Catheter Ablation of Paroxysmal Atrial Fibrillation Originating from Non-pulmonary Vein Areas

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Abstract
Pulmonary veins (PVs) are a major source of ectopic beats that initiate AF. PV isolation from the left atrium is an effective therapy for the majority of paroxysmal AF. However, investigators have reported that ectopy originating from non-PV areas can also initiate AF. Patients with recurrent AF after persistent PV isolation highlight the need to identify non-PV ectopy. Furthermore, adding non-PV ablation after multiple AF ablation procedures leads to lower AF recurrence and a higher AF cure rate. These findings suggest that non-PV ectopy is important in both the initiation and recurrence of AF. This article summarises current knowledge about the electrophysiological characteristics of non-PV AF; suitable mapping and ablation strategies, and the safety and efficacy of catheter ablation of AF initiated by ectopic foci originating from non-PV areas.

Keywords
Atrial fibrillation, non-pulmonary vein, trigger, catheter ablation

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Electrophysiological Features of AF Originating from Non-pulmonary Vein Areas

Incidence of Initiators
Several important concepts have been proposed regarding the role of non-PV ectopy in initiating AF.2-7 AF is initiated by non-PV disturbance of the cardiac rhythm in up to 39 % of cases.1,19,22-28 The left atrium (LA) (25.3 %), superior vena cava (SVC) (22.2 %), coronary sinus (CS) (18.0 %), right atrium (RA) including the crista terminalis (17.4 %), interatrial septum (7.9 %), and ligament of Marshall (LOM) (3.9 %) are the areas in which non-PV triggers of de novo AF are most commonly found (Table 1), whereas the SVC, interatrial septum and LA are the most common non-PV trigger sites in recurrent AF (Table 2).6-30 Furthermore, there is a higher incidence of non-PV triggers initiating AF in females and in patients with an enlarged LA.38

Pathophysiology
Histological analysis of the embryonic sinus venosus has identified areas capable of spontaneous depolarisation at the junctions between different embryonic tissues, such as the RA–SVC junction, crista terminals and CS ostium.31,42 The SVC is a major origin of non-PV triggers of AF.5-8,33-38,43-47 Heterogeneity of the SVC sleeve and arrhythmogenicity of cardiomyocytes isolated from the SVC have been reported.41,42 An excitation from the SVC can conduct to the RA through the myocardial extensions of the SVC sleeve.46-50 Disease human atria are hypopolarised in comparison to normal atria, which may account for the abnormal automaticity and/or activity originating from the LA wall.51-53 The crista terminals, which is an area exhibiting abnormal automaticity, anisotropy and slow conduction, may serve...
Table 1: De Novo AF Originating from Non-pulmonary Vein Areas

| Publication | Number of patients | Mean age (years) | Number of Ectopic Foci | Mapping Modality | Origin of Ectopy (No of Foci) |
|-------------|--------------------|-----------------|------------------------|-----------------|-------------------------------|
| Lin et al. 2003 | 640 | 61 ± 13 | 43 | C, basket, ICE | RA (20 %), SVC (28 %) |
| Shah et al. 2003 | 36 | 36 (23 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Beldner et al. 2004 | 401 | 68 (17 %) | 58 | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Suzuki et al. 2004 | 127 | 18 (14 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Yamada et al. 2007 | 147 | 31 (21 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Valles et al. 2008 | 45 | 57 (61 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Lo et al. 2009 | 85 | 17 (20 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Yamaguchi et al. 2010 | 65 | 17 (20 %) | 62x8 | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Chang et al. 2013 | 660 | 51 ± 12 | 86 | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Zhang et al. 2014 | 300 | 29 (10 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Cheng et al. 2014 | 76 | 13 (17 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Kurie et al. 2015 | 446 | 26 (6 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Hayashi et al. 2015 | 304 | 59 (19 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Lo et al. 2015 | 540 | 70 (13 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Hayashi et al. 2016 | 74 | 60 (80 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Hasebe et al. 2016 | 39 | 13 (17 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Zhao et al. 2016 | 720 | 66 (37 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Santangeli et al. 2016 | 1531 | 165 (11 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Hung et al. 2017 | 579 | 95 (16 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Narui et al. 2017 | 255 | 34 (13 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Allamsetty et al. 2017 | 32 | 11 (34 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Takigawa et al. 2017 | 865 | 68 (8 %) | NA | C, ICE, CARTO | RA (20 %), SVC (28 %) |
| Total | 7,823 | 1,273 (16.3 %) | 1597 | C, ICE, CARTO | RA (20 %), SVC (28 %) |

*Includes persistent left superior vena cava; †38 parasympathetic and 52 non-parasympathetic AF patients in (1) et al.; ‡28 and 18 in Chang et al., † 190 and 105 in Narui et al., † and 26 and 6 in Allamsetty et al. †‡Atrioventricular nodal re-entrant tachycardia and atrioventricular re-entrant tachycardia triggered AF. †§Five foci were speculated to have an epicardial origin. †¶Non-PV triggers were observed in 34 % of the total population (26 parasympathetic and 6 non-parasympathetic AF). A total of 45 % of non-PV triggers (16 % of the total population) were observed in the aortic encroachment area. Array = EnSite™ Array™ noncontact mapping system (Abbott); Basket = basket catheter; C = conventional mapping; CARTO = CARTO® system BiosenseWebster; CS = coronary sinus; CT = crista terminalis; ER = Eustachian ridge; F = femoral; FO = fossa ovalis; IAS = interatrial septum; ICE = intracardiac echocardiography; LA = left atrium; LOM = ligament of Marshall; M = male; MA = mitral annulus; NA = data not available; NAVX = EnSite™ NAVX™ system (Abbott); PLVS = persistent left superior vena cava; PV = pulmonary vein; PV os = ostia of an ablated pulmonary vein including the zone between ipsilateral veins; PW = left atrial/posterior wall; RA = right atrium; RAF = right atrial free wall; SVC = superior vena cava; SVT = supraventricular tachycardia; TA = tricuspid annulus; Velocity = EnSite™ Velocity™ cardiac mapping system (Abbott). Some data reproduced with permission from Higa et al., 2011. 34
as an arrhythmogenic substrate for AF initiation and perpetuation.\textsuperscript{14,15} Catecholamine-sensitive ectopy arising from the crista terminalis exhibits high-frequency depolarisations with fibrillatory conduction.\textsuperscript{6} The LOM is an embryological remnant of the left SVC and contains arrhythmogenic myocardial fibres with sympathetic innervation. Several reports have demonstrated the existence of catecholamine-sensitive tissue within the LOM that has abnormal automaticity, and which could be a potential source of AF initiation.\textsuperscript{54,55}

The musculature within the CS also has arrhythmogenic activity, with spontaneous depolarisations induced by catecholamine loading.\textsuperscript{29,30} Abnormal dilatation due to an unroofed CS can be an arrhythmogenic focus of AF initiation.\textsuperscript{14} A recent study found that 45% of non-PV triggers of AF were in the area of aortic encroachment, which equates to 16% of the total population with AF. There is also an arrhythmogenic substrate exhibiting low voltage and fractionated electrograms with a prolonged duration in the anterior part of the LA at the site of aortic encroachment.\textsuperscript{27}

Diagnosis

Proving Ectopy

To successfully provoke ectopy with AF initiation, antiarrhythmic drugs should be discontinued for a period of at least five half-lives before the patient undergoes electrophysiological study. Spontaneous initiation of ectopic beats preceding AF should be observed at baseline or after isoproterenol loading.\textsuperscript{20–23} In the case of deep sedation or general anaesthesia, it is necessary to give the patient a high dose of isoproterenol to induce ectopy with AF initiation. Adenosine or adenosine triphosphate can also be used, especially in young patients with vagal AF and with a family history of AF.\textsuperscript{15}

If ectopy does not occur, short-burst atrial pacing can be delivered with intermittent pauses or, failing that, atrial burst pacing to induce sustained AF. Careful monitoring for spontaneous reinitiation of AF is required after internal or external cardioversion. The induction of spontaneous AF initiation should be attempted at least twice to confirm the location of ectopy, the initiation pattern of spontaneous AF, and the earliest activation site (the AF initiator).\textsuperscript{2,4–7,20–24}

Mapping

Localisation of AF triggers is important for the catheter ablation of AF. If it is suspected that the trigger is based in the LA, a decapolar catheter should be inserted into the CS via the internal jugular vein and a circular mapping catheter placed in the LA using a transseptal approach. If the initiator is likely to be in the RA, a duodecapolar catheter can be placed from the crista terminalis to the distal SVC for the simultaneous mapping of the right PVs, crista terminalis and SVC. Endocardial activation timing from the high RA, His bundle and distal/proximal portion of the CS can be used to predict non-PV ectopy (Figure 1).\textsuperscript{2,4–7,20–24} It is 100% accurate in discriminating ectopy from the SVC or upper portion of the crista terminalis from PV ectopy.\textsuperscript{20–24,50} The interatrial septum should be the suspected initiator in cases with a monophasic positive narrow P wave in lead V\textsubscript{1}, or a relatively short activation time (≤15 ms) preceding P wave onset during ectopy. Simultaneous mapping of the right- and left-sided interatrial septum should be performed to avoid any misdiagnosis.\textsuperscript{20–24,63,64}

AF Initiators with Right Atrial Origin

Careful observation of P wave morphology is useful for predicting the approximate location of AF ectopy.\textsuperscript{20–24} A negative P wave or the presence of a negative component in V\textsubscript{1} is predictive of an RA origin of AF initiation. Ectopy originating from the SVC or upper portion of the crista terminalis exhibits upright P waves in the inferior leads; ectopy from the CS ostium produces negative P wave polarity in the inferior leads; and ectopy from the middle portion of the crista terminalis results in biphasic P waves. Negative P waves with a long duration in V\textsubscript{1}, may be associated with RA free-wall ectopy, including the tricuspid annulus.

If RA AF ectopy is suspected, the use of a duo-decapolar catheter is useful for mapping along the crista terminalis to the SVC.\textsuperscript{2,4–7,20–24} Bipolar signals from the proximal portion of the SVC usually exhibit a blunted atrial signal followed by a discrete sharp SVC signal during sinus rhythm.\textsuperscript{20–24} The activation sequence of these double potentials is reversed during SVC ectopy. Bipolar signals from the distal part of the SVC usually exhibit double potentials; the first component represents a SVC near-field sharp potential; and the second component, a right superior PV far-field blunted signal. During SVC ectopy, the activation sequence of these double potentials remains unchanged. The activation sequence is reversed during right PV ectopy. Intracardiac recordings along the crista terminalis also exhibit double potentials during sinus rhythm, with a high-to-low activation sequence.\textsuperscript{20–24} During crista terminalis ectopy, the atrial activation sequence of the double potentials is reversed. Noncontact mapping using an EnSite™ ArrayTM (Abbott) can accurately localise the ectopic foci with discrete depolarisations and clarify crista terminalis gap conduction-related small radius re-entry.\textsuperscript{20–24,64}

### Table 2: Recurrent AF Originating from Non-pulmonary Vein Areas

| Publication | Number of patients Total (Mean age) | Number of Ectopic Foci Total | Mapping Modality | Origin of Ectopy (Percentage of Foci) |
|-------------|------------------------------------|-----------------------------|-----------------|-------------------------------------|
| Takigawa et al. 2005\textsuperscript{a} | 207 (95 (46 %)* | 63±11 | 69 male/ 26 female | NA | 92 | C | 34 | 16 | 12 | 38\textsuperscript{a} |
| Lo et al. 2015\textsuperscript{a} | 94 | 11 (12 %)* | NA | NA | 102 | 12 (12 %) | NavX | 8 | 25 | 8 | 42 | 17 |
| Lo et al. 2015\textsuperscript{a} | 52 | 15 (29 %) | NA | 75 | 24 (32 %) | NavX | 17 | 25 | 4 | 42 | 13 |
| Mahony et al. 2017\textsuperscript{a} | 84 | 74 (88 %) | NA | NA | NA | CARTO | 9\textsuperscript{a} | 64 | 22 | 69 |

*Incidence of non-PV foci during a second session of catheter ablation of paroxysmal AF. \textsuperscript{20} In this study,35 foci (38 %) were unmappable non-PV foci. †Incidence of non-PV foci during the third to fifth catheter ablation of paroxysmal AF. ‡Incidence of non-PV foci during a second session of catheter ablation of paroxysmal AF with severe left atrial scarring. The non-PV triggers were mostly (90.5 %) located in areas outside the scar region. †Incidence of non-PV triggers of AF were in the area of aortic encroachment, which equates to 16 % of the total population with AF. There is also an arrhythmogenic substrate exhibiting low voltage and fractionated electrograms with a prolonged duration in the anterior part of the LA at the site of aortic encroachment. " Incidence of non-PV foci during a second session of catheter ablation of paroxysmal AF. § Incidence of non-PV foci during a second session of catheter ablation of paroxysmal AF with severe left atrial scarring. The non-PV triggers were mostly (90.5 %) located in areas outside the scar region. || Incidence of non-PV foci during a second session of catheter ablation of paroxysmal AF. ¶ Incidence of non-PV foci during a second session of catheter ablation of paroxysmal AF with severe left atrial scarring. The non-PV triggers were mostly (90.5 %) located in areas outside the scar region. ‡ Incidence of non-PV triggers of AF were in the area of aortic encroachment, which equates to 16 % of the total population with AF. There is also an arrhythmogenic substrate exhibiting low voltage and fractionated electrograms with a prolonged duration in the anterior part of the LA at the site of aortic encroachment. \textsuperscript{27}
AF Initiators with Left Atrial Origin

The time interval between the atrial activation of the decapolar catheter in the proximal CS and that in the distal CS is useful for predicting ectopic foci located near the right (>0 ms) or left PV antrum (<0 ms) (Figure 1). During sinus rhythm, the fusion potentials of a blunt signal and a rapid, deflecting sharp signal can be observed in the areas between the LA posterior wall and the PV antrum. The fusion potential consists of atrial and PV signals and can be found at the earliest activation site during LA posterior or PV antral ectopy. An alternating pattern of atrial and PV potentials can also be seen during ectopy.6,32–34

The Marshall ligament has multiple electrical connections to the musculature of the CS, LA posterior free wall and left PV; therefore, it is essential to differentiate a Marshall potential from a left PV or LA posterior free wall potential. A differential pacing method and/or direct recording of the LOM potential by a microelectrode catheter cannulated into the vein of Marshall can distinguish a PV potential from a Marshall potential (Tables 3 and 4).7,32–34,56,67,68

According to expert consensus statements, complex fractionated atrial electrogram (CFAE)-targeted ablation after PV isolation is feasible for substrate modification.2,4–7,32–34

Recently, the efficacy of a novel self-reference mapping technique using a PentaRay® catheter (Biosense Webster) to localise non-PV triggers originating from the LA has been reported.72

Limitations of Mapping

AF ablation can be a challenging and sometimes cumbersome task in cases of unmappable infrequent beats originating from uncommon areas. Activation mapping using fixed multipolar catheters and point-by-point mapping are not efficient for the identification of target ectopies in such cases. Single-beat analysis by noncontact mapping using the Array™ system (Figure 2) or non-invasive body-surface mapping using the CardioInsight™ Mapping Vest system (Medtronic) can be useful tools in these situations.73

Ablation

The earliest bipolar electrogram site with unipolar QS pattern recorded from the origin is the ablation target for non-PV ectopy.2,4–7,32–34

Ablation of an ectopic focus and/or electrical isolation of an arrhythmogenic thoracic vein can be achieved with the application radiofrequency energy for around 30 seconds with a non-irrigated tip at 50–55 °C or with an irrigated tip at <25–30 W.2,4–6,32–34 A contact force catheter can be used to create durable transmural lesions. This method has a lower arrhythmia recurrence and a lower incidence of atrial tachyarrhythmias resulting from incomplete ablation due to proarrhythmic lesion gaps. However, caution should be taken to avoid the application of excessive

Figure 1: Stepwise Algorithm for the Localisation of Non-pulmonary Vein AF Initiators

Δ (high right atrium – His) interval >0 ms

(CSp – CSd) interval >0 ms

Mean AF cycle length during 1 min recording at RA free wall < proximal or distal CS

Reentrant right atrium AF

Reentrant left atrium AF

Earliest site shows SVC potential inside or at SVC ostium

Earliest site shows LA potential followed by PV potential

Earliest site shows PV potential inside or at RPV ostium

Earliest site shows PV potential inside or at LPV ostium

Non-SVC

SVC

Non-PV near RPV

Non-PV near LPV

LOM

Earliest site shows SVC potential inside or at SVC ostium

Earliest site shows LA potential followed by PV potential

Earliest site shows PV potential inside or at RPV ostium

Earliest site shows PV potential inside or at LPV ostium

Non-SVC

SVC

Non-PV near RPV

Non-PV near LPV

LOM

Δ (high right atrium – His) represents the time interval from the high right atrial electrogram onset to the onset of the His atrial electrogram during sinus beats minus the same interval measured during ectopic atrial activity. CSp – CSd represents the difference in the atrial activation time between the proximal (p) and distal (d) CS atrial electrograms during an ectopic atrial beat. Source: Higa et al., 2006. Reproduced with permission from Elsevier. CS = coronary sinus; LOM = ligament of Marshall; LPV = left pulmonary vein; PV = pulmonary vein; RPV = right pulmonary vein; SVC = superior vena cava.
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Catheter Ablation of Paroxysmal AF

Persistent left SVC is also a well-recognised trigger site for AF.\textsuperscript{19,21,78–85} and the catheter position during the procedure.\textsuperscript{19,21,78–85} Monitoring of the anatomical relationship between the crista terminalis and conduction block between the RA and SVC.\textsuperscript{5,32–34,47} Circular and basket catheters, and 3D mapping systems including the CARTO\textsuperscript{©} ( Biosense Webster), EnSite\textsuperscript{™} NavX\textsuperscript{™} Velocity (Abbott), EnSite\textsuperscript{™} Array\textsuperscript{™} noncontact mapping system, and Rhythmia HDx\textsuperscript{™} mapping system with IntellaMap Orion\textsuperscript{™} catheter (Boston Scientific) can guide SVC isolation.\textsuperscript{32–34,63,64–77}

Persistent left SVC is also a well-recognized trigger site for AF.\textsuperscript{32–34,64–77} The connecting musculature means that multiple electrical signals are conducted to the posterolateral LA and middle portion of the CS from the left SVC trigger site. Complete left SVC isolation may be challenging, as it is close to the oesophagus and left phrenic nerve. There have been rare reports of inferior vena cava triggers.\textsuperscript{84,85} In these cases, the IVC triggers were successfully eliminated with a focal/isolation strategy.

Interatrial Septal Triggers

Focal ablation of the earliest activation site preceding the onset of AF should be performed until a complete elimination of the ectopy is achieved in patients with interatrial septal triggers. Near-simultaneous atrial activation of the multielectrode catheters located in the high RA, His bundle region and CS ostium can be observed in such cases. Simultaneous mapping of the right and left atrial septum is crucial to successfully locate and ablate this trigger.

Crista Terminalis Triggers

Focal ablation of the earliest activation site in the crista terminalis during ectopy preceding AF onset should be performed until complete elimination of the ectopy initiating AF or >50% reduction in the amplitude of the initial local electrogram at the ablation site.\textsuperscript{6,32–34} A region with transverse gap conduction in the crista terminalis can be an arrhythmogenic source of re-entry and also ectopy initiating AF. Linear ablation of the transverse gap should address both of these problems.\textsuperscript{12–26,44} Intracardiac echocardiography can provide real-time monitoring of the anatomical relationship between the crista terminalis and the catheter position during the procedure.

Coronary Sinus Triggers

For patients with a CS trigger, electrical isolation of the arrhythmogenic CS musculature from the atrium by endocardial and/or epicardial ablation under the guidance of a 3D mapping system is preferable.\textsuperscript{20–24,71} The aim is to eliminate (entrance block) and/or dissociate (exit block) the CS potential.\textsuperscript{86–91} Care must be taken if an inappropriate impedance rise occurs during CS ablation, and the application of radiofrequency energy should be stopped immediately to prevent any steam pops.

Marshall Ligament Triggers

For patients with Marshall ligament triggers, the earliest site with a LOM potential preceding the onset of AF is targeted using an endocardial and/or epicardial approach.\textsuperscript{20–24,92} The isolation of both the LOM and left PVs from the LA can be monitored with simultaneous mapping of the LOM and left PV ostia, maximising the chance of a successful procedure.\textsuperscript{20–24,54,56,93} Ethanol infusion into an arrhythmogenic vein of Marshall through angioplasty guidewire and balloon catheter in addition to PV isolation has recently been reported to have beneficial outcomes.\textsuperscript{94,95}

Left Atrial Triggers

For ectopy from the LA posterior wall, focal ablation of the earliest activation site should be performed (Figure 2). If unsuccessful, a box-shaped linear ablation needs to be added around the ectopy.\textsuperscript{20–24,36} Box isolation of the LA posterior wall in combination with PV isolation may be a therapeutic option in cases refractory to extensive focal ablation. The endpoint is complete elimination of the ectopy initiating AF, >50% reduction in the electrogram amplitude of the ectopic focus, or isolation of the posterior LA wall.\textsuperscript{20–34,73}

The left atrial appendage (LAA) has been reported to be a trigger of AF.\textsuperscript{96} Due to its large structure, triggers may arise from the LAA ostium, body or tip. Simultaneous mapping of the left superior PV and LAA can differentiate between a near-field sharp and a far-field blunt signals and identify true LAA triggers. Focal ablation can be applied to avoid LAA isolation. LAA isolation is only indicated when the patient can tolerate long-standing anticoagulation or a LAA occlusion device is indicated.
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Table 3: Diagnostic Criteria for Non-pulmonary Vein Ectopy Initiating AF

| Location                              | Criteria                                                                 |
|---------------------------------------|--------------------------------------------------------------------------|
| AF initiators from the right atrium   | Difference in the time interval between the atrial activation at the high right atrium and His bundle area during sinus rhythm and ectopy of >0 msec |
| Inferior vena cava, superior vena cava| Positive (superior vena cava) and negative (inferior vena cava) P waves in the inferior leads and positive or biphasic P waves in V₁ (superior vena cava) |
|                                       | Earliest ectopic activity in the vena cava during simultaneous mapping of the vena cava and right pulmonary vein (PV) |
|                                       | Reversal of the double-potential sequence during ectopy (vena cava potentials with a rapid deflection-far-field atrial potential sequence; distal-to-proximal venous activation sequence) |
| Crista terminals (CT)                 | Polarity of the P waves in the inferior leads: upper portion of the CT, positive; middle portion, biphasic; lower portion, negative |
|                                       | Earliest ectopic activity along the CT during simultaneous mapping of the CT; vena cava and right PV |
| Coronary sinus ostium                 | Negative P waves in the inferior leads |
|                                       | Earliest ectopic activity in the coronary sinus ostium |
| AF initiators from left atrium        | Difference in time interval between the atrial activation at the high right atrium and His bundle area during sinus rhythm and ectopy of >0 msec |
| Left atrial free wall or left atrial appendage | Atrial potentials with a rapid deflection-PV potential found after the earliest atrial activation |
| Ligament of Marshall (LOM)           | Earliest activation site along the vein of Marshall, posterolateral portion of the mitral annulus or left PV ostium |
|                                       | Reversal of the triple-potential sequence; the LOM potential is earlier than the left atrium or left PV potentials (LOM–left atrium–PV potentials sequence) |

CT = crista terminalis; LOM = ligament of Marshall; PV = pulmonary vein. Source: Higa et al., 2006. Reproduced with permission from Elsevier.

Table 4: Targets for Ablation of AF Originating from Non-pulmonary Vein Areas

| AF Initiators                          | Target Sites                                                                                      | Mapping Tools                                                                                     |
|----------------------------------------|---------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Right Side                             |                                                                                                  |                                                                                                   |
| Inferior vena cava, superior vena cava | Breakthrough sites around right atrium–vena cava junction for an isolation                     | Circular catheter, Array, Grid, PentaRay or Rhythmia                                            |
| Crista terminals                       | Earliest crista terminals activation site for a focal ablation                                   | Unipolar recording with a multipolar catheter, Array, Grid, PentaRay or Rhythmia                 |
| Coronary sinus                         | Connection sites between the coronary sinus and atrial musculature for an isolation              | Array, PentaRay or Rhythmia                                                                     |
| Left Side                              |                                                                                                  |                                                                                                   |
| Left atrial free wall, septum, appendage, mitral annulus | Earliest activation site for a focal ablation                                                    | Unipolar recording with a multipolar catheter, Array, Grid, PentaRay or Rhythmia                 |
| Ligament of Marshall (LOM)             | Earliest LOM potential for a focal ablation                                                       | Multipolar recording of triple potentials during ectopy and direct mapping of LOM potentials by microelectrode catheter, Array, Grid, PentaRay or Rhythmia |
|                                       | Connection sites between the left atrium and LOM for an isolation                                | Multipolar recording of triple potentials during ectopy and direct mapping of LOM potentials by microelectrode catheter, Array, Grid, PentaRay or Rhythmia |

Array = EnSite™ Array™ Noncontact Mapping System (Abbott); Grid = Advisor™ HD Grid Mapping Catheter (Abbott); LOM = ligament of Marshall; PentaRay = PentaRay® Catheter (Biosense Webster); Rhythmia = Rhythmia Mapping System and InntellaMap Orion™ Mapping Catheter (Boston Scientific). Source: Higa et al., 2006. Reproduced with permission from Elsevier.

Efficacy and Safety of Catheter Ablation

Ablation Outcomes
A relatively high success rate has been demonstrated following the ablation of RA triggers of AF. There is a comparatively higher recurrence rate following the ablation of LA triggers. The average success, recurrence and complication rates are 99.3 %, 18.5 %, and 1.9 %, respectively, for AF originating from the vena cava. These rates are 78.0 %, 16.7 %, and 2.4 %, respectively, for AF originating from the Marshall ligament.

A higher incidence of recurrent AF and non-PV AF sources has been reported in patients with metabolic syndrome and obstructive sleep apnoea. Patients who have a greater extent of left atrial delayed enhancement on MRI have a higher recurrence rate after PV isolation, suggesting the existence of AF triggers in non-PV areas.

Managing Complications
Overall complication rates are now relatively low as a result of vast improvements in our understanding of the nature and ablation of non-PV ectopy AF triggers. Injury to the sinus node, atrioventricular node, and phrenic nerve, thoracic vein stenosis, peri-oesophageal damage, gastric hypomotility, and pyloric spasms can all be caused by a non-PV trigger ablation.

Complications can be minimised by using a titrated and minimum power setting, short duration of radiofrequency energy, and by monitoring for any sinus rate accelerations, PR or RR interval prolongations and for oesophageal temperature rises. An upstream pacing technique to monitor the phrenic nerve and/or compound muscle action potential can minimise phrenic nerve injury. To reduce the risk of atrio-oesophageal fistula formation, which carries a 60–75 % chance of mortality,
Clinical Perspective

• The mechanisms of paroxysmal AF originating from non-pulmonary vein areas are automatically, triggered activity, and microreentry.
• The diagnosis is made on the basis of a spontaneous onset of the ectopic beats initiating AF during baseline or after provocative maneuvers.
• The earliest activation sites are the targets for focal ablation.
• The myocardial sleeve surrounding the ostium of the vena cava is the target for isolation.
• Success rates are >99 % for the vena cava and 78 % for the ligament of Marshall.

Conclusion

Evidence suggests that inducing the non-PV ectopic trigger responsible for initiating AF both before and after PV isolation is an indispensable step in both initial and repeat isolation/procedures. Advances in mapping and alternative energy modalities with 3D navigation are likely to play an important role in the ablation of non-PV ectopy.

Together, these advances and the systematic identification of the trigger foci and their successful elimination will improve overall AF ablation outcomes.

surgery should avoid extensive high-power ablation on the non-PV areas to avoid scar formation.
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ablation of paroxysmal AF

for impulse initiation in isolated human atrial fibers.

for atrial fibrillation originating from the superior vena cava.

in patients with paroxysmal atrial fibrillation.

of atrial fibrillation originating from the superior vena cava.

of atrial fibrillation: factors related to its arrhythmogenicity.

for atrial fibrillation.

node: Significance of mapping both sides of the interatrial septum.

and catheter ablation of complex atrial arrhythmias from non-pulmonary vein foci.

by ectopic beats originating from the ostium of the coronary sinus.

an arrhythmogenic focus in patients with paroxysmal atrial fibrillation.

and catheter ablation of paroxysmal AF.

originating from the non-pulmonary vein foci.

of the coronary sinus by radiofrequency catheter ablation.

right atrial tachycardia.

of atrial fibrillation originating from the superior vena cava.

atrial fibrillation.

by intracardiac echocardiography.

atrial fibrillation originating from the superior vena cava.

ablation of nonparoxysmal atrial fibrillation.

and catheter ablation of paroxysmal atrial fibrillation.

of the coronary sinus.

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