

Mapping Strategies in Focal Atrial Tachycardias Demonstrating Early Septal Activation: Distinguishing Left From Right

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Abstract: Determining the chamber of origin of focal atrial tachycardias (FATs) arising at or close to the septum might require biatrial mapping. This review focuses on the available tools and methods used to distinguish right atrial from left atrial origin before left atrial access is obtained. These include analysis of P wave morphology, assessing the timing of right atrial septal activation, the sequence of right atrial and/or biatrial activation and analysis of earliest electrogram morphology. The electroanatomical properties of the interatrial septum and coronary sinus that provide the basis for the above mentioned tools have also been briefly described.

Keywords: Focal atrial tachycardias, septal, electrogram analysis, coronary sinus musculature, biatrial mapping.

INTRODUCTION

Focal atrial tachycardia (FAT) is a relatively uncommon entity causing supraventricular tachycardia. In many cases, medical therapy is not effective and patients are referred for catheter ablation. It is well established that foci of atrial tachycardia tend to cluster at specific atrial structures. For the right atrium (RA), these foci are frequently localized along the crista terminalis [1]. Other common locations are the coronary sinus (CS) ostium [2], the tricuspid annulus [3], the perinodal region [4, 5] or rarely the CS body [6]. In the left atrium (LA), the structures most commonly giving rise to atrial tachycardia foci are the pulmonary veins' (PV) ostia [7] and the mitral annulus [8]. Less commonly foci may arise from the left aspect of the interatrial septum (IAS) [9]. Left and right atrial appendages could also be the sources of foci of atrial tachycardias [10, 11]. An increasingly recognized entity includes FATs that are successfully ablated from the non-coronary aortic sinus [12, 13]. Precise mapping and focus localization are crucial for a successful ablation. Planning mapping and ablation strategy requires accurate determination of the atrium from which the focus originates. This is relatively straightforward based on P wave morphology and mapping data when the focus originates from the lateral walls of RA or LA. However, when the focus is located at or close to the IAS differentiating between RA and LA origin often requires mapping both sides of the septum [4]. This review will focus on the mapping techniques used to overcome this obstacle and to provide reliable information to guide ablation prior to acquiring access to the LA.

ANATOMY AND ELECTRICAL ACTIVATION PATTERNS OF THE INTERATRIAL SEPTUM AND CORONARY SINUS

IAS is a complex anatomical structure comprising the oval fossa with its rim and the adjacent RA and LA walls.

This complex structure is a direct reflection of the phases of embryological septal development [14]. Numerous anatomical studies demonstrate that the only structure that is truly interatrial in this regard is the oval fossa with its adjacent rim [15, 16]. The remaining parts represent infoldings of the RA wall separated by fibrofatty tissue posteriorly and superiorly and the two atrial vestibules and the interposed aortic root anteriorly [15]. Electrical activation of the IAS also follows complex patterns reported in several studies. In an animal study using simultaneous biatrial mapping using two multipolar basket catheters deployed in the RA and LA Sun *et al.* demonstrated discordant electrical activation of the RA and LA septal aspects [17]. Similar findings have also been reported by human studies as well [18-20]. An elegant study by Lemery *et al.* used simultaneous noncontact biatrial mapping in 20 patients [19]. Their results demonstrate that in the majority of the studied patients endocardial activation of RA and LA septal aspects was discordant, independent and asynchronous during sinus rhythm and during pacing from multiple sites in the RA and LA. In all of these reports interatrial electrical conduction was found to be dependent on interatrial routes of preferential conduction. Such routes have been described in detail in anatomical studies and include mainly the Bachmann's bundle traversing the IAS anterosuperiorly, oval fossa, CS and subepicardial muscular fibers located in the posterior interatrial groove [15, 16, 21-23]. Our group has also found evidence of discordant electrical activation of the IAS [24]. We studied 8 patients undergoing transseptal access to the LA during catheter ablation procedures. The atrial electrograms (EGMs) recorded at the His bundle region were analyzed during paraseptal pacing from the tricuspid and the mitral annulus. During pacing from the tricuspid annulus the atrial EGM at the His bundle region was found to be fragmented or double and consisted of two distinct components. In all patients, the first component was found to have high-frequency, and large-amplitude signal and the second component was of lower amplitude and lower-frequency. The timing of the second component was found to coincide with the local atrial EGM at the mitral

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annulus in the vicinity of the IAS. During mitral annular pacing this sequence was reversed in 7 of 8 patients with the lower-amplitude, lower-frequency signal preceding the higher-frequency, higher-amplitude component (Fig. 1). Based on these findings we have concluded that atrial EGMs recorded from the His bundle region consist of two components – a high-frequency, higher-amplitude component representing a near-field potential from activation of the RA septal aspect and a lower-frequency, lower-amplitude component representing a far-field potential from activation of the LA septal aspect.

The CS also has a rather complex anatomical structure. Its proximal and middle part is covered by a cuff of striated muscle that extends from the ostium to the valve of Vieussens and even more distally in the great cardiac vein as reported in a detailed anatomical study of 240 human hearts [25]. According to another anatomical study the myocardial cuff is continuous with the RA myocardium at the ostium and extends to an average of 40 mm from there [23]. It is

connected to the LA myocardium by discrete bundles of striated myocardium that represent the substrate for LA to CS conduction and is continuous with the RA myocardium at the ostium. This explains the role of the CS as one of the routes of preferential interatrial electrical conduction as described above. Patterns of CS electrical activation have been extensively studied by Antz *et al.* [26]. In an experiment on 8 excised canine beating hearts these authors showed that CS EGMs are fragmented or double with two distinct components. One of them is a high-amplitude, high-frequency (near-field) component arising from the myocardial cuff of the CS and the other is low-amplitude, low-frequency (far-field) component arising from the activation of the adjacent LA myocardium. The origin of the two components was confirmed by microelectrode recordings from the LA myocardium and CS myocardial cuff. Activation of the LA and adjacent CS myocardial cuff was demonstrated to be discordant as well. During lateral LA pacing activation of the atrial myocardium adjacent to the mitral annulus was shown to be

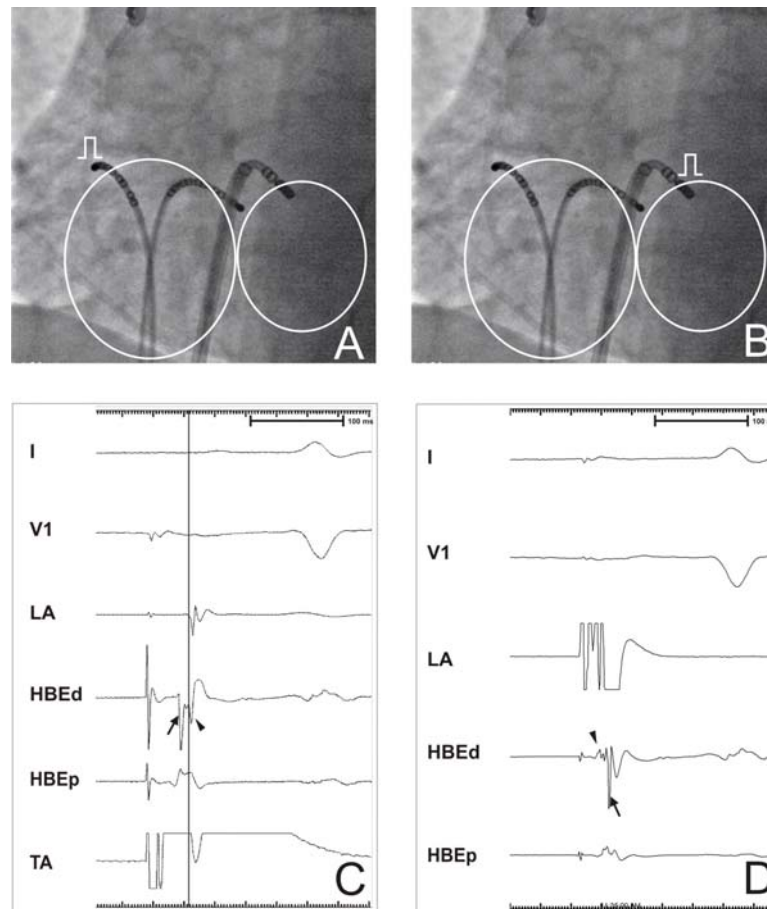


Fig. (1). Evidence of discordant electrical activation of the septum at the His bundle region. Panels A and B. Left anterior oblique (45°) fluoroscopic projection showing the position of the catheters during paraseptal pacing. HBE – catheter positioned at the His bundle region; LA – catheter positioned at the left atrial septum adjacent to the His bundle region; and TA – catheter positioned at the anterosuperior tricuspid annulus. The two circles represent the presumed location of the tricuspid and mitral annulus. Pacing site during tricuspid (panel A) and mitral annular pacing (panel B) is also shown. Panels C and D. Surface electrocardiogram leads I and V1 and intracardiac recordings from the anterosuperior left atrial septum (LA), distal and proximal His bundle region (HBE_d and HBE_p), and the anterosuperior tricuspid annulus (TA). Panel C. Double HBE electrogram with higher amplitude and higher-frequency component (arrow) and a lower frequency, lower-amplitude (arrowhead) component during right atrial paraseptal pacing. Note that the timing of the lower-amplitude, lower-frequency component on the HBE coincides with the local activation at the left atrial septum. Panel D. In the same patient the sequence is reversed during left atrial paraseptal pacing. Paper speed 300 mm/s. Modified and reproduced from [24] with permission from Oxford University Press.

activated from lateral to septal while the CS myocardial cuff was activated in a centrifugal pattern with a breakthrough at the middle CS where the presumed LA-to-CS connection is located. This study also demonstrated the presence of RA-to-CS electrical connection located at the ostium of the CS. Isolation of the CS ostium from the remaining part of the RA myocardium by a set of incisions resulted in complete reversal of atrial activation during RA pacing: LA was found to be activated via the septum and Bachmann's bundle. The near-field component in the CS electrograms followed the far-field component indicating activation of the CS myocardial cuff in a reversed fashion via an LA-CS connection. With all these complex electrical activation patterns the CS seems to play an important role in interatrial conduction.

SURFACE P WAVE MORPHOLOGY

P wave morphology during FAT has been used to predict the ectopic focus location. Ideally, the P wave morphology should be assessed during episodes of spontaneous or induced AV block or during ventricular pacing. Many FATs demonstrate 1:1 atrioventricular conduction necessitating carotid sinus massage or administration of AV nodal blocking drugs (e.g. adenosine) to disclose P wave morphology. These maneuvers not infrequently result in tachycardia termination making analysis of P wave morphology impossible or inaccurate. Despite these limitations P wave morphology is a classical tool to determine the site of origin of FATs. A couple of algorithms have been created for this purpose. In an early study Tang *et al.* analyzed P wave morphology in 31 patients with FAT [27]. They have found that P wave polarity in leads aVL and V1 was most helpful to distinguish between LA and RA foci. Positive or biphasic P wave in lead aVL was able to predict RA focus with a sensitivity of 88% and a specificity of 79%. Positive P wave in the surface ECG lead V1 during FAT predicted LA origin of the focus with a sensitivity of 93% and a specificity of 88%. However, their series did not include patients with septal foci. In an elegant study, Kistler *et al.* have designed an algorithm based on P wave morphology to predict focus location [28]. They have analyzed P wave morphology during tachycardia in 126 patients with 130 FATs undergoing successful catheter ablation. This data was used to create an algorithm that was further tested prospectively in 30 consecutive patients. The proposed algorithm could successfully predict the focus location in 93% of the studied patients. However, as stated by the authors diagnostic accuracy was much lower in foci located close to the IAS. The same issue was also touched in a study by Qian *et al.* [29]. Other groups have reported conflicting results in terms of P wave morphology in FATs arising at or close to the IAS. Frey *et al.* studied 16 patients with perinodal foci undergoing endocardial mapping of both sides of the septum and have reported that foci arising from the perinodal region on the LA aspect of the septum demonstrated a monophasic positive P wave in lead V1 while foci from the RA aspect of the septum had an isoelectric or biphasic P wave in the same lead [4]. A recent study of patients with left septal tachycardias has reported that all the 9 studied subjects demonstrated biphasic P waves with an initial negative deflection during FAT in lead V1 and negative or biphasic P waves with an initial negative component in the inferior leads [30]. With this P wave morphology differentiating left septal foci

from foci from the CS ostium or superior mitral annulus might be difficult or impossible [2, 8]. According to published series FATs successfully ablated from the non-coronary aortic sinus also demonstrate similar surface P wave morphology [12, 13]. In addition to that in a series of 5 patients Marrouche *et al.* did not find a consistent P wave morphology during FATs arising from the left aspect of the IAS as confirmed by biatrial mapping and successful catheter ablation [9]. Iwai *et al.* reported the largest series of patients with para-Hisian FAT undergoing successful catheter ablation [5]. In this study P wave morphology was also variable among study subjects with 20 of 35 patients demonstrating negative (or biphasic with terminal negative deflection) P waves in the inferior leads. The remaining 15 patients studied demonstrated positive P waves in the inferior leads. P waves in lead V1 were biphasic with the predominant component being opposite to P wave polarity recorded in the inferior leads. P wave polarity in lead aVR was also found to be opposite to that in the inferior leads. Based on all this data it can be concluded that P wave morphology, although a classical tool to define the chamber of origin of FATs, cannot be used as a highly reliable method to differentiate RA from LA origin and plan the ablation strategy in patients with FATs arising at or close to the septum. This overlap in P wave morphology might be partially explained by the obvious spatial limitations of surface ECG [31].

INTRACARDIAC MAPPING IN FATs WITH EARLY SEPTAL ACTIVATION

Assessing the local endocardial activation timing during FAT is the routine approach for localizing the focus. The first step to mapping would be to look into the timing of endocardial activation on the catheters located in the CS, His bundle region, and at the RA lateral wall. In FATs that demonstrate early activation at the RA lateral wall or show distal to proximal CS activation predicting the chamber of origin of the focus is relatively straightforward even before any mapping with a roving catheter is carried out in the RA [7]. However, when earliest endocardial activation at this first step is found at the His bundle region or at the proximal or middle CS poles, differentiating between RA and LA foci frequently requires further detailed mapping with a roving catheter and often necessitates access to the LA and biatrial septal mapping [4]. In addition, foci arising from the right pulmonary veins (esp. right superior pulmonary vein) might demonstrate early endocardial activation at the RA posterior wall due to the proximity of these two structures [7].

Many groups have worked out different diagnostic tools based on earliest EGM timing, sequence of endocardial activation or EGM morphology in an attempt to define the chamber of origin of FATs demonstrating early activation at or close to the septum. Local EGM prematurity in relation to surface P wave onset during FAT has been studied as a parameter to differentiate RA from LA origin when earliest activity after detailed RA mapping is found at the IAS. Following biatrial mapping, Marrouche *et al.* have identified 5 patients with left septal FAT in a series of 120 consecutive patients with FAT [9]. The authors used an arbitrary value of ≤ 15 ms for the earliest RA septal activation to P wave onset as a cut-off to suggest LA septal origin of the focus. However, in two of the patients in their series RF ablation was

not successful at the RA septum and necessitated LA access despite the EGM prematurity exceeding 15 ms. This suggests the absence of a dichotomous cut-off limit for electrogram prematurity that can reliably differentiate LA from RA septal origin. Another very recent study reports early atrial endocardial activation (-15 ± 5 msec ahead of surface P wave) at the His bundle region in patients with FATs arising from the LA septal aspect [30]. Values in this range can be recorded during FATs coming from other LA structures such as the mitral annulus or in those FATs successfully ablated from the non-coronary aortic sinus [8, 12, 13]. In a study of 16 patients Frey *et al.* have not found a significant difference in the timing of the earliest electrogram (recorded at the His bundle region in all patients) in perinodal FATs ablated from the RA septal aspect, compared to those arising from LA septum [4]. In contrast FATs arising from the left septum demonstrated significantly earlier EGMs on the left septal aspect compared to those originating from the RA septal aspect. Therefore, the authors have concluded that biatrial septal mapping is necessary for reliable determination of the chamber of origin in FATs arising in the vicinity of the AV node. This is of extreme importance given the fact that applying ablation lesions in the region of the AV node is associated with increased risk of iatrogenic AV block.

Endocardial activation sequence can also be used to differentiate RA from LA origin of FAT. A focus at a specific region would generate a wavefront that would follow a specific pattern of endocardial activation. This pattern, compared to the endocardial activation pattern during sinus rhythm might serve to differentiate RA from LA foci. In a series of patients with paroxysmal atrial fibrillation undergoing catheter ablation Lee *et al.* studied the endocardial activation timing of the high RA, His bundle region and CS during sinus rhythm and during ectopic foci initiating atrial fibrillation [32]. In 37 patients the sequence of endocardial activation was retrospectively correlated to foci location as confirmed by successful ablation. Then, the difference in timing of high RA EGM and the atrial EGM at the His bundle region during atrial ectopy compared to that obtained during sinus rhythm was further prospectively studied in other 38 patients. When the difference in EGM timing at the high RA and the His-bundle region during atrial ectopy subtracted from the same difference during sinus rhythm was ≤ 0 msec a right PV focus could be differentiated from an RA focus with a diagnostic accuracy of 100% before LA access was obtained. Chang *et al.* studied inter- and intraatrial activation sequence during FAT and ectopic activity in comparison to sinus rhythm in 8 patients with foci originating from superior vena cava and 8 patients with ectopic activity from right superior pulmonary vein [33]. They examined the difference in activation timing of high RA and distal CS as a reflection of interatrial activation and of high RA and His-bundle region as a measure of intra-RA activation. In an attempt to provide a simple measure of the difference in endocardial activation sequence during sinus rhythm and during ectopic activity they subtracted the values of interatrial and intra-RA activation during ectopic activity or FAT from those during sinus rhythm. Their results demonstrate that the difference in interatrial activation was significantly larger for ectopic activity arising from right superior PV in comparison to that originating from the superior vena cava. With a cut-

off of 20 msec for this difference these authors could predict the focus location in all of the studied patients. From an electroanatomical standpoint these results could be explained by the fact that an ectopic beat from the superior vena cava and a sinus beat will follow the same or similar pattern of propagation across the atria. Despite close anatomical proximity an ectopic beat from the right superior pulmonary vein would demonstrate a different pattern of electrical activation of the atria hence a different endocardial activation sequence that could explain the observed difference.

Analysis of EGM morphology is another tool that might aid distinguishing between RA and LA foci. Unipolar electrogram showing QS morphology at the earliest site on the RA septal aspect might also signify RA origin while the presence of an R wave might support LA septal origin as suggested by Wetzel *et al.* [34]. Schwartzmann *et al.* reported that in a porcine model "batrial" potentials consisting of components reflecting RA activity and right superior pulmonary vein activity may be recorded at the posterior RA due to the close anatomical proximity of these two structures [35]. Following this report Soejima *et al.* studied 16 patients with LA FAT [36]. In their series 14 patients had earliest RA activation recorded at the high posteromedial RA where double potentials were identified. During FAT these double potentials consisted of a smaller first component and a larger second component. The sequence of these two components was reversed during sinus rhythm. The timing of the smaller component during FAT coincided with the timing of the local LA electrogram recorded at the same area on the LA septum. Ablation lesions at the sites of earliest electrograms during FAT on the RA septum resulted in reduction of the amplitude of the larger component without any impact on the amplitude of the smaller component. Based on these findings the authors concluded that the smaller component is a far-field signal from the activation of the left aspect of the posterior septum while the larger component is a near-field activation of the posteromedial RA myocardium. However, their series did not include patients with RA septal foci and pacing was used to simulate RA FAT. In a prospective study Yamada *et al.* studied 26 patients with FATs arising from the posterior RA and right PVs [37]. Similar dual-component EGMs were recorded at the posterior RA with the larger-amplitude, near-field component preceding the smaller-amplitude, far-field component during sinus rhythm and during FAT in all cases of posterior RA foci. The sequence was reversed during FAT in all patients with foci from the right PVs providing an excellent diagnostic accuracy in differentiating RA from LA origin in these cases. Despite its very high diagnostic accuracy the technique proposed by the two investigator groups is limited to FATs originating from the right pulmonary veins and the posterior RA. It is not applicable to cases when earliest RA activation is found at other septal sites or proximal to middle CS. Our group has recently reported a novel technique, based only on EGMs from His bundle region and CS, that can aid in differentiating RA from LA origin of FAT prior to any detailed mapping [24]. We studied a series of 27 patients with FAT demonstrating early activation of the His bundle region or proximal or middle CS assessed using a decapolar catheter in the CS and a quadripolar catheter at the His bundle region. FATs demonstrating early activation at the RA lateral wall or at the distal

CS clearly suggesting the chamber of origin were excluded. Prior to any detailed conventional or three-dimensional mapping, we analyzed the morphology of the earliest EGM recorded with the above mentioned catheter setting with regard to the sequence of near-field/far-field components. As already shown, atrial EGMs recorded from the CS and His bundle region are fragmented or double due to the recording of a near-field component from RA septal aspect or CS myocardial cuff and a far-field component from the LA. We hypothesized that radially spreading wavefronts from a LA tachycardia focus would likely activate the LA septal aspect or the LA myocardium adjacent to the CS earlier than the RA septal aspect or CS myocardial cuff, respectively. The activation of the latter two structures would occur via one or several interatrial connections. In this case the far-field component at the earliest bipole at the HB or proximal or mid-CS would precede the near-field one. The opposite sequence would occur in FATs arising from the RA or from CS myocardial cuff. In both cases, due to the different timing of the two components the earliest electrogram would be double or fragmented, especially if the focus is in its immediate proximity (Fig. 2). Electrogram recordings of the 27 cases were

assessed by two independent observers with an interobserver agreement of 93% ($\kappa=0.83$). In this series, a far-field/near-field sequence of the earliest EGM could predict the need for left-sided ablation with a sensitivity of 78 and 89%, specificity of 94 and 89%, positive predictive value of 88 and 80%, and negative predictive value of 89 and 94%, respectively, for the two observers. This high diagnostic accuracy was achieved for a wide range of foci locations in comparison to other reports studying only FATs originating from circumscribed areas as the LA septal aspect [9], perinodal region [4] or posterior septum [36, 37] (Fig. 3).

CONCLUSION

Determining the atrium of origin of foci located at or in the vicinity of the interatrial septum might be challenging and frequently necessitates biatrial septal mapping with all the risks associated with transeptal or transaortic access. While surface P wave morphology might be useful in this regard when the focus arises from RA or LA structures located laterally, its utility remains limited for atrial tachycardia foci arising at or close to the septum. Endocardial

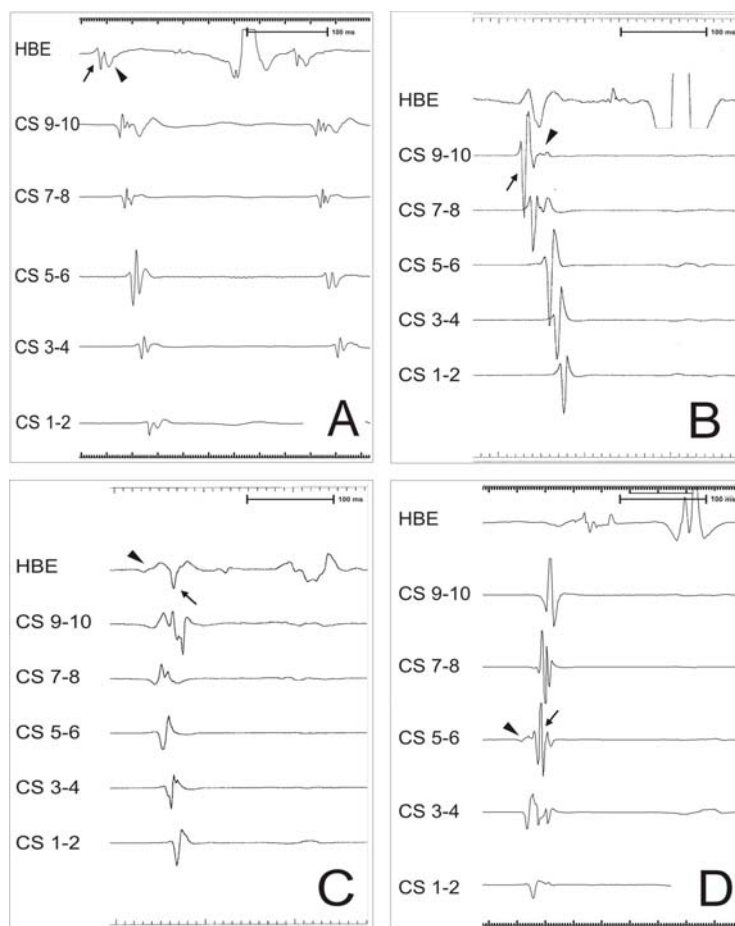


Fig. (2). Representative examples of intracardiac recordings as presented for analysis to the observers showing single beats of FATs successfully ablated in the RA (panels A and B) and in the LA (panels C and D). Panel A. Earliest activation at the HBE with the near-field component preceding the far-field one (N-F sequence). Panel B. Earliest activation at CS 9–10 with N-F sequence. Panel C. Earliest activation at the HBE with the far-field component preceding the near-field one (F-N sequence). (D) Earliest activation at CS 5–6 demonstrating F–N sequence. CS 9–10 is positioned at the ostium. CS - coronary sinus. The other abbreviations are the same as in Figure 2. Arrows and arrowheads denote near-field and far-field EGM components, respectively. Paper speed 300 mm/s. Reproduced from [24] with permission from Oxford University Press.

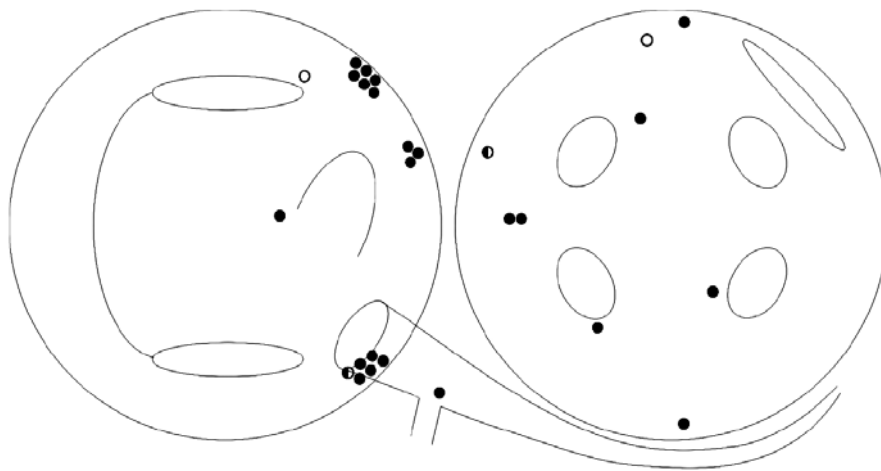


Fig. (3). Schematic representation of the anatomical distribution of the foci included in the studied series. The two atria are presented as viewed from the atrioventricular annuli. Foci that were correctly identified by both observers are presented by the filled circles, those that were misclassified are denoted by the open circles, and half-filled circles represent the foci that were misclassified by only one of the observers. Reproduced from [24] with permission from Oxford University Press.

atrial activation mapping remains a very important step in pinpointing the focus. Data from several studies shows that transseptal LA access is crucial in determining the chamber of origin of these foci. However, numerous other studies have attempted to use endocardial activation sequence or electrogram morphology in an attempt to acquire that information before gaining LA access. The results of some of these studies are promising and the techniques they use may be applied routinely in practice. However, none of them provides a definite solution for all foci locations. The exact technique or combination of techniques that is most likely to differentiate RA from LA foci should be cautiously selected.

CONFLICT OF INTEREST

The author confirms that this article content has no conflict of interest.

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