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Role of the Vein of Marshall in Patients with Atrial Fibrillation

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Introduction

Myocardial fibers and nerves adjacent to the vein of Marshall (VOM), have been implicated as a source of ectopic beats initiating paroxysmal atrial fibrillation (AF)¹, as a connection pathway between the left atrium (LA) and left pulmonary veins (PVs)^{2,3}, and as a source of arrhythmogenic autonomic innervation.^{4,5} This various complex nature of the VOM can constitute the genesis of AF.

Philippe Coumel put forward the concept of Coumel's triangle of arrhythmogenesis. The concept is composed of three main ingredients required for the generation of a clinical arrhythmia. The arrhythmogenic substrate, the trigger factor, and the modulation factors are proposed as the three main ingredients, respectively. Of these, the modulation factors are commonly the autonomic nerves system.⁶

Based on the viewpoint of the triangle of arrhythmogenesis, herein I describe the role of the VOM in patients with AF.

The Arrhythmogenic Substrate

It is well-known that PVs play a critical role in substrate

of AF. And left atrial linear lesions (mitral isthmus line, roof line) are effective in substrate modification for AF.⁷

The VOM location coincides with the areas usually ablated during PV isolation. It has recently been reported that VOM ethanol infusion creates a low voltage area in the LA adjacent to the VOM and facilitates left PV isolation for AF ablation.⁸

Figure 1 shows the location of the VOM and PV potentials recorded from the left PVs during ethanol infusion into the VOM. Following the ethanol infusion, all left inferior PV potentials disappeared. This illustrates that VOM ethanol infusion, therefore, could contribute to a reduction in radiofrequency energy application for isolation of the left PVs.

The reduction in radiofrequency energy application by VOM ethanol infusion might also help relief the esophageal damage caused by radiofrequency energy applications for isolation of the left PVs. This is because the esophagus is most commonly close to the left PVs, the esophagus could be damaged seriously by radiofrequency energy applications for isolation of the left PVs.⁹

Radiofrequency catheter ablation has been the standard tool for mitral isthmus (MI) ablation, but it is usually difficult to achieve bidirectional MI block. Báez-

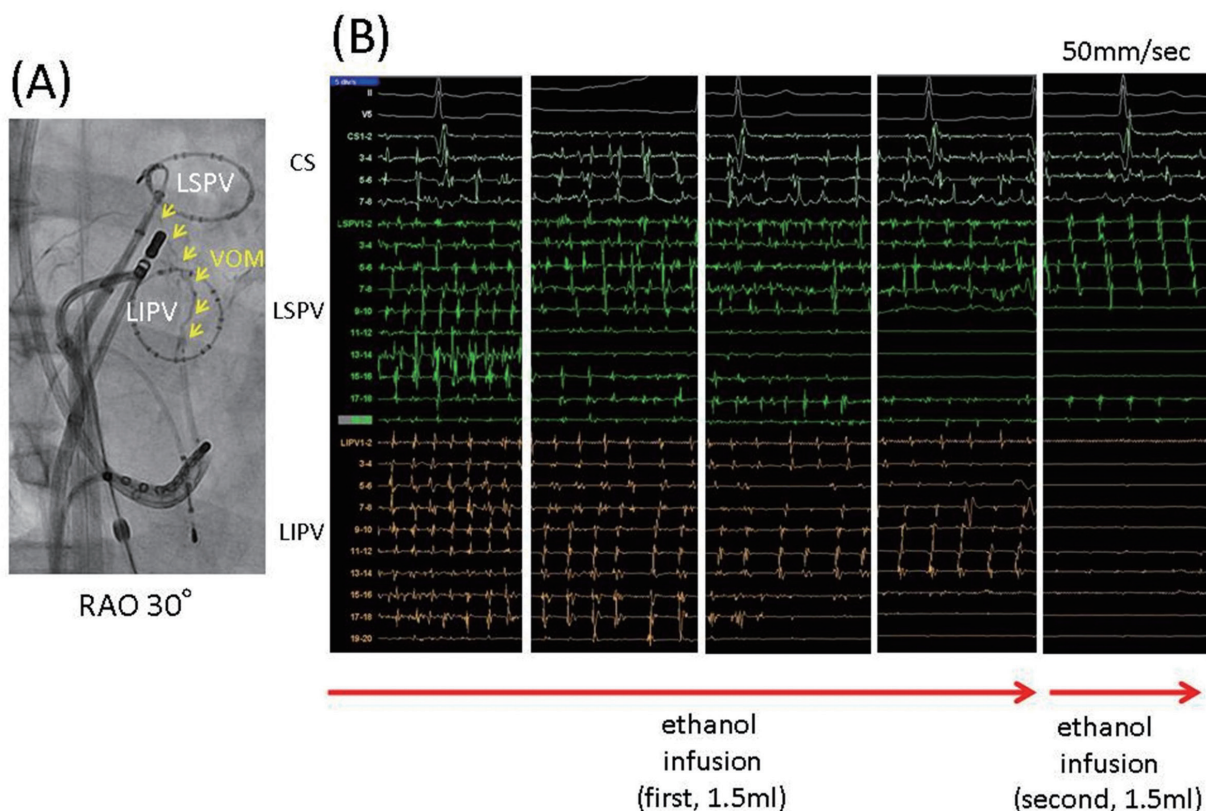


Figure 1. Retrograde subselective venograms of the VOM (A): Arrows indicate the VOM extending upward near the anterior site of the LSPV. Intracardiac electrogram during ethanol infusion for VOM (B): Ethanol infusion leads to complete elimination of LIPV signals. VOM= vein of Marshall; LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein.

Escudero et al. reported the use of ethanol infusion in the VOM with radiofrequency catheter ablation facilitates achievement of bidirectional MI block.¹⁰ That the VOM is located in the epicardial aspect of the MI is thought to be the main cause of the facilitation of bidirectional MI block. Figure 2 shows the location of the VOM and voltage maps before and after VOM ethanol infusion.

In this case, VOM ethanol infusion creates a low-voltage area along the MI. As a result, bidirectional MI block was achieved solely by VOM ethanol infusion.

The Trigger Factor

The VOM has focal automatic activity that could be revealed or accelerated by isoproterenol, and it may contribute to the development of AF.^{1,11} We reported that VOM ethanol infusion eliminated frequent supraventricular extrasystoles (SVEs) that had been the probable trigger for his paroxysmal AF.¹² A 46-year-old man presented with a 5-year symptomatic drug refractory paroxysmal AF. The 24-hour Holter monitoring had revealed frequent SVEs (10,402 beats/day) and paroxysmal AF preceded by an SVE. For this patient, the identification of the

VOM with a retrograde coronary sinus venogram (Figure 3A) and a subsequent VOM ethanol infusion were performed. Immediately after 4ml of >99.5% ethanol infusion into the VOM (Figure 3B), frequent SVEs that had observed since the patient entered the electrophysiology laboratory disappeared (Figure 4). The voltage maps constructed with 3-dimensional mapping system (CARTO 3, Biosense Webster, Diamond Bar, CA) showed that VOM ethanol infusion created a low-voltage area along course of VOM (Figure 3C and 3D). We could hypothesize different kinds of potential mechanisms for the elimination of non-PV foci in this case. VOM ethanol infusion might directly abolish the non-PV foci originating from the VOM or the tissue near the VOM, might injure the arrhythmogenic autonomic innervation, might disconnect non-PV foci to the LA or the left PV, and might affect some of these complex functionalities simultaneously.

The Autonomic Nervous System

The intrinsic cardiac autonomic nervous system (ICN) plays a significant role in the initiation and maintenance of AF.¹³ ICN contains clusters of autonomic ganglia located in epicardial fat pads and in the ligament of Marshall (LOM).

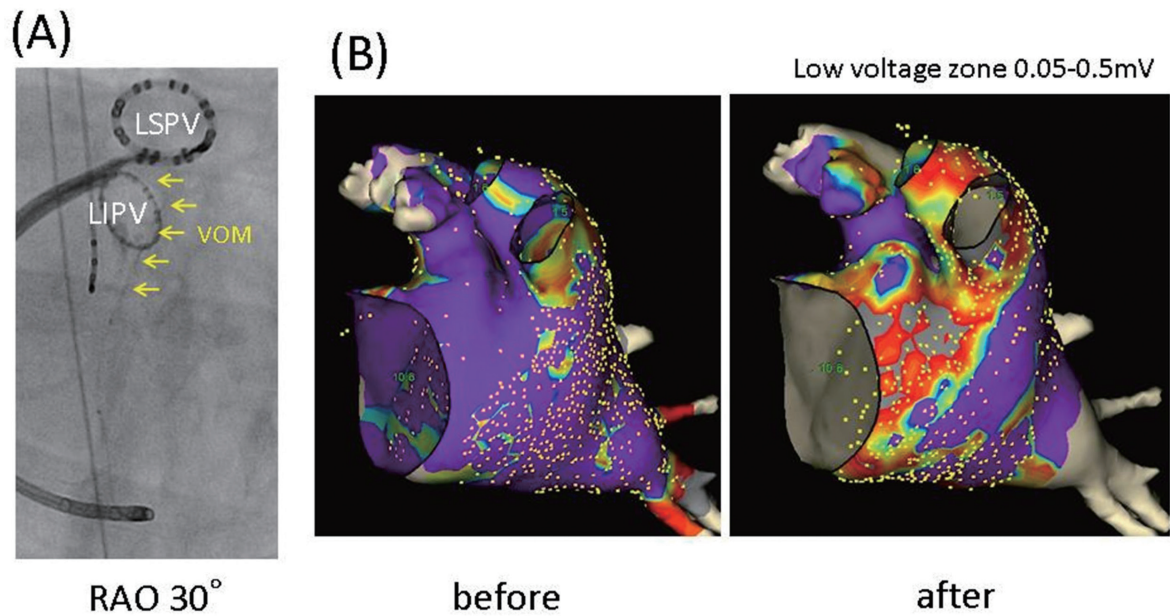


Figure 2. Retrograde subselective venograms of the VOM (A): Arrows indicate the VOM extending upward near the carina of the LIPV.

Left atrial 3-dimensional voltage maps constructed before and after VOM ethanol infusion (B): A low-voltage area emerged along the course of the VOM after VOM ethanol infusion.

VOM= vein of Marshall; LIPV = left pulmonary vein.

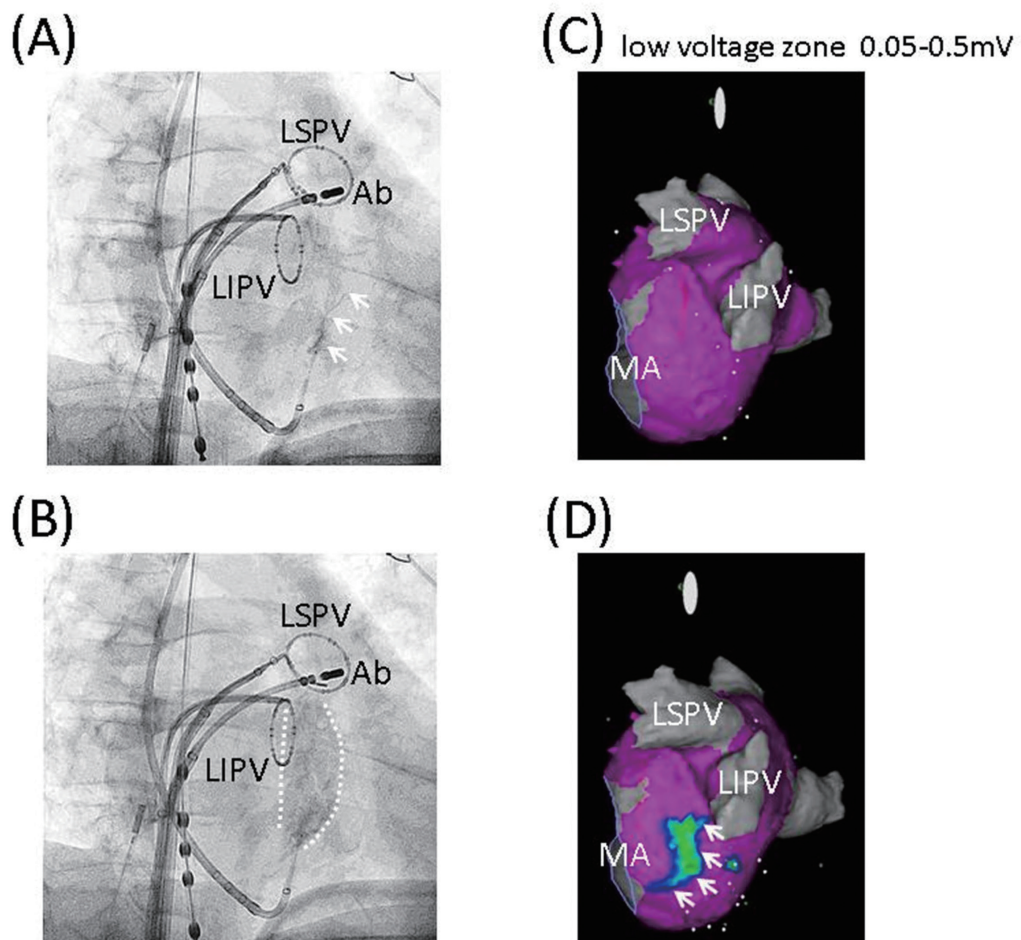


Figure 3. Retrograde subselective venograms of the VOM. (A): Arrows indicate the threadlike VOM extending upward near the anterior site of the LIPV. (B): Area surrounded with dashed lines indicates the area stained by the contrast medium injection following VOM ethanol infusion. Left atrial 3-dimensional voltage maps constructed before (C) and after (D) VOM ethanol infusion. Arrows indicate a low-voltage area emerged along the course of the VOM after VOM ethanol infusion. VOM= vein of Marshall; LIPV = left inferior pulmonary vein.

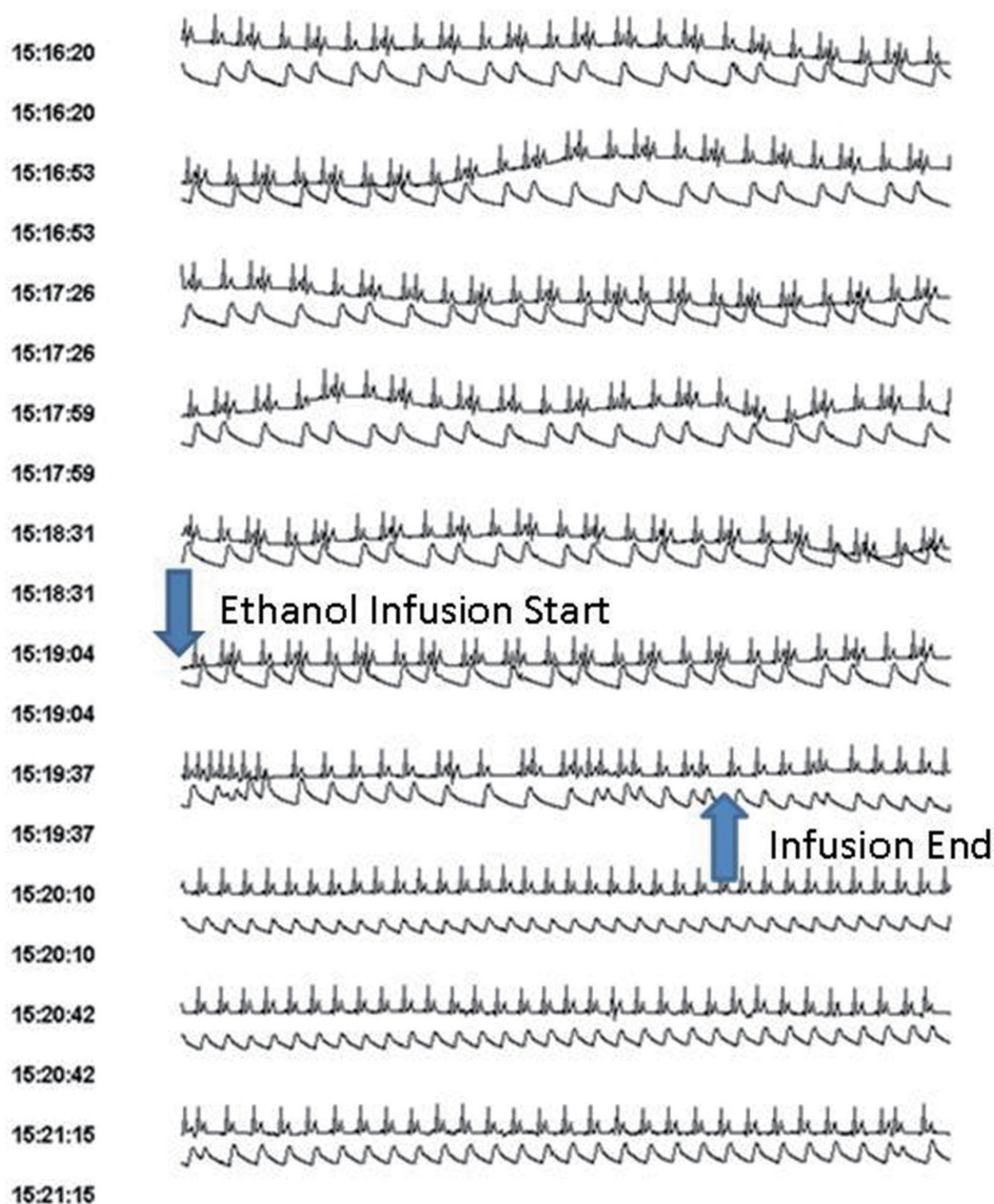


Figure 4. Electrocardiographic tracings recorded before, during, and after the VOM ethanol infusion. A downward-pointing arrow indicates the timing of the initiation of the VOM ethanol infusion, and an upward-pointing arrow indicates the timing of the completion of the infusion. VOM= vein of Marshall.

We reported the use of the VOM as a vascular route for the ablation of ICN neurons.⁵ In this study, a multipolar catheter was introduced in the VOM and used for high-frequency stimulation (HFS). Atrioventricular (AV) nodal conduction slowing (asystole >2 s or R-R interval prolongation >50%) and AF inducibility were assessed before and after VOM ethanol infusion. Up to 4 1-ml infusions of 98% ethanol were delivered via an angioplasty balloon in the VOM. Burst HFS was performed in 32 patients undergoing de novo AF ablation (Group 1) and 40 patients undergoing repeat ablation (Group 2).

Parasympathetic responses were found in all Group 1 patients and in 75% of Group 2 patients. After VOM ethanol infusion, parasympathetic responses were abolished in all patients (both groups).

An important implication of this study is that the VOM can be used as a vascular route to deliver therapies targeting the ICN.

Figure 5 shows vagal response before the ethanol infusion of the VOM. After the ethanol infusion, this vagal response disappeared.

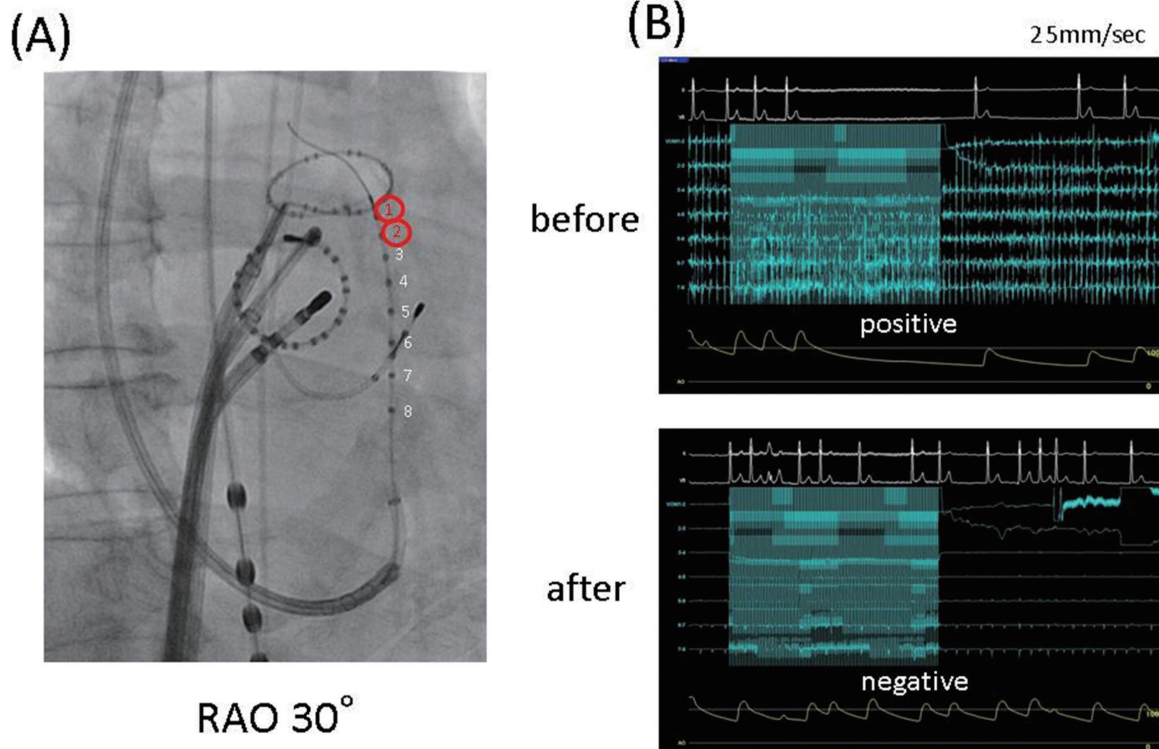


Figure 5. (A) shows the 3Fr monorail type octapolar electrode inserted in the VOM. (B) shows vagal response before and after VOM ethanol infusion. Positive vagal response turned into negative after ethanol infusion.

Conclusion

The VOM or the tissues adjacent to the VOM relate closely to the arrhythmogenic substrate, the trigger factor as well as the modulation factor for AF occurrence. At least, the VOM mediates the triangle of arrhythmogenesis in patients with AF and VOM chemical ablation (e.g. ethanol infusion) could be one of the promising therapeutic options for AF in the future.

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EP Image: Left Atrial Pouch

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Welcome remark:

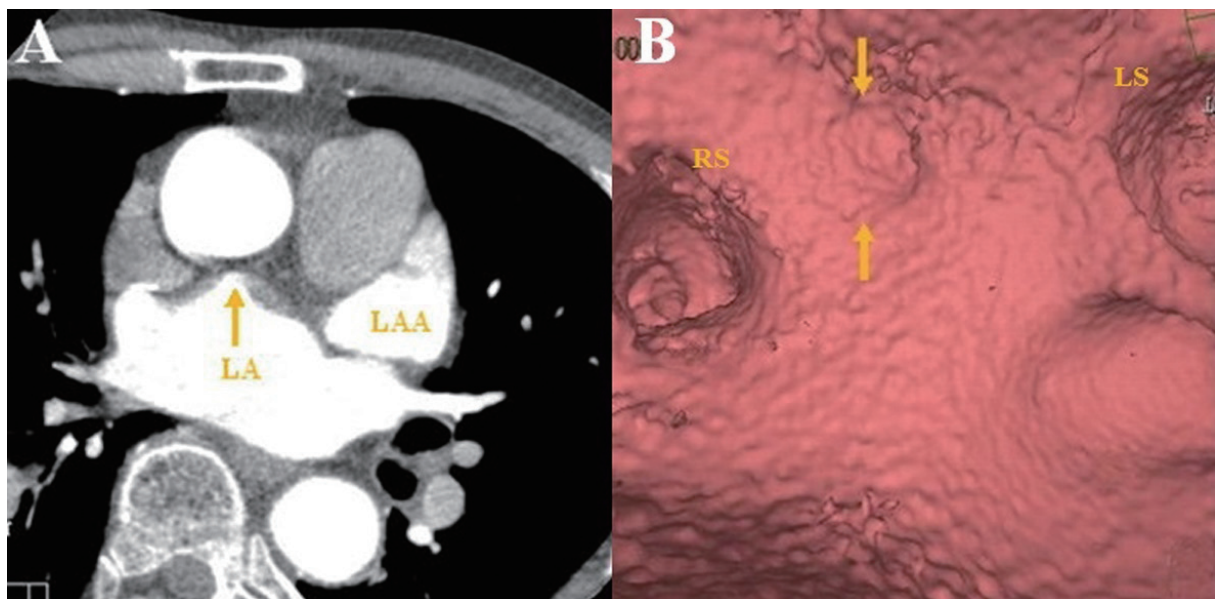
We are pleased to announce that the APHRS News will open a new column entitled “Images of Cardiac Arrhythmias”. Images play an important role in the diagnosis and management of cardiac arrhythmias. This feature is intended to capture the sense of visual discovery and variety that clinicians have experienced. The editorial board actively encourages our colleagues to submit the original and intriguing images with direct relevance to arrhythmic patient care. And we accept submissions from all areas of cardiovascular imaging including echocardiography, magnetic resonance, computed tomography, nuclear and invasive imaging. This platform is suitable for you to share the interesting experience and disseminate the essential knowledge. We look forward to your participation.

A 66 year-old male was admitted due to sudden onset of right limb weakness and numbness. Computed tomography of brain showed acute infarction of left thalamus. 12 lead ECG showed atrial fibrillation (AF) which was converted to sinus rhythm 2 days later. Aspirin (100mg), dipyridamole (75mg) and cordarone (200mg) were prescribed. A 64-slice multidetector computed tomography was performed and showed a pouch of LA roof (arrows in figure). However, no LA appendage thrombus could be delineated.

LA pouch is not an uncommon finding in patients with AF or ischemic stroke. However, the asso-

ciation between the presence of LA pouch and stroke is not clear. Previous reports had suggested that the pouch could be the potential source of thrombus in patients with ischemic stroke. In contrast, several studies showed no significant difference regarding the incidence of pouch between the stroke patients and control.

The identification of LA pouch is also important during catheter ablation of AF. The inadvertent catheter manipulation could be avoided and the ablation lines could be modified according to the location of pouches.



A left atrial roof pouch between right superior (RS) and left superior (LS) pulmonary veins. A. Axial view of 64-slice multidetector computed tomography showed a roof pouch (arrow) and no thrombus could be detected within appendage (LAA). B. Virtual endoscopic view showed the pouch (between arrows) of LA roof.

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ECG Quiz

The model commentary will be provided in the next issue No.15

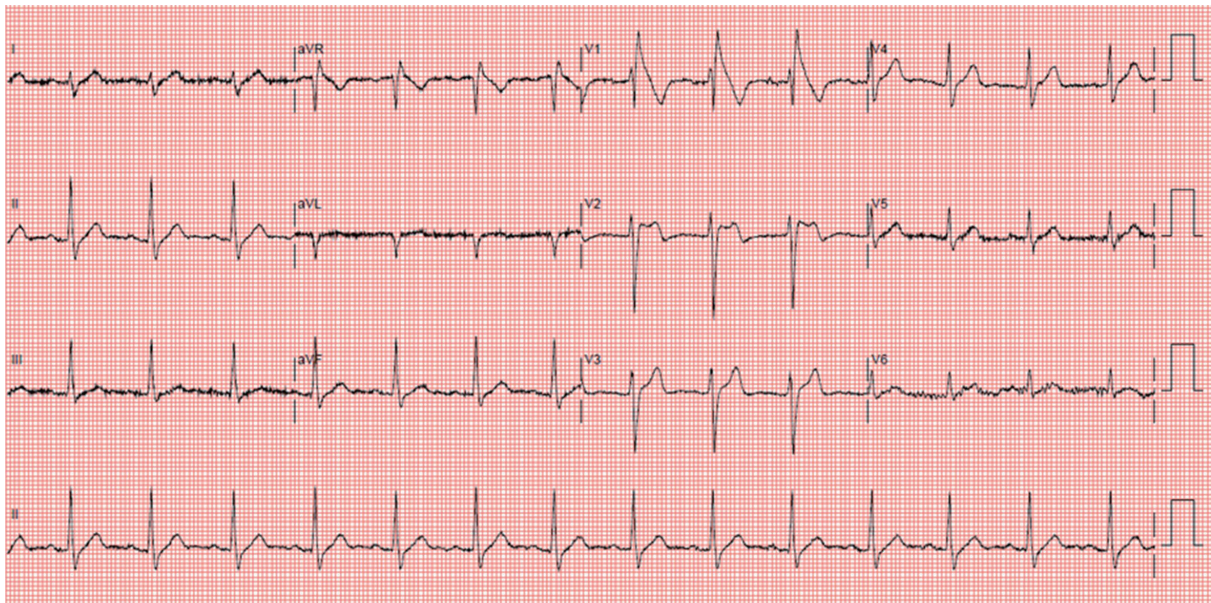
**Paul C Y Lim, Eric T S Lim, Kah Leng Ho, Boon Yew Tan,
Chi Keong Ching, Wee Siong Teo**

National Heart Centre Singapore

Case:

A 23 year old male presented with a febrile upper respiratory tract infection and near syncope with no chest pain. The following is an electrocardiogram performed at the emergency department while he is pyrexemic with a temperature of 38.3 degrees celcius.

Figure: ECG performed at 28/10/2010 when his temperature was 38.3 degrees celcius.



Question:

What is the diagnosis?

1. Anterior ST segment elevation myocardial infarction
2. Pulmonary embolism
3. Pericarditis
4. Type 1 Brugada pattern ECG – Fever sensitive Brugada

Arrhythmia Center, Yonsei University College of Medicine, Seoul, Korea

**Boyoung Joung, Jin-Kyu Park, Nam-kyun Kim, Jae-Sun Uhm,
Hui-Nam Pak, Moon-Hyoung Lee**

Arrhythmia Center in Severance Cardiovascular Hospital provides the highest level of treatments and procedures while leading arrhythmia treatments in Korea (Figure 1 and 2). Looking through its history, the center first performed His bundle recording in 1973; and in 1986, it not only started electrophysiologic study but also conducted catheter ablation using direct current electricity on bypass tract with WPW syndrome for the first time in Korea by Dr Sungsoon Kim. Since 1990, radiofrequency catheter ablation has been fully implemented where it still makes a great deal of contributions to the arrhythmia treatments. Currently, six EP faculties (Moon-Hyoung Lee, Hui-Nam Pak, Boyoung Joung, Jae-Sun Uhm, Nam-kyun Kim and Jin-Kyu Park) and 4 EP fellows are working in the arrhythmia center (Figure 3).

We have two and half electrophysiology rooms, a pacemaker clinic and a heart station. Magnetecs, remote catheter controlling system is equipped in one of the electrophysiology rooms (Figure 4). For specific procedures such as lead extractions and LAA occlude, we are also using a hybrid operation room. In recent years, over 1,000 radiofrequency catheter ablations including 300 atrial fibrillation ablations are being offered to maintain its highest level in Korea. For the patients with congenital heart disease and



Figure 1. Main Building, Severance Hospital



Figure 2. Severance Cardiovascular Hospital



Figure 3. Electrophysiology team in Severance Arrhythmia Center



heart failure, we are providing multidisciplinary therapy with pediatrician and heart failure physician.

In research, we are publishing clinical papers about ablation, imaging tools for electrophysiology, anticoagulation and congenital heart disease. For basic research, we have two basic research laboratories dedicated for electrophysiology, and 6 researchers (including 2 PhDs) are working together. One laboratory is developing computer simulation model for the treatment of arrhythmia (Figure 5). The other laboratory is developing animal model with arrhythmia, and is equipped with basic research tools including dual optical mapping (Figure 6), patch clamp, telemetry system for rat and mouse, and confocal microscope. Also, a variety of researches including national research projects are being conducted in order to develop new medical devices as well as treatment procedures.

A variety of training programs are currently being offered for doctors, nurses, radiologic technicians and medical equipment personnel; furthermore, 'Electrophysiology Review Course', a special lecture on arrhythmia, is being held biannually based on vast experiences accumulated by the center. Concurrently, the center rigorously maintains close collaboration with world-renowned scholars through regularly-held symposiums.

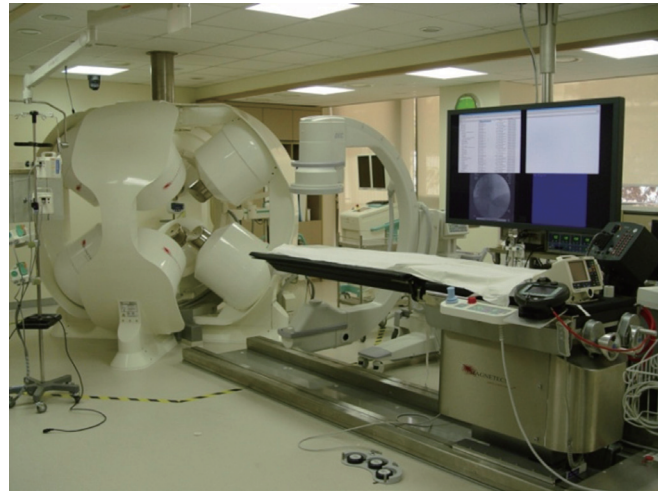


Figure 4. Remote catheter controlling system in EP room 2

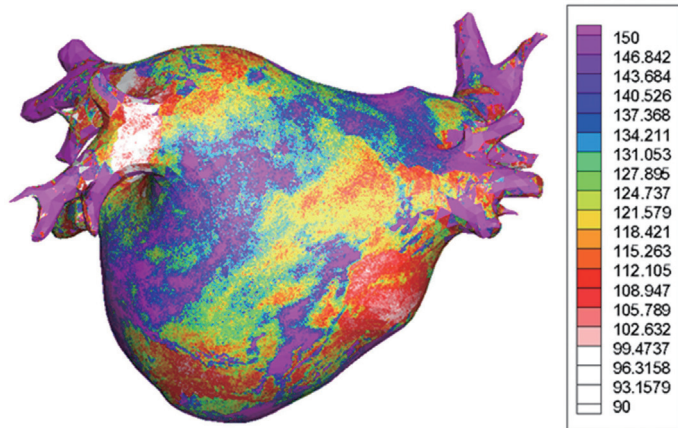


Figure 5. CFAE mapping by Three-dimensional computer simulation

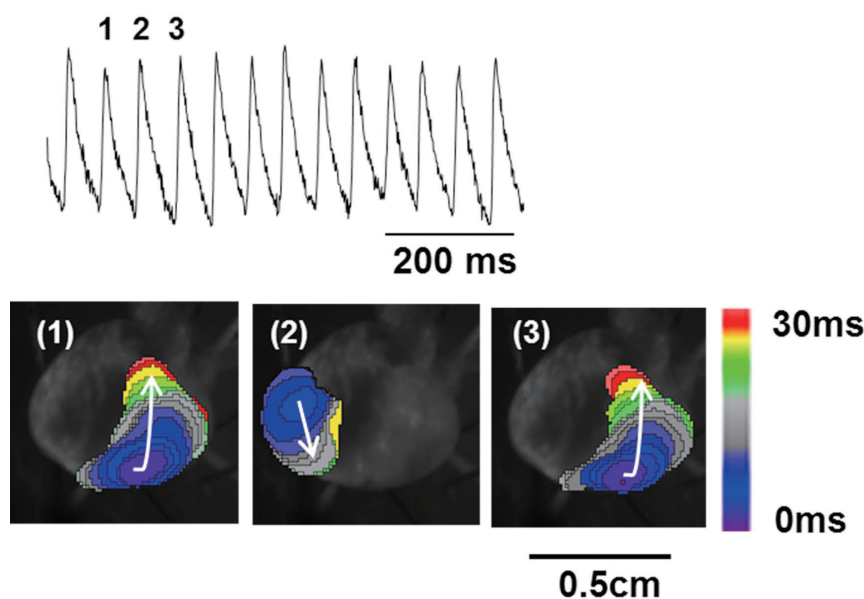


Figure 6. Optical mapping of ventricular tachycardia induced in Htr3 knock-out mouse

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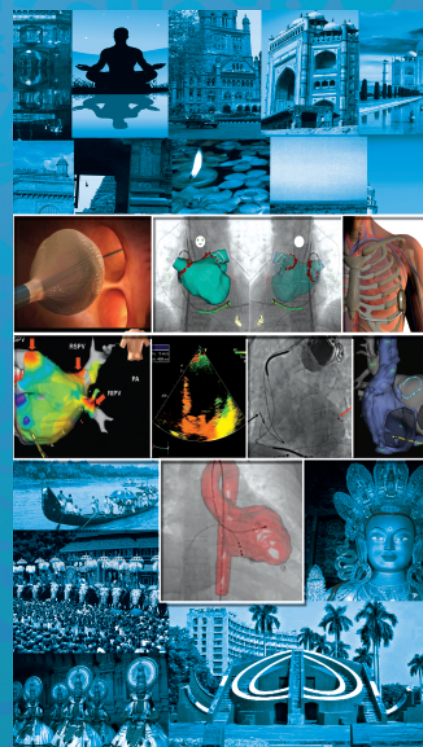
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Notification of Acceptance :	August 01, 2014
Deadline for Early-bird Registration :	July 31, 2014

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ECG Commentary Related to the Quiz in the No. 13 Issue

Yoshinori Kobayashi MD

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Tokai University Hachioji-hospital, Tokyo, JAPAN

Answer:

- 1) Subepicardial Kent bundle (posteroseptal)
- 2) Diverticulum (diverticula) of coronary sinus (CS) or mid-cardiac vein (MCV)

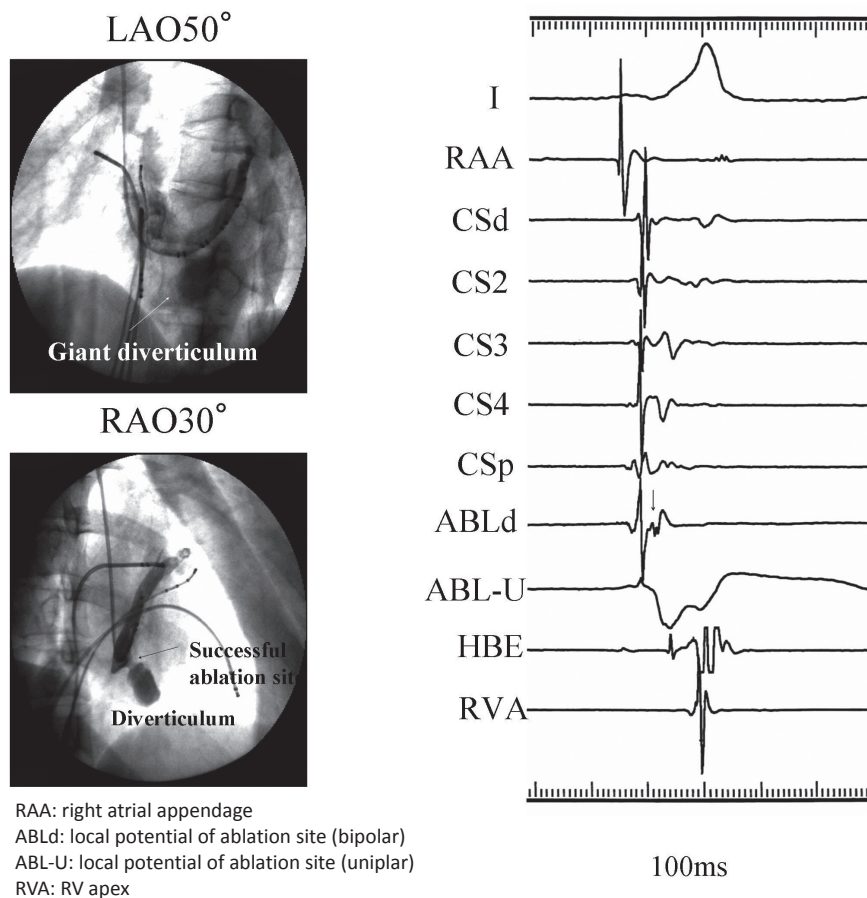


Figure 2. coronary sinus angiography and the local potential of successful ablation site

ECG commentary related to the quiz

The ECG before ablation shows characteristic features of WPW syndrome with obvious ventricular pre-excitation (delta wave). According to the diagnostic algorithm for the localization of Kent bundle developed by correlating a resting ECG with successful ablation site, a negative delta wave in lead II is shown to identify the subepicardial posteroseptal accessory pathway with very high accuracy. In the ablation of subepicardial Kent bundle, a radiofrequency (RF) delivery applied at the earliest activation site from endocardium usually results in the failure, and the RF application from inside of the CS are needed for the successful

result. In this patient, CS angiography revealed a presence of a giant CS diverticulum (Figure 2: the left panels). Several RF deliveries applied at the neck of diverticulum at which the local electrogram showed the earliest ventricular activation (shown by an arrow in the right panel), eliminated the ventricular pre-excitation.

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