

# Hybrid Atrial Fibrillation Ablation

## Current Status and a Look Ahead

**T**reatment of atrial fibrillation (AF) has evolved significantly during the last 3 decades. Successful surgical AF ablation was developed by the pioneering work of Dr James Cox in 1987 resulting in the development of the Cox-maze (CM) procedure.<sup>1</sup> Further experience and incorporation of ablation technology allowed subsequent modifications to increase efficacy and decrease morbidity, resulting in the latest iteration—the CM IV.<sup>2</sup> Despite the excellent results of open SA of AF, its widespread use has been limited by its morbidity, especially for stand-alone surgical procedures. Ablation lines from alternate energy sources to replace many of the surgical incisions in the cut and sew maze led to a thoracoscopic, minimally invasive, off-pump beating heart approach.<sup>1</sup> Minimally invasive thoracoscopic surgery may improve on the results of AF catheter ablation but may not be as effective as open surgery because of limitations in creating transmural lesions in roof and floor of the left atrial posterior wall in some patients.<sup>3</sup>

In 1998, the observation by Haïssaguerre et al<sup>2</sup> that the pulmonary veins (PVs) serve as common sources of AF triggers in patients with paroxysmal AF paved the way for catheter AF ablation (CA) using radiofrequency energy. Although CA is associated with relatively low morbidity, it has been characterized by higher AF recurrence rates, especially in persistent and long-standing persistent AF.<sup>4</sup> Because thoracoscopic SA and CA interventions may lead to incomplete isolation of the PVs and the posterior wall of left atrium, a hybrid option combining these 2 techniques was developed. The so-called hybrid strategies proposed to increase procedural success. In fact, single-center studies have demonstrated that catheter ablation may be effective in completing some of the lines created by the thoracoscopic-based SA procedure.<sup>5</sup> Hybrid AF ablations in various centers have been variable in terms of surgical approach (thoracoscopic versus pericardioscopic), lesion sets applied by surgeon and electrophysiologist, timing of the staged procedures, type of energy used, exclusion of left atrial appendage (LAA), and the rigor and length of patient follow-up (Table 1).

Despite the presence of observational data supporting the safety and efficacy of this approach, lack of prospective trials and the remaining unanswered questions temper its widespread use. This article will review the evidence behind hybrid AF ablation and provide a rationale for the US Food and Drug Administration–sponsored prospective multicenter trials to provide more meaningful data on the safety and efficacy of hybrid approaches to AF ablation.

### CONCEPT

Hybrid AF ablation consists of subsets of the CM IV lesion set applied epicardially via minimally invasive thoracoscopically based approach followed by CA, which treats gaps in ablation lesions and any additional atrial reentrant circuits. There are variations about the energy sources used, the surgical approach, the timing of the

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**Table 1. Summary of Studies Evaluating Hybrid AF Ablation**

First Author	y	Patients, n	P-LSP, %	Access	Timing	Mortality, %	Complications, %	Follow-Up, mo	AF Freedom, %
Mahapatra	2011	15	100	B-Thor	Staged	0	0	20	87
Lee	2011	25	36	B-Thor	Staged	0	4	14	79
La Meir	2013	28	54	B-Thor	Concomitant	0	0	12	91
Pison	2012	26	42	B-Thor	Concomitant	0	0	12	92
Pison	2014	78	63	B-Thor	Concomitant	0	8	24	87
Kurfirst	2014	30	100	B-Thor	Staged	0	24	0	90*
Bulava	2015	50	100	B-Thor	Staged	0	24	12	94
Richardson	2016	83	99	B-Thor	Both	1.2	11	12	71
Bisleri	2013	45	100	R-Thor	Staged	0	0	28	89
Gehi	2014	29	94	R-Thor	Concomitant	0	10	12	56
Kiser	2010	28	100	SubX	Concomitant	0	11	6	76
Gehi	2013	101	84	SubX	Concomitant	0	6	12	73
Gersak	2014	73	100	SubX	Concomitant	0	7	12	73
Zembala	2012	27	100	SubX	Staged	3.7	7	12	80
Edgerton	2016	24	100	SubX	Concomitant	14	10	24	19

AF indicates atrial fibrillation; B-Thor, bilateral thoroscopic; P-LSP, persistent and long standing persistent; R-Thor, right thoroscopic; and SubX, subxiphoid.

\*Freedom of AF was reported at the completion of procedures; no outcomes reported at follow-up for this study.

surgical and catheter components, the ablation lesion set applied, management of the LAA, and the medical management of these patients.

## ADVANTAGES AND CHALLENGES OF HYBRID AF ABLATION

Hybrid AF ablation has been developed with several advantages because it combines the strengths of both SA and CA. The strength of SA stems from the ability of the surgeon to visualize the antrum of the PVs and perform a proximal or antral PV isolation (PVI)—the cornerstone of AF ablation in most patients. The bipolar radiofrequency clamp is arguably the surgeon's best tool in developing long linear lesions on the heart without the need for cut and sew incisions. The surgeon visually avoids ablating important anatomic structures, such as the phrenic nerve, PV orifices, and the esophagus. The surgeon has access to the ganglionic plexi and ligament of Marshall, which may play roles in the genesis of AF. Moreover, the LAA may be excluded during the same procedure, which may reduce the lifetime stroke risk and has the potential to electrically isolate any AF triggers from the LAA.<sup>6</sup>

The strength of CA stems from the electrophysiologist's ability to identify isolation of the PVs and the posterior wall box lesion. Catheter ablation can close any gaps in the epicardial ablation lines that are identified. Furthermore, identification of epicardial ablation line gaps provides feedback to the surgeon to result in improved surgical techniques. The electrophysiologist can also ablate sites that are otherwise inaccessible

to the surgeon from the epicardial side, such as near the coronary sinus and left circumflex artery as part of the mitral isthmus lesion and the cavotricuspid isthmus in the right atrium. Additionally, CA allows for ablation of additional triggering foci or other electrogram-guided or mapping-using approaches, such as Focal impulse and rotor modulation, although the benefit of this additional mapping is yet to be established by controlled trials (Table 1).

Some of the challenges inherent in a hybrid approach include the additional potential risks from performing a second procedure in a staged approach, the additional costs of a second procedure, potentially longer or second hospitalization, and the logistics involved in coordinating both the surgical and electrophysiology teams, especially when performed in the same hospitalization. The added risks and costs of a second procedure may be offset by the risks and costs of repeat catheter ablations, multiple hospitalizations, and medication costs. Decision analysis and comparative and cost-effectiveness studies will help elucidate these challenges.

## REVIEW OF THE EVIDENCE

Significant interest in hybrid AF ablation began ≈8 years ago. Although there were no randomized clinical trials, several observational studies, largely from single centers, have been published describing the results of this relatively new strategy as a feasible and effective approach to the treatment of AF (Table 2). We present the literature supporting the hybrid approach to AF. The studies involving thoroscopic approaches

use bipolar radiofrequency and access the left atrium through the right and left pleura. On the contrary, the studies involving pericardioscopic approach are using monopolar radiofrequency, approaching the left atrium through the diaphragm or subxiphoid access. This may explain differences in midterm outcomes between the approaches. Two major US Food and Drug Administration (FDA) prospective studies discussed later in this article will provide the most definitive results.

## Thoracoscopic Approach

In the first report on hybrid AF ablation, Mahapatra et al<sup>7</sup> described their experience with a staged hybrid AF ablation on 15 patients with persistent and long-standing persistent AF who failed antiarrhythmic drugs (AADs) and at least one attempt at CA. They applied the Dallas lesion set through a bilateral thoracoscopic approach, which included bilateral antral lesions, connected through a floor and roof line; lesions connecting right and left superior PVs to the non/left coronary commissure of the aortic valve and a lesion connecting left superior PV to LAA followed by LAA occlusion.<sup>8</sup> CA followed 3 to 5 days later this lesion set, which confirmed the epicardial lines and ablated any gaps, as well as residual and induced arrhythmia. They compared these patients to a matched CA-alone group and found higher freedom from atrial arrhythmia off AADs in the hybrid group at 20 months of follow-up (87% versus 53%;  $P=0.04$ ). There were no complications in this report.

Lee et al<sup>9</sup> compared a minimally invasive hybrid maze (HM) in 25 patients to a classic cut and sew CM in 38 patients. The first stage of the HM consisted of bilateral PVI through a bilateral thoracoscopic approach in addition to ablation of autonomic ganglia and LAA exclusion through stapling. Entrance and exit block was confirmed in all patients. Stage 2 was performed in patients with recurrent AF >3 months since stage 1 and consisted of transvenous catheter ablation connecting the PVs in addition to a mitral annulus line and touch-up of any gaps in the PVI. Freedom from AF and AADs at 1 year was 52% in the HM group and 88% in the CM group ( $P<0.001$ ). However, data at 1 year were only available for 23 patients with HM and 32 with CM. At the latest follow-up (mean follow-up of 14 and 26 months in the patients with HM and CM, respectively), the freedom from AF and AADs was 79% for the HM group and 89% for the CM group (0.298). There were no operative deaths in either group; however, 1 patient with CM experienced an in-hospital stroke, which eventually resolved. Although this early study showed that the new hybrid approach did not achieve the level of efficacy of the CM III, it did show safety and feasibility.<sup>10</sup> This study was limited by significant differences between the 2 groups at baseline, including a higher proportion of paroxysmal AF in the HM group.

La Meir et al<sup>11</sup> compared a hybrid approach in 35 patients to an epicardial-only approach in 28 patients. Forty-six percent of their patients had paroxysmal AF. Bilateral thoracoscopic approach was used to perform PVI and a posterior box lesion formation in addition to ganglionic plexi ablation. In the hybrid group, a mitral isthmus line and superior vena cava isolation was added endocardially during the same procedure (concomitant hybrid approach). The LAA was excluded in patients with CHADS<sub>2</sub> score  $\geq 1$ . At 1-year follow-up, the hybrid group had a nonsignificantly higher freedom from atrial arrhythmias off AADs (91% versus 82%;  $P=0.07$ ), especially in patients with nonparoxysmal AF. No complications were reported in this series.

Pison et al<sup>12</sup> reported on 26 patients undergoing hybrid AF ablation, of which 58% had paroxysmal AF. Their criteria for a hybrid approach was failed CA, nonparoxysmal AF, or an enlarged left atrial volume. A PVI was performed through a bilateral thoracoscopic approach followed by concomitant endocardial mapping and confirmation of PVI on all patients. In patients with nonparoxysmal AF, additional lines included the posterior box, superior vena cava isolation, intercaval line, and mitral isthmus line. At 1-year follow-up, freedom from atrial arrhythmia off AADs was 92% (93% in paroxysmal AF versus 90% in nonparoxysmal AF). There were no reported complications in this study.

Pison et al<sup>13</sup> reported on a second series of 78 patients undergoing hybrid AF ablation using bilateral thoracoscopic surgical approach with concomitant CA. The ablation lines were described as in their previous study. At median follow-up of 24 months, freedom from atrial arrhythmias off AADs was 87% and 92% on AADs. However, 13% of the patients required repeat CA for recurrent atrial arrhythmia after the hybrid procedure. In contrast to the previous study, the complication rate was 8% (3% pneumonia, 3% permanent pacemaker insertion, 1% experienced bleeding not requiring intervention, and 1% experienced bleeding requiring reoperation).

Kurfurst et al<sup>14</sup> evaluated their staged hybrid AF approach in 30 patients with nonparoxysmal AF using a bilateral thoracoscopic epicardial ablation followed by CA 3 months later. The SA consisted of PVI, posterior box, mitral isthmus line, dissection of the ligament of Marshall, ablation of ganglionic plexi, and LAA clip. The CA entailed mapping and ablation of any gaps to complete the epicardial lesions. A cavotricuspid isthmus line was also added during CA. Freedom from atrial arrhythmias after completion of the hybrid procedures was 90% off AADs and 93% with AADs. The article does not report 1-year results. The complication rate was 24% in this study (7% wound infections, 7% phrenic nerve palsy, 7% conversion to sternotomy because of intraoperative bleeding, and 3% delayed tamponade). The majority of these complications occurred early in

**Table 2. The Rationale of Hybrid Ablation of Atrial Fibrillation**

Creation of Completed Lines
1. Surgical approach may be more complete in making transmural ablation lines
(a) Ablation tools are designed for making lines
(b) Smooth epicardial surface ideal for surgical tools
(c) Visual imaging reveals the atrial surface, ablation lines, and gaps in lesions
2. Catheter ablation may be most effective in targeting specific lesions
(a) Catheter ablation is designed to create point lesions
(b) Catheter can slip off endocardial ridges or trabeculations, thus breaking up lines
(c) Even with ultrasound imaging, assessing continuing of endocardial lesions may be difficult
Complementary nature of epicardial and endocardial ablation
1. Epicardial ablation
(a) Heat sink of the circulating blood in the atrial chamber limits depth
(b) Epicardial lesions may be limited by fat
(c) Depth of ablation lesions may be insufficient
(d) May fail to penetrate the endocardium
2. Endocardial ablation
(a) Creating transmural lesions may be difficult
(b) Endocardial ablation may result in collateral damage to epicardial structures
Together these techniques complement each other!
Role of mapping
1. Epicardial mapping may be limited
(a) Constrained by pericardial reflections
(b) Absence of sophisticated tools and mapping systems designed for epicardial use
(c) Epicardial fat may limit mapping
2. Endocardial mapping
(a) Extensive experience in mapping
(b) Large range of tools and technology
(c) Formally trained
(d) Mature enabling technology
Together these techniques complement each other!
3. Unique targets
(a) Surgical epicardial ablation
(i) Full division of ligament of Marshall
(ii) LAA removal
(iii) Targeted ganglionic plexi ablation
(iv) Safer superior vena cava isolation
(b) Transcatheter endocardial ablation
(i) More effective cavotricuspid isthmus line
(ii) Atrial flutter and atrial tachycardia ablation
(iii) Coronary sinus ablation
(iv) Map for flutter
(v) Mapping techniques, such as FIRM or CFAE
Together these techniques complement each other!

CFAE indicates complex fractionated atrial electrograms; FIRM, focal impulse and rotor modulation; and LAA, left atrial appendage.

their experience without further complications in the latter half of the series.

Bulava et al<sup>15</sup> reported on their experience with a staged hybrid approach wherein 50 patients with long-standing persistent AF and dilated left atrium (mean 4.8±0.4 cm) underwent a bilateral thoracoscopic ablation followed by a CA 6 to 8 weeks later. The surgical component included a PVI, posterior box, trigone line, ganglionic plexi ablation, and LAA exclusion. During CA, the epicardial lines were confirmed and completed, and any inducible atrial arrhythmias were mapped and ablated. At 1-year follow-up, freedom from atrial arrhythmia off AADs was 94% and 84% on AADs. The complication rate was 24% (14% insignificant PV narrowing and 10% phrenic nerve palsy). All complications occurred in the first 15 patients, and modification of technique eliminated any further complications.

Recently, Richardson et al<sup>16</sup> published a series of 83 patients undergoing a totally thoracoscopic epicardial ablation combined with endocardial catheter ablation. The study compared safety, outcomes, and the identification of incomplete surgical PVI between a same-day concomitant procedure versus a staged endocardial procedure. The rate of any recurrence through 12-month follow-up was similar, and the overall rate of morbidity and mortality was low. Detection of incomplete epicardial PVI was statistically higher in the same-day procedure as was postoperative bleeding. It was speculated that bleeding was associated with use of immediate heparinization after epicardial and thoracoscopic surgery, which is not required in a staged procedure. AF burden reduction for the entire cohort through 12 months of continuous monitoring was 91%.

These publications used a bilateral total thoracoscopic approach with bipolar radiofrequency technology. Two other groups have used different technology through a right thoracoscopic approach. Bisleri et al<sup>17</sup> reported their experience with a staged hybrid AF ablation approach in 45 patients with long-standing persistent AF. The surgical component consisted of a right thoracoscopic approach with an internally cooled vacuum-assisted unipolar radiofrequency device, creating the posterior box lesion surrounding all 4 PVs. CA was performed after 30 to 45 days to confirm and complete the epicardial lines, adding a cavotricuspid isthmus line, and then performing complex ablation of fractionated atrial electrograms. After a mean follow-up of 28 months, freedom from AF was 89%. There were no reported complications in this study.

Gehi et al used a similar approach as Bisleri et al with differing results. In 29 patients with mostly nonparoxysmal AF (94%), a right thoracoscopic approach using a vacuum-assisted bipolar/unipolar radiofrequency ablation device was used followed by immediate CA.<sup>18</sup> Epicardial ablation consisted of PVI, posterior box, and an intercaval line, whereas the endocardial CA consisted of

confirming and completing the epicardial lines, complex fractionated atrial electrogram ablation, and ablation of any residually induced atrial arrhythmias. At a median of 356 days, 56% of patients were free of AF recurrence >2 minutes duration and 84% had a partial success, defined by as AF burden <5%. The complication rate was 10%, consisting of bleeding requiring intervention.

### Pericardioscopic Approach

Another 5 groups described yet a different surgical strategy in their hybrid AF series, which consists of pericardioscopic approach through a transdiaphragmatic/sub-xiphoid access. Kiser et al<sup>19</sup> reported their experience in 28 patients with persistent or long-standing persistent AF undergoing the convergent procedure consisting of concomitant epicardial radiofrequency ablation and transeptal endocardial ablation to exclude the entire posterior left atrium and isolate the PVs. They reported no deaths. However, 2 patients developed symptomatic pericardial effusions requiring pericardiocentesis, and 1 patient developed phrenic nerve paralysis. Patients were followed  $\leq 6$  months, and freedom from AF and AADs at that point was 76%.

Gehi et al<sup>20</sup> reported their experience with 101 patients with mostly nonparoxysmal AF (84%). The surgical portion consisted of PVI, posterior box, and connecting lesion to the coronary sinus. Concomitant CA consisted of endocardial ablation of complex fractionated atrial electrograms, superior vena cava isolation, and cavotricuspid isthmus line. Furthermore, any residual atrial arrhythmias were mapped and ablated. The 12-month freedom from atrial arrhythmia was 73% off AADs. The complication rate was 6% in this study.

Gersak et al<sup>21</sup> reported the experience of 4 centers performing hybrid AF ablation using an irrigated unipolar epicardial device on 73 patients with nonparoxysmal AF through a pericardioscopic approach followed immediately with endocardial CA. The surgical component was limited to PVI and posterior box lesion, whereas CA served only to ensure completeness of the epicardial lesions. The 12-month atrial arrhythmia-free survival was 73%. Zembala et al<sup>22</sup> used a slightly different strategy in that the surgical component included connecting lesions to the coronary sinus, the CA component was staged (15–20 days after surgery) and included a mitral isthmus and cavotricuspid isthmus lines. Their 1-year freedom from atrial arrhythmia off AADs was 80%. The complication rates of these 3 studies ranged from 5% to 11%.

A recent study by Edgerton et al<sup>23</sup> deserves mention for 2 reasons. First, it is the only prospective study comparing a hybrid AF ablation approach (24 patients) to an endocardial-only ablation (35 patients). Second, it is the only study to highlight their high-complication rates and lower efficacy of a hybrid approach, possibly

tempering the results of the aforementioned studies. Their hybrid group underwent SA through a pericardioscopic approach followed immediately by CA. They used a unipolar radiofrequency device to perform PVI, posterior box, ablate the ligament of Marshall (without dissection), and the lateral right atrium. The endocardial portion entailed verification and completion of epicardial lines, line to the coronary sinus, isolation of the LAA, and ablation of complex fractionated atrial electrograms. At 12-month follow-up, the hybrid group had lower arrhythmia-free survival (24% versus 63%;  $P < 0.001$ ). At 24 months, the hybrid group continued to have inferior results (19% versus 54%;  $P > 0.001$ ). Furthermore, the complication rates were significantly higher in the hybrid group (21% versus 3%;  $P = 0.036$ ), including 3 deaths, 1 tamponade, and 1 phrenic nerve palsy in the hybrid group compared with 1 tamponade in the CA group. The overall rate of mortality because of atrioesophageal fistula and the sudden deaths was felt to be unacceptable. The authors attribute the results to the type of technology used (unipolar radiofrequency) and the approach (pericardioscopic and concomitant CA). The unipolar ablation device used for pericardioscopic ablation has been redesigned with an electrocardiogram-sensing tip and an irrigation port to reduce the rate of atrioesophageal fistulas.

Table 1 is an overview of results of these single-center studies. It highlights the variability of how hybrid AF ablations are conducted in each clinical program. There are differences in terms of surgical approach (unilateral thoracoscopic, bilateral thoracoscopic, pericardioscopic), lesion sets applied by surgeon or electrophysiologist, timing of the staged procedures (concomitant, staged during same hospital stay, staged at later hospitalization), type of energy used (unipolar versus bipolar radiofrequency), and the rigor and length of AF recurrence follow-up. This review highlights an overall superior outcome in centers using bilateral thoracoscopic ablation compared with the pericardioscopic approach (Table 1). Aside from lower rate of morbidity and mortality in the bilateral thoracoscopic approach compared with the pericardioscopic route, the former also excludes LAA. LAA exclusion in this cohort of patients with persistent or long-standing persistent AF may reduce the lifetime stroke risk, and has the potential to electrically isolate any AF triggers from the LAA.<sup>6</sup> The potential benefit of surgical LAA ligation/excision remains to be proven, but from the start, it has been an integral part of SA. Two trials are underway, which may shed light on this topic. Both are trials of LAA closure concomitant to another open cardiac procedure. LAAOS III (Left Atrial Appendage Occlusion Study III; [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01561651) identifier: NCT01561651) is evaluating closure of the LAA in patients with a history of AF. The ATLAS trial (Atri-Clip Left Atrial Appendage Exclusion Concomitant to Structural Heart Procedures; [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01561651) identifier

NCT02701062) is examining LAA closure in patients without a history of AF but at increased risk of developing it postop as determined by CHA<sub>2</sub>DS<sub>2</sub>-VASc score. There is also an ongoing trial of epicardial LAA exclusion during transvenous catheter AF ablation with the LARIAT device under study with the AMAZE trial (LAA Ligation Adjunctive to PVI for Persistent or Longstanding Persistent Atrial Fibrillation; US FDA IDE# G150107).

## Prospective Multicenter Clinical Trials of Hybrid AF Ablation

There are currently 2 FDA-approved industry-sponsored clinical trials involving thoracoscopic and pericardioscopic approaches ([clinicaltrials.gov](http://clinicaltrials.gov) identifiers NCT01984346 and NCT01661205, respectively). The CONVERGE trial (Convergence of Epicardial and Endocardial Radiofrequency Ablation for the Treatment of Symptomatic Persistent AF) is a multicenter, prospective, open-label, randomized 2:1 (convergent procedure versus endocardial catheter ablation) pivotal study. The hybrid portion is completed under general anesthesia: using a pericardioscopic approach, the posterior left atrial wall is ablated using the unipolar radiofrequency device. The endocardial procedure (PVI and cavotricuspid lesion) is subsequently performed with irrigated unipolar radiofrequency. The primary efficacy end point is freedom from AF, atrial tachycardia, and atrial flutter without class I and III AADs (except for a previously failed or intolerant class I or III AADs with no increase in dosage after the 3-month blanking period) through the 12-month post-procedure follow-up visit. The CONVERGE trial will enroll ≤153 subjects in ≤17 sites, and to date, there have been 51 patients enrolled. This is an industry-sponsored study (AtriCure, Mason, OH).

The DEEP approach (dual epicardial and endocardial procedure) is the other multicenter industry-sponsored clinical trial for treatment of patients with persistent or long-standing persistent AF. DEEP is a staged hybrid prospective, single-arm, pivotal study to establish the safety and effectiveness of hybrid ablation procedure. The totally thoracoscopic procedure is performed from 2 pleural cavities, and the LAA is excluded using a commercially available clip at the end of the procedure. After basic epicardial mapping for ganglionic plexi and entrance and exit block at the PVs, the following lesions are performed using bipolar radiofrequency: right and left antral lesions (isolating both PVs), left atrial roof and floor lesions, and a lesion at the base of the LAA. After 90 days, the endocardial mapping and ablation procedure uses a commercially available radiofrequency-based, irrigated, power-controlled ablation system to ablate any gaps in the previous lesions and to complete a cavotricuspid isthmus lesion.

The primary outcome end point is freedom from any AF, atrial flutter, or atrial tachycardia through the

12-month follow-up visit in the absence of class I or III AADs (with the exception of any previously failed AADs at the same or lower doses). Similar to the CONVERGE trial, the rhythm status used for evaluation of this end point will be derived from regularly scheduled monitoring (ie, Holter, Zio-Patch, or 30-second 12-lead ECG) and any symptom-driven monitoring that is performed. The primary safety end point is a composite end point consisting of serious adverse events within 30 days of the epicardial SA procedure, or within 7 days of the index endocardial procedure, or within 7 days after a repeat endocardial procedure within the blanking period. The DEEP trial will enroll ≤220 subjects in ≤25 sites.

## CONCLUSIONS

Management of AF remains challenging in patients with nonparoxysmal AF, particularly when AF is long standing or in the presence of large left atria or after failed CA. Hybrid AF approach seems to be a promising tool supported by many single-center reports. This review found a significant variability among hybrid AF ablations performed in various centers in terms of surgical approach, lesion sets applied by surgeon or electrophysiologist, timing of the staged procedures, type of energy used, exclusion of LAA, and the rigor and length of patient follow-up. Furthermore, adverse outcome in bilateral thoracoscopic approach seems to be lower than the pericardioscopic route. The 2 ongoing FDA-sponsored, prospective, multicenter clinical trials will add significantly to our understanding of the efficacy and safety of the hybrid AF approach using a uniform epicardial and endocardial protocol.

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## DISCLOSURES

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## FOOTNOTES

*Circ Arrhythm Electrophysiol* is available at <http://circep.ahajournals.org>.

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