



# A hybrid approach to complex arrhythmias

Bart Maesen <sup>1,2\*</sup>, Justin G.L.M. Luermans <sup>2,3</sup>, Elham Bidar <sup>1,2</sup>,  
Sevasti-Maria Chaldoupi <sup>2,3</sup>, Sandro Gelsomino <sup>1</sup>, Jos G. Maessen <sup>1,2</sup>,  
Laurent Pison <sup>4</sup>, and Mark La Meir <sup>1,5</sup>

<sup>1</sup>Department of Cardiothoracic Surgery, Maastricht University Medical Center, Maastricht, the Netherlands; <sup>2</sup>Cardiovascular Research Institute Maastricht, Maastricht University, Maastricht, the Netherlands; <sup>3</sup>Department of Cardiology, Maastricht University Medical Center, Maastricht, the Netherlands; <sup>4</sup>Department of Cardiology, ZOL, Genk, Belgium; and <sup>5</sup>Department of Cardiothoracic Surgery, UZ Brussels, Brussels, Belgium

Received 6 November 2020; editorial decision 16 January 2021; accepted after revision 20 January 2021

## Abstract

Despite many years of research, the different aspects of the mechanism of atrial fibrillation (AF) are still incompletely understood. And although the latest guidelines recommend catheter ablation with pulmonary vein isolation as a rhythm control strategy, long-term results in persistent and long-standing persistent AF are suboptimal. Historically, a mechanistic-based patient-tailored approach for the treatment of AF was impossible because of the lack of real-time mapping techniques and advanced ablation tools. Therefore, surgeons created lesion sets based upon the anatomy of both atria and the safety of the incisions made by the knife. These complex open-heart procedures had to be performed through a sternotomy on the arrested heart and were therefore not generally adopted. The use of controlled energy sources such as cryotherapy and radiofrequency where the first step to make the creation of these lesions less complex. With the development and improvement of electrophysiology techniques and catheters, this invasive and solely anatomical approach could again be partially redesigned. Now less invasive, it prepared the way for collaboration between electrophysiologists working on the endocardial side of the heart and cardiac surgeons providing epicardial access. The introduction of video-assisted technology and hybrid procedures has further increased the possibilities of new successful therapies. Now more than 40 years since the beginning of this exciting maze of AF procedures and still working towards a less aggressive and more comprehensive approach we give an overview of the history of the different minimally invasive surgical solutions and of the hybrid approach.

## Keywords

Atrial fibrillation • Hybrid atrial fibrillation ablation • Catheter ablation • Surgical ablation Minimally invasive surgery • Cardiac arrhythmia • Thoracoscopic ablation • Persistent atrial fibrillation • Endocardial–epicardial ablation • Review • History of arrhythmia surgery • Historical overview

## Introduction

Despite the fact that numerous groups have addressed the different aspects of the mechanism of atrial fibrillation (AF), <sup>1–6</sup> to date, the precise pathophysiological processes underlying the initiation and perpetuation of persistent AF remain to be unraveled.<sup>7</sup> While it is generally accepted that AF paroxysms are triggered by ectopic activity arising from anatomical locations where cardiac muscle intermingles with non-excitable vascular tissue, as, for example, in the muscular sleeves of the pulmonary veins,<sup>8,9</sup> no consensus exists as to which AF drivers form the sustaining mechanism leading to

persistence of AF.<sup>7</sup> Over the years, several potential AF driving mechanisms, often assessed with the use of advanced mapping techniques, were studied, resulting in the identification of novel substrate targets.<sup>6,10–19</sup> In most cases, despite promising initial results, the significant improvement in treatment outcome could not be confirmed in large independent multicentre randomized controlled trials.

To date, the complexity of AF pathophysiology prevents a true mechanistic-based patient-tailored approach for the management of AF. Therefore, current invasive AF treatment, catheter-based or surgical, is based on anatomical landmarks or general electrophysiological findings regarding AF triggers. Surgical treatment of AF can be

\* Corresponding author. Tel: +31433871125; fax: +31433875073. E-mail address: b.maesen@mumc.nl

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author(s) 2021. For permissions, please email: journals.permissions@oup.com.

performed on the arrested or on the beating heart. While the on-pump Cox-Maze procedure<sup>20</sup> is a surgical approach mainly based upon anatomical landmarks, off-pump beating-heart thoracoscopic approaches are more 'trigger-driven', focusing on the pulmonary veins and the posterior left atrial wall. Over the years, surgical treatment of so-called 'lone-AF' has shifted from the Cox-Maze procedure, remaining the golden standard, to minimally invasive thoracoscopic approaches.

Given the complexity of AF conduction patterns,<sup>1,2,21,22</sup> it was decided in 2010 in Maastricht to combine forces. Because one of the major weaknesses of endocardial catheter ablation techniques is the inability to create long-lasting linear transmural lesions,<sup>23</sup> and modern surgical AF ablation techniques, on the other hand, are less affected by incomplete lesions but lack the ability to define the specific properties of the underlying atrial electrical substrate in order to customize the ablation strategy, a hybrid approach that combines a transvenous endocardial and thoracoscopic epicardial approach in a single procedure was developed in order to overcome their mutual shortcomings.<sup>24,25</sup> Here, we give an overview of the history of the different minimally invasive surgical approaches and of the hybrid approach. With the goal of providing a comprehensible overview, a summarized version of the history of arrhythmia surgery is illustrated with the help of a 'maze'-diagram (Figure 1).

## Minimally invasive atrial fibrillation surgery

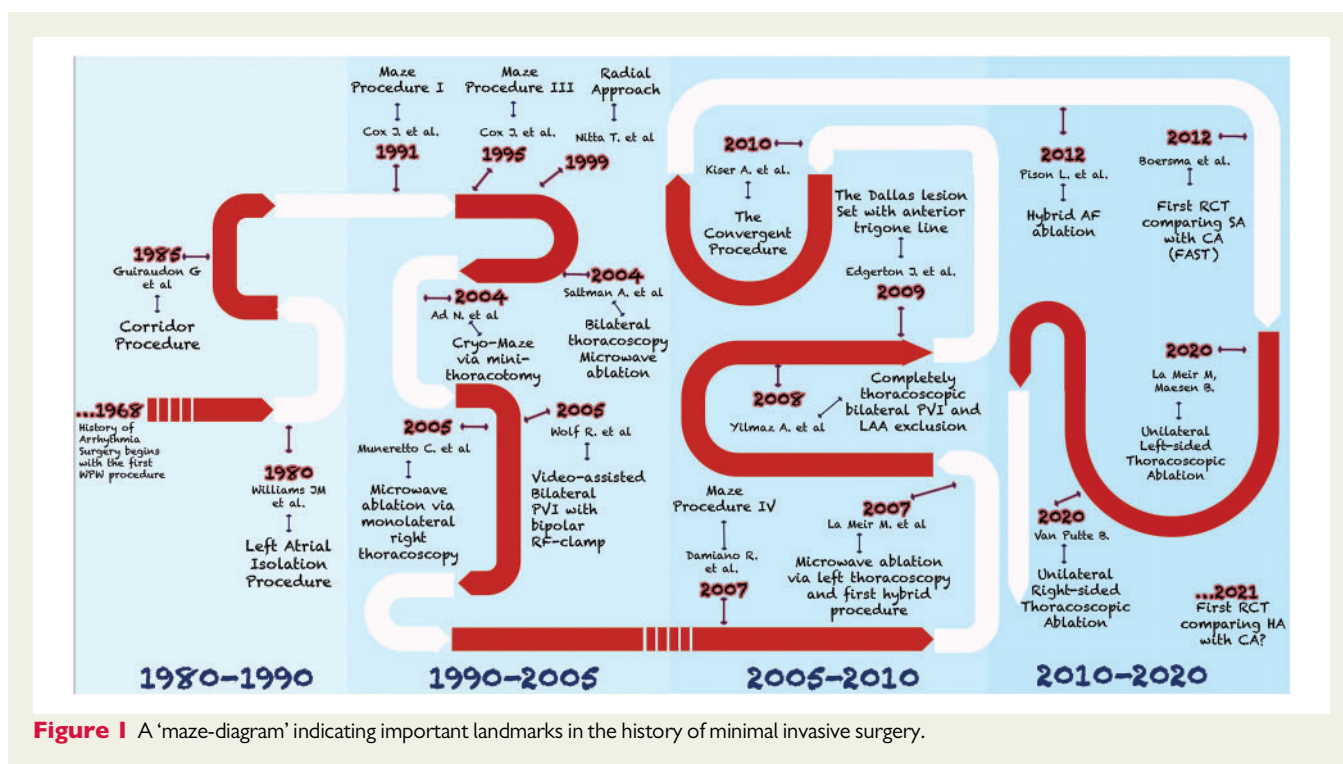
The difficulty with surgical treatment of AF is that it was, in its early years, solely based on atrial isolation or on atrial incisions to prevent re-entry and allow the sinus node (SA node) to activate the atrial myocardium in a channelled manner. In 1980, Williams *et al.* described the left atrial isolation procedure to try to confine AF to the left atrium while leaving the remainder of the heart in sinus rhythm.<sup>26</sup> In 1985, Guiraudon *et al.* presented the corridor procedure for the treatment of AF, a technique that isolated a 'corridor' harbouring the SA node and the atrioventricular node, thereby obtaining a regular ventricular rhythm driven by the SA node.<sup>27</sup> In their quest to try to stop AF, Cox *et al.* searched for a surgical technique that could be capable of interrupting all macro-reentrant circuits that might potentially develop in both atria.<sup>28</sup> An anatomic electrophysiological basis of AF was developed, the Maze procedure was born. Later on, modifications to this procedure were developed such as the use of bipolar RF clamps instead of cut-and-sew technique<sup>29</sup> and the radial approach based on alternative incision pattern.<sup>30</sup> For all procedures, the potential treatment of AF was based upon a complex surgical procedure. Therefore, for many years, any interventional treatment of a patient with AF had to be based upon an extensive surgical technique.

A simplified insight into the mechanisms of AF made a significant impact on our current approaches. In 1998, Haïssaguerre *et al.* demonstrated that the pulmonary veins are an important source of ectopic beats, initiating frequent paroxysms of AF. The understanding that it is often not necessary to perform a full Maze lesion set in stand-alone AF patients and the development of new ablation technologies to create transmural lesions on the beating heart has allowed us, in the last two decades, to treat AF through a less-

invasive access. Pulmonary vein isolation, isolation of the posterior wall combined with ganglionic plexi destruction and left atrial appendage exclusion can now be performed safely without extracorporeal bypass assistance.

Already in 2000, limitations of catheter ablation led to the concept of transthoracic epicardial application of radiofrequency (RF) energy on the beating heart using a video-assisted approach.<sup>31</sup> One of the first steps to minimally invasive surgery was reported in 2004 by Saltman *et al.*<sup>32</sup> Via a bilateral thoracoscopic technique, a flexible microwave ablation catheter was used to encircle the four veins, thereby creating a posterior left atrial wall isolation, a so-called box lesion. This technique was improved in 2005 to a unilateral approach by Muneretto *et al.* via the right side<sup>33</sup> and via the left side to be able to address the left atrial appendage by La Meir *et al.*<sup>34,35</sup> The difficulty to start these programs of thoracoscopic procedures was that for the first time beating heart surgery necessitating dissection of pericardial reflections and manipulation of catheters within the transverse and oblique sinuses had to be done with a port-access. The rationale of the creation of a box lesion was based on maximal AF trigger reduction by isolating the 4 pulmonary veins and the ligament of Marshall, reduction of substrate mass by isolation of the posterior wall, and partial cardiac denervation by ablation of the ganglionated plexi. Although the idea of creating a box lesion by encircling the four veins with a catheter was very innovative, the use of microwave as an energy source later appeared to be incapable in creating of long-lasting transmural lesions. Around this time, Wolf *et al.* reported a video-assisted technique to isolate the veins via a small thoracotomy on both sides of the chest with the use of the bipolar radiofrequency clamp.<sup>36</sup> The left atrial appendage was excised using a surgical stapler. The radiofrequency clamp was shown to be able to create long-lasting transmural lesions, specifically around the PVs. Although a thoracotomy facilitated the teaching of the approach, a less invasive approach was looked for and in 2008 Yilmaz *et al.* reported a completely thoracoscopic technique for bilateral pulmonary vein isolation and left atrial appendage exclusion.<sup>37</sup> As it was clear that linear lesions connecting the superior PVs by a roof line and inferior PVs by an inferior line could improve the outcome in terms of SR, a bipolar yet unidirectional device was introduced to create these lines, resulting in a box lesion similar to the original minimal invasive microwave procedure.

Although the success of minimally invasive AF ablation is large attributable to the important advantages of epicardial ablation, a complete mitral isthmus line cannot be performed via an epicardial approach. In 2009, Edgerton *et al.* introduced the interesting concept of creating an additional lesion, by connecting the roof line with the subaortic root left fibrous trigone, as part of the so-called 'Dallas lesion set'.<sup>38</sup> From an electrophysiological point of view, application of such an anterior trigone line is an intelligent way to mimic the effect of a mitral isthmus for the prevention of left atrial macro-reentrant circuits. However, considering that the path from the roofline to the subaortic non-conducting tissue can be long and treacherous on the beating heart, and taking into account that the protective effect of a trigone line, as it is with all ablation lines, requires complete block of electrical conduction over its full length, its benefit needs to outweigh the proarrhythmic risk. More recently, a left sided unilateral thoracoscopic technique to isolate left and right pulmonary veins, to create a box lesion and to address the left atrial appendage was introduced by



**Figure 1** A 'maze-diagram' indicating important landmarks in the history of minimal invasive surgery.

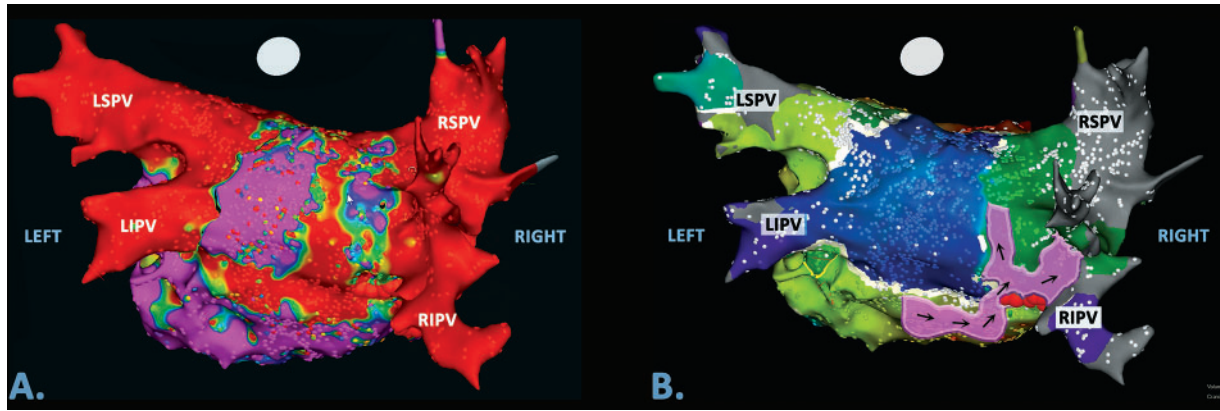
our group.<sup>39</sup> Later on, also a right-sided technique was introduced by the group of van Putte *et al.*<sup>40</sup> It remains to be determined if a left or a right sided technique is to be preferred, but the potential advantages of a left sided technique are a dissection of the pericardial reflections away from the heart instead of towards the heart, per-procedural right instead of left single lung ventilation and a clear visualisation of the left atrial appendage during exclusion. Anyhow, any unilateral technique has the big advantage that one avoids complications and postoperative pain at the contralateral side.

Another very promising technique is the subxiphoid approach to obtain direct access to the pericardial sac, the convergent procedure.<sup>41</sup> In most centres, an epicardial unipolar RF ablation of the posterior left atrial wall between the 4 PVs is performed and in a second procedure completed with a conventional endocardial catheter ablation of the PVs. Recently, the results of the Converge study, that randomized patients with non-paroxysmal AF to the convergent procedure vs. endocardial catheter ablation, 2:1, were reported.<sup>41</sup> In this trial, apart from posterior wall isolation, a more complete epicardial PV ablation was done (along the lateral sides of the PVs and the inferior side of the LIPV). Although the hybrid convergent arm had significant better freedom from AF than the catheter arm, the arrhythmia-free survival at 1 year off AAD, 53.5% vs. 32%, is low compared to other hybrid strategies.<sup>42-44</sup> Clearly, the subxiphoid route represents the most promising less invasive direct approach to the epicardium, has the potential to avoid thoracic complications and is a mandatory hybrid procedure. Therefore, this ablation strategy could be more acceptable to the EP community, the learning curve for the surgeon could be less and the adaption rate could be higher. However, in its current form it has the disadvantage that it does not allow bipolar bidirectional isolation of the pulmonary veins<sup>45</sup> and it is difficult (unless you add a left thoracoscopy or use cardiologic

closure device) to address the left atrial appendage. Both are potential explanations of the differences in reported outcomes.<sup>41-44</sup>

## Hybrid atrial fibrillation ablation

Surgical treatment by thoracoscopic or subxiphoid procedures has seen important improvements by combining these techniques with an endocardial EP approach since transmural of a lesion set cannot be guaranteed with current ablation catheters on the beating heart. Given the complexity of the arrhythmia, it is only logical to combine both approaches into one procedure. An epicardial approach has the advantage of being anatomical and fast, creating transmural lines and addressing the ganglionated plexi and the left atrial appendage. The latter may be an important determinant of success, as it not only has to potential to reduce the stroke risk,<sup>46</sup> but also isolates ectopic foci located in the LAA<sup>47,48</sup> and, in case of a large appendage, reduces the atrial mass needed to perpetuate the arrhythmia.<sup>49</sup> On the other side, an endocardial approach has the advantage of using advanced high-resolution mapping systems, evaluating hard end points and creating isthmus lines. The benefit of these endocardial advantages is obvious.<sup>50</sup> Epicardial testing of ablation lesions lacks the knowledge on the pre-existing AF substrate. *Figure 2A*, for example, represents a voltage map of the left atrium after epicardial ablation. As can be appreciated from the figure, there is a pre-existing cranio-caudal strand of fibrosis in the oblique sinus in between right and left pulmonary veins (red colour represents low voltage). Epicardial evaluation of exit or entrance block of the box lesion at this location would lead to the false assumption that the box is isolated. Pacing at a location where the tissue is still 'healthy' (purple colour represents normal voltage) would reveal that the box is not isolated, but leaves the



**Figure 2** (A) Voltage map of the posterior left atrial wall. (B) Still image of an activation map in the same patient. The site of ‘breakthrough’ where conduction enters the box is indicated by the purple ‘wave’. LIPV, left inferior superior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.

operator blinded to the exact location of the gap and thus requires re-ablation of all lines. In contrast, endocardial mapping (Figure 2B, still image of an activation map in the same patient, with location of the gap depicted in purple) enables easy location of gap and complete box isolation following the application a few targeted ablation points. Furthermore, epicardial approaches do not allow to create complete isthmus lesions. And although epicardial right atrial ablation allows to mimic most of the right atrial lesions of the Cox-Maze procedure,<sup>40</sup> it fails to complete its most important lesion, the cavo-tricuspid isthmus line.

Several RCTs have shown that adding linear lesions or additional targets on PVI does not necessarily increase the SR outcome. The FAST trial,<sup>51</sup> the CASA-AF trial,<sup>52</sup> the STAR-AF trial<sup>53</sup> should have made us aware that, apart from a consistent PVI, we are still having difficulties to achieve consistent reliable linear lesions. However, a hybrid procedure, whether performed in a single step or within 6 months after the epicardial approach, not only combines the advantages of an epicardial and endocardial approach, but also has shown to dramatically improve the quality of these linear lesions created by non-clamping devices, whether from the epicardium or endocardium.

In 2012, the first 26 patients (42% persistent AF) in which a thoracoscopic surgical ablation (consisting of PV isolation, a box lesion  $\pm$  additional lesions) was combined with endocardial validation and touch-up (if needed) were reported. The single procedure success rate was 83% at 1 year, off anti-arrhythmic drugs (AAD).<sup>54</sup> Recently, we reported the 3-year follow-up of this patient group.<sup>42</sup> This resulted in an overall 3-year freedom from AF/AT/AFL off after 1 hybrid procedure of 80% in paroxysmal AF (24 of 30 patients) and 79% in non-paroxysmal AF (26 of 33 patients).<sup>42</sup> But also other groups clearly demonstrated the benefit of such a hybrid approach. In 2019, Al-Jazairi *et al.* reported on hybrid AF ablation in 50 consecutive patients with persistent or long-standing persistent AF, or paroxysmal AF with two or more failed catheter ablations.<sup>44</sup> At 1 year, 76% of patients were in sinus rhythm without repeated ablation or the use of AAD. In the same year, we performed a meta-analysis in patients with persistent and longstanding persistent AF that demonstrated

that hybrid ablation is associated with higher success rates in maintaining SR compared to catheter ablation. Although hybrid ablation has a slightly higher complication rate than catheter ablation, over-all mortality and morbidity of both techniques is low.<sup>55</sup> These findings were included in the 2020 ESC guidelines<sup>56</sup> and are important take-home messages for the physician when discussing the different invasive rhythm control options in the informed consent with the AF patient.

The clear rationale for a hybrid approach in the treatment of non-paroxysmal AF and the lack of randomized clinical data comparing catheter ablation and hybrid ablation stimulated us to initiate the HARTCAP-AF study in 2017.<sup>57</sup> In this study, we randomized 40 patients to either hybrid (performed in one stage) or transvenous endocardial catheter ablation (allowing repeated ablation procedures) to compare the safety, efficacy, and cost-effectiveness of both procedures. The primary effectiveness endpoint was defined as freedom of documented supraventricular arrhythmias without the use of AAD throughout 12 months of follow-up. Failure in this endpoint was specified as a recurrence  $> 5$  minutes, considering that  $>30$  seconds does not *per se* predict clinical meaningful AF and taking into account that the AF patient’s quality of life is mainly affected by the amount of symptomatic AF burden.<sup>57,58</sup> For the primary safety endpoint, we assessed a composite endpoint of major adverse events and complications—including death, stroke, cardiac tamponade/perforation and bleeding requiring transfusion or reoperation, among others—during 12 months post procedure. The first patient was included on 30 January 2017 and as the 12-month follow-up of the last included patient was recently completed, the results will be reported in the very near future.

## Conclusion

In an editorial in response to our first report on hybrid AF ablation in 2012,<sup>54</sup> Dr Calkins wondered if hybrid thoracoscopic and transvenous catheter ablation of AF represented the answer we were searching. The success of minimally invasive surgical approaches using bipolar

biparietal RF tells us that a fixed lesion set resulting in adequate isolation of the pulmonary veins, the posterior left atria wall, including the ligament of Marshall and the LAA can successfully treat 70% of all persistent AF patients. As such, the difference in outcome between a surgical approach and an endocardial approach is not based on a 'secret ingredient', but is the consequence of the creation of long-lasting transmural lines. But it also demonstrates the limitations of a one-size-fits-all treatment, it cannot be adapted to the differences in AF substrate and in AF complexity between patients. The hybrid approach has the benefit of surgery, and creates the platform to combine it with a substrate-based approach. At the time, Dr Calkins stated that the hybrid strategy represents a 'logistical nightmare'. However, to date most cardiovascular centres dispose of 1 or more hybrid rooms and the number of surgeons performing minimally invasive AF ablation has significantly increased. In any case, it can be stated that 8 years later hybrid AF ablation represents a valid treatment option for patients with (longstanding) persistent AF, or patients with paroxysmal AF and two or more failed endocardial ablations. We think that the results of the HARTCAP-AF trial will, at least partly, answer the question raised by Dr Calkins in 2012.

**Conflict of interest:** B.M. has a contract for speaking services with Atricure. B.M., J.L., and L.P. are consultant for Medtronic. M.L.M. is a consultant for Atricure. All remaining authors have declared no conflicts of interest.

## References

- Maesen B, Zeemering S, Afonso C, Eckstein J, Burton RA, van Hunnik A et al. Rearrangement of atrial bundle architecture and consequent changes in anisotropy of conduction constitute the 3-dimensional substrate for atrial fibrillation. *Circ Arrhythm Electrophysiol* 2013;**6**:967–75.
- Eckstein J, Zeemering S, Linz D, Maesen B, Verheule S, van Hunnik A et al. Transmural conduction is the predominant mechanism of breakthrough during atrial fibrillation: evidence from simultaneous endo-epicardial high-density activation mapping. *Circ Arrhythm Electrophysiol* 2013;**6**:334–41.
- Narayan SM, Krummen DE, Rappel W-J. Clinical mapping approach to diagnose electrical rotors and focal impulse sources for human atrial fibrillation. *J Cardiovasc Electrophysiol* 2012;**23**:447–54.
- Lau DH, Maesen B, Zeemering S, Kuklik P, van Hunnik A, Lankveld TA et al. Indices of bipolar complex fractionated atrial electrograms correlate poorly with each other and atrial fibrillation substrate complexity. *Heart Rhythm* 2015;**12**:1415–23.
- 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**:1665–80.
- Nademanee K, McKenzie J, Kosar E, Schwab M, Sunsaneewitayakul B, Vasavakul T et al. A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. *J Am Coll Cardiol* 2004;**43**:2044–53.
- Schotten U, Verheule S, Kirchhof P, Goette A. Pathophysiological mechanisms of atrial fibrillation: a translational appraisal. *Physiol Rev* 2011;**91**:265–325.
- Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;**339**:659–66.
- de Bakker JM, Ho SY, Hocini M. Basic and clinical electrophysiology of pulmonary vein ectopy. *Cardiovasc Res* 2002;**54**:287–94.
- 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**:628–36.
- Kottkamp H. Fibrotic atrial cardiomyopathy: a specific disease/syndrome supplying substrates for atrial fibrillation, atrial tachycardia, sinus node disease, AV node disease, and thromboembolic complications. *J Cardiovasc Electrophysiol* 2012;**23**:797–9.
- Marrouche NF, Wilber D, Hindricks G, Jais P, Akoum N, Marchlinski F et al. Association of atrial tissue fibrosis identified by delayed enhancement MRI and atrial fibrillation catheter ablation: the DECAAF study. *JAMA* 2014;**311**:498–506.
- Lee G, Kumar S, Teh A, Madry A, Spence S, Larobina M et al. Epicardial wave mapping in human long-lasting persistent atrial fibrillation: transient rotational circuits, complex wavefronts, and disorganized activity. *Eur H J* 2014;**35**:86–97.
- Haissaguerre M, Hocini M, Denis A, Shah AJ, Komatsu Y, Yamashita S et al. Driver domains in persistent atrial fibrillation. *Circulation* 2014;**130**:530–8.
- Kottkamp H. Human atrial fibrillation substrate: towards a specific fibrotic atrial cardiomyopathy. *Eur Heart J* 2013;**34**:2731–8.
- Cuculich PS, Wang Y, Lindsay BD, Faddis MN, Schuessler RB, Damiano RJ, Jr. et al. Noninvasive characterization of epicardial activation in humans with diverse atrial fibrillation patterns. *Circulation* 2010;**122**:1364–72.
- Di Biase L, Burkhardt JD, Mohanty P, Sanchez J, Mohanty S, Horton R et al. Left atrial appendage: an underrecognized trigger site of atrial fibrillation. *Circulation* 2010;**122**:109–18.
- Kalifa J, Tanaka K, Zaitsev AV, Warren M, Vaidyanathan R, Auerbach D et al. Mechanisms of wave fractionation at boundaries of high-frequency excitation in the posterior left atrium of the isolated sheep heart during atrial fibrillation. *Circulation* 2006;**113**:626–33.
- Pappone C, Rosanio S, Oreto G, Tocchi M, Gugliotta F, Vicedomini G et al. Circumferential radiofrequency ablation of pulmonary vein ostia: a new anatomic approach for curing atrial fibrillation. *Circulation* 2000;**102**:2619–28.
- Cox JL, Jaquiss RD, Schuessler RB, Boineau JP. Modification of the maze procedure for atrial flutter and atrial fibrillation. II. Surgical technique of the maze III procedure. *J Thorac Cardiovasc Surg* 1995;**110**:485–95.
- Eckstein J, Maesen B, Linz D, Zeemering S, van Hunnik A, Verheule S et al. Time course and mechanisms of endo-epicardial electrical dissociation during atrial fibrillation in the goat. *Cardiovasc Res* 2011;**89**:816–24.
- de Groot NM, Houben RP, Smeets JL, Boersma E, Schotten U, Schalij MJ et al. Electropathological substrate of longstanding persistent atrial fibrillation in patients with structural heart disease: epicardial breakthrough. *Circulation* 2010;**122**:1674–82.
- Kuck KH, Hoffmann BA, Ernst S, Wegscheider K, Tressl A, Metzner A et al. 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. *Circ Arrhythm Electrophysiol* 2016;**9**:e003337.
- Pison L, Vroomen M, Crijns HJ. Catheter ablation for persistent atrial fibrillation. *N Engl J Med* 2015;**373**:877–8.
- La Meir M, Gelsomino S, Luca F, Lorusso R, Gensini GF, Pison L et al. Minimally invasive thoracoscopic hybrid treatment of lone atrial fibrillation: early results of monopolar versus bipolar radiofrequency source. *Interact Cardiovasc Thorac Surg* 2012;**14**:445–50.
- Mark Williams J, Ungerleider RM, Lofland GK, Cox JL, Sabiston DC. Left atrial isolation: new technique for the treatment of supraventricular arrhythmias. *J Thorac Cardiovasc Surg* 1980;**80**:373–80.
- Guiraudon G, Campbell C, Jones DL. Combined sinoatrial node atrio-ventricular node isolation: a surgical alternative to His' bundle ablation in patients with atrial fibrillation. *Circulation* 1985;**72**: 220.
- Cox JL, Canavan TE, Schuessler RB, Cain ME, Lindsay BD, Stone C et al. 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**:406–26.
- Damiano RJ, Jr, Bailey M. The Cox-Maze IV procedure for lone atrial fibrillation. *Multimed Man Cardiothorac Surg* 2007;**2007**: mmcts 2007 002758.
- 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**:27–35.
- Inoue Y, Yozu R, Cho Y, Kawada S. Video-assisted thoracoscopy system guidance in linear radiofrequency ablation. *Surgery Today* 2000;**30**:811–5.
- Salenger R, Lahey SJ, Saltman AE. The completely endoscopic treatment of atrial fibrillation: report on the first 14 patients with early results. *Heart Surg Forum* 2004;**7**:E555–8.
- Bisleri G, Muneretto C. Innovative monolateral approach for closed-chest atrial fibrillation surgery. *Ann Thorac Surg* 2005;**80**:e22–5–e25.
- La Meir M, De Roy L, Blommaert D, Buche M. Treatment of lone atrial fibrillation with a right thoracoscopic approach. *Ann Thorac Surg* 2007;**83**:2244–5.
- La M, M De RL, Gourdin M. A Hybrid Approach for Treatment of Patients with Atrial Fibrillation with Radiofrequency Catheters. In: JCH Maessen, ed. *Hybrid and Minimally Invasive Cardiac Intervention*: Turin: Minerva Medica; 2010. p. 9–13.
- Wolf RK, Schneeberger EW, Osterday R, Miller D, Merrill W, Flege JB, Jr. et al. Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. *J Thorac Cardiovasc Surg* 2005;**130**:797–802.
- Yilmaz A, Van Putte BP, Van Boven WJ. Completely thoracoscopic bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. *J Thorac Cardiovasc Surg* 2008;**136**:521–2.

38. Edgerton JR, Jackman WM, Mahoney C, Mack MJ. Totally thorascopic surgical ablation of persistent AF and long-standing persistent atrial fibrillation using the "Dallas" lesion set. *Heart Rhythm* 2009;**6**:S64–S70.
39. Maesen B, La Meir M. Unilateral left-sided thorascopic ablation of atrial fibrillation. *Ann Thorac Surg* 2020;**110**:e63–e66.
40. Fleerackers J, Hofman FN, van Putte BP. Totally thorascopic ablation: a unilateral right-sided approach. *Eur J Cardiothorac Surg* 2020;**58**:1088–1090.
41. DeLurgio DB, Crossen KJ, Gill J, Blauth C, Oza SR, Magnano AR et al. Hybrid convergent procedure for the treatment of persistent and long-standing persistent atrial fibrillation: results of CONVERGE clinical trial. *Circ Arrhythm Electrophysiol* 2020;**13**:e009288.
42. Maesen B, Pison L, Vroomen M, Luermans JG, Vernoooy K, Maessen JG et al. Three-year follow-up of hybrid ablation for atrial fibrillation. *Eur J Cardiothorac Surg* 2018;**53**:i26–i32.
43. de Asmundis C, Chierchia GB, Mugnai G, Van Loo I, Nijs J, Czaplaj J et al. Midterm clinical outcomes of concomitant thorascopic epicardial and transcatheter endocardial ablation for persistent and long-standing persistent atrial fibrillation: a single-centre experience. *Europace* 2017;**19**:58–65.
44. Al-Jazairi MIH, Rienstra M, Klinkenberg TJ, Mariani MA, Van Gelder IC, Blaauw Y. Hybrid atrial fibrillation ablation in patients with persistent atrial fibrillation or failed catheter ablation. *Neth Heart J* 2019;**27**:142–51.
45. Maesen B, Weberndörfer V, Bidar E, Linz D. The importance of bipolar bidirectional radiofrequency in surgical AF ablation. *Int J Cardiol Heart Vasc* 2020;**26**:100478.
46. van Laar C, Verberkmoes NJ, van Es HW, Lewalter T, Dunnington G, Stark S et al. Thorascopic left atrial appendage clipping: a multicenter cohort analysis. *JACC Clin Electrophysiol* 2018;**4**:893–901.
47. Romero J, Michaud GF, Avendano R, Briceno DF, Kumar S, Carlos DJ et al. Benefit of left atrial appendage electrical isolation for persistent and long-standing persistent atrial fibrillation: a systematic review and meta-analysis. *Europace* 2018;**20**:1268–78.
48. Starck CT, Steffel J, Emmert MY, Plass A, Mahapatra S, Falk V et al. Epicardial left atrial appendage clip occlusion also provides the electrical isolation of the left atrial appendage. *Inter CardioVasc Thorac Surg* 2012;**15**:416–8.
49. Moe GK, Abildskov JA. Atrial fibrillation as a self-sustaining arrhythmia independent of focal discharge. *Am Heart J* 1959;**58**:59–70.
50. Vroomen M, Maesen B, Luermans JL, Maessen JG, Crijns HJ, La MM et al. Epicardial and endocardial validation of conduction block after thorascopic epicardial ablation of atrial fibrillation. *Innovations (Phila)* 2020;**15**:525–31.
51. Boersma LV, Castella M, van Boven WV, Berrueto A, Yilmaz A, Nadal M et al. Atrial fibrillation catheter ablation versus surgical ablation treatment (FAST): a 2-center randomized clinical trial. *Circulation* 2012;**125**:23–30.
52. Haldar S, Khan HR, Boyalla V, Kralj-Hans I, Jones S, Lord J et al. Catheter ablation vs. thorascopic surgical ablation in long-standing persistent atrial fibrillation: CASA-AF randomized controlled trial. *Eur Heart J* 2020;**41**:4471–80.
53. Verma A, Jiang CY, Betts TR, Chen J, Deisenhofer I, Mantovan R et al. Approaches to catheter ablation for persistent atrial fibrillation. *N Engl J Med* 2015;**372**:1812–22.
54. Pison L, La Meir M, van Opstal J, Blaauw Y, Maessen J, Crijns HJ. Hybrid thorascopic surgical and transvenous catheter ablation of atrial fibrillation. *J Am Coll Cardiol* 2012;**60**:54–61.
55. van der Heijden CAJ, Vroomen M, Luermans JG, Vos R, Crijns H, Gelsomino S et al. Hybrid versus catheter ablation in patients with persistent and longstanding persistent atrial fibrillation: a systematic review and meta-analysis. *Eur J Cardiothorac Surg* 2019;**56**:433–43.
56. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C et al. ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2020:ehaa612.
57. Vroomen M, La Meir M, Maesen B, Luermans JGL, Vernoooy K, Essers B et al. Hybrid thorascopic surgical and transvenous catheter ablation versus transvenous catheter ablation in persistent and longstanding persistent atrial fibrillation (HARTCAP-AF): study protocol for a randomized trial. *Trials* 2019;**20**:370.
58. Steinberg JS, O'Connell H, Li S, Ziegler PD. Thirty-second gold standard definition of atrial fibrillation and its relationship with subsequent arrhythmia patterns: analysis of a large prospective device database. *Circ Arrhythm Electrophysiol* 2018;**11**:e006274.