Mapping of Focal Atrial Tachycardia with an Un-Interpretable Activation Map Following Extensive Atrial Ablation: Tricks and Tips

Running title: Ju et al.; Mapping of Focal ATs

Weizhu Ju, MD*; Bing Yang, MD*; Hongwu Chen, MD; Fengxiang Zhang, MD; Kai Gu, MD; Jinbo Yu, MD; Mingfang Li, MD; Gang Yang, MD; Kejiang Cao, MD; Minglong Chen, MD

Department of Cardiology, the First Affiliated Hospital of Nanjing Medical University, Nanjing, China

*contributed equally

Correspondence:
Minglong Chen, MD
the First Affiliated Hospital of Nanjing Medical University
Guangzhou Road
Nanjing, 210029
China
Tel: 0086-25-6813-6965
Fax: 0086-25-8378-1867
E-mail: chenminglong@njmu.edu.cn

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Abstract:

Background - Atrial tachycardias (ATs) following extensive ablation are increasingly common and challenging arrhythmias. The prolonged intra-atrial conduction time (IACT) during ATs in the milieu may complicate the mapping of focal ATs. The present study characterized the electrophysiological features of ATs in this unique setting and to further delineate an effective mapping strategy.

Methods and Results - In total, 13 patients (average age of 59±7 years) in a cohort of 80 patients referred for AT ablation were selected into the study. The patients all demonstrated an undistinguishable map not ready to be interpreted the three-dimensional mapping. A total of 13 ATs were mapped with mean tachycardia cycle length 296±70ms. Two activation patterns were identified, which were referred to as "pseudo macro reentry" and "chaotic activation", respectively. The former was a focal AT originating from the vicinity of an area of conduction block with the IACT less than the window of interest duration (4 cases, IACT/WOI ratio range 0.93-0.98). The latter refers to a focal AT exhibiting a disorderly color mapping display with IACT exceeding the WOI duration (9 cases, IACT/WOI ratio range 1.02-1.29). The IACT was determined after resetting the annotation. All ATs were successfully eliminated at the originating site.

Conclusions - We delineated a series of focal ATs in the setting of a significantly prolonged IACT encountered in patients following previous extensive ablation. Two activation patterns were identified, which may help facilitate the mapping of focal ATs in this setting.

Key words: atrial tachycardia, reentry, mapping, focus
Introduction

For more than a decade, focal atrial tachycardias (ATs) have been effectively treated by catheter ablation.\(^1,2\) Generally speaking, focal ATs tend to occur in structurally normal hearts and manifest a typical centrifugal activation pattern, with the total atrial activation time accounting for less than 50% of the tachycardia cycle length. However, in patients who have undergone previous ablation for atrial fibrillation (AF) or those with structural heart disease, focal ATs may have a heterogenous anatomical distribution and co-existing scar substrate, which can add to difficulties in mapping.\(^3,4\) Prior extensive ablation and/or pre-existing substrate may significantly prolong the conduction time in the chamber, which in turn would alter the typical pattern of focal ATs seen with three-dimensional mapping and make the diagnosis more difficult. In the present study, we aim to characterize the electrophysiological features of these arrhythmias in this unique setting and to further delineate the mapping strategy to localize the site of origin.

Methods

Study population

From January 2009 to August 2013, there were 80 patients who underwent a second ablation procedure post AF ablation or ablation for ATs in the setting of structural heart disease (post atriotomy, valvular heart disease). In the 80 patients, a total of 146 ATs were mapped, in which 55 ATs were macro-reentrant, the other 91 cases of ATs proved to be focal ATs (including micro-reentry and true focus). Among the 91 focal ATs, 78 cases of AT exhibited an unambiguous centrifugal activation map in the three dimensional mapping and were successfully
ablated at the original site, while the other 13 cases of AT (in 13 patients) demonstrated an undistinguishable map not ready to be interpreted. Thus, the 13 patients were included (8 males, average age of 59±7 years) in the study. Among them, 9 cases were encountered in the context of ablation for recurrent AF and the other 4 were cases for recurrent AT originating from the right atrium. The study was approved by the institutional review committee and written informed consents were obtained before the procedure in all subjects.

**Electrophysiological Study**

All procedures were performed under conscious sedation and local anesthetized state. A 6F quadripolar and a decapolar catheter were advanced into the high right atrium and coronary sinus via the left femoral and left subclavian veins, respectively. Data were recorded with a Prucka system (Prucka Cardiolab EP, GE Healthcare, Milwaukee, WI) or BARD system (BARD), and filtered at 30 to 400 Hz, and 0.05 to 500 Hz for intracardiac electrograms and surface electrogram recordings, respectively.

**Three-dimensional Activation Mapping**

Three-dimensional activation mapping was performed to identify the origin of ATs and to delineate the activation pattern of the tachycardia using the CARTO (Biosense-Webster Inc., Diamond Bar, CA, USA) or EnSite NavX/Velocity (Endocardial Solutions, Inc., Minneapolis, MN) systems. Typically, a coronary sinus atrial electrogram was used as the reference signal. For each AT, the beginning of the mapping window of interest (WOI) was set to be 50–70 ms earlier than the onset of P wave, allowing the local activation time of the assumed origin or mid-diastolic isthmus to be allocated within the beginning of the WOI. In cases where the onset
of the P wave could not be clearly distinguished, the WOI was set to make the reference signal located at the middle of the interval. The duration of the WOI was set to be 10~20ms less than the tachycardia cycle length (TCL). Generally, 100~200 points (in CARTO system) or 200~300 points (in EnSite system) were collected to reconstruct the geometry of the atrial chamber and to delineate the AT mechanism. Sites with the voltage ≤0.05 mV were defined as electrical silence and displayed in gray color. For each point sampled by the system, an automated algorithm was employed to annotate the potential. Generally, the maximum dv/dt part of the signal was annotated in EnSite-NavX/Velocity system, while the “down slope” algorithm was applied to annotate the electrogram when CARTO was used. The manual adjusting was necessary in the case that the catheter induced premature beat or far field ventricular potential was sampled.

Analysis, Validation of ATs and Re-setting of the Activation Map

In general, for cases of macro-reentrant AT, the total activation time would span the entire WOI, and the phenomenon of “early meets late” would be displayed on the map. Meanwhile, a focal AT would reveal itself as a centrifugal source spreading radially, and consequently no “early meets late” area will be observed. In all subjects, a multi-site entrainment strategy was employed to validate the exact nature of ATs. A post pacing interval (PPI) ≤ TCL+20 ms was considered to be a good PPI implicating the location or course of an AT circuit. A macro-reentrant AT should demonstrate a good PPI near at least two distinct segments. On the contrary, a focus usually demonstrates a centrifugal PPI response with good PPI only at the vicinity of the site of origin. Furthermore, the site of origin was verified by the elimination of tachycardia with localized

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energy delivery. Additionally, substrate analysis was performed to delineate the slow conduction area resulting in prolonged conduction time in atrium during ATs.

Once a site of origin was confirmed, the annotation of each mapping point was then reset based on a comprehensive analysis. In general, the signal in the assumed site of origin would be annotated as the earliest, while the most remote site within the same atrial chamber or the opposite site of the blocking area would be tagged as the latest part in the WOI. The intra-atrial conduction time (IACT) during AT was determined. The IACT was defined as the interval from the earliest to the latest activation after resetting of the activation map.

**Catheter ablation of the focal ATs**

Radiofrequency energy was applied at the earliest activation site based on mapping using an irrigated ablation catheter (Navistar catheter, Biosense Webster, Diamond Bar, CA or IBI, St. Jude Medical, St. Paul, MN) with a power of 30W, temperature limit of 43°C and irrigation rate of 17ml/min. The endpoint of the procedure was defined as termination of AT and noninducibility of sustained AT by programmed stimuli with or without isoproterenol infusion.

**Post ablation care and follow-up**

All patients were given warfarin to maintain the international normalized ratio between 2 to 3 for at least 3 months. All patients were asked to undergo 24 hour Holter monitoring at 1, 3, and 6 months post procedure and to be reassessed for any recurrence of symptoms. **Statistical analysis**

Continuous variables were expressed as mean ± standard deviations or median (range).
Results

Patient characteristics

Patient characteristics are provided in Table 1. The mean age of the patients was 59±7 years. The mean left atrial size was 43±3mm and mean left ventricular ejection fraction was 61±2%. Four patients had documented hypertension, including one subject with prior inferior wall myocardial infarction. Two patients had undergone prior surgical atriotomy, one for mitral valve repair and another for atrial septal defect. The median duration of AF or AT symptoms was 18 months (range, 9-60 months). All patients had undergone at least one prior ablation procedure for AF or AT. The time from the prior index ablation procedure to the current procedure was 1-30 months.

Electrophysiological characteristics

A total of 13 sustained ATs were mapped. The mean TCL was 296±70ms (range, 209-450ms). In the initial three-dimensional activation map before re-set, two types of activation pattern were identified, which were referred to as “pseudo macro-reentry” (4 cases) and “chaotic activation” (9 cases), respectively.

As the name suggests, a “pseudo macro-reentry” pattern demonstrated a focus mimicking as a macro-reentry in the three-dimensional map attributed to its “early meets late” activation pattern, which was found in 4 cases. An example of “pseudo macro-reentry” is shown in Figure 1. The map demonstrates a focus located at the ridge between the left pulmonary vein and left atrial appendage. The patient had previously had circumferential pulmonary vein ablation plus mitral isthmus line lesions for persistent AF. Due to block at the mitral isthmus line, the focus depolarizes the atrium in a uni-directional fashion rather than a centrifugal pattern, consequently
mimicking macro-reentry around the mitral annulus. Multi-site entrainment along the mitral annulus also ruled out the possibility of macro-reentry. Tachycardia was terminated by focal ablation at the site of origin, and the block of mitral isthmus line was subsequently demonstrated. In this pattern, the IACT/WOI ranges from 0.93 to 0.98.

A “chaotic activation” pattern was seen in 9 cases. In these cases, the map before re-setting demonstrated a disorderly color arrangement, not readily differentiated as focal or macro-reentrant. As shown in the upper panel of Figure 2, neither a centrifugal site of origin nor macro-reentry was obvious before re-setting the map. Entrainment mapping revealed a centrifugal post pacing interval response at the posterior wall. Therefore, the tachycardia was assumed to be a focus originating from posterior wall. The latest activation part in the window of interest was re-set as the earliest part, thus a focus originating from the posterior wall was revealed as depicted in the lower panel of Figure 2. The IACT was determined after annotation reset, with IACT/WOI range from 1.02 to 1.29.

**Ablation**

All ATs were successfully eliminated by radio frequency ablation at the site of origin.

**Follow up**

No complication in any of patients undergoing AT ablation was observed. After a median follow-up of 40 months (range, 5-51 months) months, all patients were free of tachycardia.

**Discussion**

The present study investigated the electrophysiological characteristics of focal ATs encountered
in patients that have had prior extensive atrial ablation. In this situation, focal ATs may not be readily distinguished from other mechanisms based on three-dimensional mapping because of significantly prolonged IACT. Based on the relationship between the duration of WOI and IACT, two types of activation patterns were identified, and the mapping strategy was further delineated.

In terms of left atrium, the IACT during sinus rhythm usually takes about 75-82 ms in control normal hearts and 105-108ms in persistent AF atria, based on our previously published data and other published reports.\textsuperscript{12,13} Meanwhile, the shortest TCL for ATs should be about 200ms. Taking these two factors into account, it may be safely concluded that during ATs, electrical activity may only be recorded in only one half of the TCL. This may serve as one of the key points by which to differentiating the focal ATs and macro-reentry. However, the rule would become invalid in an atrium with significantly prolonged conduction time, whether in the case of diseased atria delineated in a previous report\textsuperscript{10} or atria post extensive ablation as demonstrated in the present series.

The two types of activation patterns were identified in accordance with the relationship between IACT and duration of WOI. In the “pseudo macro reentry” pattern, the IACT approaches but does not exceed the WOI, with the focal AT always originating from the vicinity of an area of anatomical or functional block. This milieu allows for the residual part of atrium to be activated in a uni-directional pattern, with the contralateral part of the blocked region being the latest depolarized site. If the total activation time is more than 85% of the WOI duration, the three-dimensional map may display the illusion of macro reentry (Figure 3). In the “chaotic
activation” pattern, the IACT exceeds the WOI, making the annotation of the signal as compared to the reference difficult, which is critical for locating ATs. There may be three possible scenarios in this setting as demonstrated in Figure 4. The major difference among the types depends on the relationship between the WOI and true activation route of the focal AT. Figure 5 demonstrates a case of “chaotic activation”, which is in line with the “B type” of Figure 4.

When faced with this setting of focal ATs, we provide some useful tricks and tips to identify the site of origin in a straightforward way, which has proven to be efficient in our experience. First, standard entrainment mapping and substrate analysis may help to differentiate between macro-reentry and focal or localized re-entry in the localization of ATs. However, entrainment mapping may not be feasible, due to either inability to capture the atrium or degeneration into another AT or AF. More importantly, neither entrainment mapping nor substrate analysis can localize focal ATs accurately. A resetting of the signal annotation based on the two patterns would make it possible as shown in Figure 4. We provided a solution in face of the mapping of ATs post extensive ablation in Figure 6.

**Clinical Implications**

The evolution of three-dimensional electro-anatomic mapping system has dramatically reduced the difficulty of mapping for complex tachycardia, as well as expanded the scope of clinically curable arrhythmias by catheter ablation. By projecting the activation time as compared with a selected electrical signal reference on the 3-D geometry of the mapped cardiac chamber point by point, the system allows intuitive review of the activation mode of the whole chamber through the various isochrones in a 3-D fashion. However, the 3-D system per se does not always
accurately represent the mechanism of the tachycardia. The rigid interpretation of the map could lead to a false diagnosis, which may in turn result in a protracted and unsuccessful procedure. Generally speaking, macro-reentry always presents with continuous propagation around a central obstacle while a focal AT exhibits itself as a focus spreading centrifugally. Nevertheless, settings such as those as delineated in the present series would subvert the rule. The present study raises the necessity to be alert to this situation. Successful interpretation of the colors in the map has important therapeutic implications.\textsuperscript{14,15}

In clinical practice, the IACT exceeding 85\% of TCL in focal ATs is extremely rare in the setting of no prior atrial ablation or surgery\textsuperscript{10} but not uncommon in atra post extensive ablation, especially when linear lesions were performed. In this sense, linear lesions and defragmentation within the atrium not only lead to iatrogenic arrhythmias, but also result in complex substrate complicating the mapping of ATs. In order to avoid this situation, it is proposed that defragmentation in the atrial body should be cautiously performed, and that the location and course of linear lesions should be carefully designed.\textsuperscript{14,16}

**Study Limitations**

The study cohort was relatively small and from a single center. Furthermore, the patients were highly selected, and the actual prevalence could not been determined. We also speculate that this may be related to the degree of previous atrial ablation, and the prevalence may consequently vary based on an individual center.

The true mechanism of the focal ATs remains to be determined. Nevertheless, based on the stable entrainment response, localized reentry may be the most likely mechanism accounting
for ATs in the present series, which is commonly encountered in the context of prior AF ablation.15

At the end of procedure, the IACT during sinus rhythm was not routinely investigated. It could not be determined whether the prolonged conduction time was resulted from delayed conduction during high rate activation or pre-existing slow conduction or both.

Conclusions

We report one series of focal ATs in the unique milieu resulting from extensive ablation in the atrium body. The markedly prolonged IACT makes the mapping of focal ATs challenging. Two activation patterns were identified and the corresponding straightforward approaches were delineated to assist in characterization of these ATs. Further studies are needed to explore the relationship between previous ablation strategies, the degree of conduction time prolongation and prevalence of ATs in this particular setting.

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Conflict of Interest Disclosures: None
Reference:


**Table 1** Clinical Characteristics of Focal AT Patients with Prolonged Intra-atrial Conduction Time

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age (years)</th>
<th>LAD (mm)</th>
<th>Context</th>
<th>Index Ablation</th>
<th>TCL (ms)</th>
<th>WOI (ms)</th>
<th>IACT (ms)</th>
<th>% IACT/WOI</th>
<th>Location of focus</th>
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<tr>
<td>1</td>
<td>F 58</td>
<td>41</td>
<td>CAF</td>
<td>CPVI, R,A</td>
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<td>256</td>
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<td>2</td>
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<td>CAF</td>
<td>CPVI, R,A,P</td>
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<td>243</td>
<td>313</td>
<td>1.29</td>
<td>Septum of LA</td>
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<tr>
<td>3</td>
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<td>40</td>
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<td>CTI, F</td>
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<td>264</td>
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<td>440</td>
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<td>0.98</td>
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<td>CPVI,R,MI,CFAE</td>
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<td>CAF</td>
<td>CPVI,A,S,CFAE</td>
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<td>1.15</td>
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LAD: left atrial diameter; TCL: tachycardia cycle length; WOI: window of interest; IACT: inter-atrial conduction time; CAF: continuous atrial fibrillation; aAFL: atypical atrial flutter; CTI: cavo-tricuspid isthmus; CPVI: Circumferential pulmonary vein isolation; R: roof; A: anterior wall; P: posterior wall; F: right atrial free wall; S: left atrial septum; MI: mitral isthmus line; CFAE: complex fractionated atrial electrogram.
Figure Legends:

**Figure 1.** Shown is a three dimensional activation map of an AT focus located at the ridge between the left atrial appendage and left pulmonary vein (Case-7). Due to previous mitral isthmus ablation and block, the map shows macro-reentry rotating around the mitral annulus. However, the results of entrainment mapping demonstrated a centrifugal post pacing interval response. An attempt of radiofrequency ablation terminated the tachycardia. Panel A shows activation map, panel B shows voltage map. See Figure 3 for schematic diagram.

**Figure 2.** Shown is the three dimensional activation map of a focal atrial tachycardia (TCL=305ms, WOI=290ms) located at the left atrial upper posterior wall with intra-atrial conduction time exceeding the WOI duration (Case-5). A: Before re-setting, the map shows a chaotic activation pattern not readily differentiated (left panel: modified posterior-anterior view; right panel: anterior-posterior view). Entrainment mapping at three different sites located at distinct segments of the atrium showed a centrifugal post pacing interval response at the posterior wall. B: Based on entrainment mapping, the AT was assumed to have a focal origination from the posterior wall. The latest activation was re-set as the earliest activation in the WOI. Focal AT was revealed and was terminated by single radiofrequency energy delivery at the site of origin. Note the low voltage areas on the roof, septum and lateral wall, which may account for the significantly prolonged intra-atrial conduction time (IACT=344ms). See Figure 4A for schematic diagram.
**Figure 3.** Shown is the schematic diagram of a “pseudo macro-reentry” pattern. When the focus is located in the vicinity of an area of conduction block, the residual part of atrium is activated in a uni-directional fashion with the contralateral side of the area of block being the latest depolarized site, thus making the tachycardia appear macro-reentrant. The yellow area indicates the original site of AT. The gray area represents the blocking area. A prolonged IACT approaching the TCL will falsely make the map exhibit a macro-reentrant pattern.

**Figure 4.** Shown is the schematic diagram of a “chaotic activation” pattern. In A, B and C, the upper panel represents the activation detour of the focal AT, with the yellow area indicating the true site of origin and the lower panel demonstrating the window of interest (WOI). The diagram represents three scenarios where the IACT exceeds the duration of the WOI. As shown in A, the true original activation is tagged as the earliest part in WOI, however, due to the prolonged IACT, the whole activation of the cycle would not be covered by the WOI. As a consequence, the later part of the index cycle would be annotated as the head of next cycle, giving an “early meets late” appearance. In panel B, the true original activation part is not tagged as the head of WOI, which makes a region in the midst of the conduction course to be tagged as the earliest part in the WOI. In panel C, the terminal end of the WOI does not cover the original activation of the focus, making the true origin to be tagged within the latest part of WOI. IACT indicates intra-atrial conduction time during AT.

**Figure 5.** Shown are the three dimensional activation maps of a focal atrial tachycardia (TCL=267ms, WOI=250ms, Case-12) located at the septal side of a previously ablated cavo-tricuspid isthmus. A: Before re-setting, the map shows a chaotic activation pattern not
readily differentiated. However, entrainment mapping raises the possibility of a focus located at the septum. B: Based on this assumption, the annotation was re-set as shown in the figure from inside the WOI to outside the WOI (yellow arrow). A focal AT that activated the atrium with a counterclockwise rotation was revealed. At the end of procedure, the conduction time from coronary sinus ostium to low lateral right atrium was shown to be 328ms. See Figure 4C for schematic diagram. IACT indicates intra-atrial conduction time during AT.

**Figure 6.** The flow-chart for the mapping of ATs encountered in the setting of prior extensive ablation. In the annotation resetting of chaotic pattern, the principle is to set the activation of the region that demonstrates good post pacing interval at the earliest part of the window of interest.
PPI = TCL + 25ms

PPI = TCL + 90ms

PPI = TCL + 180ms
Unidirectional conduction

Origin

Blocking area

IACT

WOI
PPI = TCL + 216 ms

PPI = TCL + 36 ms
3-D Activation Mapping in the Original Chamber

- Macro-reentry Pattern
- Chaotic Pattern A, B and C
- Focus

Entrainment and Substrate Analysis

- Reset the Annotation
  - True Macro-reentry
  - Pseudo Macro-reentry

True origin
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