



# European multicentre experience of staged hybrid atrial fibrillation ablation for the treatment of persistent and longstanding persistent atrial fibrillation

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## ABSTRACT

The management of non-paroxysmal atrial fibrillation (AF) remains controversial. We examined the efficacy and safety of the 2 stage Hybrid AF ablation approach by analysing the largest series of this technique reported so far.

**Methods:** The approach aims to electrically isolate the left atrial posterior wall incorporating the pulmonary veins ('box-set' pattern). An initial video-assisted thoracoscopic (VATS) epicardial ablation is followed after a minimum of 8 weeks by endocardial radiofrequency catheter ablation.

**Results:** Of 175 patients from 4 European cardiothoracic centers, who underwent the surgical (COBRA Fusion, AtriCure Inc) 1st stage ablation, 166 went on to complete 2nd stage catheter ablation. At median follow up of 18 months post 2nd stage procedure 93/166 (56%) had remained free of AF or atrial tachycardia (AT) recurrence off antiarrhythmic drugs. 110/175 62.9% were in sinus rhythm off all antiarrhythmic drugs at last clinic follow-up (132/175 75.4% including those on antiarrhythmic drugs). 18 patients (10.8%) underwent a further re-do ablation (mean of 1.1 ablations per patient) 105/166 (63%) remained free of AF/AT recurrence off antiarrhythmic drugs following last ablation procedure.

Latterly, ILRs have been implanted in patients (n = 56); 60% have remained fully arrhythmia free and 80% have shown AF burden < 5% at a median 14 months follow-up [IQR: 13.5 (8–21.5)]. Only 10.9% have reverted to persistent AF. 5 patients (2.9%) had a perioperative stroke and 4 patients (2.3%) exhibited persistent weakness of the right hemidiaphragm following stage 1 VATS epicardial ablation. One patient died following stroke (overall mortality 0.6%).

**Conclusions:** In patients with non-paroxysmal AF with unfavourable characteristics for catheter ablation, the staged hybrid approach results in acceptable levels of freedom from recurrent atrial arrhythmia, however, complication rates are higher than with catheter ablation alone.

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## 1. Introduction

Arrhythmia free survival after catheter ablation for non-paroxysmal AF ablation is lower than that for paroxysmal atrial fibrillation and carries a class IIa rather than a class I recommendation in current guidelines [1]. At major centres, success rates at 18 months of follow up range from single procedure success rates of around 30% [2,3] to multiple procedure success rates of 59% [4] and are not improved by the addition of roof and mitral isthmus

lines or the targeting of complex fractionated electrograms (CFAE) [4]. In most series, the higher the proportion of longstanding persistent patients, the poorer the results.

Surgical treatment for AF has been available for almost 25 years in the form of the Cox-MAZE procedure. Yet despite good outcome data [5] from the procedure, its complexity has limited widespread use [6]. Interest in epicardial surgical AF ablation for non-concomitant AF ablation has been revived by the development of minimally invasive techniques either as standalone procedures or as part of hybrid ablation in combination with catheter ablation. Initial non-randomised published data in mixed AF populations reported variable success rates of between 37% and 90% freedom

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from AF at one year for all AF types and 28–80% free from AF in those with persistent atrial fibrillation [7,8] In the 2017 HRS/EHRA/ECAS/APHS/SOLAECE expert consensus statement on atrial fibrillation (AF) ablation [1], hybrid ablation of atrial fibrillation combining surgical epicardial and catheter endocardial ablation has a IIa recommendation.

The 2 stage Hybrid AF ablation procedure comprises an initial video-assisted thoracoscopic (VATS) epicardial ablation by means of the COBRA Fusion catheter (AtriCure Inc), followed after a minimum of 8 weeks by an endocardial radiofrequency catheter ablation. The method is intended to isolate the 4 pulmonary veins within a circumferential lesion set enclosing the roof and posterior wall of the left atrial chamber ('Box Set' lesion pattern). At the operator's discretion, this can be combined with cavo-tricuspid isthmus line ('CTI line') and/or a mitral isthmus line.

All patients had persistent or long-standing persistent AF (LSPAF).

This series of patients using the same surgical tool and very similar electrophysiological endpoints, represents the largest series of patients with this type of ablation reported so far.

In this study, we report:

- (1) time to first documented episode of atrial arrhythmia, defined as lasting at least 30 s on monitoring, following the 3-month blanking period after the second stage electrophysiology procedure,
- (2) the atrial fibrillation burden post blanking period in those with ILR implants and
- (3) the prevalence of sinus rhythm at the time of most recent review in all patients who have undergone both stages of the hybrid procedure.
- (4) The frequency of complications at each stage of the procedure.

## 2. Methods

Patients included in this study were referred to the Departments of Cardiology or Cardiothoracic Surgery of: University Hospitals Plymouth UK, University Hospital Kralovske Vinohrady Prague Cz, Cardiocenter, Clinic of Cardiac Surgery, University Hospital Kralovske Vinohrady, Prague, Cz, San Raffaele Hospital, Vita-Salute San Raffaele University, Milan Italy and Castle Hill Hospital, Hull UK. The study received institutional review board approval from the Clinical Effectiveness Review Board for the introduction of new procedures and practices, University Hospitals Plymouth NHS Trust.

Patients were included if they had symptomatic persistent or LSPAF with a minimum of one characteristic judged unfavourable for standard catheter ablation. Unfavourable characteristics were: continuous AF duration of longer than one year, increased body mass index (BMI), enlarged left atrium (LA volume indexed greater than 33 ml/m<sup>2</sup> or echocardiographic equivalent) or previous failed catheter ablations (Table 1).

Exclusion criteria were: Previous cardiothoracic or right sided thoracic surgery, LA diameter greater than 7 cm, need for surgical coronary revascularisation or other cardiac surgical procedure, Left ventricular ejection fraction less than 20%.

In each centre prospective patients are reviewed by an AF heart team comprised of cardiologists, cardiothoracic surgeons, arrhythmia care nurses and administrators. Symptoms, cardiac investigations (including cardiac CT and/or invasive angiography) and comorbidities are reviewed. Patients are subsequently offered either catheter ablation, hybrid ablation or medical management with rate control only.

**Table 1**  
Patient demographics table.

Total patients	175
Female	48/175 (27.4%)
Mean Age (in years)	62.2 ± 8.5
Mean BMI (kg/m <sup>2</sup> )	30.7 ± 4.4
AF Syndrome	
Persistent AF (<1 year)	71 (41%)
Longstanding persistent (>1 year)	104 (59%)
Median Longest continuous period in AF (months)	17.0 (IQR 27)
Prior DCCV (mean per patient)	2.1
Patients with prior AF ablation (%)	35 (20%)
mean no. per patient	0.19
Failure of antiarrhythmic drugs (AAD)	135 (77.1%)
Mean LA diameter (AP, in cm)	
Male /	4.7 ± 0.5 /
Female	4.3 ± 0.5
Mean LV Ejection Fraction (%)	53 ± 10

Those suitable for hybrid ablation are informed that when left atrial appendage thrombus or significant pericardial adhesions are found, the procedure may be converted to an open sternotomy.

### 2.1. The surgical 1st stage

The anticoagulation regime has been modified as expertise has developed with the procedure. Patients now undergo surgery with as minimal interruption of anticoagulation as possible. This includes continuation of warfarin or DOAC up to 48 h prior to surgery and / or heparin bridging before and after the procedure. Imaging to exclude left atrial appendage thrombus is undertaken immediately prior to surgery.

The operative procedure is previously described in the literature [9]. In summary the procedure is a thoracoscopic unilateral epicardial radiofrequency ablative procedure. The transverse and oblique sinuses are opened with blunt dissection. Suction assisted, mono and bi-polar epicardial ablation is performed after removal of epicardial fat with heparin given to maintain an ACT greater than 300 sec. The epicardial fat is removed from the roof of the left atrium and interatrial groove under direct thoracoscopic vision using a mixture of dissection with thoracoscopic scissors and traction on the fat with diathermy until the left atrial muscle is denuded of fat and the left atrium is clearly visible.

The aim is to produce a box lesion isolating the posterior left atrium and the four pulmonary veins.

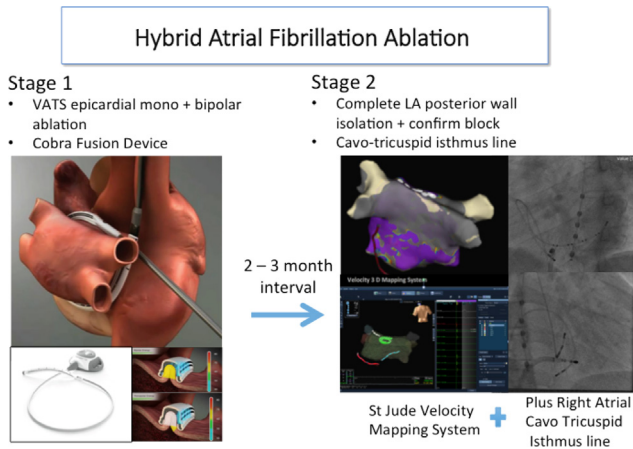
In selected patients with high CHADSVASC score the left atrial appendage was closed via an additional left thoracotomy using the AtriClip PRO (AtriCure Inc).

Up to eight cycles of mono and bipolar radiofrequency are performed using the temperature controlled COBRA Fusion ablation system (cycling up to 50 W to deliver 70 °C to tissue) and the presence/absence of left atrial posterior wall conduction block following the ablation is documented by intra-operative pacing within the isolation zone post direct current cardioversion (DCCV) if required.

The patients are mobilised the day after surgery. Discharge is between 48 h and 5 days postoperatively depending on the different centers' protocols.

### 2.2. The electrophysiological 2nd stage

The second stage procedure is performed a minimum of 8 weeks following the epicardial surgical ablation to allow time for conduction to recover at any non-permanent sections of the surgical ablation line. (Fig. 1) The study is performed under anaesthesia or sedation via vascular access from the right femoral ± right subclavian/internal jugular veins.



**Fig. 1.** The Hybrid Ablation process involves an initial surgical epicardial ablation with a staged second catheter ablation. The site of a gap in the surgical ablation line on the roof of the left atrium has been closed by radiofrequency catheter lesions indicated by white dots.

Atrial trans-septal puncture is performed and unfractionated heparin is given to maintain an activated coagulation time of greater than 300 s. SL1 and Agilis sheaths (St Jude Medical, St. Paul, Minnesota, USA) are passed to access the left atrial chamber. If the patient is in atrial fibrillation, cardioversion to sinus rhythm is advisable. We have found voltage mapping to be inconsistent in atrial fibrillation and sinus or paced rhythm permits propagation mapping.

A three-dimensional voltage map of the left atrium is created using a 3D mapping system and a multipole mapping catheter. Our standard settings for hybrid procedures are between 0.1 mV and 0.13 mV (grey colour scale) to 0.5 mV (purple colour scale) with healthy tissue identified by areas of higher voltage and areas

of low electrical amplitude indicating scar. Surgical ablation lines are shown as areas of scar (grey, yellow and orange) (Figs. 1&3). Propagation mapping in sinus or paced rhythm is used to identify areas of breakthrough in the surgical lines.

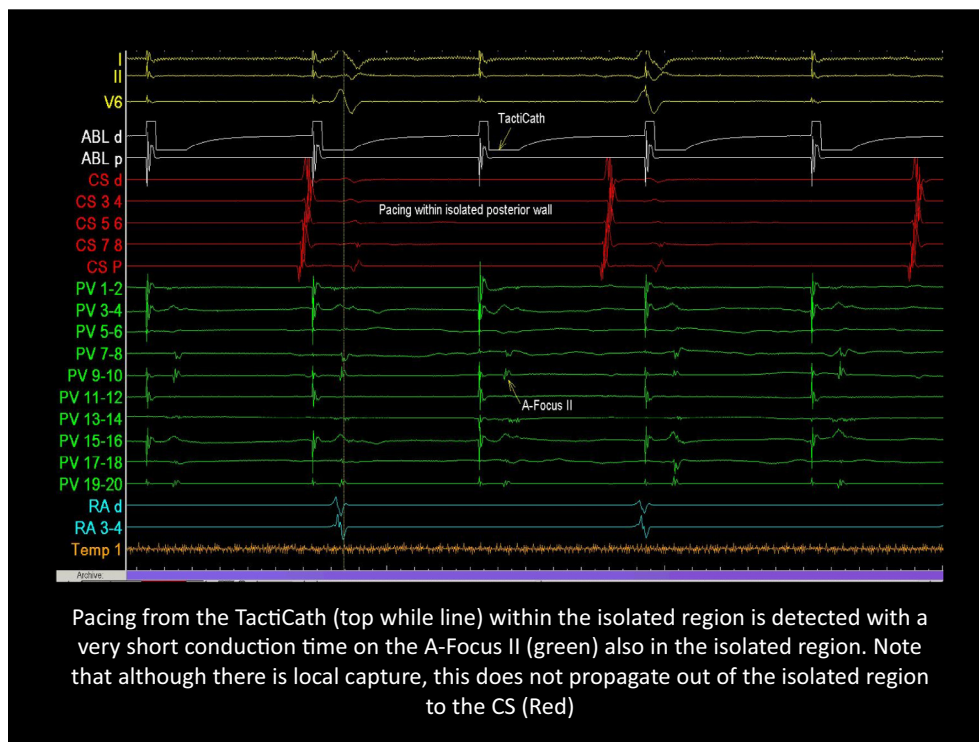
The pulmonary veins and the posterior wall of the left atrium are checked for electrical isolation by placing the mapping catheter and ablation catheter inside the veins and against the posterior wall of left atrium. An electrophysiological study is performed to test for entrance block (absence of sinus beats conducted inside the box lesion) and exit block (absence of capture of the atrium by pacing and sensing within the box lesion above the sinus rate (Fig. 2). According to center preference, evidence of block was re-checked following adenosine administration sufficient to provoke transient complete heart block.

Gaps identified in the ablation lines (Fig. 3) are closed by irrigated radiofrequency ablation lesions delivered with a contact force sensing ablation catheter. Ablation criteria sought are: greater than 1 g continuous contact force above baseline, mean force greater than 10 g and optimal stability with minimal lesion duration compatible with transmural. Precise identification of the position of residual electrical connection across the surgical line of block is achieved by placing the mapping catheter against the left atrial posterior wall, close to areas identified as defective, and using the earliest electrical signals seen at a particular pole of the mapping catheter to guide RF lesion delivery. Ablation is delivered with 25–30 Watts on the left atrial posterior wall and 30–35 Watts elsewhere.

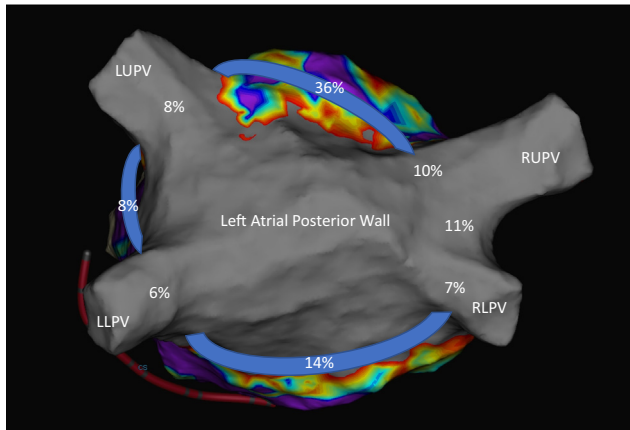
Additional ablation lines such as cavo-tricuspid isthmus or mitral isthmus lines were added at operators discretion depending on features such as the degree of atrial chamber dilatation.

All patients are prescribed one month of proton-pump inhibitors as part of the oesophageal protection protocol post-procedure.

In the latter part of this series, implantable loop recorders were placed post hybrid procedure to allow assessment of atrial fibrillation burden.



**Fig. 2.** Confirmation of left atrial posterior wall exit block at the second stage electrophysiological procedure.



**Fig. 3.** Sites of gaps in the epicardial ablation lines that were identified at the electrophysiological second stage procedure. Gaps in the ablation lines were most commonly seen in the roof lines. Left upper pulmonary vein (LUPV), left lower pulmonary vein (LLPV), right upper pulmonary vein (RUPV), right lower pulmonary vein (RLPV).

### 2.3. Follow-up

Patients who underwent hybrid ablation for atrial fibrillation were followed-up a minimum of twice in the first year and at six monthly intervals thereafter. This includes an assessment of symptoms and resting ECG 48 h to seven-day ambulatory monitoring at one and two years (depending on centre) and ILR downloads are made repeatedly during follow up. Patients are asked to undertake ECG documentation at the time of any symptoms outside these times and to send in the ECGs obtained.

### 2.4. Statistical methodology

All statistical analysis is performed using 'R' version 3.2.2 (C. 2015. The R Foundation for Statistical Computing).

Continuous variables are expressed as mean + SD. Categorical variables are presented as absolute number and percentages. Comparison between continuous variables was made using the Student *t*-test and between categorical variables the Chi-squared test. A  $p < 0.05$  was considered as statistically significant.

## 3. Results

### 3.1. 1st stage epicardial surgical procedure

175 patients underwent surgery for the 1st stage hybrid VATS procedure. Patient demographics are shown in Table 1. In two there were extensive pericardial adhesions so the procedures were abandoned. In 4 further patients, the surgery was converted to open sternotomy due to adhesions or was performed via mini-thoracotomy at operators discretion. A total of 169 patients underwent the procedure by VATS. 92 patients (54.4%) were shown to have isolation of LAPW at the end of the 1st stage surgical procedure. The median procedure duration including anaesthesia was 150 min.

Following the procedure 30% were discharged within 72 h with mean length of stay of 5.2 days (range 3.7 to 6.3 days at the different centres).

### 3.2. 2nd stage endocardial catheter procedure

166/175 patients were admitted for the second stage procedure a median of 90 days after the 1st stage procedure [IQR: 92.5

(63.25–155.75)]. The other 9 patients did not undergo 2nd stage catheter ablation; one patient died following stroke post the 1st stage procedure, the other 8 were deferred due to: patient preference (3), new diagnosis of cancer (2) and risk factors such as LAA thrombus or unfavourable inter-atrial septum (3).

On presentation for the second stage EP study 84 were in sinus rhythm (50.6%), 11 patients presented in an atypical atrial flutter (6.6%), 12 in an atrial tachycardia (7.3%) and 59 were in atrial fibrillation (35.5%).

The LA posterior wall was isolated at the start of the 2nd stage EP study in only 42 patients (25%). In 124 (75%) further LA ablation was required. Of the 92 patients with confirmed epicardial LA posterior wall isolation following surgical ablation, 33 remained isolated at the electrophysiological study second stage (35.9%). LA posterior wall isolation was achieved in 143/166 patients (86.1%). A Cavo-tricuspid isthmus line was added in 119 patients (72%). Mitral isthmus line was performed in 52pts (31%) (Fig. 4).

Mean procedure duration was 189 min.

### 3.3. Complications

#### 1st Stage Surgical Ablation Procedure (Table 2)

Evidence of immediate post procedural right phrenic nerve praxis with raised hemidiaphragm on chest X ray was demonstrated in 20 (11.4%) but during follow-up over 3 to 12 months only four (2.3%) had evidence of residual right hemi-diaphragm impairment. The frequency of phrenic nerve injury decreased as experience with the surgical technique progressed.

Five patients (2.9%) suffered a thromboembolic stroke following the surgical procedure. Three of these showed residual signs of neurological deficit. One had transient facial weakness with negative CT Head scan. One of the first patients enrolled suffered a fatal thromboembolic stroke 24 h after the surgical procedure, in this case the patient had normal coagulation preoperatively and heparin was not administered during surgical ablation (mortality 0.6%). Following this case practice changed regarding anticoagulation. In the latter part of the trial patients were either bridged to the time of the surgical procedure with subcutaneous heparin or had  $\leq 24$  h of withdrawal of direct oral anticoagulants. In addition, heparin was administered during the surgical ablation procedure.

Other complications are shown in Table 2.

#### 2nd stage catheter ablation procedure (Table 3).

Complications following catheter ablation are shown in Table 3. No revision was required for the right atrial lead damage as pacing was not required.

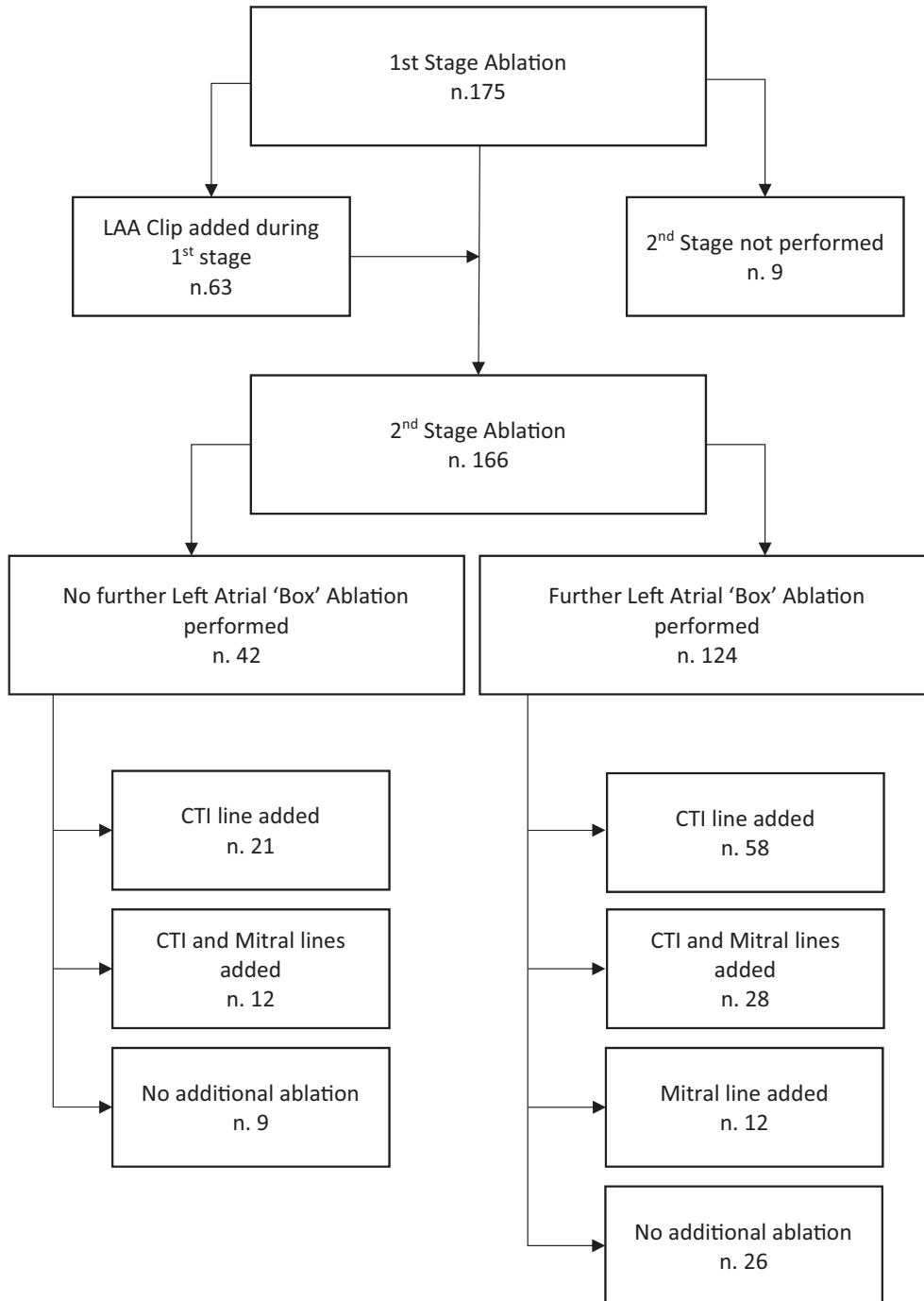
### 3.4. Outcomes at Follow-up

166 patients underwent both stages. 18 patients (10.8%) underwent a further re-do ablation (mean of 1.1 ablations per patient), with median follow-up since last ablation of 18 months [IQR: 17.5 (10.75–28.25)].

105/166 (63%) have had no AF recurrence  $>30$  s off antiarrhythmic drugs (110/166 66% including those on antiarrhythmic drugs). Treating patients who underwent a re-do ablation as a treatment failure, 93/166 (56%) have had no AF recurrence  $>30$  s off antiarrhythmic drugs.

Considering all patients who underwent at least the 1st stage procedure, outcomes in persistent and LSPAF patients were not significantly different. At the last clinic follow up, 110/175 62.9% were in sinus rhythm off all antiarrhythmic drugs (132/175 75.4% including those on antiarrhythmic drugs).

In patients with ILR implants (N = 56) following a single second stage procedure, 60% have remained fully arrhythmia free with 80% showing AF burden  $< 5\%$  at a median 14 months follow-up [IQR: 13.5 (8–21.5)].



**Fig. 4.** Flow diagram of ablations undertaken on patients (CTI = Cavotricuspid Isthmus, LAA = Left Atrial Appendage, Left atrial 'Box' = Epicardial surgical 'box' of ablation on left atrial posterior wall as shown in Fig. 1, stage 1 and in Fig. 2).

In total, 10.9% have reverted to persistent AF.

The proportion of patients at each stage of follow-up with ILR monitoring, versus holter monitoring or symptom reporting with ECG, is shown in Table 5.

**3.5. Symptom level**

The European Heart Rhythm Association AF symptom score was recorded at each follow-up visit and the median EHRA symptom score reduced from 2 to 1 following completion of both hybrid ablation stages

**3.6. Gaps in the epicardial ablation lines**

Gaps in the box lesion-set from the 1st stage surgical ablation were found in 73% (n. 126). The mean number of gaps noted was 2.1 (±1.0) per patient. The majority of gaps were found in the roof line (36%) and around the right pulmonary veins (28%) (Fig. 3). Full break-down included in Table 4.

**4. Discussion**

The 2 stage hybrid ablation approach reported here is based on achieving durable LAPWI by combining the delivery of radiofre-

**Table 2**  
Complications of First Stage Surgical Ablation (35 of 175 patients – 20%).

Persisting Phrenic nerve injury	Partial recovery (n. 3) No/minimal recovery (n. 1)
Bleeding	Haemothorax (n. 6) Gastrointestinal (n. 1) Liver abrasion (n. 1)
Pulmonary	Pleural effusion (n. 3) Pneumonia (n. 3)
Pericardium	Pericarditis (n. 1) Pericardial effusion (n. 1)
Embolic	Transient Ischaemic Attack (n. 1) Stroke (n. 5)
Dysrhythmia	Bradycardia requiring pacemaker (n. 3)
Gastrointestinal	Obstructive ileus requiring hemicolectomy (n.1)
Renal	Temporary acute kidney injury (n. 3)
Conversion to open sternotomy	Pericardial adhesions (n. 1) LAA thrombus (n. 1) on pre-operative transesophageal echo

**Table 3**  
Complications of Second Stage Catheter Ablation (4 of 166 patients – 2.4%).

Pericardium	Pericarditis (n. 1)
Dysrhythmia	Bradycardia requiring permanent pacemaker insertion (n. 2)
Miscellaneous	Damage to Right atrial lead of Permanent pacemaker system (n. 1)

**Table 4**  
Frequency of location of gaps in box-set lesion at 2nd stage EP study.

Roof line	36%
Floor line	14%
Right pulmonary veins	28%
RSPV	10%
Right PV carina	11%
RIPV	7%
Left pulmonary veins	22%
LSPV	8%
Left PV carina	8%
LIPV	6%

**Table 5**  
Mode of monitoring during follow-up.

	4 months	12 months	18 months
No. of patients followed	n. 174	n. 132	n. 103
% ILR interrogation	41%	34%	22%
% Holter	42%	51%	47%
% Clinical with ECG	17%	15%	31%

quency energy from the epicardial surface of the heart with endocardial radiofrequency ablation where necessary. This multicentre study provides outcome and safety data from 175 patients using the Cobra Fusion (AtriCure Inc.) surgical device and very similar second stage catheter ablation. This is the largest series of such an approach so far reported. Previous reports of thoracoscopic surgical and hybrid ablation methods have reported widely varying outcomes [10,7,11].

This technique aims to achieve not only pulmonary vein isolation but also left atrial posterior wall isolation involving an extensive area of the left atrial posterior wall and roof region. This is a unique lesion set which was not tested in the STAR AF II trial [4]. STAR AF II has been highly influential in attitudes to additional lines in ablation lesion sets as it showed no advantage over PVI alone of either complex fractionated atrial electrogram (CFAE) ablation, or additional roof and mitral isthmus lines. However, the trial excluded LSPAF patients and did not isolate the posterior

wall or roof region. At 18 months in STAR AF II with PVI only, freedom from atrial arrhythmia recurrence on or off drugs was 59% following a mean of 1.2 ablations.

Outcomes at 18 months in patients undergoing catheter ablation with paroxysmal AF are generally better [12]. There is evidence that as the duration of continuous atrial fibrillation increases, the triggers and sites sustaining atrial fibrillation start to extend outside the pulmonary veins and their immediate antral regions and involve the surrounding atria [13], the left atrial posterior wall appears to become a key area. Lines of functional conduction block appear to be correlated to underlying fibre orientation in the posterior LA and may form the substrate for functional re-entry [14]. Marked levels of conduction anisotropy in the posterior left atrial wall with functional conduction block in the mid left posterior atrial wall has also been shown [15]. The arrhythmogenicity of the posterior LA wall may reflect the fact that the myocardium in this part of the atrium arises from the same embryological origin as the pulmonary veins [16]. When isolation of the left atrial posterior wall incorporating the pulmonary veins is confirmed, atrial fibrillation has been observed to be inducible in the isolated posterior wall region whereas atrial fibrillation could not be induced in the larger surface area of the remainder of the atrial chambers [17].

In a randomised study [18] particularly relevant as a comparison to the STAR AF II study, 120 patients with persistent atrial fibrillation underwent either PVI plus a roof line (leaving the posterior wall in electrical connection with the rest of the atria, as in the STAR AF II 'linear' plus group) or PVI plus posterior left atrial wall isolation (LAPWI). At one year, AF recurred in 36.7% of patients without LAPWI and only 16.7% with. This trial reported a high level of success in achieving LAPWI with no cases of atrio-esophageal fistula, but RF applications at the floor line are often limited by evidence of esophageal temperature rise where careful esophageal temperature monitoring is employed. In the technique described in this report, the floor line is usually intact from the epicardial 1st stage procedure.

Similarly, recent reports of PVI versus left atrial posterior wall isolation based on cryoballoon approaches have shown superior outcomes from left atrial posterior wall isolation [19,20]. These findings alongside studies showing increased freedom from AF recurrence where the posterior LA wall is isolated in surgical procedures [21,22] all point to the 'box set' lesion pattern being a potentially superior approach to AF ablation in patients with persistent and long-standing persistent atrial fibrillation and meta-analyses of studies reporting LAPWI supports an advantage over PVI alone [23,24].

The 175 patients reported in our series had a high level of long-standing persistent drug refractory atrial fibrillation with a median of 17 months of continuous AF prior to ablation for the entire cohort. The outcome at 18 months of 62.9% freedom from recurrent atrial arrhythmia appears realistic and advantageous compared to comparable approaches. In terms of patient experience, the fact that 78% of the 175 patient cohort are maintaining stable sinus rhythm at last follow up with only 10.9% back in persistent AF is encouraging. Similarly, in the patients implanted with loop recorders in our series we observed a reduction of  $\geq 95\%$  in AF burden in 80% of patients, with 60% arrhythmia free during 14 month follow-up, a significantly higher level of efficacy than in the persistent AF series reported by Scharf et al. [25] using endocardial multi-electrode RF array catheters.

As noted in a recent review article of the different approaches to hybrid AF ablation [26], it is difficult to compare the safety and efficacy of the many different methodologies that have been reported in the literature. The patient populations differ in the percentage of paroxysmal and early stage persistent AF patients included and in the analysis of results. Few studies report the percentage freedom from atrial fibrillation recurrence off anti-arrhythmic drugs, more

commonly, the percentage in sinus rhythm at particular time points such as one year follow-up are reported. In addition the methods of monitoring vary, some using data from implantable loop recorders and others using periodic holter monitoring. The most widely employed hybrid approaches other than the method described here (Unilateral thoracoscopic staged hybrid ablation), are the bilateral thoracoscopic bipolar clamp and the transabdominal, transdiaphragmatic 'convergence' unipolar vacuum assisted monopolar hybrid approaches. Most are reports of single centre experience.

Probably the two most informative series using the bilateral thoracoscopic bipolar clamp approach for groups of patients with longstanding persistent and persistent atrial fibrillation comparable to our series are single centre studies [22,27]. The study from Haldar et al. [22] reported 51 patients and used electrophysiological study at the time of surgical ablation but did not involve subsequent hybrid catheter ablation; freedom from recurrence of AF/AT off drugs at 12 months was 73% with complications in 27%. The study from Kurfurst et al. [27] reported 30 patients who underwent bilateral bipolar clamp surgical ablation followed after 3 months by catheter ablation in all patients; at 7 months 83% were free of recurrence of AF/AT with complications in 23%. Monitoring was by 3 monthly holter monitoring in both studies and longer follow-up was not reported.

Comparative results from series reported using the transabdominal, transdiaphragmatic 'convergence' unipolar vacuum assisted monopolar hybrid approach can be considered from a multicentre European trial in 73 patients with LSPAF or Pers AF [28] and a single centre US study of 64 patients with Pers AF [29]. Follow-up was for 12 months and 16 months respectively and monitoring was with either 3 monthly holter monitoring or 30 s rhythm strip ECG at follow-up visits. In these studies, freedom from AF/AT was reported for both patients on or off anti-arrhythmic drugs with close to 50% in each study still on anti-arrhythmic drugs during follow-up. With these caveats, freedom from AF/AT recurrence was reported as 73% and 63% respectively. Complications were reported as 11% and 3% respectively.

Given these observations it appears that the transabdominal 'convergence' approach may have the lowest complication rate of the hybrid ablation techniques and the bilateral bipolar clamp approach the highest success rate with the unilateral thoracoscopic hybrid approach reported here lying in between the other techniques on these criteria.

A further difference, the value of which has not been studied in any comparative trials of hybrid ablation is inclusion of left atrial appendage closure. In the bilateral thoracoscopic approach the left sided access permits an atrial clip to be placed on the appendage whereas in the right sided unilateral thoracoscopic approach and the transabdominal approach this is not part of the standard procedure. Potentially, isolation of the left atrial appendage may enhance freedom from arrhythmia recurrence as well as reducing long term risk of thromboembolic events, but this remains to be proven. Favourable results have been reported using a unilateral left sided hybrid approach with left atrial appendage isolation [30].

#### 4.1. Study limitations

This is a report of a consecutive series of patients and is not a randomised trial of the 2 stage Hybrid method compared to a control group. In patients with gaps in the surgical ablation lines found at the second stage catheter ablation study, closure of the gaps with catheter ablation at the time of the study resulting in LAPWI may not have resulted in long-term LAPWI as some may have subsequently developed reconnection across the ablation lines. If this occurred it may have adversely affected the outcome results.

## 5. Conclusions

In this multicentre series using staged hybrid AF ablation in patients with persistent or LSPAF, we observed increased levels of medium term freedom from atrial fibrillation compared to series containing similar patient populations. Complication rates were higher than for catheter ablation alone, but patients with unfavourable characteristics for catheter ablation alone, who are severely affected by atrial fibrillation symptoms, may accept this level of risk in order to gain the increased level of efficacy represented by this approach.

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## CRedit authorship contribution statement

**G.A. Haywood:** Conceptualization, Investigation, Methodology, Project administration, Supervision, Validation, Writing - original draft, Writing - review & editing. **R. Varini:** Data curation, Formal analysis, Software, Validation. **P. Osmancik:** Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Validation, Writing - original draft. **M. Cireddu:** Conceptualization, Data curation, Investigation, Methodology, Validation, Writing - original draft. **J. Caldwell:** Conceptualization, Data curation, Investigation, Methodology, Validation, Writing - original draft. **M.A. Chaudhry:** Data curation, Investigation, Methodology, Validation, Writing - original draft. **M. Loubani:** Data curation, Investigation, Methodology, Validation, Writing - original draft. **P. Della Bella:** Data curation, Investigation, Methodology, Validation, Writing - original draft. **P. Budera:** Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Validation, Writing - original draft. **M. Dalrymple-Hay:** Conceptualization, Investigation, Methodology, Project administration, Supervision, Validation, Writing - original draft, Writing - review & editing.

## Declaration of Competing Interest

Dr Guy A Haywood, meeting support AtriCure inc.  
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## Appendix A. Supplementary material

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