

# Cox-maze procedure: One-size-fits-all for different choices. Concomitant and stand-alone atrial fibrillation. Techniques and evolution.

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The Cox-maze procedure is a surgical technique that has been especially designed in order to eliminate all possible cause for atrial fibrillation or flutter. It is composed by a set of surgical incisions or burn lines strategically placed in both atria, so the electric impulse can be conducted from the sinus node to the atrioventricular one whilst preserving the contractile and transport function in the atria. With the current incessant ebb and flow towards minimally invasive surgical techniques, several possibilities of performing the Cox-maze procedure are now at hand. The endocardial Cox-maze, epicardial surgical ablation, hybrid procedure and convergent procedure are just a mere example for this kind of procedures. While the approach for the concomitant AF is by on-pump procedures, in the case of the stand-alone AF is eminently through off-pump techniques. In this article, we sought to review the current status and applications for the Cox-maze procedure accordingly the type of AF, as concomitant or stand-alone AF.

**Key words:** Atrial Fibrillation; Atrium; Arrhythmia; Cox-maze procedure; Concomitant atrial fibrillation; Left atrial appendage; Stand-alone atrial fibrillation.

El procedimiento de Cox-maze es una técnica quirúrgica que ha sido especialmente diseñada para eliminar todas las posibles causas de fibrilación auricular (FA) o flutter. Está compuesto por un conjunto de incisiones quirúrgicas o líneas de quemaduras estratégicamente colocadas en ambas aurículas, de manera que el impulso eléctrico se pueda conducir desde el nódulo sinusal al atrioventricular, conservando la función contráctil y de transporte de ambas aurículas. Con el flujo y reflujo incesante actual hacia técnicas quirúrgicas mínimamente invasivas, existen varias posibilidades de realizar el procedimiento de Cox-maze. El procedimiento de Cox-maze endocárdico, la ablación quirúrgica epicárdica, el procedimiento híbrido y el procedimiento convergente son solo un mero ejemplo de este tipo de procedimientos. Mientras que el abordaje de la FA concomitante es mediante procedimientos con bomba, en el caso de la FA aislada es eminentemente a través de técnicas sin bomba. En este artículo, buscamos revisar el estado actual y las aplicaciones para el procedimiento de Cox-maze de acuerdo con el tipo de FA, como FA concomitante o aislada.

**Palabras clave:** Fibrilación auricular; Aurícula; Arritmia; procedimiento de Cox-maze; Fibrilación auricular concomitante; Orejuela izquierda; Fibrilación auricular aislada.

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Atrial fibrillation (AF) is the most sustained cardiac arrhythmia world-wide [1]. Approximately 2.3 million US adults currently have AF. Overall general prevalence is 0.95% in adult population, being more common in men (1.1% vs 0.8%,  $p < 0.001$ ), with an ever increase from 0.1% in adults younger than 55 years to 9.0% in older than 80 years or older [2]. It is estimated that 12.1 million people

in the United States will have AF in 2030, with an increase of 2.5-fold by 2050 [3-6].

The sole presence of AF increases 5-fold the chance for stroke [7], 3-fold for heart failure [8-10], and 2-fold for dementia [11] and mortality [8].

The progression from paroxysmal AF to persistent or long-term persistent AF at 1 year is from 10% to 20%, with a progression up to 50% - 77% after 12 years of follow-up [12].

Regarding the number of patients having preoperative AF undergoing cardiac surgery, an analysis from the STS National Database between July 1, 2011 and June 30, 2014, a total amount of 837,978 cardiac operations were registered. Out of them, 112,401 (13.4%) had preoperative AF. Of them, 86,941 (non-endocarditis nor emergent cardiac surgery) were candidates for surgical ablation. In turn, 42,066 of 86,941 of these patients (48.3%) underwent surgical ablation for AF [13]. Of note, only 3.26% (2,836 of 86,941) were stand-alone AF cases, and 96.7% were concomitant AF. The mitral valve group with or without concomitant procedures (CABG, AVR) had the highest rate for surgical ablation [13].

### BASIC CONCEPTS IN ATRIAL FIBRILLATION AND THE COX-MAZE PROCEDURE

#### *First concept: paroxysmal and non-paroxysmal AF.*

In paroxysmal AF, the pulmonary vein triggers are the main responsible for the ectopic electric impulses generating the AF. Under normal circumstances, such as normal or nearly normal atrial myocardium, these electric impulses tend to disappear on their own. The same situation can be repeated over and over again, giving rise to a new "paroxysm". In such a way, it can be called paroxysmal AF. However, after certain special circumstances in the atrial myocardium [14,15], the paroxysmal AF can become non-paroxysmal AF. Now, the arrhythmia can stay in the atrial myocardium for longer. Since it is not dependent on the pulmonary vein triggers anymore, the non-paroxysmal AF is self-sustained by means of some macro reentrant circuits (also known as rotors, mother-ro-

tors, or drivers) located anywhere in both atria. In this context, it is quite understandable that the simple pulmonary veins isolation is not enough to eliminate the non-paroxysmal AF. A much more complex strategy is necessary in order to eliminate this arrhythmia [16]. (Fig. 1).

#### *Second concept: the size of the macro reentrant circuits.*

The minimum size of these rotors to sustain AF in the human atria is 6 cm in diameter or even longer [17]. Considering that the fibrocyte does not conduct the electricity, any consequential fibrotic line can act as a wall or barrier. Surgical incisions or burn lines both produce fibrocytes. Hence, if two separate incisions or burn lines are placed on the atrial myocardium less than 6 cm one from the other, then no enough space for the development of the macro reentrant circuit. That means to say that there is no more AF as final result. By strategically placing some surgical incisions or burn lines through both atria (not just in the left atrium), a labyrinth (or maze) can be obtained (Fig. 2).

#### *Third concept: The map for the Cox-maze procedure.*

With this framework, a map of the procedure can be achieved and translated from the theory into the practice. The electric impulse must be conducted from the sinus node to the atrioventricular node while preserving the contractile and transport atrial function (Fig. 3). When all anatomic structures in both atria are considered, all incisions can be placed all along both atria. Thus, the map of the Cox-maze procedure is conceived in a bi-atrial fashion. The Cox-maze procedure must be understood as a full bi-atrial procedure [18,19]. (Fig. 4).

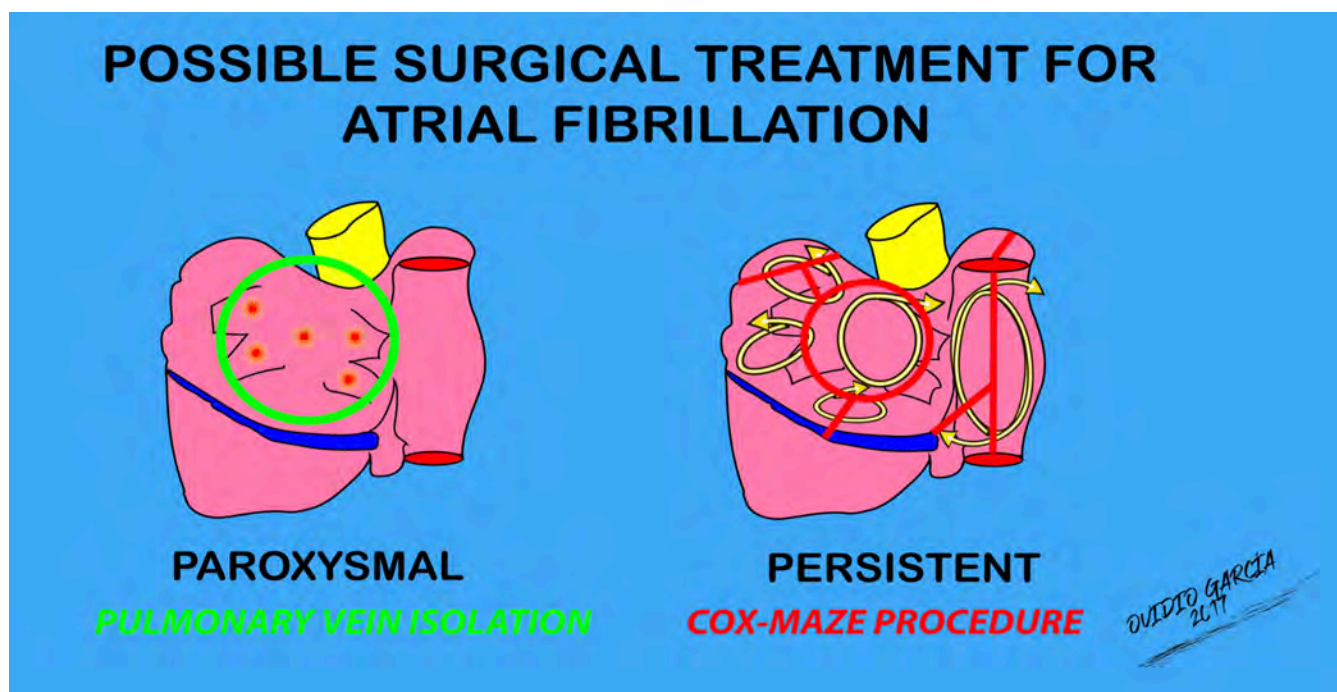


Figure 1. The two main types of atrial fibrillation and the proposed different surgical ablative strategies according the type of atrial fibrillation.

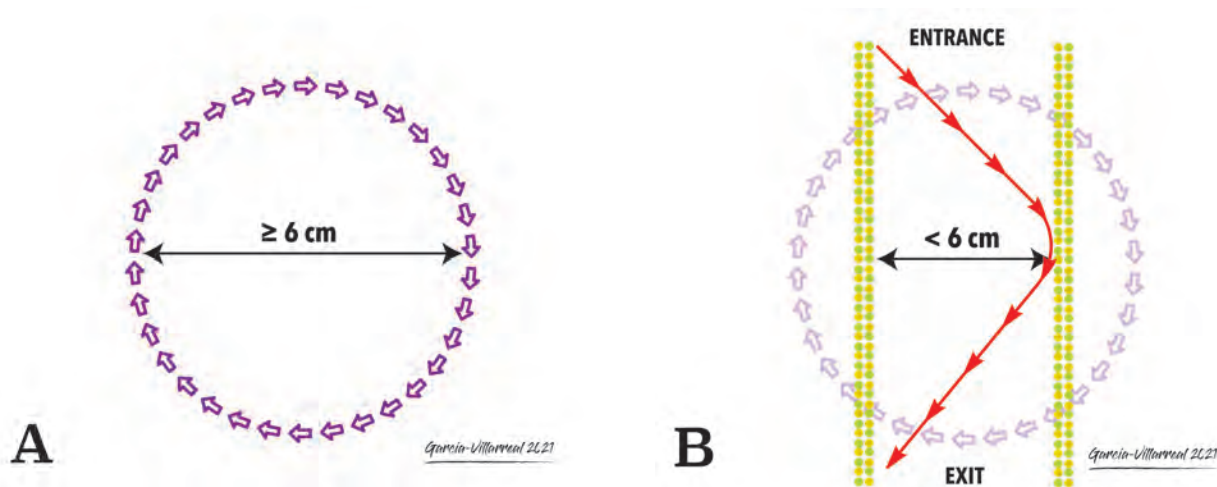


Figure 2. A: The macro reentrant circuit (also called driver, rotor or mother-rotor) sustaining the atrial fibrillation in the human atria. B: Two burn lines or surgical incisions, represented by the dotted lines, which are separated less than 6 cm one from the other. Red arrows represent the electric impulse which is not able to move in circles anymore to generate macro reentrant circuits. So, if no enough space or continuous tissue, therefore, there cannot be atrial fibrillation anymore. This is the principle of the Cox-maze procedure.

#### The evolution of the Cox-maze procedures.

From the very beginning to the present time, there have been several iterations in order to improve the efficacy of the Cox-maze procedure. The first reported procedure used to treat AF in the human being was the left atrial transection. It took place in October 13, 1986, at the Barnes Hospital, in St Louis, Missouri, US [15]. It goes without saying it was not a true Cox-maze procedure. The first true Cox-maze procedure goes all the way back to September 25, 1987, and it was performed by Dr. James L. Cox at the aforementioned Barnes Hospital. Interestingly, the previously mentioned left atrial transection was surgically converted to Cox-maze procedure in September 07, 1988, being the second officially recognized Cox-maze procedure [20]. By the first days of January 1992, after having several inconveniences regarding the chronotropic issue, the Cox-maze II procedure was brought into existence. Shortly thereafter, in April 1992 the original Cox-maze III procedure was developed and performed as it stands now [personal communication by Dr. James L. Cox]. However, all these procedures are made by means of “cut-and-sew” Thus, all of them are very time-consuming procedures. Nevertheless, by replacing most of these surgical incisions by burn lines utilizing some alternative energy sources, we can obtain an easier, faster and safer procedure, known as Cox-maze IV procedure, ever since 2002 [21]. Certainly, in 2003, the U.S. Food and Drug Administration cleared one of the marketing available bipolar surgical radiofrequency ablation tool. Therefore, since 2004, the industry launched the widespread use of the bipolar radiofrequency devices for AF surgery [22].

#### ALTERNATIVE ENERGY SOURCES FOR THE COX-MAZE IV PROCEDURE.

The only proved alternative energies getting full transmural in the burn lines are the bipolar radiofrequency ablation and cryolesion. The epicardial unipolar radiofrequency or unidirectional bipolar RF ablation have a questionable efficacy [23]. Cryolesion has demonstrated to have high efficacy when is used to perform the Cox-maze IV procedure. Consequently, we assume that a full transmural is guaranteed by using cryolesion as ablation device [24-26]. In fact, cryosurgery has revolutionized the surgery for cardiac arrhythmia improving the efficacy of the procedure getting full transmural in a consistent way [27].

With respect to radiofrequency (RF) ablation, it has been demonstrated that the only useful in terms of getting consistent full transmural is the bipolar RF. Unipolar RF has very limited power to produce transmural lesions [28, 29]. Nevertheless, several issues are to be considered in the daily practice. Bipolar RF is highly dependent on the time of application. However, the longer the application time and the more intensity, the greater the possibility of bubble formation between the burned tissue. In addition, steam pop formation is related to a greater drop in impedance than lesions with no steam pop formation [30]. In common parlance, it means incomplete transmural in burn lines. Another problem we have to analyze is the despair pressure force in the bipolar clamp for bipolar RF ablation. This clamp has different pressure profiles affecting the degree of transmural [31]. In addition, every 1 mm increase in overlying fat decreased the possibility of transmural by 11% [31]. Because of the

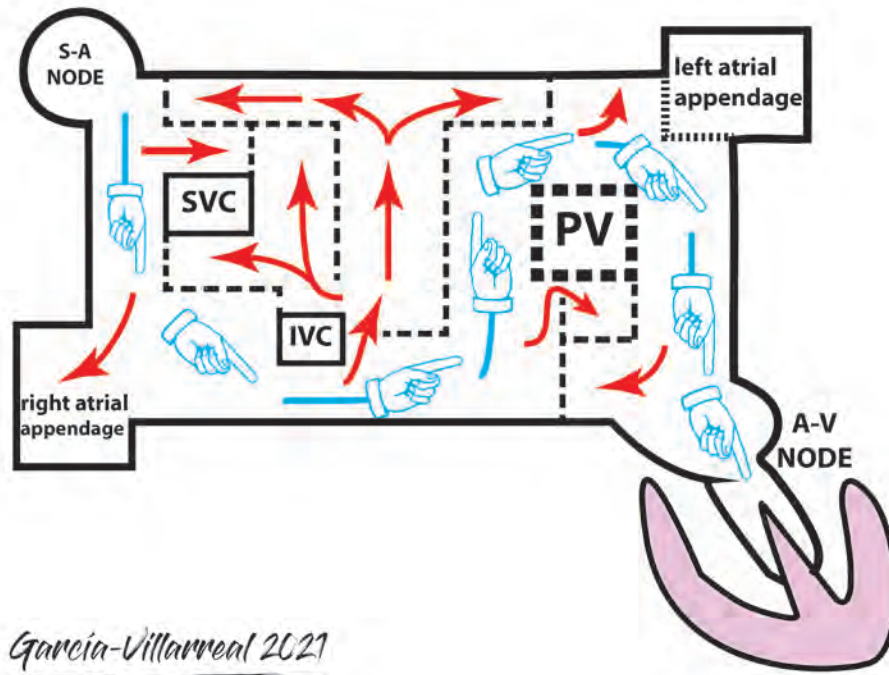


Figure 3. Map for the Cox-maze procedure. Of note, both atria are involved in the design of the Cox-maze procedure. It results more than impossible to conceive the Cox-maze procedure out of the continuum of the both atrial myocardium.

epicardial fat, one single ablation can fail to create a transmural lesion in 35% of the times; hence, two ablations without releasing the clamp resulted in 100% of transmural lesion with the bipolar RF clamp [32]. Finally, the importance of producing ischemia between the clamp jaws for delivering bipolar RF is a matter of great concern, since it can affect the algorithm for full transmural lesion: Hence, we cannot be sure if transmural lesion is due to colliquative necrosis or just simple temporary ischemia in the atrial tissue [33].

Needless to say, all the other alternative energy sources have not demonstrated true consistency to produce full transmural lesion in the human alive atrial tissue.

#### EFFECTIVENESS OF THE COX-MAZE PROCEDURE

After all information that we have reviewed thus far, the question arises as to how effective is the maze procedure. We analyze both modalities, the classic Cox-maze III procedure by means of “cut-and-sew” as well as the Cox-maze IV utilizing bipolar RF ablation with cryoablation or just cryoablation. We analyzed the results from studies showing the outcome from 1-year to 8.5-years follow-up. We only included those reports working under the form of full bi-atrial lesion pattern, regardless the treatment for concomitant or stand-alone AF. The standard “cut-and-sew” Cox-maze III remains as the gold standard for surgical ablation of AF, with results around 90% of effectiveness in terms of freedom from AF [34-44] (Fig. 5). The Cox-maze IV, only including papers using bi-atrial ap-

proach by means of bipolar RF ablation in combination with cryoablation, or just cryoablation for the whole procedure, the development of the procedure is reflected in the statistics, from 2-years to 7-years follow-up, between 90% and 61% for recovery of sinus rhythm [45-52] (Fig. 6). Despite there was a large variability in the outcome for different surgical groups in the CURE-AF trial ranging between 33% and 100% for freedom from AF [53], the Cox-maze IV is highly recommended to be used for our daily practice nowadays.

#### HOW TO DO IT THE COX-MAZE IV PROCEDURE IN THE CURRENT ERA

To answer this question, we have to recognize that there is a critical need to make a gross division between the two types of AF which we can figure out in our daily practice. Firstly, the most common type of AF seen in patients undergoing cardiac surgery is the concomitant AF. In turn, the most frequent association is with mitral valve disease, although it may be seen in combination with aortic valve disease or coronary artery disease, among many other pathologies. In patients undergoing primary non-emergent cardiac surgery, up to 13.4% had preoperative AF. Out of them, 96.7% had concomitant AF, and only 3.26% as stand-alone AF [13].

In recent years, there has been a growing interest in the possible therapeutic usefulness as mini-invasive procedures. The Cox-maze procedure is not the exception to that trend. Ever since 2002 when the Cox-maze IV, also called “electric”

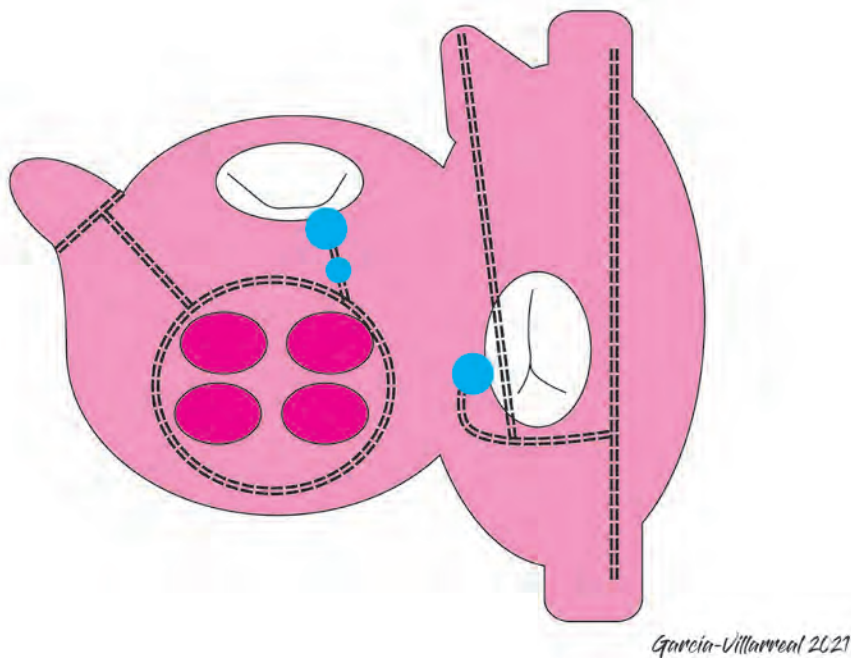


Figure 4. Schematic representation of the full bi-atrial lesion pattern of the Cox-maze procedure. The same pattern is applicable to the Cox-maze III as "cut-and-sew" as well as to the Cox-maze IV with alternative energy sources, regardless the approach, through full median sternotomy, bilateral or unilateral approach by videoscropy, etc.

Cox-maze, was brought to light [54], the possibility of performing the same operation through a right mini-thoracotomy began to take root. Nowadays, it is a well standardized technique which has been previously published yet [55, 56]. Needless to say, the key point is always performing the procedure as a full bi-atrial procedure [57].

The author has previously published how to perform the classic Cox-maze IV procedure through a full median sternotomy [58].

## CONCOMITANT AF

### Endocardial Cox-maze procedure

In the context of concomitant AF, we previously cited above, the mitral valve disease is the most common underlying pathology in cases with concomitant AF. As such, the whole matter can be approached through the same right mini thoracotomy. However, the procedure must be performed on pump including aortic-cross clamping [56]. The so-called endocardial Cox-maze procedure is a very good case in point in order to illustrate this technique [59]. Apparently, this represents a real disadvantage when compared to other lesser invasive procedures. Nevertheless, this on-pump technique has proved that it can be as safe as the other off-pump procedures, in term of mortality and morbidity, as well as efficacy in freedom from AF [60]. Overall freedom from AF of 90% and 79% off-ADD has been described with the endocardial Cox-maze procedure [61]. Another point to underline is the efficacy and

safety in terms of mortality, morbidity and the like by using the mini-invasive Cox-maze IV. No differences in mortality or freedom from atrial tachyarrhythmias between the classic approach and the endocardial one for the procedure [62]. Overall complication rate was lower when compared to the standard approach (6% vs. 13%,  $p=0.044$ ), as well as the early mortality rate (0% vs. 4%,  $p=0.039$ ) [63].

Now, in terms of concomitant AF, how safe is the procedure? does it add morbidity or mortality? By using the classic Cox-maze IV procedure by median a full sternotomy, we previously knew that there is no important difference in this regard. No additional perioperative morbidity is added with the Cox-maze procedure [23, 64]. In fact, in the setting of mitral valve disease, the concomitant AF (persistent or long-standing persistent AF) is currently a recommendation class I level of evidence A to be treated in the course of the mitral valve operation [57].

Nonetheless, specifically speaking about the combination of mitral valve surgery with Cox-maze IV procedure by means of mini-invasive operation, as endocardial Cox-maze, Jiang et al. [65] have demonstrated that not only was it possible to perform, but that the results were much better when the right mini-thoracotomy approach was used for this purpose. Postoperative ventilation time, length of stay in ICU, in-hospital stay, and blood transfusion were in favor of right mini-thoracotomy as approach for the endocardial Cox-maze procedure and mitral valve surgery ( $p < 0.001$ , for each of the subsets above) [65].

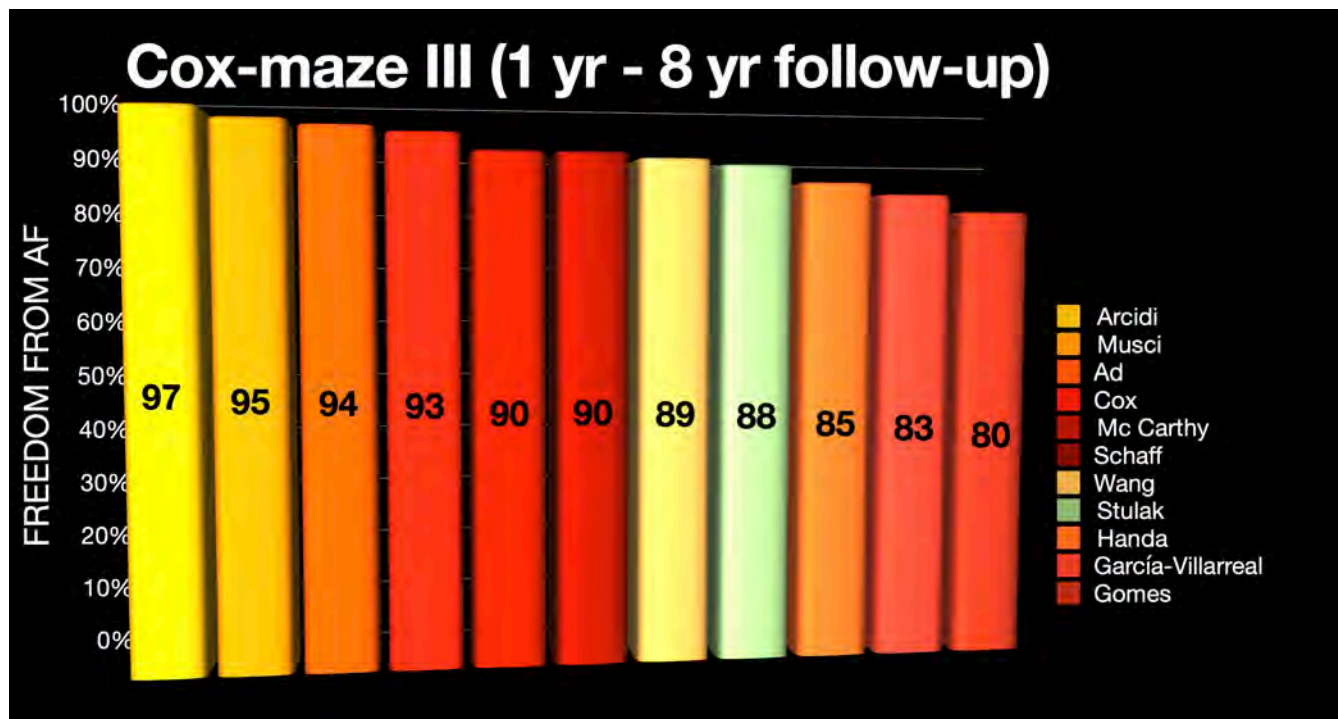


Figure 5. Results of the Cox-maze III procedure using the classic "cut-and-sew" technique.

Given the fact that the mitral group is the large one exhibiting concomitant AF, all the aforementioned constitutes the core part of this discussion. However, shall we say that, in the setting of aortic valve disease and CABG with concomitant AF, the procedure can be added with no additional risk of operative mortality or important morbidity. Actually, this represents an indication I, level of evidence B [57].

We should emphasize the fact that no additional risk for operative mortality or morbidity is observed after utilizing the on-pump endocardial Cox-maze procedure. On that note, cardiological community should be reeducated in order to be more expansive with our spreading recommending the endocardial Cox-maze procedure in a more extensive way, regardless the underlying type of AF.

#### STAND-ALONE AF

This special type of AF is presented with no underlying structural cardiac pathology explaining the presence of the AF. Most often, this is the result of a failure in the antiarrhythmic medical treatment, or after several failed attempts of catheter ablation. To the best of our knowledge, operative morbidity or mortality remains unaltered when using the mini-invasive Cox-maze procedure IV as a treatment for stand-alone AF [23, 57]. When the stand-alone AF is the result of refractoriness to AAD or catheter ablation or both, the Cox-maze procedure is recommended under the form of Class IIA, Level B randomized. Moreover, the full bi-atrial lesion pattern is recommended to be used in this kind of patients [57].

In the light of the foregoing, the premise of being more invasive, more lethal and with more potential complications when using "on-pump" procedures, such as endocardial Cox-maze procedure, cannot be sustained for longer [60-63]. Unfortunately, the general feeling towards lesser invasive procedures seems to exceed up to expectations. The concept about "off-pump" procedures turns out to be very attractive for people who are not plunged into these special procedures, even when no solid arguments underpinning this ebb and flow of information can be identified as of yet. As a result, a second wave as "off-pump" surgical ablation procedures have been proposed in order to surgically treat the stand-alone AF. In this connection, several procedures stand out; viz, epicardial surgical ablation, hybrid approach, and convergent procedure. Shall we tackle every single one of them in the remainder of this article.

#### Epicardial surgical ablation

This procedure is performed without needing cardiopulmonary bypass, as off-pump procedure, on beating heart, and usually using just videoscropy. For all these reasons, these types of procedures have become so popular in recent years. Nevertheless, a word of caution should be remarked before using these special techniques. For this purpose, a closer look at these techniques is mandatory.

The critical part on which this modality is based on is the box lesion set in the left atrium. That is, it is not only necessary to bilaterally isolate the pulmonary veins, but to complete the

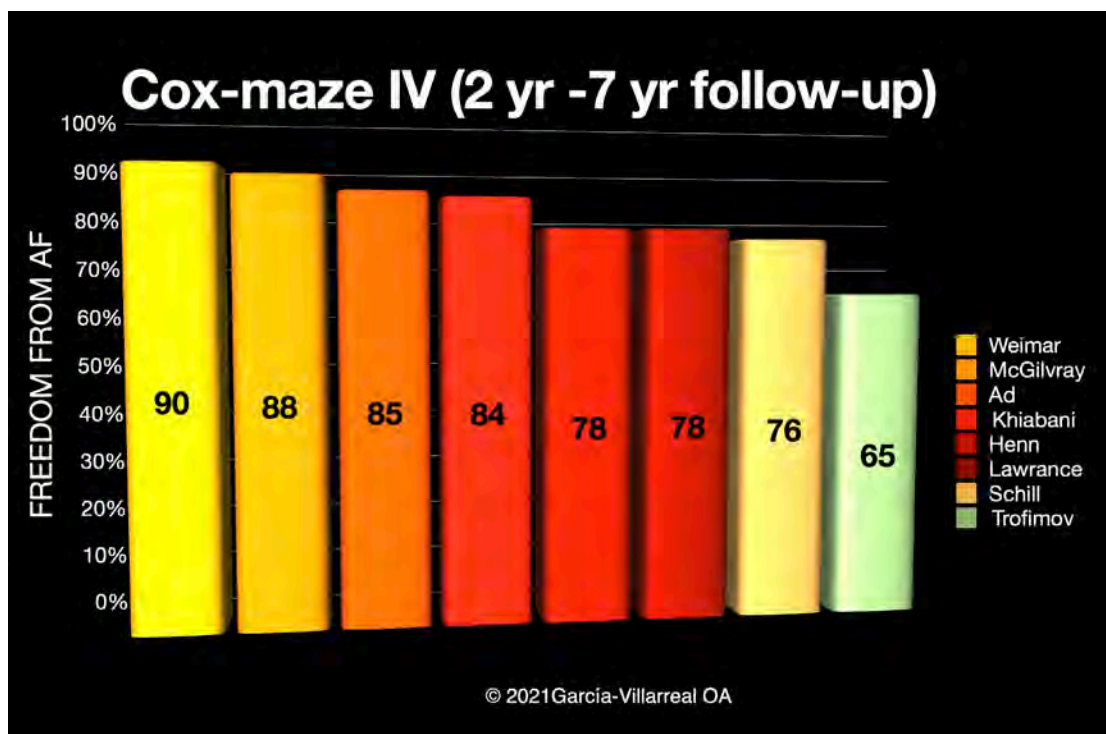


Figure 6. Results of the Cox-maze IV procedure using alternative energy sources, such as bipolar radiofrequency and/or cryoablation.

entire box lesion set including connecting lines in the roof and the floor of the antrum containing the pulmonary veins. It has been well demonstrated the box lesion set is an essential step of the Cox-maze procedure [66]. All the other additional lines of the Cox-maze procedure can be checked out in the article by Dr. Cox in the context of the electrophysiologic basis for lesions of the contemporary Maze operation [18]. The sole pulmonary vein isolation is not sufficient to eliminate the non-paroxysmal AF [67,68]. In addition, the procedure must be performed as a full bi-atrial procedure, as stated out by Dr. Cox [69,70] and some other authors [71]. Postoperative AF may be developed on the right atrium, despite the right atrial size [70]. Thus, there no room for doubting about the imperative necessity of performing the Cox-maze procedure to the fullest of the completeness [72,73].

The epicardial surgical ablation was brought to light as an “off-pump” alternative to the endocardial Cox-maze procedure, which is made “on-pump” including aortic-cross clamping [59]. Since the stand-alone AF is commonly the result of a failure in the medical antiarrhythmic treatment as well as after several failed attempts of catheter-based ablation, there is no underlying structural cardiac pathology justifying the primary surgical procedure. As such, the lesser invasive the procedure, the better the acceptance of it. According to all the aforementioned concepts in this section above, we can identify several ways of performing the same procedure. There are three ways to perform the same procedure, which vary depending on the device used for this purpose [74]. The ultimate goal is to achieve complete transmural in every burn line. As we have already mentioned

previously, only bipolar radiofrequency and cryoablation offer consistency in this regard [23]. On the grounds previously laid down, other than these alternative energies should be avoided when performing the Cox-maze procedure.

In the case of using the device by Atricure, the ablation clamp (Isolator Synergy, AtriCure, OH, USA) is used to get the pulmonary vein isolation through a bilateral approach by videoscopy [75]. Thus, the transmural at these spots around the pulmonary veins may be assured. However, all the other additional lines for the box lesion set and trigone line are made using a linear pen device (Bipolar Linear Pen, AtriCure, OH, USA). Despite described as bipolar energy, truth be told, this kind of energy is not a true bipolar radiofrequency ablation. Energy is going between two poles of the pen, which makes the power of its penetration very limited and highly dependent on tissue thickness. In a study by Sakamoto et al. using this device, 80% of ablations on the arrested heart and 67% on the beating heart were transmural. The deepest penetration of the burn in the atrial tissue was 6.1 mm. No transmural lesions were observed when the tissue was thicker than 6.7 mm [76]. An analysis of the box lesion set 6-8 weeks after having applied the epicardial ablation time has shown that the highest degree of full transmural was observed around the pulmonary veins at the site of application of the bipolar clamp, 80% in the left pulmonary veins, and 96% in the right ones. In stark contrast, the lowest degree of complete transmural was observed in the lines made by the linear pen device, 34% in the roof line, 60% in the floor line, and 5% in the trigone line [77].

With the COBRA Fusion™ 150 (Estech, an AtriCure® Company, San Ramon, CA, USA), a final catheter loop is placed around the pulmonary veins through a right unilateral approach using videoscapy [78]. Then, a suction system is applied up to 500mmHg, to get a consistent contact between the atrium and the electrodes. According to the specifications by the manufacturer, bipolar and monopolar can be delivered by means of this multisegmental catheter. However, getting an eyeful of this procedure after 6-8 weeks of the epicardial procedure, only 25% of cases had a complete posterior left atrial isolation [79].

The third possibility to perform the epicardial surgical ablation is by using the Medtronic Cardioblate™ Gemini™-S Surgical Ablation System, including the bipolar clamp (Medtronic, Inc., Minneapolis, USA). This is a bilateral thoracoscopic approach using only the bipolar clamp delivering bipolar radiofrequency ablation in order to isolate the PV as well as the entire left atrial antrum [80]. While the full transmural may be obtained, it is exclusively limited to box lesion set in the left atrium. So, the success rate is very limited in cases of non-paroxysmal AF. Doty et al. [81] demonstrated with this GALAXY technique an overall freedom from AF of 63% at 24 months in cases of non-paroxysmal AF.

As we could realize, the chief problem with all these lesser invasive off-pump procedures, all of them are missing the left-sided additional lines and right-sided lesions of the original Cox-maze IV procedure, which underpins all these procedures. The results for the non-paroxysmal AF are not that convincing. It has been previously stated out by Dr. Cox, the aim of the set of lesions in the Cox-maze procedure is to interrupt all macro-reentrant circuits that might theoretically be sustaining AF in both atria. Hence, the complete pattern as described by Dr. Jim Cox should be always applied [18].

Regarding the right-sided lesions, it turns out to be more than impossible to confine the Cox-maze procedure only to one atrium. The atria should be understood as a continuum of muscle electrically speaking. So, the Cox-maze procedure should always be conceived as a full bi-atrial procedure. Several publications have demonstrated the lack of efficacy when the right-sided lesions are missed, at the time of full efficacy when a bilateral approach is performed [82-86]. In this setting, it is imperative to improve the previous results of the epicardial surgical ablation procedures. Natural next step is to add something else to the previous epicardial procedure. By adding endocardial approach to the previous one, we can get the so-called hybrid approach [87].

#### *Hybrid approach*

The hybrid procedure can be called Hybrid Maze IV procedure as long as provided it is adhered to the same principle underpinning the Cox-maze IV procedure: the full bi-atrial lesion pattern [87]. With this endocardial approach, all epicardial lesions previously made can be now checked in terms of the degree of transmural by catheter-based techniques. If any gap is discovered, then it is burned from inside the heart getting in this way a complete transmural burn line. This second endocardial stage is classically performed after

6-8 weeks after the initial epicardial approach. Every single one of the epicardial lesions is now checked out by means of electrophysiological studies from inside the heart. Every gap is closed by burning with a tip catheter. Finally, two important lines are performed by catheter ablation. The mitral and the cavo-tricuspid lines. For this purpose, in order to make easier and safer the procedure, during the epicardial procedure the surgeon is encouraged to leave some “landmarks” by placing some small surgical clips (as those used of the internal mammary artery dissection) as a reference points on the mitral annulus as well on the coronary sinus from outside the heart. In this way, the electrophysiologist can deliver in a safer and faster way the RF energy, usually as unipolar RF working as tip-by-tip technique from inside the heart [87].

#### **RESULTS FROM HYBRID APPROACH**

The epicardial surgical ablation is much better than the sole catheter ablation approach to treat other than paroxysmal AF, viz, persistent or long-standing persistent AF. The literature is full of corroborative articles in this regard [88-93]. In this way, the existence of the hybrid approach seems to be fully justified.

With respect the hybrid approach, a search in the website ClinicalTrials.gov (<https://clinicaltrials.gov/ct2/home>) with the key words “hybrid ablation” and “atrial fibrillation” and “convergent procedure” showed that there are currently 19 studies registered. Out of them, 15 met criteria for our purpose. Thirteen trials have not completed or published the results yet. Only two of them have had some publication automatically indexed to the ClinicalTrials.gov Identifier number. As of yet, 13 trials have not completed or published the results. The complete list of these trials can be consulted in **Table 1**.

The overall results for the hybrid procedure using a bilateral or unilateral thoracoscopic approach complemented by catheter-based techniques are observed in a very wide range from 56% to 78% freedom from AF between 12 and 18 months of follow-up [94-97]. Interestingly, the best results were observed using the convergent approach as a combination of subxyphoid pericardial approach and percutaneous catheter ablation. These results ranged between 74% and 92% from 12 and 24 months after the full procedure [98-99]. Thus, further studies with longer follow-ups are absolutely necessary in order to get a better overview with stronger conclusions.

In addition, one of the most important limitations with the analysis of this studies is the large variability in the surgical technique, lesion sets, alternative energies used, left atrial appendage management, among many other variables. What is truth is that actually there is a lack of standardization with the Cox-maze procedure in our daily practice [100-101].

As a conclusion, we can highlight two main facts. The first of them is the necessity of always understanding the Cox-maze procedure as a bi-atrial procedure with the inherent full bi-atrial lesion pattern regardless the approach. The second important fact is the comprehension that there are only two



Table 1. Trials listed in the website ClinicalTrials.gov regarding the hybrid approach, including the convergent procedure, to treat the non.paroxysmal atrial fibrillation

NAME OF THE TRIAL	ClinicalTrials.gov Identifier	Status	Completion Date	Publications automatically indexed
Hybrid Ablation of Persistent and Long-standing Persistent Stand-alone Atrial Fibrillation	NCT02832206	Complete with no results posted yet.	Not applicable	no
Two-stage Hybrid Ablation or Thoracoscopic Epicardial Ablation for Long-standing Persistent Atrial Fibrillation (THAT-LSPAF)	NCT03708471	Recruiting	December 2022	no
Comparison Between One-stage Hybrid Ablation and Thoracoscopic Surgical Ablation for Intractable Atrial Fibrillation.	NCT03127423	Recruiting	December 2022	no
Hybrid Versus Catheter Ablation in Persistent AF (HARTCAP-AF).	NCT02441738	Complete with no results posted yet.	Not applicable	no
Serial Hybrid Atrial Fibrillation Ablation (SHAFT)	NCT01582828	Unknown with no results found as published yet.	December 2017	no
One Staged Hybrid Approach of Surgical/Catheter Ablation for Persistent Atrial Fibrillation.	NCT02968056	Unknown with no results found as published yet.	October 2019	no
Hybrid Staged Operating Room and Interventional Catheter Ablation for Atrial Fibrillation (HISTORIC-AF).	NCT01622907	Complete	Not applicable	doi: 10.1093/ejcts/ezx162.
Hybrid Therapy and Heart Team for Atrial Fibrillation (HT2AF)	NCT03737929	Recruiting	Juanuary 2022	no
Hybrid Procedure in Patients with Persistent Atrial Fibrillation	NCT02392338	Complete	Not applicable	doi: 10.1016/j.amj-card.2019.12.046.
Subxyphoid Hybrid MAZE Registry for Patients with Persistent Atrial Fibrillation (SubXMAZE)	NCT04148625.	Enrolling	December 30, 2021	no
Comparison of Treatment Outcomes Between Convergent Procedure and Catheter Ablation for Persistent and Longstanding Persistent Atrial Fibrillation	NCT04509180.	Recruiting	September 1, 2024	no
CONVERGE CAP Study-For the Treatment of Symptomatic Persistent or Long-standing Persistent AF (CAP)	NCT04239534.	Suspended for Covid19	November 2026	no
Combined Endoscopic Epicardial and Percutaneous Endocardial Ablation Versus Repeated Catheter Ablation in Persistent and Longstanding Persistent Atrial Fibrillation (CEASE-AF)	NCT02695277	Active, not recruiting.	December 2024	no
Dual Epicardial Endocardial Persistent Atrial Fibrillation (AF) Study (Staged DEEP) (Staged DEEP)	NCT01661205	Complete with no results posted yet	Not applicable	no

alternative energies capables to produce consistency on getting full transmuralty in burn lines: bipolar radiofrequency ablation and cryoablation. Other than these becomes questionable to use. When all these principles are rigorously and severely applied to the surgical ablation for AF, regardless the approach, the results can be impressive.

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