Spatial Relations between the Standard Deviation of Complex Fractionated Atrial Electrogram Intervals and Low-Voltage Areas in Patients with Atrial Fibrillation

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**Background:** Rapid focal activity and rotor activity have been reported to play important roles in the maintenance of atrial fibrillation (AF). Identification of rotor/focal activity by spectral and phase analyses have been demonstrated. We hypothesized that if the drivers of AF are present, their characteristics may exhibit temporal stability rather than their voltage.

**Methods:** In patients with paroxysmal AF (n = 18) and persistent AF (n = 7) LA mapping with a 20-pole spiral catheter was performed for 5 seconds during AF. Low voltage area (LVA during AF, < 0.2 mV), complex fragmented atrial electrogram (CFAE, cycle length < 120 ms) sites, and standard deviation (SD) of the cycle length were compared.

**Results:** Smaller SD sites (< 20 ms) overlapped with LVAs at 11 sites (14%), were located adjacent to a LVA (within 15 mm from the LVA edge) at 36 sites (47%), and were located away from the LVA (> 15 mm from the LVA) at 29 sites (38%).

**Conclusion:** Organized activation sites located mainly at the periphery of LVAs may represent sites of rotor/focal activity.

**Key words:** catheter ablation, atrial fibrillation, AF driver, organized activation, low voltage area

1. Introduction

Termination of persistent AF (PerAF) often requires extensive ablation, including ablation at sites of complex fractionated atrial electrograms (CFAEs) and high dominant frequency and/or multiple linear ablations in addition to pulmonary vein isolation (PVI)⁴⁻⁶. Unfortunately, a recent study showed no reduction in the incidence of recurrent AF when either linear ablation or CFAE ablation was performed in addition to PVI in patients with PerAF⁷. However, rotor ablation⁹, driver ablation⁷, and tailored atrial substrate modification based on low-voltage areas (LVAs) in addition to PVI have prevented AF recurrence in many patients with PerAF⁸⁻¹⁰. These reported successes prompted us to examine spatial relations between LVAs and rotor and/or driver sites.

2. Materials and methods

2.1 Study patients

The study involved 25 patients (18 men, 7 women; mean age 66.5 ± 4.9 years) scheduled for their first catheter ablation of AF. Characteristics of these patients are shown on Table 1. Eighteen had paroxysmal AF (PAF; AF lasting less than 7 days), and 7 had PerAF (AF lasting 7 days or more). Patients with continuous AF duration > 1 year were excluded from the study. The study protocol was approved by the Institutional Review Board of Nihon University Itabashi Hospital (May 25, 2016; RK-160614-...
and all 25 patients provided written informed consent for their participation.

### 2.2 Electrophysiologic study

Electrophysiologic study was performed in all patients under conscious sedation achieved with dexmedetomidine, propofol, and fentanyl. After 2 long sheaths (1 SL0 sheath and 1 Agilis sheath; St. Jude Medical, Inc., St. Paul, MN, USA) were inserted into the left atrium (LA) via a transseptal puncture, the 3-dimensional (3D) geometry of the LA and 4 pulmonary veins (PVs) was reconstructed with the use of a 20-pole circular mapping catheter with 4-4-4-mm interelectrode spacing (AFocus II 20-pole double ring catheter, St. Jude Medical, Inc.) and an EnSite NavX Classic system (St. Jude Medical, Inc.). We recorded multiple bipolar signals (filter setting: 30–300 Hz) from the AFocus II catheter with the EnSite Velocity Cardiac Mapping System (St. Jude Medical, Inc.). If the patient was in sinus rhythm, AF was induced by rapid atrial pacing from the coronary sinus ostium, and bipolar signals were recorded starting 5 minutes after AF induction.

### 2.3 Bipolar electrogram recordings

Nineteen bipolar electrograms (1-2…19-20) were recorded simultaneously from the 20-pole circular electrodes (AFocus II 20-pole double ring catheter) with 4-mm spacing for 5 seconds during AF, and high-density 3D electroanatomic mapping (> 400 signals) of the entire LA was performed. Peak-to-peak bipolar voltages during AF were averaged from the 5-second recordings. Bipolar electrogram amplitudes were measured during AF, and low voltage was defined as < 0.2 mV during atrial fibrillation.

The atrial electrogram intervals were analyzed as follows: the NavX mapping parameters were set to CFAE-mean, and an algorithm was used to determine the average time of the atrial electrogram interval (fractionation intervals; FIs). The FI was taken as the average time between consecutive deflections over the 5-second recording period, and both the FI and its standard deviation (SD) were calculated. An SD of < 20 ms was considered small. Local bipolar activation time was defined as the peak negative dV/dt point. The settings included a refractory period of 40 ms, peak-to-peak sensitivity of 0.05 mV to 0.1 mV, and an electrogram duration of < 10 ms.

### 2.4 Determination of the spatial relations between complex fractionated atrial electrogram sites and low-voltage areas

Sites where the SD of the FI was small were identified from the electroanatomic maps and, the spatial relations between these sites and the LVAs was assessed. The sites were described as overlapping an LVA, as adjacent to an LVA if they were located within 15 mm from an LVA edge, or as remote from an LVA if they were farther than 15 mm from an LVA edge.

### 3. Results

FIs with a small SD were identified at 76 sites in 25 patients (3.0 ± 1.1 sites per patient). Eleven (14%) of these sites overlapped an LVA, 36 (47%) were adjacent to an LVA (within 15 mm from the LVA edge), and 29 (38%) neither overlapped nor were adjacent to an LVA (> 15 mm from the LVA) (Table 2).

Representative electroanatomic maps acquired during AF are shown in Fig. 1. The patient in this case was a 70-year-old man. LVAs are shown at the left, and sites where the SD of the FI was small (< 20 ms) are shown on the right. In comparing the LVA and SD FI maps, it is evident that that sites in which the SD of the FI was small were located adjacent to the LVA, within the LVA (left superior PV), and remote from the LVA (roof and floor of the LA).

Representative electroanatomic maps are also shown in Fig. 2. The patient in this case was a 65-year-old man. Sites where the SD of the FI was small are shown at the left, and LVAs are shown on the map in the middle. Local activation is shown on the map at the right. On this map, sites where the SD of the FI is small are adjacent to an LVA, and the activation sequence at these sites (shown by AFocus II catheter shadow) is indicative of rotational activity. The electrogram (lower right panel) is that of a “small SD site.”

### 4. Discussion

#### 4.1 Major finding

We found in our patient group that areas where the SD of the FI is small (< 20 ms) exist mainly at LVA border-zones.

#### 4.2 Our findings in light of previously reported findings

Ghoraani et al. reported that areas of very low voltage (< 0.1 mV) were present in 23% of localized rotational activation sites. Schade et al. studied the relation between focal impulse and rotor sources in the LA and LVZs or PV antra and showed definite non-association between 30% of the sources and the target sites. Lin et
Fig. 1  Electroanatomic maps from a 70-year-old man showing low voltage areas (LVA) (< 0.05 mV) and areas in which the standard deviation (SD) of the fractionation interval (FI) during atrial fibrillation was small (< 20 ms). Left panel: grey indicates areas of low voltage. Right panel: white indicates areas in which the SD of the FI is small. The patient was a 70-year-old man.


Fig. 2  Electroanatomic maps from a 65-year-old man showing low voltage areas (LVA) (< 0.05 mV) and areas in which the standard deviation (SD) of the fractionation interval (FI) during atrial fibrillation was small (< 20 ms). Left panel: white indicates areas in which the SD of the FI is small. Middle panel: grey indicates LVA. Right panel: map of local activation. Lower right panel: Bipolar electrogram recorded from the LVA site shows clockwise rotational activation.
al. reported that regions with a high degree of electrogram similarity localized within an abnormal substrate—either the bipolar low voltage border zone (> 0.5 mV) or low voltage zone (0.5–0.1 mV) but not in the scar tissue (< 0.1 mV)—involved rotors and focal sources, and they found similarity index ablation to be an independent predictor of freedom from AF recurrence. Kurian et al. showed that, in comparison to ablation of non-substrate based rotors, incidental ablation of substrate-based rotors (rotors that, in comparison to ablation of non-substrate based study.

organized activation.

Sites where the SD of the FI is small may be sites of organized activation.

Conflict of Interest

The authors have no conflicts of interest related to this study.

References


