Selection of Patients for Hybrid Ablation Procedure

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Abstract

Catheter ablation for treatment of symptomatic non-paroxysmal atrial fibrillation remains challenging. Clinical failure and need for continued medical therapy or repeat ablation is common, especially in more advanced forms of atrial fibrillation. Hybrid ablation has emerged as a more effective and safe therapy than endocardial-only ablation particularly for longstanding persistent atrial fibrillation as demonstrated by the randomized controlled CONVERGE trial. Hybrid ablation requires collaboration of electrophysiologists and cardiac surgeons to develop specific workflows. This review describes the Hybrid Convergent approach in the context of available ablation options and offers guidance for workflow development and patient selection.

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Abstract

Catheter ablation for treatment of symptomatic non-paroxysmal atrial fibrillation remains challenging. Clinical failure and need for continued medical therapy or repeat ablation is common, especially in more advanced forms of atrial fibrillation. Hybrid ablation has emerged as a more effective and safe therapy than endocardial-only ablation particularly for longstanding persistent atrial fibrillation as demonstrated by the randomized controlled CONVERGE trial. Hybrid ablation requires collaboration of electrophysiologists and cardiac surgeons to develop specific workflows. This review describes the Hybrid Convergent approach in the context of available ablation options and offers guidance for workflow development and patient selection.

Keywords:

Longstanding persistent atrial fibrillation

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Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with estimates that over 37 million people were impacted globally in 2017 and that number is expected to continue to rise. Future estimates of AF

burden predict an increase of over 60% by the year 2050, with 6-12 million patients in the US alone.[1] Not only is AF a major risk factor for ischemic stroke, but it also causes economic burden, significant morbidity, and mortality.[1]Non-paroxysmal AF, or continuous AF sustained longer than 7 days, is associated with higher rates of thromboembolism (TE) and mortality compared to paroxysmal AF based on a meta-analysis of 12 studies.[2] Treatment options for paroxysmal AF include antiarrhythmic drugs (AADs), cardioversion, and ablation.[3] While the first line of therapy for paroxysmal AF is often AADs, a meta-analysis of 6 trials indicated that ablation was more effective and reducing arrhythmia recurrences and hospitalizations with a similar safety profile as that of AADs.[4] Unfortunately, AAD and ablation options for non-paroxysmal AF have lesser and varying levels of success such that many patients find themselves with long durations of AF or experience recurrent AF that has to be re-addressed.[5,6]Trials have demonstrated improved quality of life with ablation versus only AADs in patients with non-paroxysmal AF[7], who are typically patients that have failed AAD treatment, thus leading to decisions on the type of ablation based on the individual patient's clinical history and current clinical picture.

Collaborative heart teams must discuss the individual characteristics and specifics surrounding each patient with AF seeking care to determine the best course of treatment.[8] With this approach, the role of the collaborative heart team is to determine patient selection based on their need or lack of need for concomitant surgery, risk/benefit, compliance, and other patient specific factors. Although AADs are still often the first line of defense, they are frequently ineffective or poorly tolerated. Options for cardiac ablation to treat AF have expanded over time, with both approved and emerging catheter, surgical, and hybrid epicardial-endocardial techniques supported by clinical evidence. Determining the patient groups most likely to benefit from each of these approaches allows the multi-disciplinary team to select the best treatment option for a particular patient. The focus of this review is on Hybrid Convergent ablation, a minimally invasive, closed chest combined epicardial-endocardial approach, and the selection of patients most appropriate and most likely to benefit from this procedure.

Surgical Ablation

There are several cardiac ablation options for AF treatment that may be considered: surgical, endocardial only, or hybrid ablation. While the focus of this review is on hybrid ablation, surgical and endocardial ablation are described briefly as relevant for patient selection. Surgical ablation is typically utilized when there is a concomitant open-heart surgery for a structural issue coupled with pre-existing AF. It is done via a median sternotomy or a right thoracotomy, both of which require the patient undergo cardiopulmonary bypass, which is why it is typically reserved for those undergoing cardiac surgery for concomitant structural heart issues. The surgical ablation technique that is considered by many to be the gold standard is the Cox-Maze procedure, which involves bi-atrial ablation including isolation of the pulmonary veins and left atrial posterior wall as well as left atrial appendage (LAA) exclusion.[9]Published studies have reported high long-term success rates to restore sinus rhythm and mortality benefits of Cox-Maze surgical ablation. Other surgical ablation approaches may utilize reduced lesion sets including those focused only on the left atrium or epicardial only ablation, which may not achieve transmurality. Several societies have designated concomitant surgical ablation as a Class I recommendation to perform concomitantly during structural heart procedures such as valve repair/replacement or CABG.[10-12] However despite these recommendations, a study of almost 80,000 patients over three years from a 2014 Medicare database indicated that an average of 22% of patients had concomitant AF surgical ablation, with rates varying by specific surgery type.[13] Badhwar et al report an increase from 52% to 61.5% of patients undergoing surgical ablation concomitant with AF at the time of mitral valve repair in an analysis of the Society of Thoracic Surgeons database.[10]

Endocardial Ablation

Standalone endocardial catheter ablation is less invasive than surgical concomitant ablation and involves a catheter being guided through venous access points, entering the right atrium, and ultimately the left atrium where the endocardial ablation is performed. Patients with paroxysmal AF have higher success rates, such as freedom from atrial arrhythmias and less recurrences of repeat ablations compared to those with non-paroxysmal AF. After a secondary repeat ablation, paroxysmal AF patients experienced over 92% freedom

from AF, whereas patients with persistent AF and long-standing persistent AF had lower secondary success rates of 88.1 and 80.9%, respectively.[14] In a single center study, long-term success rates ranged from 28.4 to 51.1% recurrence-free rates after a single or three procedures, respectively, leaving a large percentage of patients with failed treatment.[15] While contemporary trials have demonstrated that radiofrequency catheter and cryoballoon endocardial ablation may yield sufficient clinical outcomes for paroxysmal AF and even non-paroxysmal AF without advanced substrate, there are patients with advanced AF who tend to be more difficult to treat and have lower success rates and consequently more subsequent procedures after endocardial ablation.[14] Recent studies of persistent AF have demonstrated rates of effectiveness of 54.8% to 61.7% at 12 and 15 months, respectively, after a single ablation procedure.[16,17]Tsai et al. recently published longer term follow up results from a Taipei hospital. After a single index ablation procedure, 100 patients with non-paroxysmal AF were followed very-long-term for over 5 years with a target follow up of 10 years. Only 16% of patients remained free of AF at 10 years, with the majority of AF recurrence (61.9%) at the one year mark, emphasizing the need for more effective and enduring treatment options for non-paroxysmal AF.[18]

Hybrid Ablation

With such a large population undertreated or with failed treatment for advanced AF, including long-standing persistent AF, there is still an unmet need to find better treatment options that provide durable and long-lasting treatment. Hybrid epicardial-endocardial procedures are newer, minimally invasive ablation approaches that have shown promising results compared to endocardial ablation techniques. The development of hybrid ablation techniques seeks to combine the benefits of both surgical and electrophysiological catheter ablation in a multi-disciplinary care team approach, while minimizing the risks that come with both of those procedures alone. Hybrid procedures target both the endocardial and epicardial left atrium, seeking to ensure durable, complete transmural lesions on the beating heart. In order to access the pericardium without an open chest, access to the posterior left atrium for epicardial ablation is either gained thoracoscopically or endoscopically through a subxiphoid incision. The latter approach, sometimes referred to as the Hybrid Convergent procedure, is the focus of this review.

Several single center studies have been published describing the mid-term outcomes of the Hybrid Convergent procedure.[19,20]The CONVERGE clinical trial, a multicenter randomized controlled trial that evaluated the safety of the Hybrid Convergent combined ablation treatment and its effectiveness versus standard endocardial ablation in the persistent and long-standing persistent AF patients. Based on these results, the Hybrid Convergent procedure using the EPi-Sense device (AtriCure, Inc.) for epicardial ablation augmented by endocardial catheter ablation is the only FDA-approved minimally invasive treatment for longstanding persistent AF.

Hybrid Procedure Overview and Lesion Set

In the Hybrid Convergent procedure (Figure 1), a multidisciplinary heart care team approach is utilized, first with a surgeon performing an epicardial ablation and then with an electrophysiologist following with an endocardial ablation. The minimum aspects of this lesion set involve electrical isolation of the posterior wall and pulmonary veins, with esophageal heating mitigated by device design and procedural best practices. The epicardial ablation procedure is focused on the posterior wall, utilizing a vacuum-assisted unipolar radiofrequency device inserted through a cannula with an endoscope. A transdiaphragmatic or more commonly a subxiphoid approach is used to access the pericardium. Epicardial ablations are applied across the posterior wall of the left atrium creating contiguous, parallel lesions. Current convergent ablation relies on the homogenization of the posterior wall in a more simplified manner complementary to the endocardial ablation as opposed to prior versions that were more extensive to replicate a Maze-like lesion set including a posterior wall box and bi-atrial lesions.[21] Following the epicardial ablation by the surgeon, endocardial mapping guides the endocardial ablation performed using an irrigated radiofrequency catheter by the electrophysiologist, connecting any breakthrough gaps in lesions and thus completely isolating the left and right pulmonary veins. Confirmation of isolation is done by evaluating entrance and/or exit block to ensure the absence of conduction. Most studies on hybrid convergent procedures relied on commercially available radiofrequency endocardial catheters. Retrospective single-center and registry analyses have reported the safety and efficacy

of endocardial cryoballoon catheters in the Hybrid Convergent procedure.[22-24]

Single vs Staged Setting

The Hybrid Convergent procedure relies on procedures performed both by a surgeon and an electrophysiologist. These components can either be done in a single setting in a hybrid OR-electrophysiology lab or separate OR and electrophysiology lab, or in a staged setting with the two stages usually at least 30 days apart. Whether single setting or staged, the epicardial portion is always first, followed by the endocardial portion. A robust comparison of the clinical outcomes of single versus staged Hybrid Convergent procedures has not yet been performed, however the choice may be influenced by physician and patient preferences, institutional practices, and schedule feasibility.

The CONVERGE trial was a multi-center randomized controlled trial to evaluate the safety and effectiveness of Hybrid Convergent versus endocardial catheter ablation in advanced AF.[24] With no restrictions on duration of persistent AF at enrollment, this ensured long-standing persistent AF patients were a substantial portion of the enrolled subjects (42%), which no other trial has done to date. The primary endpoint was to determine the freedom from AF/atrial flutter/atrial tachycardia off new or increased dose of previously failed AADs through 12- months. In the Hybrid Convergent group, 67.7% of patients achieved the primary effectiveness endpoint compared to 50.0% in the catheter ablation group, with a significant absolute rate difference of almost 17.7%, favoring Hybrid Convergent (risk ratio=1.35, p=0.036). In various sub-analyses by AAD usage, Hybrid Convergent had a higher success rate than catheter ablation in almost all instances and was deemed clinically although not statistically significant for patients off amiodarone. The Hybrid Convergent arm consistently demonstrated significantly better AF burden reduction and freedom from AF at 12 and 18 months compared to the Catheter Ablation Arm.[24]

Long-Standing Persistent AF

The progression of AF from paroxysmal to long-standing persistent AF is characterized by advanced substrate remodeling of the left atrium in a stretch, inflammation, and fibrosis sequence leading to fibrillation.[25] Thus, in advanced AF, the predominant triggers have evolved from the pulmonary vein to left atrial tissue, particularly on the posterior wall, creating a need for treatment options beyond endocardial ablation to effectively and comprehensively treat long-standing persistent AF.[26,27]Success rates of endocardial ablation in this population have had limited effectiveness, ranging from 35.6 to 43% after a single procedure.[26,27]This is attributed to the lack of a standardized lesion set, limited ability to produce transmural lesions, and dissociation of electrical activity between the endocardium and epicardium. A subgroup analysis examining the effectiveness of the Hybrid Convergent procedure for long-standing persistent AF demonstrated an absolute difference of 28.8% (78% improvement; p=0.022) in 12-month freedom from AF in the Hybrid group over the endocardial only group and was sustained through 18-months.[28] The benefit of Hybrid Convergent held when compared to the Catheter Ablation arm and their respective impacts on AF burden reduction as well as freedom from cardioversion and AF symptoms, through 18-months. Along with an acceptable safety profile, these significantly improved outcomes provided the collaborative heart team a new, effective approach for the difficult to treat population of patients suffering from advanced AF.

Other Considerations for Hybrid Convergent Patient Selection

Recent studies have demonstrated that there are several clinical characteristics of patients who may benefit from Hybrid Convergent over AADs or endocardial ablation, absent an indication for a concomitant surgical ablation or contraindication. These include those with forms of advanced AF; patients in whom there is a desire to simultaneously manage the left atrial appendage (LAA)/Ligament of Marshall (LOM); patients who have failed prior catheter ablation; and others with specific considerations such as esophageal risk.

Advanced AF

In addition to the CONVERGE post-hoc analysis for LSPAF, other studies have demonstrated favorable success to eliminate atrial arrhythmia or maintain normal sinus rhythm in patients with longstanding persistent AF.[23,29]Classification of AF by duration alone is arbitrary and can be challenging based on incomplete

patient history or available rhythm monitoring. There is emerging evidence that other factors associated with advanced AF may characterize patients who could benefit from Hybrid Convergent ablation.[23,29]

Left atrial (LA) size has been shown to be related to the recurrence of AF after endocardial ablation.[30] Most studies have defined enlargement by atrial diameter although a meta-analysis of 22 studies that due to the asymmetry of the LA and thus LA dilation, LA diameter may be an underestimate of size and LA volume is more accurate in predicting AF recurrence and even new onset AF.[31] Because the imaging modalities vary in the precision of their estimates of left atrial size, the mean difference in larger atria associated with the risk of AF is actually quite small so this must be a consideration in determining the accuracy of LA size measurements. Of the 22 studies in the meta-analysis by Zhuang, et al, the mean LA diameter reported at baseline was 34.3-49mm, partly beyond normal range. Only 3 studies were identified that solely examined non-paroxysmal AF, for a total of 143 patients. The mean atrial size in those studies ranged from 45-49mm.[30] The CONVERGE trial allowed patients with left atrial diameter up to 6.0 cm, with the mean left atrial diameter in the Hybrid Convergent arm of 4.4 cm (44mm).[32] With an increased risk of developing recurring AF, patients with enlarged left atria might be best served by Hybrid Convergent ablation versus a catheter ablation that may result in recurrences and repeat ablations.

AF Associated with Heart Failure

The co-mingling of heart failure and AF was examined in a review of patients in the Framingham Heart Study enrolled between 1980 and 2012.[33] More than half of those with heart failure also had AF, typically with AF preceding rather than following heart failure. Of those with AF, more than a third had heart failure, which typically developed after the onset of AF. Regardless of the temporality between the two conditions, the increased morbidity and mortality when present together is increased compared to individual diagnoses.[34]Patients in heart failure with a reduced ejection fraction and concurrent AF have had also had low success with medical therapy including AADs and rate control medications. CASTLE-AF showed that catheter ablation for patients with paroxysmal or persistent AF, HF, and left ventricular dysfunction significantly lowered composite death and hospitalizations, improved left ventricular ejection fraction, and reduced AF burden compared to medical therapy. However, the patient population in the trial was highly selected, which potentially limits the applicability to real world practice.[35,36]Patients with LVEF <40% were excluded from CONVERGE and the mean LVEF in the Hybrid Convergent arm was 55%. Thus, patients with reduced LVEF were thought to be out of bounds for Hybrid convergent treatment. However, recently there has been interest in determining if a hybrid approach could successfully treat AF and subsequently improve LVEF in patients with reduced LVEF at baseline. Our multi-center retrospective analysis of patients included those presenting with severely reduced baseline LVEF ([?]40%) and showed significantly improved LVEF after Hybrid Convergent treatment. Kiankhooy et al. used a thoracoscopic hybrid approach for patients with depressed EF and tachycardia mediated cardiomyopathy, which demonstrated feasibility and significantly improved ejection fraction after treatment at a mean of 3.5 years (±1.9 years) follow-up and improvement in NYHA Class from baseline.[37]

Left Atrial Appendage (LAA)/Ligament of Marshall

As previously discussed, patients with advanced AF have more non-pulmonary vein triggers, such as the posterior wall, and this can also include the LAA and Ligament of Marshall (LOM).[38] Excluding the LAA at the time of the hybrid epicardial ablation stage can address a site of AF triggers through electrical isolation as well eliminating a predominant site of thrombus in AF.[39] The addition of LAA exclusion is often performed in hybrid thoracoscopic ablation, which is the subject of several clinical trials (NCT01246466; NCT02695277; NCT02441738). The LAA exclusion technique involves epicardial clip exclusion of the LAA by a simultaneous left thoracoscopic approach.[39] In the absence of randomized controlled trial data evaluating the effectiveness and safety of Hybrid Convergent with LAA exclusion, multi-disciplinary care teams are using the available evidence and determining patient selection for whom they feel the benefit-risk profile is acceptable to proceed with this approach.[40] In a study over 6 years, 139 patients with persistent AF and no history of prior ablation underwent a Hybrid convergent procedure. In April 2016, LAA exclusion was added to the study procedures. Of the 139 patients, 59 had only Hybrid ablation and 64 had the concomitant Hybrid ablation with LAA

exclusion. Both groups were similar with respect to age and gender as well as BMI, which was elevated in both groups (>32). In the Hybrid plus LAA clip group, the patients appeared to have a longer time since AF diagnosis although not statistically significant (mean of 6.4 years vs 4.6 years; p=0.15). Other baseline data and comorbidities were similar between the groups. The Hybrid plus LAA exclusion group had a greater freedom from AF recurrent compared to Hybrid ablation only group (77% vs 58%; p=0.04).[41]

Initially described by British surgeon John Marshal in the 1800s, the LOM and Vein of Marshall (VOM) are remnants of the embryonic left superior vena cava with the VOM enclosed within the LOM.[42,43]The cluster of nerve cells known as the autonomic ganglionated plexi are found in abundance in the epicardial fat, embedded along the Ligament of Marshall, near the pulmonary vein-left atrial junctions. This composition of the epicardial fat stimulates triggers, enabling the perpetuation of AF.[44]If the ablation procedure is expanded to include targeting the GP specifically located in the LOM in addition to PVI, this may improve the success rates in patients with paroxysmal as well as persistent AF.[45] These ganglionated plexi are also implicated in left atrial remodeling and substrate changes, commonly found in more progressive forms of AF.[46] In a study examining the effect of ethanol infusion added to the VOM during catheter ablation in persistent and long-standing persistent AF, patients receiving the combined catheter and VOM ethanol infusion had higher rates of freedom from AF vs the catheter only group (49.2% vs 38%; p=0.04). Due to the LOM harboring the source of AF and AT triggers, targeting this anatomical region rich with theses ganglionated plexi during epicardial ablation along with LAA exclusion is of increasing interest.[47]

Prior Failed Catheter Ablation

Posterior wall isolation is part of the complex strategy of managing advanced AF, in addition to PVI, however it is often difficult to achieve safely with only endocardial catheter ablation. This is due to the thickness of the roof of the posterior wall of the left atrium and because of the need for long connection lines between the roof and the floor of the atrium, to create the conduction block without a gap. The lower linear lesion line at the floor of the posterior wall is more difficult to create due to the proximity of the esophagus and risk of esophageal damage.[48] In a study of patients undergoing left atrial posterior wall isolation concomitant with pulmonary vein reisolation, feasibility of isolating the LAPW with endocardial ablation was successfully demonstrated, despite no outcome differences in improvement of freedom from atrial arrhythmias compared to pulmonary vein reisolation alone. Of the 196 AF patients in the study, 103 were in the LAPW plus PV reisolation group and 36 patients (35%) required additional ablation within the center "box" of the LAPW.[49]This brings increased risk to endocardial catheter ablation but has potential to be easier and safer utilizing a Hybrid ablation approach such as those with advanced AF presenting for repeat ablation treatment. In patients with advanced AF and a need to isolate the posterior wall, a hybrid ablation approach may have the advantage of better access to completely and safely isolate it primarily through epicardial ablation applying energy towards the heart followed by endocardial touchup to address any gaps particularly near the pericardial reflections. This provides a more comprehensive treatment to prevent recurrence resulting from multiple triggers, including the pulmonary vein, left posterior wall, and endocardial tissue.

While the CONVERGE trial excluded patients with prior ablations, in routine clinical practice many patients with advanced AF have undergone prior catheter ablation attempts yet are still experiencing AF recurrences. A recent meta-analysis of Hybrid Convergent ablation studies included three studies in which one-third of the total patients had prior catheter ablation. Mannakkarra et al. recently reported their single-center experience with Hybrid Convergent ablation, including 38% of patients who had received prior catheter ablation at baseline.[20] However, to date, only one study has directly compared outcomes of patients who received Hybrid Convergent as a de novo versus previous catheter ablation, finding there was no difference in arrhythmia recurrence.[22]Additionally, there may be a cumulative benefit in that those with prior ablations require less endocardial PV isolation and were more likely to convert to sinus rhythm during the Hybrid procedure compared to those with no prior ablation history.[22] Kress et al. reported 75.0% of patients with prior ablation needed endocardial PV isolation, which was significantly less than 97.9% of patients who received hybrid ablation as a first ablation procedure (p<0.001). Additionally, fewer patients who had prior

ablation needed cardioversions (26.7%) to achieve sinus rhythm intraprocedurally compared to those receiving hybrid ablation as a first ablation procedure (45.8%, p=0.038). With few comparative studies or studies exclusively looking at hybrid convergent ablation after previous catheter ablation patients, more research as well as additional cumulative real-world evidence is necessary to determine whether there are any significant differences in procedural and treatment outcomes.[19]

Other Considerations

The risk of atrioesophageal fistula remains a major concern with endocardial ablation involving the left atrial posterior wall. Endocardial ablation of non-paroxysmal atrial fibrillation often involves significant energy application in the vicinity of the esophagus, particularly when complete isolation of the posterior wall is a goal. Esophageal temperature monitoring is routinely used, but guidelines for acceptable temperature deviation are lacking. Further, evidence that temperature monitoring prevents esophageal injury is limited, as evidenced by the continued incidence of this terrible complication. The Hybrid Convergent procedure benefits from a unique catheter design which directs energy away from the esophagus and toward the epicardial left atrial posterior wall. In addition, the pericardial space is irrigated with saline during energy application. Far less endocardial ablation is required near the posterior wall to complete the lesion set. These factors result in less esophageal heating, and presumable a lower risk of esophageal injury. The ability of the Convergent procedure to provide durable transmural left atrial posterior wall isolation while minimizing risk of esophageal injury may be an important consideration in patient selection.

Relative Contraindications

There are several groups of patients who may be contraindicated for hybrid procedures or who may be deemed riskier and potentially have a longer recovery time. As with other surgical procedures, patients with gastroesophageal reflux disease, severe renal insufficiency, in ability to tolerate anesthesia, acute infection such as sepsis/systemic infection, endocarditis, and localized surgical site infections. Additionally, there are several factors that disqualify a patient as a candidate specific to Hybrid Convergent ablation. Patients with a prior pericardiotomy have scar tissue formed around the heart and between the heart and surrounding structure, including the lungs. This makes future heart surgeries and procedures more challenging and thus are not recommended for hybrid approaches. The presence of a left atrial thrombus brings an increased risk of stroke and thromboembolism surrounding catheter ablation procedures. Thus, these patients should be treated with oral AADs for at least 3 weeks with a repeat transesophageal echocardiogram or other non-invasive multimodality imaging before considering a hybrid ablation procedure.[8]

Future directions

There are several factors that a multi-disciplinary hybrid team, led by the partnership between the electrophysiologist and cardiac surgeon, should consider when assessing a patient for potential Hybrid Convergent treatment. First, the care team should ensure that it is comprised of several specialists working together to promote a robust AF care team model to optimize care of this patient population. There should be a referral process in place that transitions patients from the single electrophysiologist practitioner to this shared care team model that is expanded to also include cardiac surgeons and cardiovascular anesthesiologists, among others, where each member provides individual expertise. The Hybrid Convergent procedure does not come without risks, so several patient factors must be assessed, such as chronicity of AF, left atrial size, and other comorbidities. If the efficacy of the procedure is expected to be low and the risks high, other treatment options may be considered first. If other treatment options have been tried and were not successful or there has been a recurrence of AF, the team may weigh the potential benefits of the Hybrid convergent procedure greater than the potential risks of the procedure itself or the risks of other or no treatment.

As previously mentioned, additional, larger studies could evaluate the potential arrhythmia and thromboembolic benefit as well as any risks associated with LAA exclusion in a hybrid convergent procedure. This would be helpful to guide further procedural and patient selection best practices for closing the LAA in the context of hybrid ablation. Matched comparisons of patients who had prior ablation and those who received de novo Hybrid Convergent ablation would help determine how successful the procedure is for patients outside of the

CONVERGE trial target population. While CONVERGE allowed left atrial size up to 6.0 cm, the enrolled patient population had mildly enlarged left atrium. Upper limits for left atrial size have been established for open surgical ablation based on the rhythm benefit achieved, however it is currently unknown how Hybrid Convergent outcomes correlate with incremental increases in left atrial size.

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Disclaimer

The EPi-Sense Guided Coagulation System is intended for use in treating symptomatic long-standing persistent atrial fibrillation when augmented in a hybrid procedure with an endocardial catheter listed in the IFU, in patients: 1. Who are refractory or intolerant to at least one Class I and/or III antiarrhyhmic drug and 2. In whom the expected benefit from rhythm control outweighs the potential known risks associated with a hybrid procedure such as delayed post-procedure inflammatory pericardial effusions.

Figure 1 . Hybrid Convergent Epicardial and Endocardial Lesion Pattern