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# Surgical Treatment of Atrial Fibrillation

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Additional information is available at the end of the chapter

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## Abstract

Atrial fibrillation represents the most common supraventricular arrhythmia above all in patients undergoing cardiac surgery and is associated to an augmented risk of thromboembolic stroke, heart failure, and cardiovascular mortality. That is the reason why cardiac surgeons began to address their attention to how to surgically treat fibrillating patients according to pathophysiological models describing mechanisms of arrhythmia induction and maintenance. A new branch of cardiac surgery was born, leading to a progressive development of adapted surgical ablation techniques, applicable both to lone or concomitant arrhythmia treatment. Historical evolution and current available surgical treatment options are described, beginning from the first pure surgical maze, going through all its modifications in source ablation energies and lesion sets and finishing with current mini-invasive hybrid treatment of lone atrial fibrillation. Indications, patients' selection, technical options with respective advantages and disadvantages, surgical technique details, complications, and results are fully illustrated. Relationship between pathophysiologic arrhythmia mechanisms and the consequent ablation tailored procedure choice is highlighted, allowing a customized procedural offer to every single patient, resulting in a success rate ranging from 60 to 90%.

**Keywords:** atrial fibrillation treatment, maze procedure, hybrid ablation, energy sources, cardiac surgery

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## 1. Introduction

Atrial fibrillation (AF) is a common medical condition affecting over 5 million people in the United States and whose prevalence is expected to join over 12 million by 2030. Considering people aged more than 80 years, about 7% experiences at least one episode of such supraventricular arrhythmia in their life. Dangers of AF are well known; they range from troubling symptoms to a fivefold increased risk of thromboembolic stroke and heart failure and

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culminate in excess mortality [1]. Cardiac surgeons are frequently faced to AF, since data from the Society of Thoracic Surgeons (STS) database demonstrate that preoperative AF is present in 11% of patients presenting for nonemergent, first-time cardiac surgery, varying from 6.5% of coronary patients until nearly 30% in mitral ones [2]. The high AF prevalence in case of mitral stenosis or regurgitation may be explained by histological modifications occurring in enlarged left atria suggesting chronic inflammation and interstitial fibrosis which translate into electrical changes such as augmentation of effective atrial refractory period and conduction heterogeneity able to lead to an increased vulnerability to arrhythmia genesis. These epidemiologic considerations explain why, historically, cardiac surgeons were the pioneers of curative ablation of AF; their interest began in the 1980s when Cox and associates introduced the left atrial isolation procedure in dogs. A new branch of cardiac surgery was born, leading to a progressive development of adapted surgical ablation sets of lesions and devices, applicable both to lone and concomitant (a term indicating patients in whom AF is associated with another cardiac disease requiring surgery) arrhythmia treatment.

## 2. Main body

### 2.1. History: the maze (cut-and-sew procedure)

The history of the surgical treatment of AF began in 1980, when Cox described the procedure of left atrial surgical isolation. This technique was able to enclose arrhythmia in the left atrium, leaving the right one and the ventricle in a synchronized sinus rhythm (SR). In spite of its hemodynamic efficacy, thromboembolic risk remained unchanged as the left atrium continued to fibrillate. It was clear that the development of a more complete technique was necessary in order to contemporarily achieve SR and atrio-ventricular synchrony maintenance, atrial contractility restoring, and embolic risk elimination. The Cox-maze procedure was introduced in humans in 1987 (called Cox-maze I) developing from results obtained in canine models. It consisted in creating multiple incisions that could block all possible macro-reentrant circuits and direct the propagation of the sinus impulse throughout both atria. Lesions were created by a “cut-and-sew” method performed under direct vision with the advantage of increasing the probability to achieve transmural. Excision of the left atrial appendage (LAA) was also performed alongside [1]. Even if the goal of freedom from stroke was achieved, occasional left atrial dysfunction and frequent inability to generate adequate sinus tachycardia in response to exercise (chronotrope response) led to the development of the Cox-maze II modification [3]. Sinus node incision was not included in ablation set, and the left atrial upper line was situated more posteriorly. Later, Cox-maze II rapidly evolved and perfected into Cox-maze III, whose ablation schema is represented in **Figure 1**. It consisted in a series of incisions and suture lines in both atria: lines surrounding pulmonary veins orifices with linking lesions between them and with the mitral annulus (isthmus line) and the LAA, both appendages excision and right atrial full set lesions. The Cox-maze III allowed the long-term preservation of atrial transport and sinus node function, decreasing the need for a pacemaker and the recurrence of arrhythmia, while improving the speed of the procedure with requirement of minor technical ability [4].

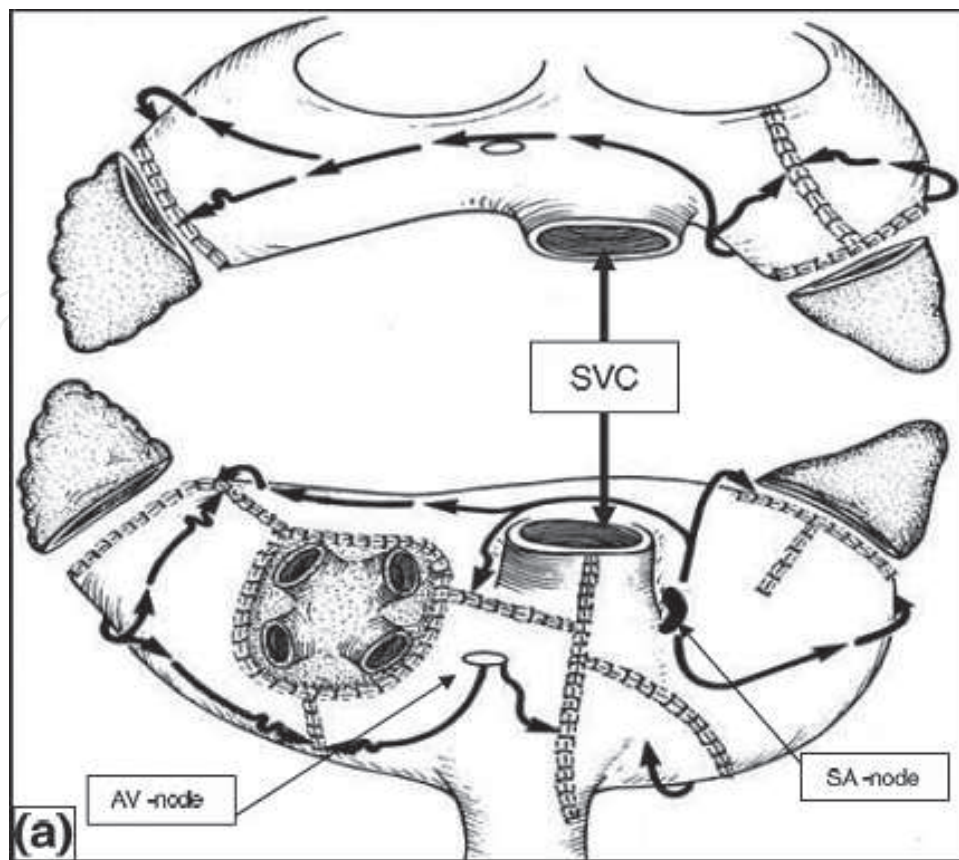
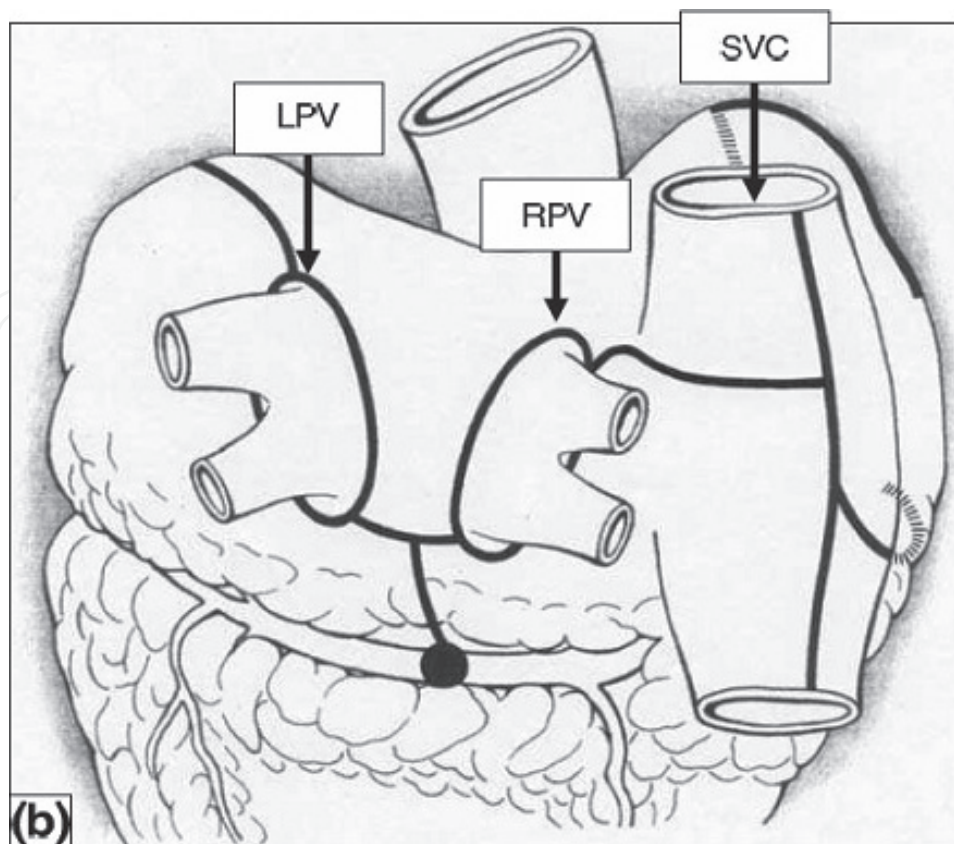


Figure 1. Cox-maze III lesions set.

Cox-maze III showed a proven efficacy with a long-term success rate superior to 90% both in concomitant and in isolated procedures [5]. Nevertheless, other works reported less encouraging results, generating a not unanimous consensus between cardiologists and cardiac surgeons, also partially due to its relevant technical complexity and possible complications. In fact, mortality rate was not irrelevant, since it ranged from 0.7 to 2% and even serious complications were frequently reported (6% following Cox JL and 3.2% in Mayo Clinic experience) including definitive pacemaker implantation due to sinus node injury, stroke, and major bleeding requiring surgical re-exploration.

## 2.2. Cox-maze evolution

In subsequent years, many attempts were made in order to improve the simplicity of the treatment, evolution which was facilitated by the increasing comprehension of AF pathophysiology thanks to the development of clinic mapping systems. In 1998, Haissaguerre [6] showed that paroxysmal arrhythmia triggers were located at the level of pulmonary veins origin, thus suggesting that an ablation action limited to this zone could be effective. Although the theory of a preeminent role played by pulmonary veins triggers is not applicable to all AF types (for instance, in case of long-standing persistent or permanent AF, other mechanisms are involved in arrhythmia beginning and perpetuating [7]), such discovery paved the way to the trial, by one side, to reduce lesions set by concentrating onto the arrhythmia real sources



**Figure 2.** Cox-maze IV lesions set.

and maintaining pathways and, by the other, to minimize surgical risk by replacing lines of incisions by lines of transmural necrosis using other energy sources. In 1999, the first “non cut-and-sew” maze was performed by the use of the cryoenergy as the sole ablation modality for all lesions described in the Cox-maze III; later, Dr. Cox introduced the so-called Cox IV which preserved the entire lesions set of the previous version, but used bipolar radiofrequency (RF) instead of the cut-and-sew technique (**Figure 2**). Minor variations of the ablation procedure have been proposed over time, namely concerning the extension of the lesions set, but the original schema of the Cox-maze IV will remain as the reference for every complete biatrial surgical ablation of long-standing persistent or permanent AF [8].

## 2.3. Energy sources

### 2.3.1. Requirements for surgical ablation

In order to perform an effective and durable AF ablation with alternative energy sources replacing surgery, devices and technologies must possess several features [9]:

1. **Transmurality:** heart lesions, either performed from the epicardial or the endocardial surface, have to go homogeneously through the whole thickness of cardiac wall for producing a complete conduction block with the aim of stopping activation wave fronts or isolating trigger foci. Especially in case of epicardial application on the beating heart, transmurality may be very difficult to achieve due to the heat sink effect of the circulating intracavitary

blood. That is the reason why some energy sources, incapable to overcome such an obstacle, have been quickly abandoned.

2. **Safety:** excessive or inadequate ablation needs to be avoided by the creation of precise dose–response curves specific for each device. Moreover, energy sources may have different harmful effects onto surrounding vital structures, including coronaries, valves, and esophagus which must be fully known and prevented.
3. **Facility and speed:** this presupposes that the device must rapidly act and be flexible and easy to handle.
4. **Adaptability for minimally invasive approaches:** this would require a specific device design allowing its insertion into small thoracotomies or ports.

Over the years, different energy sources have been tested in order to achieve all these requirements [9]: actually, only cryoenergy and radiofrequency (RF) are available and still used, because microwave devices, lasers, and high-frequency ultrasound were progressively abandoned due to their incapacity to produce reliable transmural lesions, thus resulting in high AF recurrence rates. A summary of all energy sources features is shown in **Table 1**.

### 2.3.2. Anatomic considerations

Human atrial wall thickness is far to be homogeneous in all regions and in every subject [10]; such anatomic consideration plays a major role when a new ablation device performance is tested since it has a direct repercussion onto its ability of creating transmural lesions. In normal individuals, the atrial thickness in the left atrium ranges from 2.3 to 6.5 mm. In patients with any cardiac disease, the mean left atrium thickness is  $5.2 \pm 1.8$  mm. These values encompass muscle thickness only and did not include overlying fat or underlying free-running pectinate muscles, which exist in both atria (which are not continuous with the epicardial surface). In normal individuals, the fat layer at the posterior mitral annulus can be 10-mm thick or more, which is important because epicardial fat can be an obstacle to achieve an adequate depth of penetration for most ablation technologies. Finally, as patients grow older, their chamber size and wall thickness increase. All these anatomic variations and physiologic changes provide a challenge to any unidirectional device to achieve transmural lesions and must be carefully taken into account during ablation procedure.

### 2.3.3. Cryoablation

Actually, two sources of cryothermal energy are used in cardiac surgery [9]:

1. Nitrous oxide technology (older): its name is cryoICE (AtriCure, Inc., Cincinnati, OH) and uses a 10-cm malleable probe on a 20-cm shaft.
2. Argon technology (Medtronic ATS, Minneapolis, MN): it can be used in two ways, either as a malleable single-use cryosurgical probe with an adjustable insulation sleeve for varying ablation zone lengths or as a two-in-one convertible device that incorporates a clamp and surgical probe (**Figure 3**).

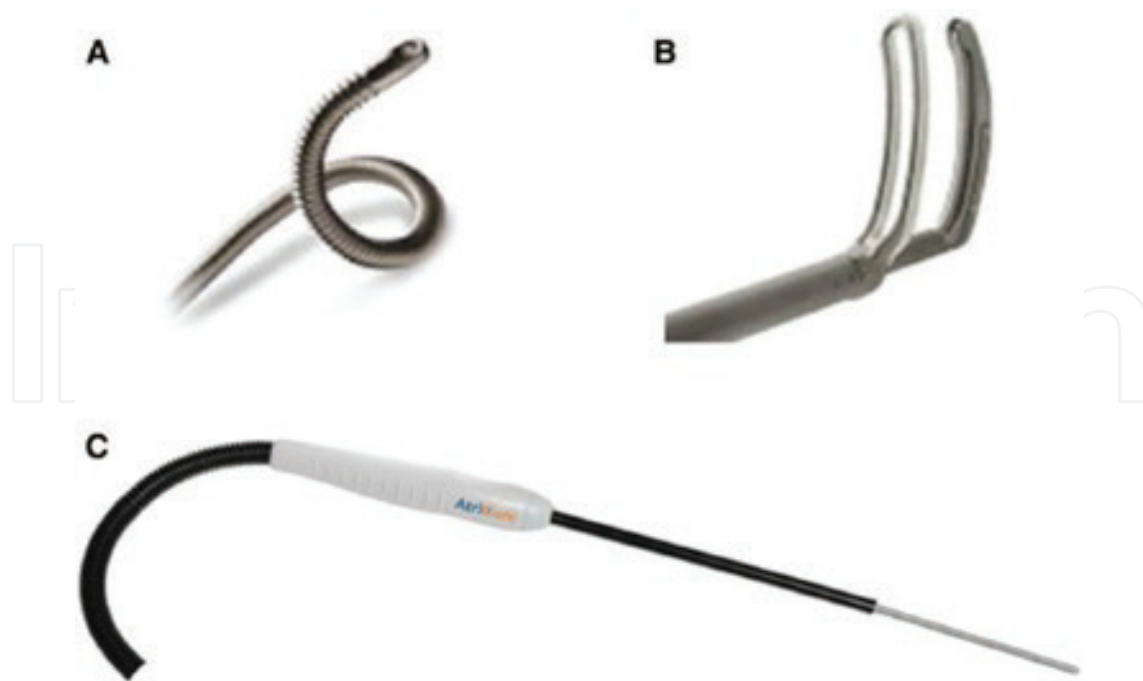
Energy source	Pros	Cons	Application
Cryo	Transmural	Time-consuming	Stand-alone maze, concomitant maze, and lesion subsets Adjunct to RF especially for lesions in perivalvular tissue
Bipolar RF	Transmural Quick Real-time conductance control	Endocardial access need Multiple applications	Stand-alone maze, concomitant maze, and lesion subsets
Unipolar RF	Epi- and endocardial	Low transmural rates No real-time transmural control Collateral damage	Stand-alone maze, concomitant maze, and as adjunct with other energy sources
Laser	Quick Epi- and endocardial Good penetration of adipose tissue	No real-time transmural control Collateral damage	Not currently used
Microwave	Epi- and endocardial	Low transmural rates Time-consuming No real-time transmural control Collateral damage	Not currently used
High-intensity focus ultrasound	Epi- and endocardial Defined depth-limiting collateral damage	Time-consuming No real-time transmural control	Not currently used

**Table 1.** Comparison of ablation energy sources.

These two devices reach different minimal tissue temperatures ( $-89.5$  and  $-185.7^{\circ}\text{C}$ , respectively) but both deliver energy to myocardium by a cryoprobe. In both cases, a console houses the tank containing the liquid refrigerant which is pumped under high pressure to the electrode through an inner lumen. Once the fluid reaches the electrode, it converts from a liquid to a gas phase, absorbing energy and resulting in rapid cooling of the tissue. At the tissue-electrode interface, there is a well-demarcated line of frozen tissue, sometimes termed an “ice ball.”

Ablation mechanism consists in cell membrane and cytoplasmic organelle destruction secondary to the formation of extra- and intracellular ice crystals. In the first 48 h after cryoablation, hemorrhage, edema, inflammation and extending, and irreversible apoptosis occur. Healing is characterized by extensive fibrosis, which begins approximately 1 week after lesion formation.

Cryoablation is unique among the presently available technologies, in that it destroys tissue by freezing instead of heating. The biggest advantage of this technology is its ability to preserve tissue architecture and the collagen structure, making it an excellent energy source for ablation close to valvular tissue or the fibrous skeleton of the heart.



**Figure 3.** Available devices for cryoablation.

Concerning transmural and safety profile, nitrous oxide technology provides good performances [11] but may cause injury to coronary arteries. Argon is relatively recent, but it seems to be able to reliably create endocardial safe transmural lesions on the arrested heart. Potential disadvantages of this technology include the relatively long time necessary to create an ablation (2–3 min; **Table 1**) and the detrimental effect of hot circulating blood volume onto cryoenergy when applied in the beating heart without cardioplegic arrest. In order to overcome such problem, a cryoclip equipped with two arms catching the tissue to be ablated has been recently proposed: in preliminary works, it showed, by one side, a 93% transmural rate on the beating heart, but, by the other, an increased risk of thromboembolism due to coagulation of the frozen blood.

#### 2.3.4. Unipolar radiofrequency energy

RF energy has been used for cardiac ablation for many years in the electrophysiology laboratory and can be delivered by either unipolar or bipolar electrodes [9].

Several devices are available (**Figure 4**):

1. Estech developed two unipolar surgical probes, the Cobra Adhere XL Probe (Atricure, Inc.) and the Cobra Cooled Surgical Probe (Boston Scientific Corp., Marlborough, MA, USA). These flexible and malleable devices with multiple electrodes, suction system stabilization, and internal saline cooling present the same mode of operation but the second one is specifically designed for minimally invasive approach;
2. VisiTrax (nContact, Raleigh, NC): a coiled electrode that is held in place with suction and irrigated with saline for cooling;

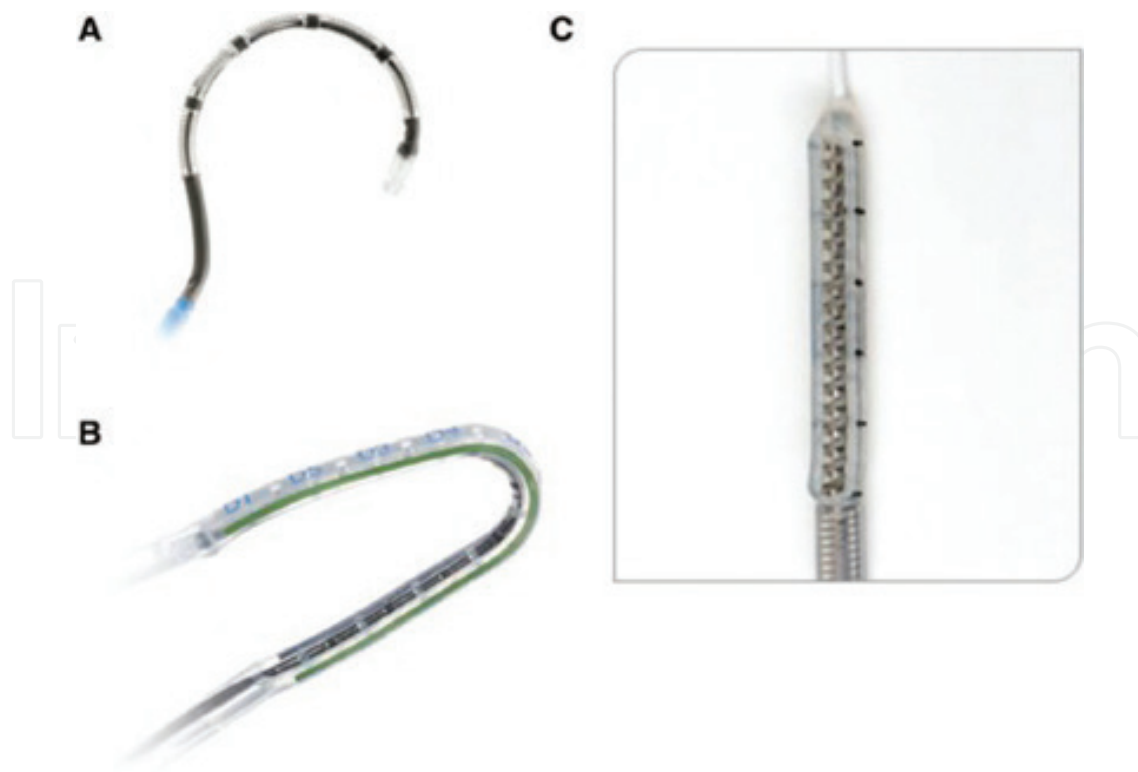


3. **Cardioblate Standard Ablation Pen and Cardioblate XL Surgical Ablation Pen by Medtronic:** these are pen-like, irrigated unipolar RF devices used to make point-by-point ablations by dragging them across the tissue to make a linear lesion. The Cardioblate XL has a 20-cm shaft and is designed to be used through a port or a small thoracotomy.

RF mode of operation consists in the application of an alternating current in the range of 100–1,000 kHz (high enough to prevent ventricular fibrillation and yet low to prevent tissue perforation) which induces a resistive tissue heating within a narrow rim of <1 mm in direct contact with the electrode and a passive heating in the deeper tissue via conduction. In unipolar technology, a passive electrode must be applied to the patient to allow energy dispersion from the electrode. RF catheters are usually irrigated with saline solutions in order to lower tissue warming and limit scar formation at the interface electrode tissue which greatly limits deep energy penetration and thus ablation efficacy. These irrigated catheters have been shown to create larger volume lesions than dry RF devices [12].

Just after unipolar RF ablation, focal irreversible coagulation necrosis occurs; later, it transforms into contraction and scarring. In case of very high temperature application (>100°C), char formation predominates.

One of the main problems of unipolar RF is its lack of transmuralty in a great percentage of cases and this despite long ablation time: more in detail, if on the arrested animal heart transmuralty achievement was satisfactory, after 2-min endocardial ablation in humans, only 20% of lesions were transmural and only 7% in case of epicardial application at a temperature of 90°C.



**Figure 4.** Available devices for unipolar RF ablation.

The complications of unipolar RF devices have been described after extensive clinical use and include coronary artery injuries, cerebrovascular accidents, and the devastating creation of esophageal perforation, leading to atrioesophageal fistula.

### 2.3.5. Bipolar radiofrequency energy

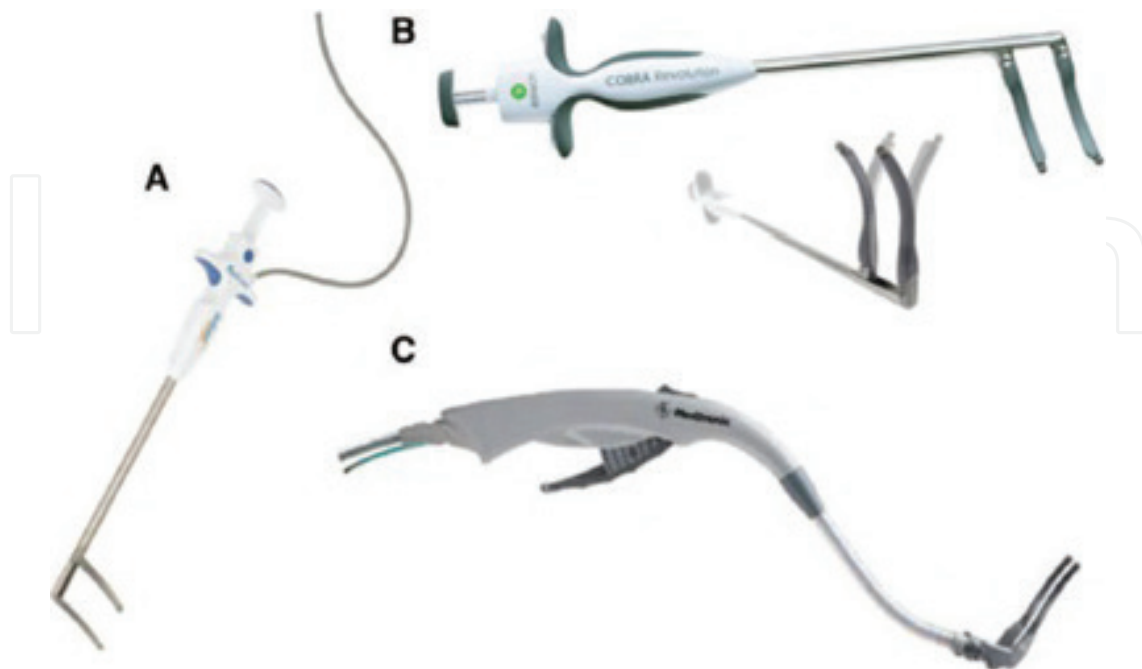
Bipolar technology is incorporated into devices (**Figure 5**) in two ways [9]:

1. a clamp with two ablating jaws each equipped with electrodes;
2. a device with two side-by-side electrodes applicable both endo- and epicardially.

Various examples of both technologies are commercially available: Atricure Inc., for instance, developed, in the first group, the Isolator Sinergy clamp showing different models and curvatures with a continuous measurement of tissue impedance as a marker of transmuralty, or, in the second one, the Isolator Multifunctional Pen able to record electrograms or pacing in addition to ablation function. Atricure has also developed the Coolrail Linear Pen, a 30-mm side-by-side electrode internally cooled with irrigated saline. Both these pens are applied for a fixed period because algorithms assessing transmuralty are not available for side-by-side devices.

Medtronic markets three bipolar clamp devices, all with irrigated flexible jaws and an articulating head: the Cardioblade BP2 (arms length of 7 cm), the Cardioblade LP for mini-invasive approach, and the longer Cardioblade Gemini.

Finally, Estech (San Ramon, CA) offers two bipolar clamps (one reusable and another single use), both called the Cobra Bipolar Clamp.



**Figure 5.** Available devices for bipolar RF ablation.

In bipolar devices, alternating current is generated between two closely approximated electrodes. This results in a more focused ablation than with unipolar technology. As for unipolar technology, ablation occurs by resistive heating, but, as the energy passes between the two electrodes, temperatures reach 60–70°C between the electrodes but drops off quickly in neighboring tissue. Bipolar RF ablation results in discrete, transmural lesions, with no evidence of contraction or scarring.

In an animal model using bipolar clamps, microscopic examination showed that 99–100% of all lesions were transmural, continuous, and discrete with a single ablation using the conductance algorithm. Bipolar clamps are the fastest and most reliable devices for creating transmural lesions in open procedures, both on the beating and the arrested heart, with average ablation times between 5 and 10 s [13]. Compared to cryoablation, which can also effectively create transmural lesions when used for adequate time (2.5–3 min), bipolar RF use is faster. Pen devices can be effective but must be used with caution. The Isolator pen has been shown to be reliable in creating transmural lesions in tissue up to 8 mm in thickness. In several studies, the Coolrail linear pen created transmural lesions only 80% of the time with a single application of the devices, but it is reasonable to speculate that multiple applications may improve performance. With all RF devices, most non-transmural lesions occur at the ends of the line of ablation. Therefore, it is important to overlap the lesions when making an extended linear lesion to insure transmurality.

The more fearsome complication of unipolar RF (esophageal perforation) has been ward off by bipolar clamps, because, since energy application is between the jaws, extensive radiation of heat is impossible, thus preventing penetrating lesions of surrounding tissues. Nevertheless, side-by-side devices safety has not been still deeply evaluated.

The risk of creating pulmonary veins stenosis especially in case of multiple and repeated RF or cryothermal lesion lines theoretically exists, but only anecdotal cases have been presented in medical literature.

## **2.4. Treatment of concomitant AF**

### *2.4.1. Indications and exclusion criteria*

The Heart Rhythm Society Task Force on Catheter and Surgical Ablation of Atrial Fibrillation (2012) released an expert consensus statement that included indications for surgical AF ablation [14]. They recommended that surgical ablation should be considered as an additional procedure in all patients with symptomatic AF, with or without trial of antiarrhythmic drugs, in cases where these patients were already scheduled to undergo cardiac surgery for other indications. This represents a class IIa indication for paroxysmal, persistent, and long-standing persistent AF failing antiarrhythmic drugs and paroxysmal and persistent AF prior to a trial of antiarrhythmic drugs. It is a class IIb indication for long-standing persistent AF prior to a trial of antiarrhythmic drugs. In 2016, the European Society of Cardiology (ESC), in collaboration with the European Association for Cardiothoracic Surgery, released guidelines for the management of AF [15]. Concerning fibrillating patients undergoing cardiac surgery, they recommended that maze surgery should be considered in symptomatic patients with AF (class IIa) and may be considered in asymptomatic patients in AF (class IIb). The ESC AF guidelines also proposed that AF surgery and extensive ablations should be discussed by an “Atrial Fibrillation Heart Team” comprising a cardiologist with expertise in antiarrhythmic drug therapy, an interventional electrophysiologist, and a cardiac surgeon with expertise in AF surgery.

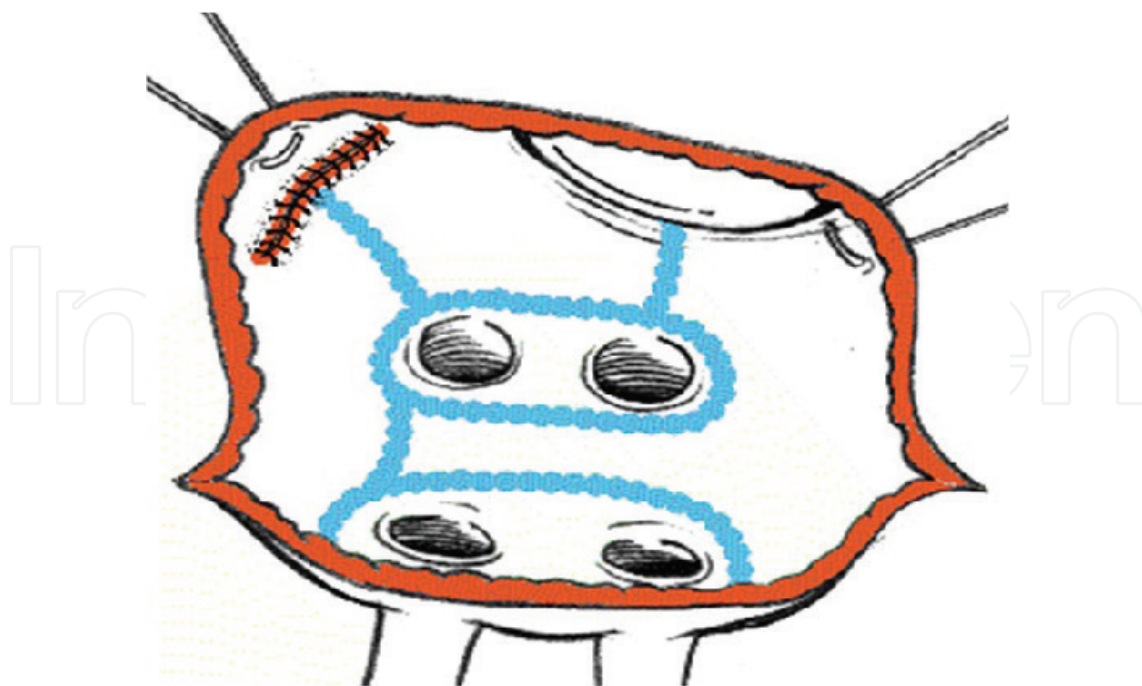
All these recommendations assume that both the patient and the surgery meet the necessary requirements for procedural success: suitable atrial anatomy (left atrial dimensions and fibrosis), AF time of evolution, favorable risk/benefit relation, and operator experience. More in detail, the main factors associated with scarce success rate of maze, thus representing a contraindication to the procedure, are [16] advanced patient's age (but no real cutoff has been identified), left atrial size superior to 60 mm or 135 ml/mq, and an arrhythmia duration longer than 60 months. All these features arise from different trials but do not play an uncontested and universally accepted role, even if it is reasonable to hypothesize that they well correlate with AF chronicity, which translates into more deeper pathophysiological changes in the left atrium rendering arrhythmia interruption more difficult.

#### *2.4.2. General surgical principles*

Many surgical variations concerning lesions sets have been proposed, ranging from the simple isolation of the pulmonary veins (PVI) to the complete biatrial approach originally described by Cox; all types of energy sources have been tested over time too. It is difficult to indicate what is the right approach for every AF category, because studies comparing the different maze variations are scarce and most frequently do not comprise large number of patients. The result is that no unanimous consensus exists and that the task of assessing if any of lesions sets or techniques is more effective is a real challenge. Nevertheless, thanks to our knowledge concerning AF pathophysiology, we can perhaps affirm that in case of paroxysmal arrhythmia not associated to mitral disease (where we may imagine that focal triggers around pulmonary veins origin play a major role in the absence of left atrial enlargement and histologic modifications leading to reentrant drivers perpetuating circuits), a simple procedure of PVI could be sufficient. On the contrary, when the patient is affected by persistent or permanent AF, a more extensive lesions set including left atrial Cox-maze IV lines (**Figure 6**) and, if possible, right atrial ablations seems to be the best option. In fact, such a wide approach should allow the highest chances of interrupting rotors maintaining arrhythmia. The same ablation protocol may also be applied if the principal pathology requiring surgery is a mitral disease, independently from AF type: as a matter of fact, mitral valve dysfunction (stenosis or regurgitation) causes left atrial dilatation, microscopic modifications, and fibrosis which constitute a perfect substrate for arrhythmia perpetuation, thus suggesting the opportunity of a more aggressive ablation treatment. An algorithm showing how the type of AF and the extension of the structural disease may affect the type of lesions set is presented in **Figure 7** [4].

#### *2.4.3. Outcomes*

Published reports of surgical ablation contain success rates of 60–90% [1]. Factors related to the probability of success include AF duration, left atrial size, patient's age, and adaptation of lesions set to arrhythmia type and underlying disease [16]. In case of Cox-maze IV lesions set application (for instance, for mitral patients or chronic AF), completed either with cryotherapy or a combination of RF and cryotherapy, 1-year and longer-term freedom from AF generally range from 65 to 85%; freedom from AF off antiarrhythmic drugs tends to be about 10% lower. Success rate dramatically drops if PVI alone is performed with persistent or long-standing persistent AF with a failure percentage joining nearly 80% of the time. Patients and surgeons must understand that



**Figure 6.** Modified left atrial Cox-maze IV.

the success of surgical ablation cannot be determined at the index hospitalization. During the first 6 months after surgery, half or more of patients experience atrial arrhythmias. One-year success is determined by a long-term Holter monitor (24 h or greater), confirming freedom from any episode of AF, atrial flutter, or atrial tachycardia that lasts more than 30 s. ECG alone overestimates the success by 10–15% when compared with long-term monitoring. According to guidelines, “true” success requires that the patient has no atrial arrhythmias and be off antiarrhythmic drugs. In practice, freedom from AF on antiarrhythmic drugs often represents a good clinical result. Annual follow-up with a Holter or other long-term monitor is necessary, as AF may recur overtime.

#### 2.4.4. Perioperative management

The two key management issues are heart rhythm and anticoagulation [1]. In the absence of evidence-based guidelines, clinical practice in these areas varies considerably. Because the Cox-maze IV does not immediately “cure” AF in most patients, both heart rhythm surveillance and management are necessary. Perioperative arrhythmia relapse occurs in at least half of all patients undergoing surgical ablation. The precise cause of perioperative AF is unknown, although changes in adrenergic tone and inflammation may contribute; these physiological conditions tend to subside with time. Preoperative  $\beta$ -blockers should be continued in all patients who do not have a contraindication. Anti-arrhythmic medications (more often amiodarone) may be administered as prophylaxis to all patients or only in case of new AF episodes, which must be aggressively treated by electric cardioversion if chemical one fails. Antiarrhythmic treatment should be maintained at least for 2 months after hospital discharge and then stopped in the absence of detected arrhythmia episodes; otherwise, it should be continued or restarted. Considering general maze success rate, about 20% of patients will have AF at 1-year mark: if antiarrhythmic medication has failed and symptoms persist, catheter ablation may be proposed with good outcomes. Concerning anticoagulation, as more than 50% of patients experience perioperative

AF after maze, warfarin should be continued for several months after the intervention. It is reasonable to discontinue such treatment if, at 6-months check, no AF episodes have been detected with a 24-h periodical Holter monitor, atrial contractility is fully restored at transthoracic echocardiography, LAA is well controlled, and no other indication for anticoagulation exists. Although some suggest that this decision should depend on the CHADS2 score, recent data advocate that it cannot be applied to the surgical patient. The effective LAA exclusion “per se” does not allow safe warfarin interruption, since the risk of stroke is reduced but not eliminated (two to four events per 1000 patient years) after a Cox-maze IV procedure.

2.4.5. Clinical benefits and risks of maze

It is commonly accepted that, by one side, AF presence in cardiac surgery patients is associated with increased risks of death and stroke in follow-up and, by the other, that freedom from symptomatic AF and warfarin taking (objectives frequently achieved by maze) represents important advantages. Nevertheless, there is no conclusive proof—a randomized, controlled

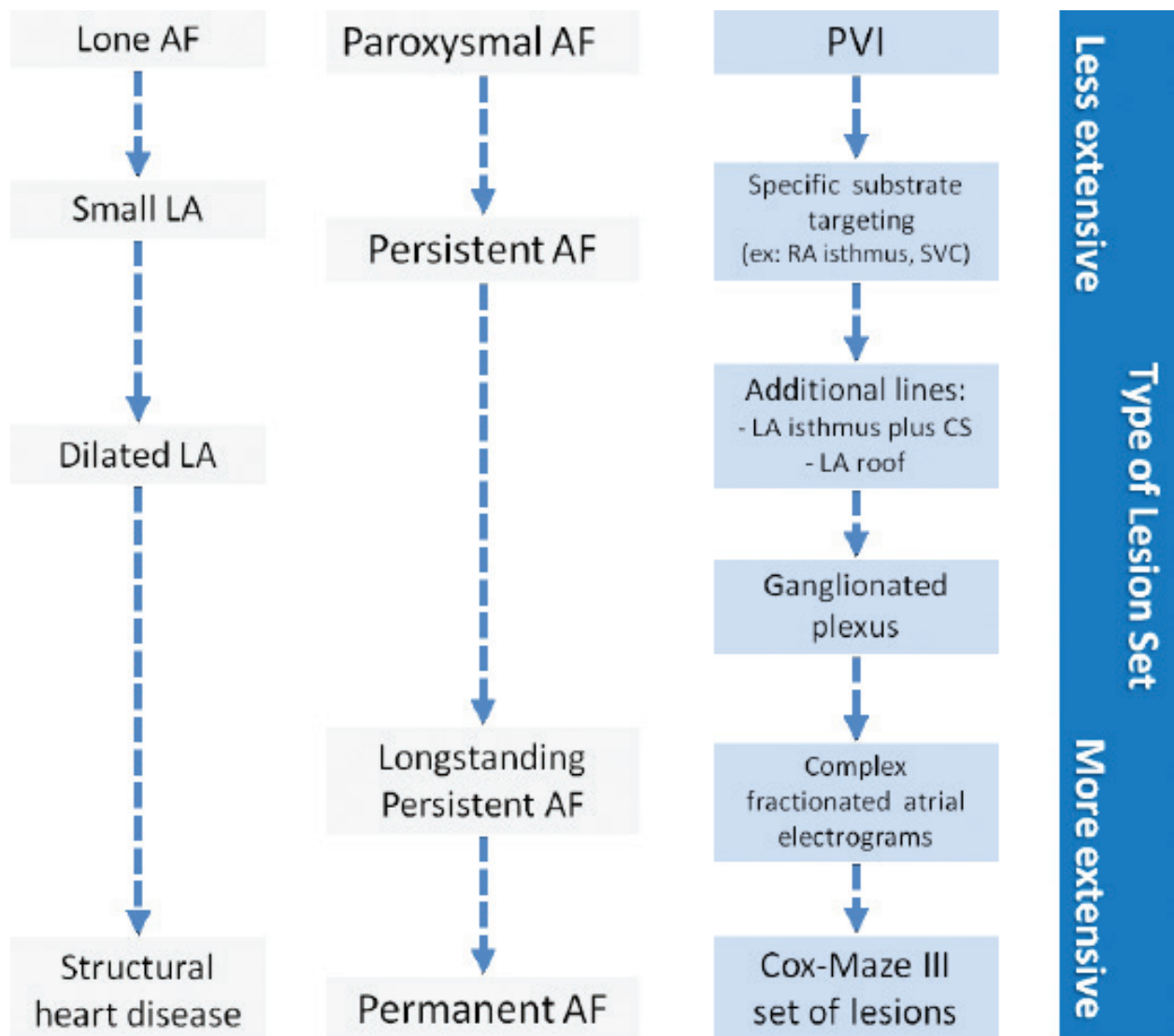


Figure 7. AF type, structural disease and lesions sets.

clinical trial—confirming that the surgical treatment of AF reduces long-term morbidity and mortality. However, we know that a successful medical and catheter-based treatment reduces late events. Observational studies, many of which employed propensity matching, suggest that successful surgical ablation has similar effects, reducing both late mortality and risk of stroke. When taking all of the available evidences together, the International Society of Minimally Invasive Cardiothoracic Surgery (ISMICS) consensus statement concluded that concomitant ablation was indicated to increase the incidence of SR at short- and long-term follow-up (class 1, level A), improve ejection fraction and exercise tolerance (class 2a, level A), and reduce the risk of stroke and thromboembolic events and improve long-term survival (class 2a, level B) [17].

In general, the addition of a Cox-maze procedure for concomitant AF ablation does not increase surgical risk as confirmed by several clinical series [18]. In addition, recent data suggest that although approximately 5% of AF patients require a permanent pacemaker after a Cox-maze IV procedure, this does not represent an increase over the pacemaker implantation rate when AF is left untreated. Finally, the surgical ablation of AF does not increase intensive care unit or hospital length of stay. Using alternate energy sources, surgical maze adds 20–25 min to the cardiopulmonary bypass time; moreover, if right atrial and PVI lesions are performed on the beating, decompressed heart, myocardial ischemic time is minimized. For most patients, the additional pump and cross-clamp times pose no supplementary clinical risk.

#### *2.4.6. Debated issues: RA ablation and LAA management*

In case of chronic AF or in mitral patients, the addition of RA lesions increases the effectiveness of surgical ablation by 10–15% [19]. The standard set proposed by Cox includes the following three distinct lesions: (1) a small (1-cm) incision in the right atrial appendage, which provides access for the creation of a cryolesion to the tricuspid annulus (tricuspid lesion at the 10-o'clock position); (2) an incision in the RA body that terminates with a second cryolesion at the tricuspid annulus (tricuspid lesion at the 2-o'clock position); and (3) an intercaval lesion that extends from the superior vena cava to the inferior one. It is a mistake to add a classic “flutter line” (cavotricuspid isthmus ablation) to this lesion set, as it is unnecessary and slows intra-atrial conduction. Creation of the standard RA lesions requires no more than 10 min and can be completed with the heart arrested or beating on cardiopulmonary bypass.

Management of the LAA is mandatory [1]. A recent prospective, randomized controlled trial confirms that percutaneous occlusion of the LAA reduces the risk of stroke in patients with AF. Successful surgical LAA management requires its complete excision or exclusion with a residual stump less than 1 cm in length [20]. Surprisingly, several studies demonstrate inadequate surgical management of the LAA, with residual flow after both endocardial and epicardial ligation and large stumps after stapled and surgical excision. New epicardial occlusion devices enable safe, rapid, and complete LAA exclusion; prospective trials confirm their effectiveness. If the surgeon chooses to use suture to exclude the LAA, a single endocardial pursestring or epicardial loop is inadequate. Endocardial exclusion should incorporate a two-layered closure and epicardial one at least two sutures.

#### *2.4.7. Comparison of available sources*

Nowadays, only RF and cryotherapy remain as available sources and are currently used in medical practice separately or in combination with a similar success rate. Due to the possibility

of associating different lesion line sets in different patients' category performed with unipolar, bipolar RF, or cryotherapy according to surgeon's preference and habits, there is a lack of randomized-prospective trials really comparing the performance of these two technologies which are thus both accepted and employed in concomitant AF ablation.

## 2.5. Treatment of stand-alone AF

### 2.5.1. Indications

The Heart Rhythm Society Task Force on Catheter and Surgical Ablation of Atrial Fibrillation (2012) recommend that surgical ablation may be considered as a stand-alone procedure in patients who have failed antiarrhythmic drugs and who have either failed catheter ablation or who prefer surgery over catheter ablation (class IIb indication) [14]. Stand-alone surgical ablation in patients who have not trialed antiarrhythmic drugs represents a class III indication [14]. ESC guidelines (2016) [15] report that catheter or surgical ablation should be considered for symptomatic control in all cases of persistent or long-standing persistent AF that is refractory to antiarrhythmic drugs (class IIa indication). They also recommend that minimally invasive PVI should be contemplated where catheter ablation failed in symptomatic AF and that maze surgery should be considered in refractory symptomatic AF or post ablation AF to reduce symptoms (class IIa indications).

### 2.5.2. Minimally invasive surgical techniques and the hybrid approach

Although surgical ablation for AF is much less frequently performed as a stand-alone procedure compared to its use as a concomitant procedure, the initial report of the Cox-maze procedure was as a stand-alone procedure and was successful in providing freedom from AF in all 22 patients at 3 months [14]. The open sternotomy, "cut-and-sew" Cox-maze III procedure, has been used as a stand-alone procedure for the treatment of AF in some centers, with reports showing a success rate of 95.9% at long-term follow-up with no significant difference when compared to Cox-maze III as concomitant procedure (97.5%). Nevertheless, maze represents a very invasive operation requiring median sternotomy and, also in experienced hands, 45–60 min of cardiopulmonary bypass and cardiac arrest; as a result, efforts have been made to reduce the operative aggression in parallel with the introduction of alternative energy sources for ablation, reducing the need for "cut-and-sew" incisions. Such an approach led to the development of minimally invasive AF surgery [14, 21]. Two main operative techniques have been described:

1. A bilateral thoracoscopic approach consisting in a video-assisted bilateral mini-thoracotomy or thoracoscopic pulmonary veins island creation and LAA removal or exclusion, usually with ganglionic plexus evaluation and destruction. A monolateral approach is also possible but is technically more demanding since the device must encircle the pulmonary veins in one time passing through the transverse and the oblique sinus.
2. A right-side thoracoscopic approach with two or three ports, presenting the limitation of the inability to remove the LAA.

Nevertheless, results of mini-invasive epicardial surgical ablation were below expectations, above all when compared with those of open Cox-maze IV and cut-and-sew maze. More in detail, this



was particularly true in case of non-paroxysmal AF, with a rate of freedom from arrhythmia recurrence equal to 43% for long-standing persistent AF patients. A recent systematic review estimated a 10–20% higher rate of recurrent atrial arrhythmias after minimally invasive surgery as compared to open ablation-based surgery. Based on these findings, the attention of cardiac surgeons and of cardiologists focused onto the comprehension of the reasons of such failure and, thanks to careful electrophysiological observations, highlighted that often transmural ablation was not achieved by current ablation tools applied endoscopically on the epicardium of the beating heart.

To overcome these limitations of minimally invasive surgical ablation as a stand-alone procedure in abolishing AF, hybrid ablation was developed, incorporating an adjunctive percutaneous catheter procedure to bridge conduction gaps in the anatomically based surgical ablation lines as well as additional targets determined electrophysiologically [22]. As a result, respective advantages and limitations were overcome and combined, allowing a relevant technical innovation.

The concept of “hybrid” procedure was first published by Pak et al. [23] who combined percutaneous epicardial catheter ablation and endocardial ablation in difficult cases of AF. According to this initial experience, other groups published their encouraging results (early freedom from AF superior to 80%) with various hybrid techniques. Actually, three different techniques are employed, each utilizing unique RF ablation tools (**Figure 8**) [21]:

1. bilateral thoracoscopy with circumferential and linear lesions (LAMP [La Meir, Ailawadi, Mahapatra, Pison] hybrid ablation) created using bipolar RF clamps and ablation pens (Atricure, West Chester, OH), respectively;
2. right-sided thoracoscopy with simultaneous isolation of PV and posterior left atrium using a suction monopolar RF catheter (Estech Cobra Adhere XL, Atricure, West Chester, OH) designed to deliver an encircling linear lesion;
3. Subxiphoid posterior pericardioscopy (through laparoscopic incision of the central diaphragmatic tendon) with linear ablation using a vacuum irrigated unipolar RF device (Numeris guided coagulation system with VisiTrax, nContact surgical, Inc., Morrisville, NC, USA) to isolate or debulk the posterior left atrium and partially isolate the pulmonary veins

PVI was a common end point in all studies. In addition to the differences in epicardial lesions created by these very different strategies and tools, the timing of the endovascular catheter component also varied widely, from being performed immediately after surgery or after a delay ranging from 4 days to 3 months. Potential advantages of the “immediate staged” strategy compared to the “delayed staged” one are (1) there is no risk of tamponade during the trans-septal puncture since the pericardium is open; (2) the surgeon can protect the phrenic nerves and the esophagus and the effective surgical ablation reduces the fluoroscopy time; (3) thromboembolic events rate consequent to endocardial ablation is reduced since the majority of lesions lines are performed epicardially.

Nevertheless, the hybrid procedure is time-consuming and the need of heparinization after septal puncture just following the “surgery time” may cause major bleeding of dissected areas.

The endovascular component itself varied significantly between studies, such as whether electroanatomical mapping was utilized, the choice of linear ablation lesions, and which patients these were performed in, whether physiological targets such as triggers and complex fractionated atrial electrograms were targeted and selection of end points including intraprocedural confirmation of conduction block and re-induction protocols. Many other aspects greatly varied among the different approaches, such as ganglion, LAA, and ligament of Marshall management and peri-procedural medical treatment. Such diversity in approach is not surprising given the relative infancy of minimally invasive surgical AF ablation and the novel ablation tools used, as well as lack of consensus within the ablation community itself on optimal strategies for persistent and long-standing persistent AF.

### 2.5.3. Outcomes of the hybrid approach

Published success rates from hybrid ablation, defined as maintained SR off antiarrhythmic medications at 12 months, are 74.3% overall (76.9% for paroxysmal and 73.4% for persistent/long-standing persistent AF patients) [21, 22]. The three described techniques failed to achieve the same results in terms of freedom from AF recurrence, with the LAMP approach showing

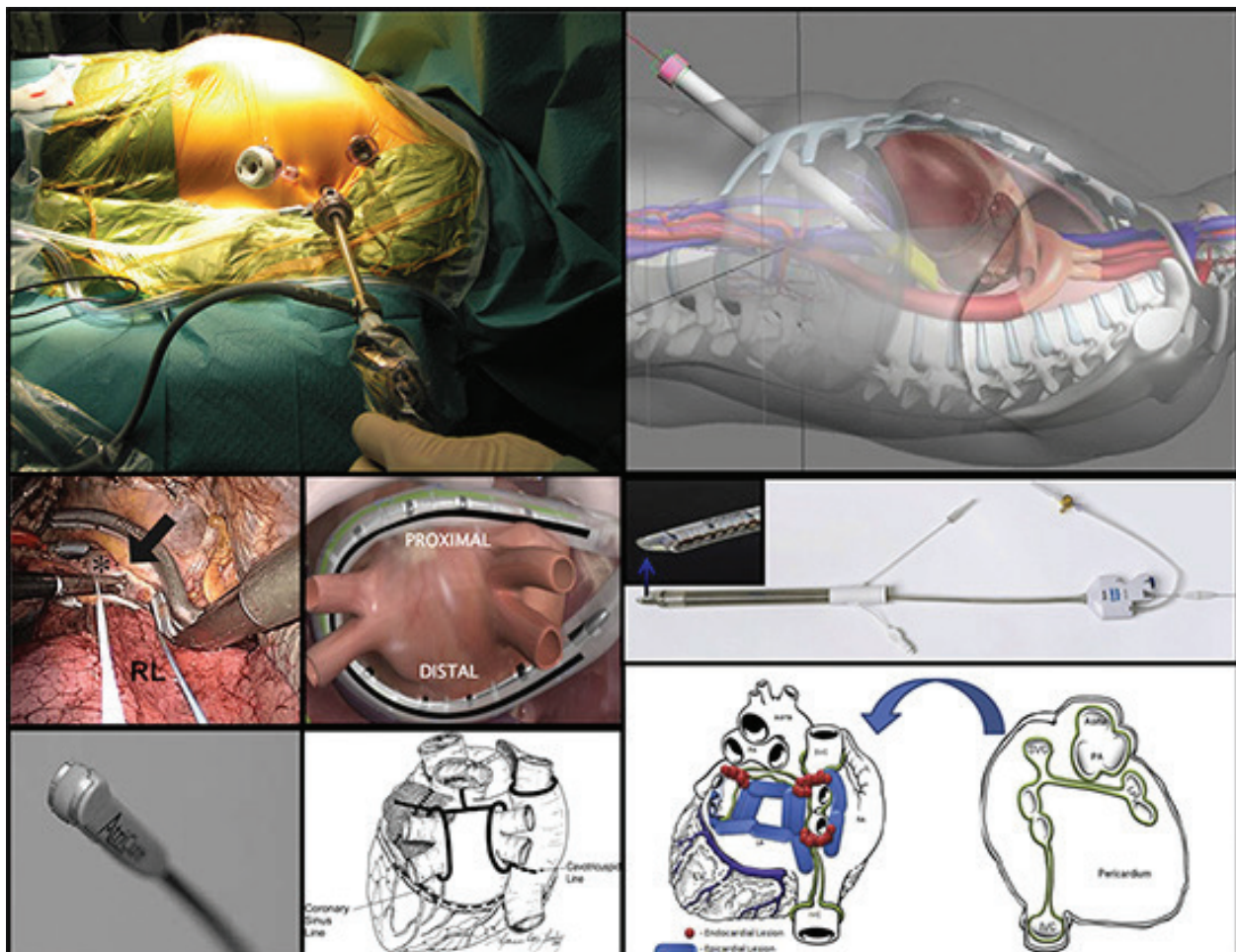


Figure 8. Hybrid ablation: access, tools and lesions sets.

the best performance (88%) and the subxiphoid posterior pericardioscopy the worst (59.3%). Even the percentage of death or non-fatal complications greatly varied from 8.5% of the bilateral approach to 0% right-sided thoracoscopy. The average length of hospital stay was between 3.6 and 7 days. A limited number of trials comparing the hybrid procedure versus sequential catheter ablation are available, but hybrid results seem to be superior than the endovascular alone ones, but with increased complications rate and longer post-procedural hospital stay.

### 3. Conclusions

The aim of the present treatise is to show that, thanks to the evolution in arrhythmia pathophysiology understanding, it has been possible to develop a series of different technological tools and options able to treat even long-standing persistent lone or concomitant AF, permitting a tailored procedural offer to every single patient including pure endocardial ablation, pure surgical procedures (especially for concomitant cases), or a cooperation of both (hybrid strategies).

Undoubtedly, the way is still long, since several aspects of the treatment require improvements: concerning concomitant chronic AF, first of all, rate success should be augmented by trying to develop energy sources and technologies able to achieve transmural ablation in the totality of cases; secondly, it should be important to join an unanimous consensus onto lesions set schema to apply, but such objective cannot be independent from a full comprehension of arrhythmia pathogenesis.

Even with reference to lone AF, understanding arrhythmia mechanisms is crucial in view of developing less invasive techniques [21]. More in detail, recent studies are now more focused on the role of autonomic ganglia in being the true triggers and perpetuators of AF and perhaps they will rapidly become the main target of future ablation techniques.

Furthermore, results of the hybrid approach are encouraging but far from perfect, especially in case of persistent and long-standing persistent AF and need to be confirmed in larger and stronger trials also allowing comparison with last-generation catheter-based ablation tools. Nevertheless, we can speculate that the success rate in the treatment of lone AF may probably rely on a close collaboration between surgeons and electrophysiologists, implying the use of “a common language” and information exchange.

In conclusion, by highlighting that midterm success results in terms of SR maintenance without antiarrhythmic drugs are satisfactory, ranging from 60 to 90% depending from AF type and ablation technique, such a comprehensive essay would like to represent a useful instrument for clinicians, allowing them to hypothesize and recommend an adapted treatment to their fibrillating patients.

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