its superior penetration, microwave energy has more potential for epicardial ablation and the early clinical experience has been promising with a sinus rhythm restoration rate of 73 to 87%.[9,10,43]

Potential advantages of microwave energy ablation include reduced time of application, long linear lesions within few applications, continuous visual checking during operation, sparing of endocardial surface with reduced risk of thromboembolic complications, capability of penetrating necrotic tissue as well as old scars, and possible epicardial applications. So far, no major complications have been linked to the use of microwave energy in cardiac surgery, although large series of patients are still to be presented.

Laser Ablation

Laser energy consists in high-energy optical waves delivered through an optical coupling fiber and a radiating fiber tip. The delivery device has a diffusing tip that contains silicone particles. The silicone causes the laser to be emitted perpendicular to the fiber direction. A mirror reflects the energy so that the ablation can only occur in one direction. The final result of this structure is a unidirectional linear ablation of 2-5 cm with a flexible configuration. This allows for a controlled but effective ablation through dielectric heating, with no mechanical effects as there are with the high power spot ablations. Although all laser ablation is hypothermic, the tissue effects are dependent on the wavelength used. The laser energy commonly used is the neodymium:yytrium-alimunium garnet (Nd:YAG). The tissue defects are caused by a combination of direct heating and mechanical damage resulting from fast cellular explosions caused by shock waves. The laser technique allows for the formation of sharp and narrow ablation lines because the laser light penetrates the tissue directly, heating the tissue within limits of the beam, with minimal lateral expansion of the lesion.

The mechanism of tissue injury is dependant on the wavelength with diode responding to the laser energy in a very similar fashion as it does to microwave energy. Still, the tissue penetration is deeper with the laser method. The first effect on the tissue is denaturation/coagulation of cells that occurs during the application of the light beam. The cells lose their normal architecture owing to membrane destruction and instant loss of water. It is believed that the characteristic sharpness and depth of the lesions are achieved by the blasting effect of the ultrasonic wave, which exceeds the myocyte membrane elasticity. Microscopic tissue examination shows the loss of cell striations, fiber separation, and mild hemorrhage near the border of the lesions. When high energy is delivered, crater formation and loss of tissue is often noted, as a result of exaggerated tissue heating.[3] As the application time increases for a given power, the lesions tend to become wider, but with high power (above 350 J) the risk of crater formation increases. The lesions can also be difficult to see immediately after the procedure so careful attention must be paid to the location of lesions as they are made. Lesions can be extended to 7 mm in depth while maintaining a narrow profile, thus significantly reducing the total area of ablated tissue. This may represent an advantage in considering the risk of thromboembolism and could result in improved recovery of atrial contractility.

The major complication associated with the laser procedure is perforation. There is no protective mechanism with laser ablation, although this can be avoided by following appropriate parameters. Despite the promising results from studies, only a small number of cases exists and more experience is mandatory before any conclusion about clinical efficacy and safety can be made.[3] Rhythm success rates are around 70-80% among studies already conducted.[10,44]

Ultrasound Ablation

The mechanism of ultrasound ablation is mechanical hyperthermia. The ultrasound wave is emitted from the transducer and the resulting wave travels through the tissue causing compression, refraction, and particle movement. The effects of ultrasound ablation are kinetic energy and heat. Since the mechanism is mechanical, if the wave is applied too aggressively shear stress and tissue disruption can occur. Since the wave can be controlled via a number of different parameters, it is not difficult to avoid this complication. Ultrasound can either be applied in a focused (HIFU-high intensity focused ultrasound) or nonfocused manner. HIFU allows for rapid, high concentration energy in a confined space and experimentally, produces transmural epicardial lesions through epicardial fat in less than 2 seconds. Nonfocused ultrasound is a slower processs, but the transducer system is simpler to create and may have more flexibility.

A potential future advantage of ultrasound (though not yet established) will be the ability to image lesions. The transducer can be used both to image and ablate, and thus it may be possible, particularly with HIFU, to determine atrial wall thick-

Table 1. Summary of energy sourcesfor AF ablation.

Types of energy	Radiofrequency	Cryothermy	Microwave	Laser	High Intensity Focused ultrasound
Linear Lesions	Coil- tip and pen-tip	With linear probes	With coil tip device	With diffusion linear tips in study	
Transmural lesion	Limited, requires optimal contact	Excellent does not penetrate	Excellent, requires optimal contact	Excellent	Excellent
Width / depth ratio	Very high	Low	Low	Very low	High
Duration of single ablation	Moderate	Moderate	Low	Low	Moderate
Endocardial application	+	+	+	+	+
Epicardial application	+	+	+	+	+
Endocardial Damage	Moderate	Low	Low	Low	Moderate
Thrombogenicity	High	Low	High	High	Low
Anticoagulation	May be required	No	No clear reccommendation	No clinical data	No clinical data
Risk for perforation	Moderate	Low	Possible at high energy	Low-high dependent on wave length	Low
No burns	-	+	+	-	+
Flexible probe	+	-	+	+	-
Clinical experience	Extensive	Extensive	Moderate	Minimal	Minimal

ness, set the focus to ablate the appropriate amount of tissue, and then confirm that the ablation is transmural.[33] Ultrasound ablation is currently a preclinical modality in the cardiac surgical field.

Infrared Ablation

There is very limited data regarding infrared coagulation, which has been performed experimentally.[45] In Table 1, data regarding status, application forms, complications, and efficacy was shown.

Conclusion

Each one of the techniques mentioned above must be capable of meeting some crucial requirements to be considered a valid solution to the puzzling challenge of atrial fibrillation. Transmurality, safety and reliability, endocardial damage, and related thromboembolism are matters of concern. RF and cryoablation systems have been used for the treatment of many different types of supraventricular arrhythmais, as well as for ventricular tachycardias. Nevertheless, microwave energy and laser technology (the latter only at an experimental level so far,) have undergone substantial development and show enough promise to be considered for further employment on a larger scale. These energy sources permit lesions to be created without the use of incisions and allow the procedure to be performed more rapidly and by an increasing number of surgeons. The future of the surgical treatment of AF is bright with the development and improvement of various AF treatment devices that can be used to make rapid, safe, and effective lesions.

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