

Surgical Ablation of Atrial Fibrillation: is Electrical Isolation of the Pulmonary Veins a Must?

Bart Maesen, MD, PhD,¹ Ines Van Loo, MD,² Laurent Pison, MD, PhD,³ Mark La Meir, MD, PhD^{1,2}

¹Department of Cardio-Thoracic Surgery, Maastricht University Medical Center, Maastricht, The Netherlands. ²Department of Cardiac Surgery, Universitair Ziekenhuis Brussel, Brussels, Belgium. ³Department of Cardiology, Maastricht University Medical Center, Maastricht, The Netherlands.

Abstract

Ablation of atrial fibrillation (AF) is a well-established treatment option for patients with symptomatic AF refractory to antiarrhythmic drugs. The cornerstone of catheter ablation is electrical isolation of the pulmonary veins, since the pulmonary veins are the most common location for triggers of AF. Electrical reconnection of the pulmonary veins is associated with arrhythmia recurrence and therefore diminishes long-term success of catheter ablation of AF. Therefore, durable pulmonary vein isolation remains a condition sine qua non for catheter ablation of AF. The Cox-Maze procedure is considered an effective surgical cure of AF, however it has never been widely adopted due to its procedural complexity. Since the development of minimal invasive techniques for surgical AF treatment, surgical ablation of AF has regained interest. Most of the minimal invasive surgical AF ablations performed around the globe include pulmonary vein isolation as a part of the procedure. In this review, we explore the necessity of electrical isolation of the pulmonary veins in surgical AF ablation.

Historical Perspective

Although the exact pathophysiology of atrial fibrillation (AF) remains unknown, different mechanisms driving the arrhythmia have been proposed. Generally it is accepted that AF requires both a trigger and a substrate capable of perpetuating AF. Mechanisms driving AF can be classified as 'hierarchical' or 'anarchical'.¹ In a hierarchical organization a single source, ranging from local automaticity or triggered activity to local reentrant circuits, drives AF. Contrary to hierarchical AF, anarchical AF indicates that multiple non-localized sources, like reentry circuits or multiple wavelets, act anarchically to drive. Also interactions of several of these mechanisms could be responsible for the initiation and perpetuation of AF.

The multiple wavelet hypothesis, introduced by Moe and coworkers, is a classic example of anarchical AF.² In this conceptual model, AF is sustained by the co-existence of multiple wavelets meandering over both atria, given that the atria are big enough (atrial mass) and the refractory period short enough.^{2,3} Early 1980s, the only interventional treatment for AF was ablation of the atrio-ventricular node and

implantation of a ventricular pacemaker.⁴ The Cox-Maze procedure was the first curative attempt in AF treatment and was performed for the first time on 25 September 1987 at the Barnes Hospital in St. Louis, USA by James Cox.⁵ The operation consisted of an extensive cut-and-sew incision set in both atria with the goal of blocking macro-reentrant conduction and (re)directing propagation from the sino-atrial node throughout both atria. The concept of this procedure was based on epicardial mapping in patients with paroxysmal AF who were undergoing surgical correction of the Wolff-Parkinson-White syndrome.⁶ In this study, Cox et al. demonstrated that, during human AF, mainly multiple wave fronts and macro-reentrant circuits occur.⁶ The numerous atrial transections were designed in such way that macro-reentrant circuits no longer could prevail. It is remarkable that, although this surgical procedure was designed long before any knowledge of the arrhythmogenicity of the pulmonary veins (PVs) existed, it did include electrical isolation of the PVs and the posterior left atrial wall (box lesion) as a part of the surgical procedure.⁵ As such, success of the Cox-Maze procedure cannot solely be attributed to the prevention of multiple waves to co-exist, but might also be partly due to abolished AF triggers.

The initiation of paroxysms of AF by repetitive discharges originating in the PVs is a typical example of a hierarchical type of AF. In 1998, Haïssaguerre et al. demonstrated that 90% of the triggers responsible for the onset paroxysmal AF were located in and around the orifices of the PVs and that these foci responded well to catheter based radio-frequency (RF) ablation therapy.⁷ Later, it was shown that the ectopic activity presumably was a consequence of micro-reentry promoted by the presence of heterogeneity in refractoriness and anisotropic conduction at the atrial junction

Key Words:

Atrial Fibrillation, Pulmonary Veins, Electrical Isolation.

Disclosures:
None.

Corresponding Author:
Mark La Meir,
UZ Brussels
Centre for Cardiovascular Diseases
(Louis Tielemans Pavilion +1)
101, Laarbeeklaan
B - 1090 Jette Belgium.

with the PVs and within the PVs.^{8,9} These findings have important implications: as frequent discharges of a few focal sources can lead to progressive pathologic changes in the atrial substrate,¹⁰ thereby entraining AF,¹¹ and ablation of these foci suppresses the trigger and reduces the potential degeneration of the atrial substrate,⁷ the underlying mechanism driving human paroxysmal AF seems to be that of multiple foci adjacent to or in the PVs.¹² Since this pioneering work of Haissaguerre et al.,⁷ PV isolation has been regarded as the cornerstone for the treatment of paroxysmal AF and even of persistent AF. However, the underlying mechanism of persistent AF maintenance is not fully understood and might be due to

- (1) cellular proarrhythmic mechanisms, like automaticity or triggers;
- (2) spiral wave reentry or rotors;
- (3) multiple wavelet reentry where the fibrillation process is actually driven by waves and no localized sources of AF exist; or
- (4) a combination of all, different in each patient.¹ This might explain the poor outcomes reported in (single procedure) PV isolation for persistent AF.¹³ After recognition of the PVs as a dominant source of triggers initiating AF, more foci were found at other locations in right and left atria. Amongst them were the ligament of Marshall,¹⁴ the proximal superior vena cava¹⁵ and the left atrial appendage.¹⁶

Based on the success of compartmentalization in open surgical ablation, addition of left atrial linear lesions to PV isolation were introduced in catheter ablation of AF.¹⁷ For example the mitral isthmus line, a linear line from the lateral mitral annulus to the left inferior PV, was added by Jais et al. based on anatomical studies suggesting that preferential propagation is closely correlated to muscle fiber orientation along the posterior LA and circumferentially around the mitral annulus.^{18,19} Another example of substrate modification was the introduction of a linear lesion connecting both superior PVs, the so-called 'roof line' ablation.²⁰

In 2004, Nademanee et al. proposed a different substrate-based approach for the treatment of AF. They identified and ablated areas with bipolar complex fractionated electrograms (CFAE),²¹ based on the earlier described finding by Konings et al. that unipolar CFAE are found in regions of conduction slowing and conduction block.²² The authors suggested that ablation of CFAE-sites alter or eliminate random reentry paths preventing fibrillation wavelets to reenter the ablated areas.²¹ Although PV isolation was not performed, PVs were identified as key areas where CFAEs were located.²¹

A new method for analyzing AF propagation was introduced by Narayan et al. in 2012. The authors unmasked sustained electrical rotors and/or repetitive focal activation in 97% of mapped human AF (combination of paroxysmal and persistent AF) by using a 64-pole basket catheter and a novel algorithm that produces a video of the computed activation process.²³ These localized sources were low in number, stable in position, mostly located in the left atrium and they controlled surrounding fibrillatory conduction.²⁴ Catheter ablation at the center of these localized sources terminated or consistently slowed persistent or paroxysmal AF in 86% of patients prior to PV isolation.²⁴ Of notice, in a recent extension of that report, more rotors and less focal sources were reported compared to earlier reports,^{23,24} which the authors attributed to 'improved software', among other things.²⁵ This might reflect a high dependence on a special software algorithm enabling the detection of rotors driving human AF.

Even more recently, Haissaguerre et al. used electrograms generated by body surface mapping and biatrial geometry relative from a

computed tomography (CT) scan to reconstruct the propagation pattern of fibrillating atria in a noninvasive way.²⁶ Signal-analysis processing combining filtering, wavelet transform, and phase mapping was used to identify drivers (focal or reentrant activity) in 103 patients with persistent AF.²⁷ Contrary to Narayan et al.,^{23,24} the authors reported more driver locations, substantial meandering, and periodic occurrence of unstable reentries requiring statistical density maps to identify them.²⁷ Also here, RF ablation at the driver location resulted in acute AF termination in 75% of persistent AF and 15% of long-lasting AF patients.²⁷ In this strategy, ipsilateral PV isolation was only performed if drivers were found in the PVs or if the endpoint was not reached.

As discussed before, surgical ablation of AF started with the Cox-Maze III operation, a surgical procedure through median sternotomy on cardio-pulmonary bypass (CPB) in which compartmentalization was created by cutting and sewing in order to interrupt and eliminate macro re-entrant circuits.⁵ Later, the Cox-Maze III procedure was changed to the Cox-Maze IV procedure: based on the findings of Haissaguerre⁷ the pulmonary veins were isolated bilaterally, most incision sets were replaced by bipolar RF ablation and cryosurgery was applied at the valve annuli.^{4,28} The Cox-Maze IV can be performed either through a median sternotomy or through a right mini-thoracotomy.²⁸ Although the right atrial ablations can be performed on the beating heart, CPB is still required for the left atrial lesion set.²⁸ Several changes to the Cox-Maze procedure have been developed, mainly based on the application of other (and now obsolete) energy sources like microwave, laser, and high-frequency ultrasound.⁴ Nitta et al. developed the radial incision procedure, an alternative approach to preserve a more physiologic atrial transport function.²⁹ This procedure consisted of atrial incisions radiating from the sinus node to allow a more physiologic atrial activation sequence and to preserve blood supply to most atrial segments.³⁰

The last decades, new technologies enabled the creation of transmural lesions using minimal invasive surgery (MIS) for treatment of stand-alone AF.³¹ Most widely used are the RF bipolar clamp devices that allow PV isolation by applying RF energy between the two jaws of the clamp. In addition, creation of a 'box'-lesion and left atrial appendage (LAA) removal or exclusion, usually with ganglionic plexi ablation, is performed via video-assisted MIS.³¹⁻³⁴ The advantage of these MIS approaches, next to the fact that they are truly minimal invasive, is that they can be performed on the beating heart (off-pump).³¹⁻³⁴ The difference, however, between these techniques and the Cox-Maze III lesion set is that the epicardial off-pump techniques lack the possibility of a mitral isthmus line as this lesion cannot be created solely from the epicardium.^{35,36} Therefore, Edgerton et al. developed the 'Dallas lesion set', an epicardial minimal invasive approach in which the mitral isthmus line is replaced by a connecting lesion -using unipolar RF energy- from the left fibrous trigone at the anterior mitral valve annulus across the anterior dome of the atrium to the 'roof' line.³⁵

Although much more efficient as unipolar, even bipolar RF energy cannot guarantee transmural lesions.³⁷ To overcome this shortcoming and to tackle the problem of the mitral isthmus line, a combination of a transvenous endocardial and thoracoscopic epicardial approach in a single procedure, the so-called 'hybrid AF ablation', has been successfully put forward as an alternative.³⁸ Almost all of the surgical ablation procedures for the treatment of concomitant and stand-alone AF include PV isolation using RF or cryo-energy.

Is Pulmonary Vein Isolation Mandatory In Catheter Ablation Of AF?

In the initial report on PV trigger ablation for the treatment of paroxysms of AF, Haïssaguerre et al. reported 80% acute success and 62% freedom of AF in a follow-up period of 8 ± 6 months after ablation.⁷ Since then PV isolation is considered to be the cornerstone of catheter-based ablation of AF.¹² Initial PV isolation consisted of electrical isolation of the PV myocardium close to the PV ostia, but identification of triggers in the PV antrum and recognition of PV stenosis resulted in a shift towards wider antral PV isolation techniques (e.g. wide area circumferential ablation or WACA).³⁹⁻⁴¹

It has been demonstrated that PV isolation is more effective in maintaining sinus rhythm compared to medical therapy.⁴² However, catheter-based PV isolation has been reported to be successful in patients with paroxysmal AF, although repeat PV isolation procedures are needed, but far less successful in patients with persistent or longstanding persistent AF.⁴³⁻⁴⁸ Teunissen et al. recently reported on the five-year freedom of atrial tachyarrhythmia after PV isolation.⁴⁷ PV isolation restored and maintained long-term sinus rhythm in 48.6% for paroxysmal AF, but only 33.1% in persistent AF and 23.5% in longstanding persistent AF.⁴⁷ When allowing multiple re-isolations, freedom of AF increased to 67.8% for paroxysmal AF, but remained disappointing for persistent AF (46.2%) and longstanding persistent AF (38.2%).⁴⁷

The consensus that complete electrical isolation of PVs is a necessity stems from the finding that AF recurrences after PV isolation for paroxysmal AF are almost always associated with electrical PV reconnection based on conduction gaps.⁴⁹ The need for durable PV isolation is clearly demonstrated by the results of the Gap-AF-AFNET 1 trial.⁵⁰ In this study, 233 patients were randomized to complete and intentional incomplete PV isolation.⁵⁰ After 3 months, rhythm follow-up showed that patients with incomplete PV isolation had far more AF recurrences than patients with complete PV isolation (62.2% vs 79.2%).⁵⁰ More surprising was the finding that at invasive reevaluation at 3 months the rate of electrical PV reconnection in patients with acute complete PV isolation was up to 70%.⁵⁰ This illustrates that initial acute PV isolation using catheter-based RF ablation techniques does not per se translate into a durable PV isolation. What about the second most frequently used catheter-based ablation technology, cryo-energy? Kuck et al recently compared cryoballoon ablation to RF ablation in a large randomized multicenter trial, the 'fire and ice trial' and demonstrated non-inferiority of cryo-ablation to RF ablation.⁵¹ In a report on redo procedures for recurrent AF in 29 out of 131 patients who initially underwent a successful cryoballoon PV isolation, PV reconnection was again found to be the underlying mechanism (PV reconnection in 2.45 ± 0.7 veins in each patient).⁵² Some techniques have been evaluated to reduce the amount of PV reconnection. Recently, a large randomized trial demonstrated that in patients with dormant PV conduction additional adenosine-guided ablation resulted in a higher freedom of AF compared to no additional ablation (69.4% vs 42.3%).⁵³ In patients without dormant PV conduction, AF freedom was only 55.7%, suggesting that adenosine is unable to identify all veins that might reconnect.⁵³ Theoretically, waiting longer after PV isolation could help to reveal early PV reconnection. Bänsch et al. demonstrated that although this resulted in the detection of more gaps, ablation of these gaps did not result in higher freedom of AF in follow-up.⁵⁴ Furthermore, demonstration of bidirectional block has

been suggested to improve results of PV isolation.⁵⁵ Electroporation is a promising technique but still needs to be evaluated in clinical practice.⁵⁶

As discussed before, the short and long term results of PV isolation are less convincing in patients with persistent and longstanding persistent AF.⁴⁴⁻⁴⁸ As a result, additional substrate modifications, such as linear lesions or ablation of CFAEs, have been proposed for catheter-based ablation of persistent AF.^{18,21,57} The initial report on CFAE ablation by Nademanee et al. presented very high acute (98%) and 1-year follow-up (91%) freedom of AF rates.²¹ In this study, no PV isolation was performed. Does this finding challenge the need for PV isolation? It might, but although PV isolation was not performed, the PVs were identified as key areas for CFAEs.²¹ Estner et al. compared CFAE ablation with PV isolation in combination with CFAE ablation in patients with persistent AF.⁵⁸ In the CFAE ablation only group, sinus rhythm off AAD was present in 9% after a mean follow-up time of 13 ± 10 months, compared to 41% in the CFAE plus PVI ablation group.⁵⁸ Moreover, Oral et al. randomized patients with long-lasting persistent AF who did not convert to sinus rhythm after PV isolation to CFAE ablation or no further ablation and failed to demonstrate an add-on value of CFAE ablation to PV isolation.⁵⁹ Because of the dynamic nature of CFAEs and the inability of current algorithms to adequately define CFAEs, it remains challenging to identify sites critical for AF termination.^{60,61}

Also addition of linear lesions has been reported with varying success. For example, Gaita et al. randomized patients with paroxysmal or persistent/permanent AF to 2 different ablation schemes: PV isolation and PV isolation plus left linear lesions.⁶² The authors reported that addition of linear lesions is more effective in maintaining sinus rhythm off anti-arrhythmic drugs.⁶² In contrast, several recent randomized trials failed to show any benefit of additional substrate modifications techniques over PV isolation alone.⁶³⁻⁶⁵ Of interest is the STAR AF 2 trial, a large randomized trial evaluating currently used substrate modifications techniques.⁶³ Verma et al. randomized 589 patients with persistent atrial fibrillation to PV isolation alone, PV isolation in combination with CFAE ablation or PV isolation with linear lesions across the left atrial roof and mitral valve isthmus.⁶³ The authors failed to show any benefit in AF freedom between the 3 techniques, independent of AAD-allowance or repeat procedures.⁶³

The poor results of additional substrate modification in patients with non-paroxysmal forms of AF should be interpreted with caution, however, as they might be due to the relative incapacity of catheter-based unipolar RF to create transmural lesions.⁶⁶ As such, it would be interesting to (re-)evaluate these 3 techniques in patients where effective PV isolation has been proven by electrophysiological testing at a fixed time point after the initial procedure.

In 2012, Narayan et al. proposed a new ablation technique, focal impulse and rotor modulation (FIRM), based on the hypothesis that localized sources or rotors sustain human AF.²³ When comparing FIRM in addition to PV isolation with PV isolation alone, FIRM-guided cases had higher freedom from AF (82.4% vs. 44.9%).⁶⁷ These promising results were confirmed in a 3-year follow up report.⁶⁸ However, in these studies FIRM ablation was always performed in combination with PV isolation. Recently, Gianni et al reported that FIRM ablation as a sole therapy, so without PV isolation, in patients with non-paroxysmal AF did not result in AF termination.⁶⁹ After a mean follow-up of 5.7 months, single-procedure freedom from atrial

arrhythmia was 17% without AADs, 28% allowing AADs.⁶⁹

In conclusion, PV isolation is not only mandatory in catheter ablation of AF; it forms the cornerstone of this therapy. Whether additional substrate modification techniques, in combination with PV isolation or as a sole therapy, are able to improve freedom of AF is unclear at this stage.

Is Pulmonary Vein Isolation Mandatory In Surgical Ablation Of AF?

The fact that all surgical AF ablation techniques include PV isolation makes it difficult to question its need in AF surgery. There are, however, some indirect arguments to support its necessity.

There are a few differences between surgical and catheter ablation techniques for ablation of AF. First, a variety of different lesion sets are performed, including right atrial lesions, extensive left atrial lesions including full isolation of the posterior left atrium (box-lesion), addition of a trigonum or mitral isthmus line and left atrial appendage exclusion. In theory, those additional lesions might be responsible for AF termination even if the PVs are not fully electrically isolated. The left atrial appendage, for example, harbors triggers that can play a role in initiation or recurrence of AF.^{16,70} Next to the prevention of clots, surgical exclusion of the left atrial appendage performed by amputation, stapler or epicardial occluding device (clip), will also electrically isolate the left atrial appendage, thereby preventing its triggers to persist. An endocardial left atrial appendage occluding device, however, will not result in electrical isolation. Secondly, the devices used to perform AF ablation are different. In several stand-alone or concomitant surgical AF procedures, cryo-ablation is performed on the arrested heart, thereby preventing the heat sink effect of endocardial (warm) blood. Also, in surgical treatment of AF, bipolar RF devices can be used to perform PV isolation (both on the beating and the arrested heart) and to create linear lesion on the arrested heart. Those bipolar devices differ from unipolar devices in the fact that RF energy is applied from two sides with the target tissue in between. In a porcine animal study, ablation of the PVs and the left atrial appendage using a bipolar RF clamp resulted in 100% acute isolation and at 30 days.⁷¹ Microscopic evaluation of the ablation lines showed that all lesions were transmural in a total of 209 samples.⁷¹ Bugge et al compared a bipolar clamping device with a handheld unipolar device in a sheep model and showed that in atrial tissue continuous transmural lesions were achieved more often with the bipolar than with the unipolar device (92.3 vs. 33.3%).³⁷ Of course these results coming from animal studies cannot be translated one-on-one into clinical practice, but they at least suggest the superiority of bipolar compared to unipolar RF devices in creating transmural lesions. As such, it might be more representative to study the success of substrate modification techniques in addition to PV isolation in AF patients who undergo surgical PV isolation using bipolar RF devices, rather than in patients undergoing percutaneous PV isolation.

There are some indirect arguments that PV isolation is mandatory in AF surgery. Surgical PV isolation using bipolar RF devices is at least as effective as catheter ablation.⁷²⁻⁷⁴ De Maat et al. reported that video-assisted PV isolation in patients with paroxysmal AF resulted in 69% freedom from atrial arrhythmias off AAD after a mean follow-up of 5 years.⁷⁵ These results do not prove that PV isolation is a must in surgical AF ablation, but they do show that surgical PV isolation is an adequate therapy to treat paroxysmal AF. In non-paroxysmal

forms of AF, additional lesions are often required to maintain sinus rhythm. In permanent AF patients with left atrial dilatation and valvular disease, PV isolation seems necessary but not sufficient to regain sinus rhythm.⁷⁶ Gaita et al. assigned patients undergoing valve surgery to 3 different groups: cryo-isolation of the PV's only, cryo-isolation of the PV's in combination with interconnecting lines between the PV ostia and the right and left lower PVs down to the mitral annulus (reversed 'U' lesion) and cryo-isolation of the PV's in combination with interconnecting lines between the PV ostia and the left lower PV down to the mitral annulus ('7' lesion).⁷⁶ A subset of patients underwent an electrophysiological study at 3 months.⁷⁶ First of all, the 'U' lesion was never achieved; in general only 65% of linear lesions or PV isolation using cryo-energy was achieved in this patient population.⁷⁶ Complete PV isolation alone resulted in 25% sinus rhythm, whereas PV isolation in combination with a complete '7' lesion (intended '7' lesion or incomplete 'reversed U' lesion) resulted in 86% sinus rhythm at 2 years off AAD.⁷⁶ In a mixed population of paroxysmal and persistent AF patients undergoing the Cox-Maze IV procedure, higher freedom of AF at 3 and 6 months and a trend towards higher freedom of AF at 12 months was reported in patients where, in addition to PV isolation, a complete posterior left atrial isolation ('box-lesion') was performed compared to a line between the inferior PVs only.⁷⁷ This suggests that in certain patients, the posterior left atrium harbors triggers that (re-)initiate AF, and that in those patients PV isolation alone is not sufficient.⁷⁷ Of course, full posterior left atrial isolation also results in reduction of the available conducting critical mass. In contrast, in a large randomized multicenter study involving patients with persistent and longstanding persistent AF, Gillinov et al. reported no differences in freedom of AF at 1 year between patients undergoing PV isolation alone compared to patients undergoing a biatrial Cox-Maze procedure.⁷⁸ However, the reported success rate of the maze group in this study is lower than expected.⁷⁹ Furthermore, a variety of bipolar and unipolar radiofrequency and cryotherapy was used (bipolar PV isolation was only performed in 43%).⁷⁸

Electrophysiological evaluation after bipolar RF PV isolation has been scarcely performed. Kron et al performed an electrophysiological study in 13 patients (69% paroxysmal AF) with recurrent atrial tachyarrhythmias at a mean of 214±162 days after minimal invasive surgical ablation of the PVs using bipolar RF, the parasympathetic ganglionated plexi and the ligament of Marshall.⁸⁰ In these 13 failures, 50% of examined PVs reconnected; in 7/8 patients with recurrent AF either 2 or 3 PVs were reconnected and in 6/8 patients, the left superior PV was reconnected.⁸⁰ Zeng et al. reported on 8 patients (3 paroxysmal AF, 5 persistent AF) with recurrent atrial arrhythmias after minimal invasive PV isolation using bipolar RF and left atrial appendage exclusion by stapler.⁸¹ An electrophysiological study revealed gaps at the PVs in 4 patients with recurrent AF, an ectopic focus between the left atrial appendage and left superior PV in a patient with atrial tachycardia, perimitral atrial flutters in 2 patients and a left atrial roof flutter in the remaining patient.⁸¹ Trumello et al. performed percutaneous ablation on 36 patients with previous surgical ablation (7 biatrial maze, 18 left atrial ablation and 11 PV isolation).⁸² Among other findings, 15 patients had reconnection around the PVs.⁸² The authors underlined the importance of an appropriate energy source as two-thirds of patients with gaps around the PVs were initially treated using unipolar RF only.⁸² Velagic et al reported on repeat catheter ablation in 14 patients out of 64

patients treated with a hybrid AF ablation including PV isolation with bipolar RF.⁸³ In all patients, conduction block of the PVs was confirmed by endocardial mapping with a Lasso catheter.⁸³ In only 5 patients PV reconnection was found and only 1 vein per patient reconnected.⁸³ Although these findings are not direct proof, they do strongly support the need for durable PV isolation in surgical AF ablation.

Hybrid AF ablation may help to detect and immediately treat conduction gaps that are not identified during epicardial ablation. The concept of hybrid AF ablation, as discussed before, consists of combining the advantages of an epicardial and endocardial approach.³⁸ It can be performed as a staged procedure or in one single procedure. On et al. reported on 97 patients (10.1% paroxysmal AF, 21.5% persistent AF, 68.3% long-standing persistent AF) who underwent staged hybrid AF ablation.⁸⁴ Surgery consisted of thoracoscopic PV isolation with a box lesion, ganglionated plexus ablation, division of the Marshall ligament and left atrial auricle resection.⁸⁴ In 61 patients an electrophysiological study was performed 5 days after surgery: cavotricuspid isthmus ablation was routinely performed in 56 patients, and mitral isthmus ablation and septal ablation because of preoperative atrial flutter.⁸⁴ In 15 patients PV conduction gaps were detected requiring additional ablation.⁸⁴ Using this staged approach, the freedom of AF after 1 year was 74% off AAD.⁸⁴ Pison et al reported on 26 patients (42% persistent AF) undergoing hybrid AF ablation in a single procedure.³⁸ Combining thoracoscopic surgical ablation (consisting of PV isolation, a box lesion +/- additional lesions) with endocardial validation and touch-up (if needed) of the epicardial lesions resulted in a single procedure success rate of 83% at 1 year, off AAD.³⁸ During the hybrid procedure, endocardial touch-up was necessary in 23% of patients because the epicardial lesions were not transmural, illustrating the immediate advantage of this approach.³⁸ Using meticulous rhythm follow-up, 4 failures were identified.³⁸ Of this 4 patients, 2 underwent an electrophysiological study: 1 conduction gap in the roofline and 1 atrial flutter but no reconnection of the PVs was documented.³⁸ In theory, endocardial validation of epicardial ablation lesions is superior to epicardial testing for several reasons. First, because of edema, epicardial testing of surgical ablation lines can lead to false negative results. Secondly, it can be challenging to adequately pace in between instead of on the performed ablation lines. Also, the border between conducting and non-conducting tissue at the distal sleeve of the pulmonary vein cannot be determined without sophisticated mapping techniques. Third, there is a timeframe of at least 30 minutes between epicardial PV isolation and endocardial validation, which can help to unmask incomplete PV isolation. Last, endocardial testing of PV isolation allows electrophysiological mapping using validated techniques (e.g. Lasso catheter). Probably these advantages result in a more durable PV isolation and thereby contribute to a higher rate of AF freedom.

Conclusion

PV isolation remains the cornerstone in AF ablation. In catheter ablation, durable PV isolation is mandatory as recurrences of AF go hand in hand with PV reconnection. In surgical ablation of AF, the necessity of PV isolation is more difficult to demonstrate, as reports on redo procedures after surgery are scarce. However, there are no obvious reasons why surgical ablation would differ from catheter ablation in necessitating PV isolation. Surgical ablation of AF seems superior to catheter ablation of AF, especially in the treatment of

non-paroxysmal forms of AF. This seems, at least in part, to be due to the use of bipolar radiofrequency devices. As such, more durable PV isolation is to be expected in surgical AF ablation. Therefore the efficacy of additional substrate modification techniques should also be evaluated in patients undergoing surgical AF ablation, and not only in patients undergoing percutaneous ablation.

References

- Schotten U, Verheule S, Kirchhof P, Goette A. Pathophysiological mechanisms of atrial fibrillation: a translational appraisal. *Physiol Rev* 2011;91(1):265-325.
- Moe GK, Abildskov JA. Atrial fibrillation as a self-sustaining arrhythmia independent of focal discharge. *Am Heart J* 1959;58(1):59-70.
- Lee AM, Aziz A, Didesch J, Clark KL, Schuessler RB, Damiano RJ, Jr. Importance of atrial surface area and refractory period in sustaining atrial fibrillation: testing the critical mass hypothesis. *J Thorac Cardiovasc Surg* 2013;146(3):593-8.
- Ad N. The Cox-Maze procedure: history, results, and predictors for failure. *Journal of interventional cardiac electrophysiology : an international journal of arrhythmias and pacing* 2007;20(3):65-71.
- Cox JL. The surgical treatment of atrial fibrillation. IV. Surgical technique. *J Thorac Cardiovasc Surg* 1991;101(4):584-92.
- Cox JL, Canavan TE, Schuessler RB, Cain ME, Lindsay BD, Stone C, Smith PK, Corr PB, Boineau JP. The surgical treatment of atrial fibrillation. II. Intraoperative electrophysiologic mapping and description of the electrophysiologic basis of atrial flutter and atrial fibrillation. *J Thorac Cardiovasc Surg* 1991;101(3):406-26.
- Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Metayer P, Clementy J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;339(10):659-66.
- Kumagai K, Ogawa M, Noguchi H, Yasuda T, Nakashima H, Saku K. Electrophysiologic properties of pulmonary veins assessed using a multielectrode basket catheter. *Journal of the American College of Cardiology* 2004;43(12):2281-9.
- Lee G, Spence S, Teh A, Goldblatt J, Larobina M, Atkinson V, Brown R, Morton JB, Sanders P, Kistler PM, Kalman JM. High-density epicardial mapping of the pulmonary vein-left atrial junction in humans: insights into mechanisms of pulmonary vein arrhythmogenesis. *Heart Rhythm* 2012;9(2):258-64.
- de Bakker JM, Ho SY, Hocini M. Basic and clinical electrophysiology of pulmonary vein ectopy. *Cardiovascular research* 2002;54(2):287-94.
- Wijffels MCEF, Kirchhof CJHJ, Dorland R, Allesie MA. Atrial Fibrillation Begets Atrial Fibrillation : A Study in Awake Chronically Instrumented Goats. *Circulation* 1995;92(7):1954-1968.
- Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ, Damiano RJ, Jr., Davies DW, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, Haines DE, Haissaguerre M, Hindricks G, Iesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim YH, Kirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky E, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao HM, Wilber D. 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Europace* 2012;14(4):528-606.
- Brooks AG, Stiles MK, Laborderie J, Lau DH, Kuklik P, Shipp NJ, Hsu LF, Sanders P. Outcomes of long-standing persistent atrial fibrillation ablation: a systematic review. *Heart Rhythm* 2010;7(6):835-46.
- Hwang C, Karagueuzian HS, Chen PS. Idiopathic paroxysmal atrial fibrillation induced by a focal discharge mechanism in the left superior pulmonary vein: possible roles of the ligament of Marshall. *Journal of cardiovascular*

- electrophysiology 1999;10(5):636-48.
15. Tsai CF, Tai CT, Hsieh MH, Lin WS, Yu WC, Ueng KC, Ding YA, Chang MS, Chen SA. Initiation of atrial fibrillation by ectopic beats originating from the superior vena cava: electrophysiological characteristics and results of radiofrequency ablation. *Circulation* 2000;102(1):67-74.
 16. Di Biase L, Burkhardt JD, Mohanty P, Sanchez J, Mohanty S, Horton R, Gallinghouse GJ, Bailey SM, Zagrodzky JD, Santangeli P, Hao S, Hongo R, Beheiry S, Themistoclakis S, Bonso A, Rossillo A, Corrado A, Raviele A, Al-Ahmad A, Wang P, Cummings JE, Schweikert RA, Pelargonio G, Dello Russo A, Casella M, Santarelli P, Lewis WR, Natale A. Left atrial appendage: an underrecognized trigger site of atrial fibrillation. *Circulation* 2010;122(2):109-18.
 17. Ernst S, Ouyang F, Lober F, Antz M, Kuck KH. Catheter-induced linear lesions in the left atrium in patients with atrial fibrillation: an electroanatomic study. *Journal of the American College of Cardiology* 2003;42(7):1271-82.
 18. Jais P, Hocini M, Hsu LF, Sanders P, Scavee C, Weerasooriya R, Macle L, Raybaud F, Garrigue S, Shah DC, Le Metayer P, Clementy J, Haissaguerre M. Technique and results of linear ablation at the mitral isthmus. *Circulation* 2004;110(19):2996-3002.
 19. Ho SY, Sanchez-Quintana D, Cabrera JA, Anderson RH. Anatomy of the left atrium: implications for radiofrequency ablation of atrial fibrillation. *Journal of cardiovascular electrophysiology* 1999;10(11):1525-33.
 20. Hocini M, Jais P, Sanders P, Takahashi Y, Rotter M, Rostock T, Hsu LF, Sacher F, Reuter S, Clementy J, Haissaguerre M. Techniques, evaluation, and consequences of linear block at the left atrial roof in paroxysmal atrial fibrillation: a prospective randomized study. *Circulation* 2005;112(24):3688-96.
 21. Nademanee K, McKenzie J, Kosar E, Schwab M, Sumsaneewitayakul B, Vasavakul T, Khunnawat C, Ngarmukos T. A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. *Journal of the American College of Cardiology* 2004;43(11):2044-53.
 22. Konings KT, Kirchhof CJ, Smeets JR, Wellens HJ, Penn OC, Allessie MA. High-density mapping of electrically induced atrial fibrillation in humans. *Circulation* 1994;89(4):1665-80.
 23. Narayan SM, Krummen DE, Rappel WJ. Clinical mapping approach to diagnose electrical rotors and focal impulse sources for human atrial fibrillation. *Journal of cardiovascular electrophysiology* 2012;23(5):447-54.
 24. Narayan SM, Krummen DE, Shivkumar K, Clopton P, Rappel WJ, Miller JM. Treatment of atrial fibrillation by the ablation of localized sources: CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) trial. *Journal of the American College of Cardiology* 2012;60(7):628-36.
 25. Miller JM, Kowal RC, Swarup V, Daubert JP, Daoud EG, Day JD, Ellenbogen KA, Hummel JD, Baykaner T, Krummen DE, Narayan SM, Reddy VY, Shivkumar K, Steinberg JS, Wheelan KR. Initial Independent Outcomes from Focal Impulse and Rotor Modulation Ablation for Atrial Fibrillation: Multicenter FIRM Registry. *Journal of Cardiovascular Electrophysiology* 2014;25(9):921-929.
 26. Haissaguerre M, Hocini M, Shah AJ, Derval N, Sacher F, Jais P, Dubois R. Noninvasive Panoramic Mapping of Human Atrial Fibrillation Mechanisms: A Feasibility Report. *Journal of Cardiovascular Electrophysiology* 2013;24(6):711-717.
 27. Haissaguerre M, Hocini M, Denis A, Shah AJ, Komatsu Y, Yamashita S, Daly M, Amraoui S, Zellerhoff S, Picat MQ, Quotb A, Jesel L, Lim H, Ploux S, Bordachar P, Attuel G, Meillet V, Ritter P, Derval N, Sacher F, Bernus O, Cochet H, Jais P, Dubois R. Driver domains in persistent atrial fibrillation. *Circulation* 2014;130(7):530-8.
 28. Damiano RJ, Jr., Bailey M. The Cox-Maze IV procedure for lone atrial fibrillation. *Multimed Man Cardiothorac Surg* 2007;2007(723):mmcts 2007 002758.
 29. Nitta T, Lee R, Schuessler RB, Boineau JP, Cox JL. Radial approach: a new concept in surgical treatment for atrial fibrillation I. Concept, anatomic and physiologic bases and development of a procedure. *Ann Thorac Surg* 1999;67(1):27-35.
 30. Nitta T, Ishii Y, Ogasawara H, Sakamoto S, Miyagi Y, Yamada K, Kanno S, Tanaka S. Initial experience with the radial incision approach for atrial fibrillation. *Ann Thorac Surg* 1999;68(3):805-10; discussion 811.
 31. La Meir M, Gelsomino S, Luca F, Pison L, Colella A, Lorusso R, Crudeli E, Gensini GF, Crijns HG, Maessen J. Minimal invasive surgery for atrial fibrillation: an updated review. *Europace* 2013;15(2):170-82.
 32. Lee AM, Melby SJ, Damiano RJ, Jr. The surgical treatment of atrial fibrillation. *Surg Clin North Am* 2009;89(4):1001-20, x-xi.
 33. Wolf RK, Schneeberger EW, Osterday R, Miller D, Merrill W, Flege JB, Jr., Gillinov AM. Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. *J Thorac Cardiovasc Surg* 2005;130(3):797-802.
 34. Edgerton JR, Edgerton ZJ, Weaver T, Reed K, Prince S, Herbert MA, Mack MJ. Minimally invasive pulmonary vein isolation and partial autonomic denervation for surgical treatment of atrial fibrillation. *Ann Thorac Surg* 2008;86(1):35-8; discussion 39.
 35. Edgerton JR, Jackman WM, Mack MJ. A new epicardial lesion set for minimal access left atrial maze: the Dallas lesion set. *Ann Thorac Surg* 2009;88(5):1655-7.
 36. Lockwood D, Nakagawa H, Peyton MD, Edgerton JR, Scherlag BJ, Sivaram CA, Po SS, Beckman KJ, Abedin M, Jackman WM. Linear left atrial lesions in minimally invasive surgical ablation of persistent atrial fibrillation: techniques for assessing conduction block across surgical lesions. *Heart Rhythm* 2009;6(12 Suppl):S50-63.
 37. Bugge E, Nicholson IA, Thomas SP. Comparison of bipolar and unipolar radiofrequency ablation in an in vivo experimental model. *Eur J Cardiothorac Surg* 2005;28(1):76-80; discussion 80-2.
 38. Pison L, La Meir M, van Opstal J, Blaauw Y, Maessen J, Crijns HJ. Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation. *Journal of the American College of Cardiology* 2012;60(1):54-61.
 39. Oral H, Scharf C, Chugh A, Hall B, Cheung P, Good E, Veerareddy S, Pelosi F, Jr., Morady F. Catheter ablation for paroxysmal atrial fibrillation: segmental pulmonary vein ostial ablation versus left atrial ablation. *Circulation* 2003;108(19):2355-60.
 40. Pappone C, Rosanio S, Oreto G, Tocchi M, Gugliotta F, Vicedomini G, Salvati A, Dicandia C, Mazzone P, Santinelli V, Gulletta S, Chierchia S. Circumferential radiofrequency ablation of pulmonary vein ostia: A new anatomic approach for curing atrial fibrillation. *Circulation* 2000;102(21):2619-28.
 41. Ouyang F, Bansch D, Ernst S, Schaumann A, Hachiya H, Chen M, Chun J, Falk P, Khanedani A, Antz M, Kuck KH. Complete isolation of left atrium surrounding the pulmonary veins: new insights from the double-Lasso technique in paroxysmal atrial fibrillation. *Circulation* 2004;110(15):2090-6.
 42. Piccini JP, Lopes RD, Kong MH, Hasselblad V, Jackson K, Al-Khatib SM. Pulmonary vein isolation for the maintenance of sinus rhythm in patients with atrial fibrillation: a meta-analysis of randomized, controlled trials. *Circulation Arrhythmia and electrophysiology* 2009;2(6):626-33.
 43. Sawhney N, Anousheh R, Chen WC, Narayan S, Feld GK. Five-year outcomes after segmental pulmonary vein isolation for paroxysmal atrial fibrillation. *Am J Cardiol* 2009;104(3):366-72.
 44. Ouyang F, Tilz R, Chun J, Schmidt B, Wissner E, Zerm T, Neven K, Kokturk B, Konstantinidou M, Metzner A, Fuernkranz A, Kuck KH. Long-term results of catheter ablation in paroxysmal atrial fibrillation: lessons from a 5-year follow-up. *Circulation* 2010;122(23):2368-77.
 45. Tilz RR, Rillig A, Thum AM, Arya A, Wohlmuth P, Metzner A, Mathew S, Yoshiga Y, Wissner E, Kuck KH, Ouyang F. Catheter ablation of long-standing persistent atrial fibrillation: 5-year outcomes of the Hamburg Sequential Ablation Strategy. *Journal of the American College of Cardiology* 2012;60(19):1921-9.
 46. Medi C, Sparks PB, Morton JB, Kistler PM, Halloran K, Rosso R, Vohra JK, Kumar S, Kalman JM. Pulmonary vein antral isolation for paroxysmal atrial fibrillation: results from long-term follow-up. *Journal of cardiovascular electrophysiology*

- 2011;22(2):137-41.
47. Teunissen C, Kassenberg W, van der Heijden JF, Hassink RJ, van Driel VJ, Zuithoff NP, Doevendans PA, Loh P. Five-year efficacy of pulmonary vein antrum isolation as a primary ablation strategy for atrial fibrillation: a single-centre cohort study. *Europace* 2016.
 48. Oral H, Knight BP, Tada H, Ozaydin M, Chugh A, Hassan S, Scharf C, Lai SW, Greenstein R, Pelosi F, Jr., Strickberger SA, Morady F. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. *Circulation* 2002;105(9):1077-81.
 49. Callans DJ, Gerstenfeld EP, Dixit S, Zado E, Vanderhoff M, Ren JF, Marchlinski FE. Efficacy of repeat pulmonary vein isolation procedures in patients with recurrent atrial fibrillation. *Journal of cardiovascular electrophysiology* 2004;15(9):1050-5.
 50. Kuck KH, Hoffmann BA, Ernst S, Wegscheider K, Treszl A, Metzner A, Eckardt L, Lewalter T, Breithardt G, Willems S, Gap AF. Impact of Complete Versus Incomplete Circumferential Lines Around the Pulmonary Veins During Catheter Ablation of Paroxysmal Atrial Fibrillation: Results From the Gap-Atrial Fibrillation-German Atrial Fibrillation Competence Network 1 Trial. *Circulation Arrhythmia and electrophysiology* 2016;9(1):e003337.
 51. Kuck KH, Brugada J, Furnkranz A, Metzner A, Ouyang F, Chun KR, Elvan A, Arentz T, Bestehorn K, Pocock SJ, Albenque JP, Tondo C, Fire, Investigators ICE. Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation. *N Engl J Med* 2016.
 52. Conte G, Chierchia GB, Sicira J, Levinstein M, Casado-Arroyo R, De Asmundis C, Sarkozy A, Rodriguez-Manero M, Di Giovanni G, Baltogiannis G, Wauters K, Brugada P. Repeat procedure using radiofrequency energy for recurrence of atrial fibrillation after initial cryoballoon ablation: a 2-year follow-up. *Europace* 2013;15(10):1421-5.
 53. Macle L, Khairy P, Weerasooriya R, Novak P, Verma A, Willems S, Arentz T, Deisenhofer I, Veenhuyzen G, Scavee C, Jais P, Puererfellner H, Levesque S, Andrade JG, Rivard L, Guerra PG, Dubuc M, Thibault B, Talajic M, Roy D, Nattel S, investigators At. Adenosine-guided pulmonary vein isolation for the treatment of paroxysmal atrial fibrillation: an international, multicentre, randomised superiority trial. *Lancet* 2015;386(9994):672-9.
 54. Bansch D, Bittkau J, Schneider R, Schneider C, Wendig I, Akin I, Nienaber CA. Circumferential pulmonary vein isolation: wait or stop early after initial successful pulmonary vein isolation? *Europace* 2013;15(2):183-8.
 55. Essebag V, Wylie JV, Jr., Reynolds MR, Baldessin F, McClennen S, Shvilkin A, Germano J, Richardson A, Zimetbaum PJ, Josephson ME. Bi-directional electrical pulmonary vein isolation as an endpoint for ablation of paroxysmal atrial fibrillation. *Journal of interventional cardiac electrophysiology : an international journal of arrhythmias and pacing* 2006;17(2):111-7.
 56. Wittkamp FH, van Driel VJ, van Wessel H, Neven KG, Grundeman PF, Vink A, Loh P, Doevendans PA. Myocardial lesion depth with circular electroporation ablation. *Circulation Arrhythmia and electrophysiology* 2012;5(3):581-6.
 57. Fassini G, Riva S, Chiodelli R, Trevisi N, Berti M, Carbucicchio C, Maccabelli G, Giraldi F, Bella PD. Left mitral isthmus ablation associated with PV Isolation: long-term results of a prospective randomized study. *Journal of cardiovascular electrophysiology* 2005;16(11):1150-6.
 58. Estner HL, Hessling G, Ndrepega G, Wu J, Reents T, Fichtner S, Schmitt C, Bary CV, Kolb C, Karch M, Zrenner B, Deisenhofer I. Electrogram-guided substrate ablation with or without pulmonary vein isolation in patients with persistent atrial fibrillation. *Europace* 2008;10(11):1281-7.
 59. Oral H, Chugh A, Yoshida K, Sarrazin JF, Kuhne M, Crawford T, Chalfoun N, Wells D, Boonyapisit W, Veerareddy S, Billakanty S, Wong WS, Good E, Jongnarangsin K, Pelosi F, Jr., Bogun F, Morady F. A randomized assessment of the incremental role of ablation of complex fractionated atrial electrograms after antral pulmonary vein isolation for long-lasting persistent atrial fibrillation. *Journal of the American College of Cardiology* 2009;53(9):782-9.
 60. Lau DH, Maesen B, Zeemering S, Verheule S, Crijns HJ, Schotten U. Stability of complex fractionated atrial electrograms: a systematic review. *Journal of cardiovascular electrophysiology* 2012;23(9):980-7.
 61. Lau DH, Maesen B, Zeemering S, Kuklik P, van Hunnik A, Lankveld TA, Bidar E, Verheule S, Nijs J, Maessen J, Crijns H, Sanders P, Schotten U. Indices of Bipolar Complex Fractionated Atrial Electrograms Correlate Poorly with Each Other and Atrial Fibrillation Substrate Complexity. *Heart Rhythm* 2015.
 62. Gaita F, Caponi D, Scaglione M, Montefusco A, Corleto A, Di Monte F, Coin D, Di Donna P, Giustetto C. Long-term clinical results of 2 different ablation strategies in patients with paroxysmal and persistent atrial fibrillation. *Circulation Arrhythmia and electrophysiology* 2008;1(4):269-75.
 63. Verma A, Jiang CY, Betts TR, Chen J, Deisenhofer I, Mantovan R, Macle L, Morillo CA, Haverkamp W, Weerasooriya R, Albenque JP, Nardi S, Menardi E, Novak P, Sanders P, Investigators SAI. Approaches to catheter ablation for persistent atrial fibrillation. *N Engl J Med* 2015;372(19):1812-22.
 64. Vogler J, Willems S, Sultan A, Schreiber D, Luker J, Servatius H, Schaffer B, Moser J, Hoffmann BA, Steven D. Pulmonary Vein Isolation Versus Defragmentation: The CHASE-AF Clinical Trial. *Journal of the American College of Cardiology* 2015;66(24):2743-52.
 65. Wong KC, Paisey JR, Sopher M, Balasubramaniam R, Jones M, Qureshi N, Hayes CR, Ginks MR, Rajappan K, Bashir Y, Betts TR. No Benefit of Complex Fractionated Atrial Electrogram Ablation in Addition to Circumferential Pulmonary Vein Ablation and Linear Ablation: Benefit of Complex Ablation Study. *Circulation Arrhythmia and electrophysiology* 2015;8(6):1316-24.
 66. Pison L, Vroomen M, Crijns HJ. Catheter Ablation for Persistent Atrial Fibrillation. *N Engl J Med* 2015;373(9):877-8.
 67. Narayan SM, Krummen DE, Shivkumar K, Clopton P, Rappel W-J, Miller JM. Treatment of Atrial Fibrillation by the Ablation of Localized Sources: CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) Trial. *J Am Coll Cardiol* 2012;60(7):628-636.
 68. Narayan SM, Baykaner T, Clopton P, Schricker A, Lalani GG, Krummen DE, Shivkumar K, Miller JM. Ablation of rotor and focal sources reduces late recurrence of atrial fibrillation compared with trigger ablation alone: extended follow-up of the CONFIRM trial (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation). *Journal of the American College of Cardiology* 2014;63(17):1761-8.
 69. Gianni C, Mohanty S, Di Biase L, Metz T, Trivedi C, Gokoglan Y, Gunes MF, Bai R, Al-Ahmad A, Burkhardt JD, Gallingshouse GJ, Horton RP, Hranitzky PM, Sanchez JE, Halbfass P, Muller P, Schade A, Deneke T, Tomassoni GF, Natale A. Acute and early outcomes of focal impulse and rotor modulation (FIRM)-guided rotors-only ablation in patients with nonparoxysmal atrial fibrillation. *Heart Rhythm* 2016;13(4):830-5.
 70. Takahashi Y, Sanders P, Rotter M, Haissaguerre M. Disconnection of the left atrial appendage for elimination of foci maintaining atrial fibrillation. *Journal of cardiovascular electrophysiology* 2005;16(8):917-9.
 71. Voeller RK, Zierer A, Schuessler RB, Damiano RJ, Jr. Performance of a novel dual-electrode bipolar radiofrequency ablation device: a chronic porcine study. *Innovations (Phila)* 2011;6(1):17-22.
 72. De Maat GE, Van Gelder IC, Rienstra M, Quast AF, Tan ES, Wiesfeld AC, Pozzoli A, Mariani MA. Surgical vs. transcatheter pulmonary vein isolation as first invasive treatment in patients with atrial fibrillation: a matched group comparison. *Europace* 2014;16(1):33-9.
 73. Boersma LV, Castella M, van Boven W, Berrueto A, Yilmaz A, Nadal M, Sandoval E, Calvo N, Brugada J, Kelder J, Wijffels M, Mont L. Atrial fibrillation catheter ablation versus surgical ablation treatment (FAST): a 2-center randomized clinical trial. *Circulation* 2012;125(1):23-30.
 74. Phan K, Phan S, Thiagalingam A, Medi C, Yan TD. Thoracoscopic surgical ablation versus catheter ablation for atrial fibrillation. *Eur J Cardiothorac Surg*

- 2016;49(4):1044-51.
75. De Maat GE, Pozzoli A, Scholten MF, Van Gelder IC, Blaauw Y, Mulder BA, Della Bella P, Alfieri OR, Benussi S, Mariani MA. Long-term results of surgical minimally invasive pulmonary vein isolation for paroxysmal lone atrial fibrillation. *Europace* 2015;17(5):747-52.
76. Gaita F, Riccardi R, Caponi D, Shah D, Garberoglio L, Vivalda L, Dulio A, Chiechio A, Manasse E, Gallotti R. Linear cryoablation of the left atrium versus pulmonary vein cryoisolation in patients with permanent atrial fibrillation and valvular heart disease: correlation of electroanatomic mapping and long-term clinical results. *Circulation* 2005;111(2):136-42.
77. Voeller RK, Bailey MS, Zierer A, Lall SC, Sakamoto S, Aubuchon K, Lawton JS, Moazami N, Huddleston CB, Munfakh NA, Moon MR, Schuessler RB, Damiano RJ, Jr. Isolating the entire posterior left atrium improves surgical outcomes after the Cox maze procedure. *J Thorac Cardiovasc Surg* 2008;135(4):870-7.
78. Gillinov AM, Gelijns AC, Parides MK, DeRose JJ, Jr., Moskowitz AJ, Voisine P, Ailawadi G, Bouchard D, Smith PK, Mack MJ, Acker MA, Mullen JC, Rose EA, Chang HL, Puskas JD, Couderc JP, Gardner TJ, Varghese R, Horvath KA, Bolling SF, Michler RE, Geller NL, Ascheim DD, Miller MA, Bagiella E, Moquete EG, Williams P, Taddei-Peters WC, O'Gara PT, Blackstone EH, Argenziano M, Investigators C. Surgical ablation of atrial fibrillation during mitral-valve surgery. *N Engl J Med* 2015;372(15):1399-409.
79. Lawrance CP, Henn MC, Miller JR, Sinn LA, Schuessler RB, Damiano RJ, Jr. Comparison of the stand-alone Cox-Maze IV procedure to the concomitant Cox-Maze IV and mitral valve procedure for atrial fibrillation. *Ann Cardiothorac Surg* 2014;3(1):55-61.
80. Kron J, Kasirajan V, Wood MA, Kowalski M, Han FT, Ellenbogen KA. Management of recurrent atrial arrhythmias after minimally invasive surgical pulmonary vein isolation and ganglionic plexi ablation for atrial fibrillation. *Heart Rhythm* 2010;7(4):445-51.
81. Zeng Y, Cui Y, Li Y, Liu X, Xu C, Han J, Meng X. Recurrent atrial arrhythmia after minimally invasive pulmonary vein isolation for atrial fibrillation. *Ann Thorac Surg* 2010;90(2):510-5.
82. Trumello C, Pozzoli A, Mazzone P, Nascimbene S, Bignami E, Cireddu M, Della Bella P, Alfieri O, Benussi S. Electrophysiological findings and long-term outcomes of percutaneous ablation of atrial arrhythmias after surgical ablation for atrial fibrillation. *Eur J Cardiothorac Surg* 2016;49(1):273-80.
83. Velagic V, CDEA, Mugnai G, Irfan G, Hunuk B, Stroker E, Hacıoglu E, Umbrain V, Beckers S, Czaplaj, Wellens F, Nijs J, Brugada P, M LAM, Chierchia GB. Repeat Procedures After Hybrid Thoracoscopic Ablation in the Setting of Longstanding Persistent Atrial Fibrillation: Electrophysiological Findings and 2-Year Clinical Outcome. *Journal of cardiovascular electrophysiology* 2016;27(1):41-50.
84. On YK, Park KM, Jeong DS, Park PW, Lee YT, Park SJ, Kim JS. Electrophysiologic Results After Thoracoscopic Ablation for Chronic Atrial Fibrillation. *Ann Thorac Surg* 2015;100(5):1595-602; discussion 1602-3.