Macroreentrant form of an adenosine 5′-triphosphate–sensitive atrial tachycardia arising from the vicinity of the atrioventricular node involving the tricuspid and mitral annuli as its reentrant circuit

Takeshi Ueyama, MD, PhD,* Akihiko Shimizu, MD, PhD,† Yasuhiro Yoshiga, MD, PhD,* Makoto Ono, MD, PhD,* Tomoko Fumimoto, MD,* Masafumi Yano, MD, PhD*

*From the *Division of Cardiology, Department of Medicine and Clinical Science, Yamaguchi University Graduate School of Medicine, Yamaguchi, Japan, and †Faculty of Health Sciences, Yamaguchi University Graduate School of Medicine, Yamaguchi, Japan.*

Introduction

Atrial tachycardias (ATs) with a unique pharmacologic response to verapamil or low-dose adenosine 5′-triphosphate (ATP) arising from the para-Hisian region have been reported, and their responsible mechanism is considered to be microreentry.[1] Recently, some investigators successfully demonstrated manifest entrainment in the right atrium (RA), indicating that the mechanism of these ATs could be RA macroreentry.[2,3] Here we describe a case with an ATP-sensitive AT that arose from the vicinity of the atrioventricular (AV) node and that demonstrated manifest entrainment from the right and left AV annuli including an earliest site in the RA.

Case report

A 72-year-old female patient was referred to our hospital for an electrophysiological study (EPS) and radiofrequency catheter ablation (RFCA) of a supraventricular tachycardia (SVT). The electrocardiogram (ECG) recorded previously at another hospital revealed a narrow QRS tachycardia with a heart rate of 154 beats per minute (bpm), which was terminated by 5 mg of verapamil. After written informed consent was obtained, an EPS was performed under deep sedation. All antiarrhythmic drugs were discontinued for ≥5 half-lives prior to the EPS. Three electrode catheters were placed in the high RA (HRA), His-bundle region (HBE), and right ventricular apex (RVA) via the femoral veins. A 7F 10-polar catheter was introduced into the coronary sinus (CS) via the right subclavian vein. There was no retrograde conduction during ventricular pacing. The SVT was easily and reproducibly induced by atrial extrastimuli or rapid atrial pacing. The earliest local atrial activation was recorded by the HBE catheter's distal electrodes during the SVT. Ventricular pacing during the SVT revealed ventriculoatrial (VA) dissociation. No VA linkage could be observed by differential atrial pacing and the SVT was reproducibly terminated without AV block by a low-dose (2-mg) bolus intravenous injection of ATP (Figure 1A). According to these findings, the SVT was diagnosed as an ATP-sensitive AT arising from near the His bundle. During the AT, electroanatomic mapping (Ensite NavX, St Jude Medical, St Paul, MN) using a 7F deflectable quadripolar catheter with a 4-mm distal electrode (Celsius, Biosense Webster, Diamond Bar, CA) was performed. The RA activation map revealed a centrifugal pattern and earliest atrial activation site on the RA anterior septum (RAAS) around the HBE. After obtaining atrial activation maps of the aortic noncoronary cusp (NCC), via a retrograde transaortic approach, and left atrium, through a transseptal puncture, the atrial activation recorded from the NCC was identical to that of the RAAS (Figure 1B). After constructing the activation maps, atrial pacing with a pacing cycle length of about 20 to 40 ms shorter than the tachycardia cycle length (TCL) was performed at various sites. Because of the discontinuous nature of the stable AT during entrainment mapping, isoproterenol (ISP; 0.8–1.0 μg/min) was given intravenously, and its TCL increased to approximately 360 ms without any obvious change in the activation sequence. As shown in Figure 2, when pacing was applied from the RAAS near the earliest activation site the RA, HRA, distal HBE, and CS were orthodromically captured (Figure 2B). Pacing from the anterior tricuspid annulus (TA), HBE, and CS captured orthodromically and the HRA captured antidromically (Figure 2A). Pacing from the septal mitral annulus (MA) obtained orthodromic capture of the HRA and HBE and antidromic capture of the CS

KEYWORDS Adenosine 5′-triphosphate; Atrial tachycardia; Catheter ablation; Entrainment; Macroreentry (Heart Rhythm Case Reports 2017;3:289–293)

Conflict of interest: The authors declare no conflict of interest associated with this article. **Address reprint requests and correspondence:** Dr Takeshi Ueyama, Division of Cardiology, Department of Clinical Science, Yamaguchi University Graduate School of Medicine, 1-1-1 Minami-Kogushi, Ube, 755-8505, Japan. E-mail address: tueyama@yamaguchi-u.ac.jp.

http://dx.doi.org/10.1016/j.hrcr.2017.03.001

KEY TEACHING POINTS

- Careful mapping including of the aortic cusp and left atrium should be required in adenosine 5′-triphosphate (ATP)–sensitive atrial tachycardias (ATs) arising from near the atrioventricular node.
- Although ATP-sensitive AT is "focal," the responsible mechanism may be "macro"-reentry among some ATP-sensitive ATs.
- Entrainment mapping via electroanatomic mapping is a useful tool for helping decide the strategy for catheter ablation in ATP-sensitive AT.

(Figure 2D). On the other hand, pacing from the NCC, HRA, HBE, and CS captured antidromically (Figure 2C). Postpacing intervals (PPIs) <20 ms longer than the TCL were also documented on the anterior TA, septal MA, and NCC. The PPI on the RAAS was identical to the pacing cycle length. RFCA applications (20–30 W, 50°C–55°C, 30 s) were applied from the anterior TA and septal MA where manifest entrainment was documented with a PPI ≤20ms longer than the TCL or the number of pacing stimuli needed to entrain (NNE) were ≤3 (Figures 3A, 3B). However, RFCA applications from the endocardial side (RF1 and RF2) were not effective. Finally, a single RFCA application (20 W, 50°C, 30 s) from the NCC (Figure 3C) terminated the AT 2.5 s after initiating the application. No junctional beats or PR prolongation were observed during the RFCA. AT could no longer be induced after the RFCA from the NCC. The patient was discharged without any medications and has been asymptomatic during a 12-month follow-up period.

Discussion

Iesaka et al[1] first described ATP-sensitive AT arising from focal sites within the triangle of Koch and speculated that their mechanism was focal reentry and that the AV node or its transitional tissues were included in part of the reentrant circuit. Subsequently, a similar pharmacologic response to adenosine or low-dose ATP has been reported among ATs originating from non–para-Hisian regions.[4–6] Thus, ATP-sensitive AT in which the earliest activation is recorded around the AV node should be considered to be among ATs arising from either the right or left AV annuli. In the current case, the AT was easily induced by burst atrial pacing or extrastimuli and was sensitive to verapamil and low-dose ATP, suggesting that its mechanism was either reentry or

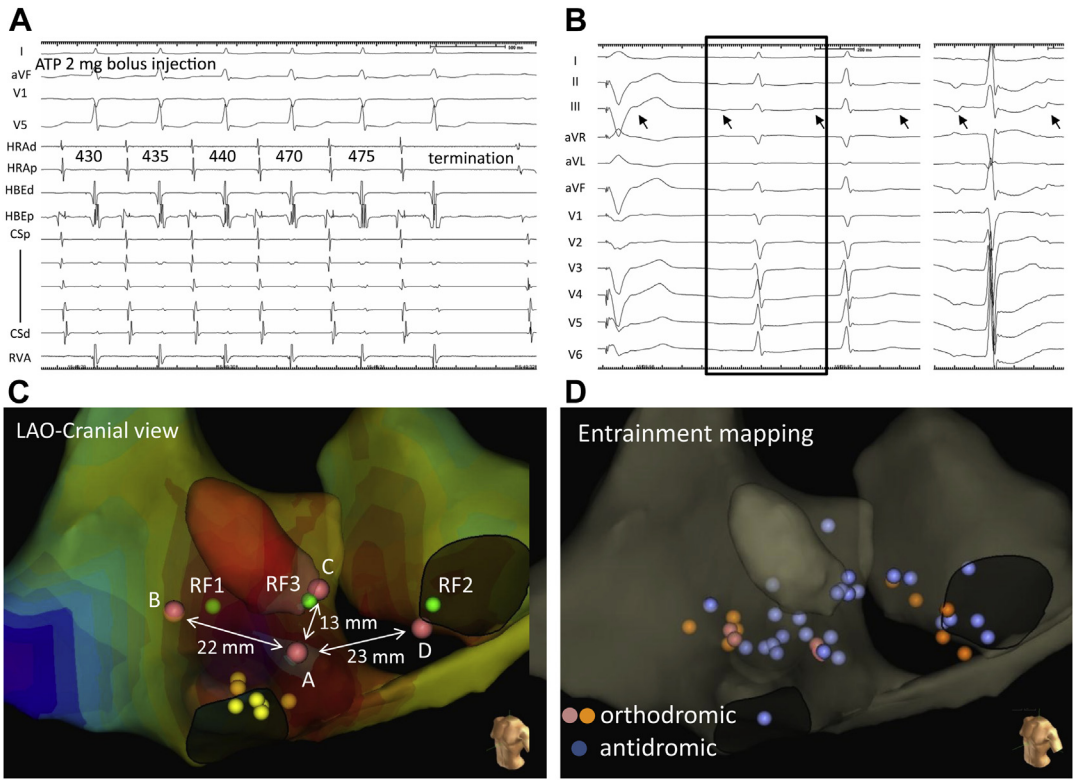

Figure 1 **A:** Intracardiac recording of the termination of the tachycardia without atrioventricular block after a bolus injection of adenosine 5′-triphosphate. **B:** P-wave morphologies during the tachycardia. The P wave (arrow) just after cessation of ventricular pacing was negative in the inferior and $V_{3–6}$ leads, biphasic (negative/positive) in I and $V_{1–2}$, and positive in aVL. **C:** Activation maps during the tachycardia (left anterior oblique-cranial view). The pink tags (sites A, B, C, and D) show the pacing sites during the tachycardia. The yellow tags show the points where the His potentials were recorded. The green tags (RF1–RF3) show the radiofrequency catheter ablation sites. **D:** Entrainment mapping during the tachycardia. The pink and golden yellow tags show the pacing sites where orthodromic capture was observed. The blue tags show the sites where antidromic capture was observed. CS = coronary sinus; HBE = His-bundle electrode; HRA = high right atrium; RF = radiofrequency; RVA = right ventricular apex.

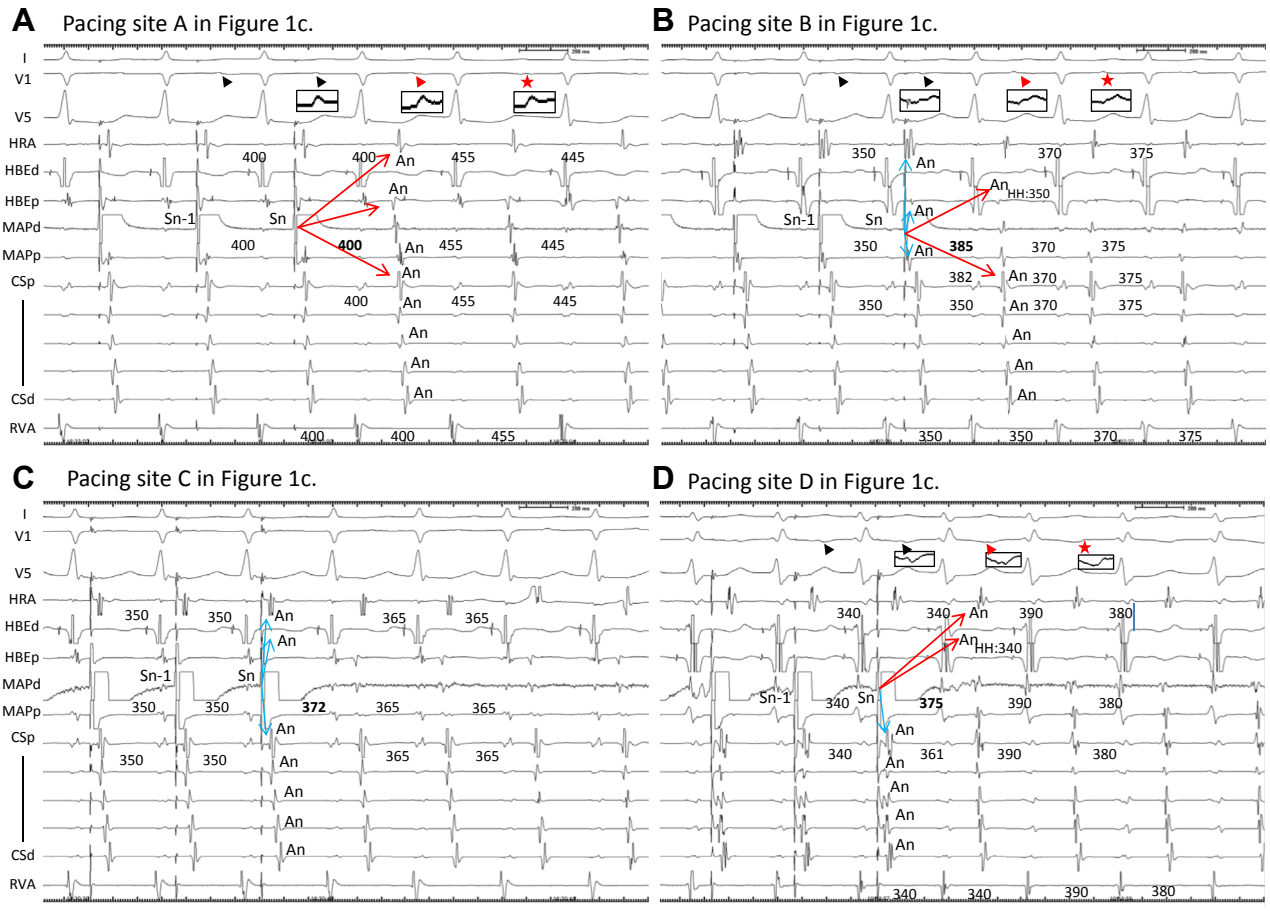

Figure 2 Intracardiac recordings during entrainment pacing during the tachycardia, with pacing from **A:** the right atrial anterior septum, **B:** anterior tricuspid annulus, **C:** noncoronary cusp, and **D:** mitral annulus. Each pacing site is shown in Figure 1C. The red arrows show the orthodromic atrial activation and the blue arrows show the antidromic atrial activation. The P-wave morphology of the last paced beat (red arrowhead) is similar to the tachycardia (red star). Magnified P wave shown in the square box. An = atrial beat paced by Sn pacing; MAP = mapping catheter, S = stimulation. The other abbreviations are as in Figure 1.

triggered activity.[6,7] The possible mechanism of this AT was reentry because of the successful demonstration of manifest entrainment during the AT; however, we were unable to show any progressive fusion due to tiny P waves (Figure 1B) during the AT. The location of the entrainment mapping revealed sites where the PPI was ≤20 ms longer than the TCL and distributed broadly from the anterior TA to the septal MA. Although the 3-dimensional map exhibited a focal activation pattern, this AT satisfied the definition of "macro"-reentry because the distance from the superior TA to the MA was ≥2 cm (Figure 1C), indicating its critical slow conduction area might have involved the region along the left-to-right atrioventricular annuli.[8] To validate this idea, we estimated the NNE.[9] According to the report, an NNE >3 is highly predictive of pacing outside the tachycardia circuit.[9] The NNEs on the anterior TA and septal MA, where manifest entrainment was observed, were ≤3, suggesting involvement of a reentrant circuit and its entrance near this area (Figure 3A, 3B). Wit et al[10,11] and McGuire et al[12,13] reported the existence of periannular cells, which are histologically similar to the atrial myocardium and have nodal-like electrophysiological properties and which respond to adenosine and have a lack of connexin 43 expression. Liu et al[14] reported anatomic insights into an AT arising adjacent to the NCC, which originated from paraseptal atrial myocardium, lying adjacent to the NCC on the epicardial side and interspersed with fibrofatty tissue on the endocardial side. These findings support the idea that the paraseptal endocardial region might provide a substrate and entrance for the reentry. Recently, Yamabe et al[2] and Okumura et al[3] clearly demonstrated manifest entrainment and successful elimination of ATs by radiofrequency applications between the earliest activation site and entrainment pacing site on the endocardial side of the RA, indicating the responsible mechanism of these ATs would be reentry with a slow conduction zone. Hence, they speculated the presence of a slow conduction zone near the area of the TA. In the present case, we demonstrated manifest entrainment with a long interval from the TA to the MA, including the earliest site of the RA, and that was the reason we could not abolish the AT from the endocardial side, probably because of multiple entrances on the endocardial side in the present AT (Figure 3D). To the best of our knowledge, this is the first observation of these findings, and it would be difficult to apply Yamabe's and Okumura's ablative strategy for such cases, and vice versa, these findings may account for the

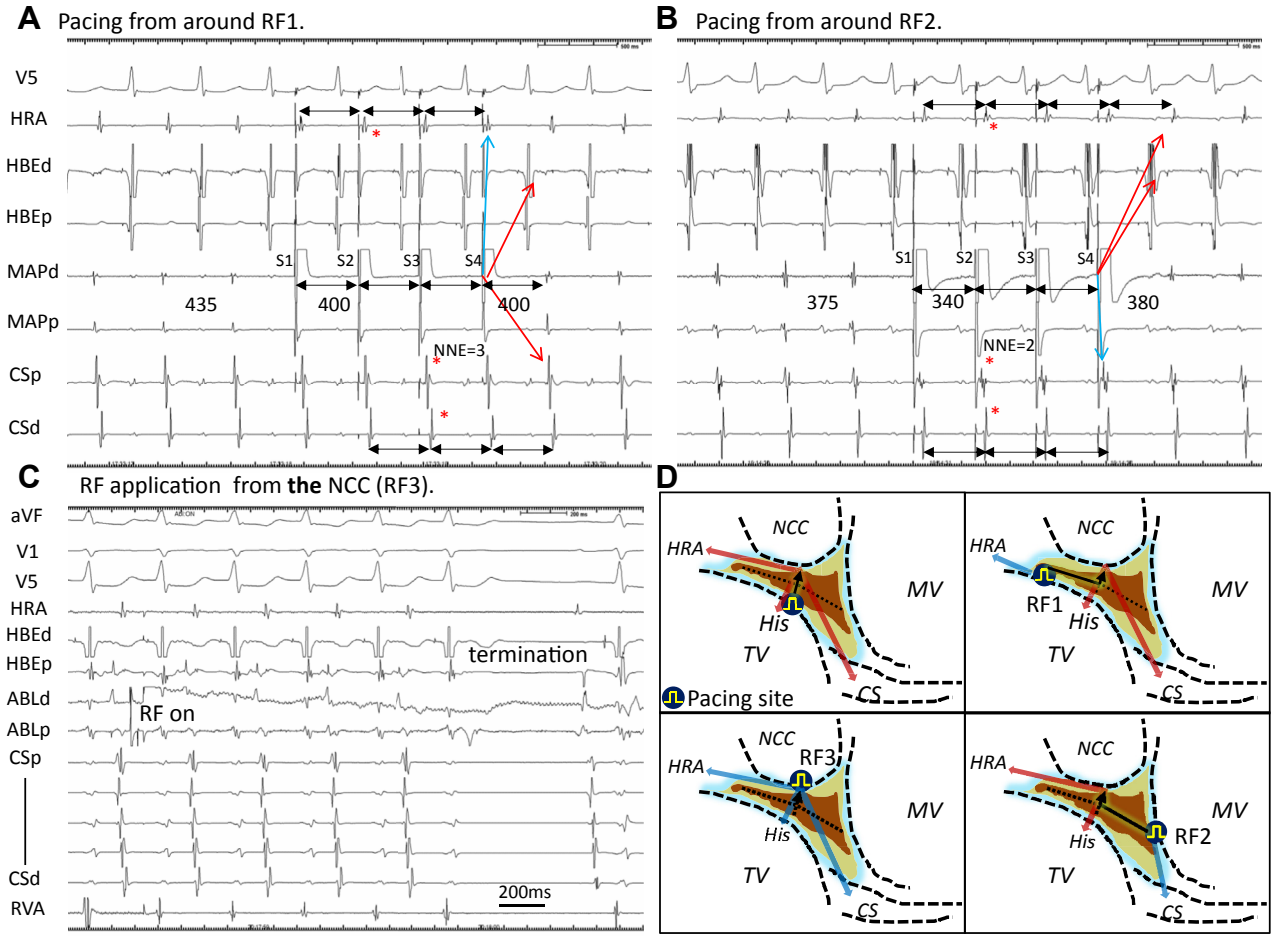

Figure 3 **A, B:** Entrainment pacing, **C:** successful catheter ablation, and **D:** schematic presentation. **A:** Entrainment pacing and number of pacing stimuli needed to entrain (NNE) for measurements at a site on the anterior tricuspid annulus (TA) near site RF1 (shown in the upper right panel of part D). The cycle length at the HRA and CS accelerated to the pacing cycle length (red asterisks) and the NNE count was 3. **B:** Entrainment pacing and the NNE measurement number at a septal mitral annulus (MA) site around site RF2 (shown in the lower right panel of Figure 3D). The cycle length at the HRA and CS accelerated to the pacing cycle length (red asterisks) and the NNE count was 2. **C:** Intracardiac recordings of the successful catheter ablation from the NCC. Ablation at the RF3 site (shown in the lower left panel of part D) terminated the tachycardia. **D:** Schematic presentation of entrainment pacing during the tachycardia. The abbreviations are as in the previous figures.

effectiveness of the radiofrequency application from the NCC in this ATP-sensitive AT arising from near the AV node.[15]

Conclusion

The mechanism of ATP-sensitive AT that we experienced could have been macroreentry, and the reentrant circuit might have involved the bilateral AV annuli. ATs with multiple entrances into the reentrant circuit are difficult to ablate from the endocardial side. When we are able to obtain manifest entrainment from both sides of the AV annulus in a case of a para-Hisian AT such as this case, ablation from the NCC may be considered a primary strategy to achieve a successful RFCA with avoidance of any potential risk of AV conduction block.

Acknowledgments

We thank Mr John Martin for his linguistic assistance with this article.

References

1. Iesaka Y, Takahashi A, Goya M, Soejima Y, Okamoto Y, Fujiwara H, Aonuma K, Nogami A, Hiroe M, Marumo F, Hiraoka M. Adenosine-sensitive atrial reentrant tachycardia originating from the atrioventricular nodal transitional area. J Cardiovasc Electrophysiol 1997;8:854–864.
2. Yamabe H, Okumura K, Morihisa K, Koyama J, Kanazawa H, Hoshiyama T, Ogawa H. Demonstration of anatomical reentrant tachycardia circuit in verapamil-sensitive atrial tachycardia originating from the vicinity of the atrioventricular node. Heart Rhythm 2012;9:1475–1483.
3. Okumura K, Sasaki S, Kimura M, Horiuchi D, Sasaki K, Itoh T, Tomita H, Ishida Y, Kinjo T. Usefulness of combined CARTO electroanatomical mapping and manifest entrainment in ablating adenosine triphosphate-sensitive atrial tachycardia originating from the atrioventricular nnode vicinity. J Arrhythm 2016;32:133–140.
4. Yamabe H, Tanaka Y, Okumura K, Morikami Y, Kimura Y, Hokamura Y, Ogawa H. Electrophisiologic characteristics of verapamil-sensitive atrial tachycardia originating from the atrioventricular annulus. Am J Cardiol 2005;95:1425–1430.
5. Matsuoka K, Kasai A, Fujii E, Omichi C, Okubo S, Teramura S, Uchida F, Makano T. Electrophysiologial features of atrial tachycardia arising from the atrioventricular annulus. Pacing Clin Electrophysiol 2002;25(pt. 1):440–445.
6. Iwai S, Markowitz SM, Stein KM, Mittal S, Slotwiner DJ, Das MK, Cohen JD, Hao SC, Lerman BB. Response to adenosine differentiates focal from macroreentrant atrial tachycardia: validation using three-dimensional electroanatomc mapping. Circulation 2002;106:2793–2799.

7. Chen SA, Chiang CE, Yang CJ, Cheng CC, Wu TJ, Wang SP, Chiang BN, Chang MS. Sustained atrial tachycardia in adult patients: Electrophysiological characteristics, pharmacologic response, possible mechanisms, and effects of radiofrequency ablation. Circulation 1994;90:1262–1278.
8. Saoudi N, Cosío F, Waldo A, Chen SA, Iesaka Y, Lesh M, Saksena S, Salemo J, Scholes W. Working Group of Arrhythmias of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. A classification of atrial flutter and regular tachycardia according to electrophysiological mechanisms and anatomical bases. A statement from a Joint Expert Group from the Working Group of Arrhythmias of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Eur Heart J 2001; 22:1162–1182.
9. Maruyama M, Yamamoto T, Abe J, Yodogawa K, Seino Y, Atarashi H, Shimizu W. Number needed to entrain. A new criteria for entrainment mapping in patients with intra-atrial reentrant tachycardia. Circ Arrhythm Electrophysiol 2014;7:490–496.
10. Wit AL, Fenoglio JJ Jr, Wagner BM, Bassett AL. Electrophysiological properties of cardiac muscle in the anterior mitral valve leaflet and the adjacent atrium in the dog. Possible implication for the genesis of atrial dysrhythmias. Circ Res 1973; 32:731–745.
11. Wit AL, Fenoglio JJ Jr, Hordof AJ, Reemtsma K. Ultrastructure and transmembrane potentials of cardiac muscle in the human anterior mitral valve leaflet. Circulation 1979;59:1284–1292.
12. McGuire MA, de Bakker JM, Vermeulen JT, Opthof T, Becker AE, Janse MJ. Origin and significance of double potentials near the atrioventricular node. Correlation of extracellular potentials, intracellular potentials, and histology. Circulation 1994;89:2351–2360.
13. McGuire MA, de Bakker JM, Vermeulen JT, Moorman AF, Loh P, Thibault B, Vermeulen JL, Becker AE, Janse MJ. Atrioventricular junctional tissue. Discrepancy between histological and electrophysiological characteristics. Circulation 1996;94:571–577.
14. Liu X, Dong J, Ho SY, Shah A, Long D, Yu R, Tang R, Hocini M, Haissaguerre M, Ma C. Atrial tachycardia arising adjacent to noncoronary aortic sinus. J Am Coll Cardiol 2010;56:796–804.
15. Ouyang F, Ma J, Ho SY, et al. Focal atrial tachycardia originating from the noncoronary aortic sinus: electrophysiological characteristics and catheter ablation. J Am Coll Cardiol 2006;48:122–131.