# Features of intrinsic ganglionated plexi in both atria after extensive pulmonary isolation and their clinical significance after catheter ablation in patients with atrial fibrillation

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**BACKGROUND** The features of intrinsic ganglionated plexi (GP) in both atria after extensive pulmonary vein isolation (PVI) and their clinical implications have not been clarified in patients with atrial fibrillation (AF).

**OBJECTIVE** The purpose of this study was to assess the features of GP response after extensive PVI and to evaluate the relationship between GP responses and subsequent AF episodes.

**METHODS** The study population consisted of 216 consecutive AF patients (104 persistent AF) who underwent an initial ablation. We searched for the GP sites in both atria after an extensive PVI.

**RESULTS** GP responses were determined in 186 of 216 patients (85.6%). In the left atrium, GP responses were observed around the right inferior GP in 116 of 216 patients (53.7%) and around the left inferior GP in 57 of 216 (26.4%). In the right atrium, GP responses were observed around the posteroseptal area: inside the CS in 64 of 216 patients (29.6%), at the CS ostium in 150 of 216 (69.4%), and in the lower right atrium in 45 of 216 (20.8%). The presence of a positive GP response was an independent risk factor for AF recurrence (hazard ratio 4.04, confidence interval 1.48–11.0) in patients with paroxysmal, but not persistent, AF. The incidence of recurrent atrial tachyarrhythmias in patients with paroxysmal AF with a positive GP response was 51% vs 8% in those without a GP response ($P = .002$).

**CONCLUSION** The presence of GP responses after extensive PVI was significantly associated with increased AF recurrence after ablation in patients with paroxysmal AF.

**KEYWORDS** Autonomic nervous system; Catheter ablation; Atrial fibrillation; Pulmonary vein

**ABBREVIATIONS** **AF** = atrial fibrillation; **AT** = atrial tachycardia; **CANS** = intrinsic cardiac autonomic nervous system; **CS** = coronary sinus; **GP** = ganglionated plexi; **HFS** = high-frequency stimulation; **LA** = left atrium; **PV** = pulmonary vein; **PVI** = pulmonary vein isolation; **RF** = radiofrequency; **SVC** = superior vena cava

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## Introduction

The intrinsic cardiac autonomic nervous system (CANS) is composed of a neural network formed by axons and autonomic ganglia concentrated at the ganglionated plexi (GP), and it is involved in the mechanism of atrial fibrillation (AF).[1–3] GP stimulation followed by autonomic nervous hyperactivity with an uncontrolled release of excess amounts of neurotransmitters[4,5] causes pulmonary vein (PV) firing by reducing the PV sleeve action potential duration[5] and shortening the fibrillation cycle length,[6] creating ideal conditions for the initiation and maintenance of AF.

The PVs are the cornerstone of catheter ablation of AF, but AF recurrence still is high after an initial pulmonary vein isolation (PVI). A wide circumferential PVI, delineating the GPs adjacent to the PVs, suppresses PV firing after an electrical PVI and includes the clinical benefit of catheter ablation despite frequent postablation PV reconnections. In addition, the presence of intrinsic GP responses, even if far from the PVs, is also likely to promote PV firing and/or circumstances for maintaining AF. However, the features and clinical significance of residual GPs after PVI have not been clarified. In this study, we examined the location and incidence of GP responses after extensive PVI in both atria and evaluated the hypothesis that GP responses were associated with an increased subsequent incidence of atrial tachyarrhythmic episodes.

## Methods

The study population consisted of 216 consecutive patients with AF episodes who underwent catheter ablation from

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October 1, 2011, to September 6, 2013. Exclusion criteria for the patient characteristics were (1) left atrial (LA) diameter >55 mm, (2) significant valvular disease requiring surgery, and (3) hypertrophic obstructive cardiomyopathy. Persistent AF was defined as that lasting >7 days, not self-terminating, and usually requiring medical intervention. All antiarrhythmic drugs were generally discontinued at least 7 days before catheter ablation. All patients provided written informed consent for electrophysiologic study and catheter ablation. The study was approved by our institutional review board.

## Electrophysiologic study and catheter ablation

A single 3000 international unit bolus of heparin was administered, and an activated clotting time >250 seconds was maintained after the transseptal puncture. A 20-pole diagnostic catheter was positioned in the coronary sinus (CS) for pacing and recording. A 20-pole catheter was placed in the right atrium to cover the area along the crista terminalis or superior vena cava (SVC). The LA and PVs were accessed by a transseptal approach. Three steerable catheters, including 2 spiral curve catheters, were introduced into the LA through a single transseptal puncture site. The upper and lower left PVs were simultaneously mapped with 2 adjustable 20-pole catheters (Optima, Irvine, CA; Figure 1).

The 3-dimensional constructed geometry of the entire LA was created using a NavX system (St. Jude Medical, St. Paul, MN), and each ablation site during radiofrequency (RF) delivery was monitored and recorded by fluoroscopy and the 3-dimensional electroanatomic mapping system. Surface ECGs and intracardiac electrograms filtered between 30 and 500 Hz were recorded simultaneously with a polygraph (EP Workmate, St. Jude Medical).

Intravenous dexmedetomidine hydrochloride was continuously administered for sedation (0.2–0.7 μg/kg/h). We initially performed the PVI procedure using a double circular mapping catheter technique during sinus rhythm. DC energy was delivered with an external biphasic waveform of up to 270 J before PVI. We confirmed the success of electrical PVI by monitoring the wide circumferential electrical isolation: approximately 2 cm from the ostium of both the right and left PVs. Complete disappearance of all potentials from all 4 PVs was confirmed in all patients.

When AF persisted after extensive PVI or dilated LA diameter >45 mm was present, creation of an LA roof line and/or a mitral isthmus line was performed. A spiral catheter was placed in the LA appendage, and constant pacing was delivered from the LA appendage base if the patient was in sinus rhythm. Complete bidirectional block was determined by the presence of widely separated local double potentials along the length of the ablation line and mapping the activation detour during pacing from either side of the line. In cases with an induced tricuspid and/or mitral annulus-dependent atrial tachycardia (AT), RF energy was appropriately applied in order to terminate each induced AT. Mapping of macroreentrant ATs was performed using multisite entrainment techniques and observing the P-wave morphology and activation sequence recorded from the atrial electrodes. RF energy with a power of 25–35 W was delivered for 20–40 seconds at each site or sequentially dragged by using a 4-mm irrigation tip catheter (St. Jude Medical).

## GP pacing

We searched for the location of the GP sites in both atria after extensive PVI (all 4 PVIs and/or additional line creation).

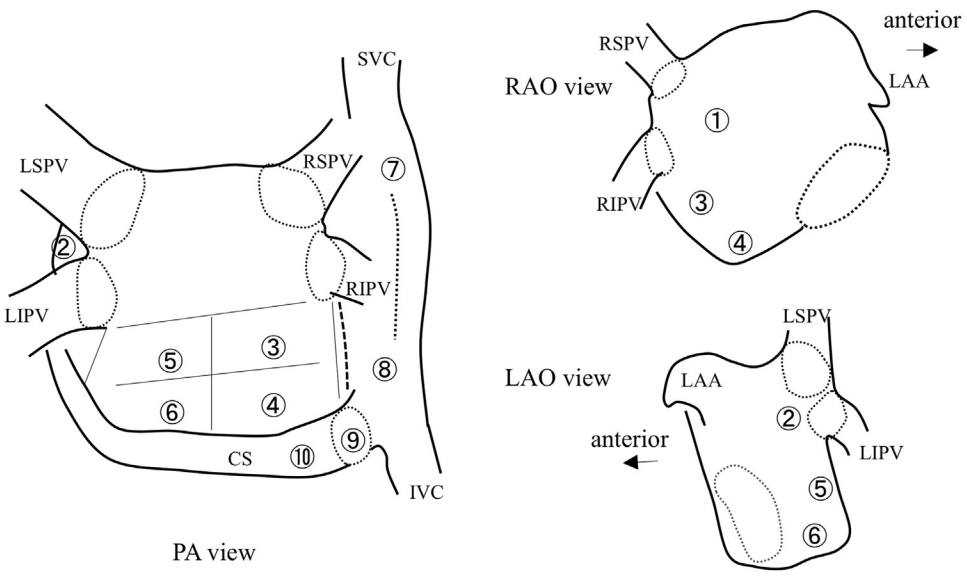


**Figure 1** Location arbitrarily divided into 10 preferable ganglionated plexi (GP) response regions. ① Anterior region of the right superior pulmonary vein. ② Lateral region of the part of the left atrium consistent with the ligament of Marshall. ③ Upper region of the right inferior GP. ④ Lower region of the right inferior GP. ⑤ Upper region of the left inferior GP. ⑥ Lower region of the left inferior GP. ⑦ Superior vena cava or crista terminalis. ⑧ Inferior septal region of the right atrium outside the coronary sinus. ⑨ Coronary sinus ostium. ⑩ Inside the coronary. The GP response inside the coronary sinus (CS) was approximately determined up to 2 cm from the CS ostium. IVC = inferior vena cava; LAA = left atrial appendage; LAO = left anterior oblique; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; PA = posteroanterior; RAO = right anterior oblique; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.