Differential Atrial Pacing to Detect Reconnection Gaps After Pulmonary Vein Isolation in Atrial Fibrillation
A Retrospective Study Using a Novel Mapping Technique

Mai Tahara, MD, Ritsushi Kato, MD, Yoshifumi Ikeda, MD, Koji Goto, MD, So Asano, MD, Hitoshi Mori, MD, Shiro Iwanaga, MD, Toshihiro Muramatsu, MD and Kazuo Matsumoto, MD

Summary
High-resolution mapping is useful to identify reconnection gaps in the pulmonary vein after pulmonary vein isolation for atrial fibrillation. However, it is sometimes difficult to differentiate pulmonary vein potentials from far-field potentials because of very low amplitudes. Our purpose was to evaluate the usefulness of a novel differential atrial pacing method to differentiate reconnected pulmonary vein potentials from isolated pulmonary vein potentials. This retrospective observational study included 34 patients with atrial fibrillation (22 men; mean age, 64 ± 14 years; 28 with paroxysmal atrial fibrillation) who underwent radiofrequency or cryoballoon ablation. Following pulmonary vein isolation, we created a high-resolution activation map during pacing from both the coronary sinus and left atrial appendage. We compared the characteristics of the pulmonary vein potentials and the pattern of activation between the reconnected and isolated pulmonary veins. We analyzed 131 pulmonary veins and found reconnections in 41 pulmonary veins (R group); 90 pulmonary veins had no reconnection (NR group). The R group had a significantly shorter distance between the earliest pulmonary vein activation sites in both activation maps, compared with the NR group (5.22 ± 0.53 mm versus 17.08 ± 0.36 mm, respectively; P < 0.0001). The amplitude of the pulmonary vein potentials was higher in the R group versus the NR group (0.61 ± 0.05 mV versus 0.04 ± 0.03 mV, respectively; P < 0.0001). Six gaps (14%) in the R group that were unrecognized using a conventional method were identified using our novel method. In conclusion, differential atrial pacing was useful to identify pulmonary vein reconnection gaps during ablation using a novel high-resolution mapping system.

Key words: Catheter ablation, High resolution mapping, Conduction gap, Radiofrequency ablation, Cryoballoon ablation

During the last decade, atrial fibrillation has become one of the most important public health problems, with a prevalence as high as 2% of the world’s population. Pulmonary vein isolation is a standard technique for catheter ablation of atrial fibrillation and is known to improve quality of life in patients with atrial fibrillation. However, the reported incidence of atrial fibrillation recurrence remains relatively high (48%-59%), and the major cause of recurrence is reconnection of the ablated area to the pulmonary vein and left atrium. Therefore, identifying pulmonary vein reconnection gaps after pulmonary vein isolation is important to complete the procedure. However, in some patients, it is difficult to identify these gaps due to very low pulmonary vein potentials. Several studies have shown the usefulness of the Rhythmia® mapping system (Boston Scientific, Natick, MA, USA) to identify pulmonary vein gaps, but due to its high sensitivity for detecting tiny potentials, it is difficult to differentiate pulmonary vein potentials from far-field potentials in some patients. Therefore, we hypothesized that if pulmonary vein gaps are present after initial pulmonary vein isolation, the earliest activation sites in the pulmonary vein using two different pacing sites will be located at the same or similar positions. We also speculated that the characteristics of the inner pulmonary vein potentials and the conduction patterns will be different between patients with and without reconnection gaps, using the high-density mapping system. The purpose of this study was to investigate the usefulness of this mapping strategy.

Methods

Patient population: This study included 34 patients (age 64 ± 14 years; 22 men (76%); 28 with paroxysmal atrial fibrillation and 6 with persistent atrial fibrillation) who underwent first ablation for atrial fibrillation (n = 16) or redo-ablation (n = 18) with either radiofrequency or cryoballoon ablation.
Figure 1. We adjusted the window of interest to exclude the most proximal posterior potential (left). We also adjusted the window of interest to exclude the LAA potential when analyzing left PV potentials (right). PV indicates pulmonary vein; and LAA, left atrial appendage.

cryoballoon ablation. All procedures were performed in our institution between August 2017 and August 2018 using the Rhythmia® high-density mapping system. Patients were eligible if they were 18 years of age or older and had symptomatic paroxysmal or persistent atrial fibrillation. The exclusion criteria were sustained atrial fibrillation lasting more than 5 years and a left atrial diameter ≥ 50 mm. Paroxysmal and persistent atrial fibrillation were defined according to the HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation11) and were documented with electrocardiography (Nihon Kohden, Shinjuku, Japan).

Mapping the left atrium: Left atrial mapping was performed using an IntellaMap Orion® catheter (Boston Scientific) following pulmonary vein isolation for the initial procedure or before ablation for the second session. Mapping was performed twice with different atrial pacing sites: coronary sinus ostium and left atrial appendage (LAA) under a pacing rate of 100 beats per minute. A 20-polar diagnostic catheter was placed in the coronary sinus for reference, and a 20-polar ring catheter was placed in the LAA for pacing. Appropriate electrocardiograms using the Orion® catheter were automatically selected by the system with predefined criteria. The initial criteria were as follows: stable cycle length with a tolerance of ± 10 ms, a propagation reference with a tolerance of ± 5 ms, and a respiratory cycle accepting beats only during the exhalation phase. A 10-polar ring catheter was also used to detect each pulmonary vein potential. Mapping was also performed after ablation to confirm the disappearance of any pulmonary vein potentials.

Identification of pulmonary vein gaps: We retrospectively analyzed the pulmonary vein potentials detected by the Orion® catheter using a propagation and voltage map. The window of interest (WOI) was adjusted according to the pacing map. For the LAA pacing map, we excluded the timing of the LAA potential. For the coronary sinus ostium map, the timing of the closest left atrial potential was excluded (Figure 1). Therefore, we set the WOI between the endpoint of the local left atrial potential and the beginning of the QRS wave. However, we sometimes prolonged the endpoint to the timing within the QRS, because left atrial-pulmonary vein conduction was very slow in some patients. First, we created the voltage map with the following settings to overlook and confirm the gap site: normal-voltage area, > 0.5 mV; low-voltage zone, < 0.05 mV; and scar zone, < 0.03 mV. Since the voltage map alone could not accurately identify the gaps, we used the activation map for all analyses. The noise confidence mask was decreased from 0.03 mV (nominal setting) to 0.005 mV to include very low potentials in the activation map. A dark red color was set as 5 ms in the activation map to detect the conductive gap. We identified the earliest activation site in the pulmonary vein during coronary sinus ostial pacing and LAA pacing and measured the difference between the two maps (Figures 2, 3). The geometry of the maps was considered the same when no error was detected by the Orion® catheter during mapping. We also measured the voltage of the pulmonary vein gap po-
PACING TECHNIQUE TO DETECT GAPS IN AF ABLATION

Figure 2. Example of a left inferior PV gap. The EAS in both coronary sinus and LAA pacing maps was located at the anterior wall (red dot in A and a, respectively) of the PV, and the potential spread to the upper side of the PV (A-C, and a-c, respectively). The potentials in both maps spread from the proximal to distal PV (white arrow in the coronary sinus pacing map and the white dashed arrow in the LAA pacing map). A fragmented PV potential is seen inside the adjusted window of interest (D). The circumferential distance between the EAS in both coronary sinus and LAA pacing maps was calculated as 3.5 mm. PV indicates pulmonary vein; EAS, earliest activation site; and LAA, left atrial appendage.

Tentials detected by the Orion® catheter for each map.

When multiple gaps were found in the same pulmonary vein, we used the same technique to identify conduction gaps (Figure 4). Multiple gaps were considered present when the deep scar or apparent conduction-blocked area was located between each different gap. The size of the reconnection gap was defined and measured at sites only where fragmented potentials were seen and/or at the site between apparent double potentials. We also analyzed the pulmonary vein potentials in the ring catheter and investigated whether the pulmonary vein potential was identified over the catheter. We considered that the pulmonary vein was reconnected when we saw at least one of the following: an apparent pulmonary vein potential recorded by the 20-polar ring catheter or a tiny pulmonary vein potential recorded by the Orion® catheter within the WOI during both LAA pacing and coronary sinus pacing, and these pulmonary vein potentials were eliminated by catheter ablation.

Ablation procedure after pulmonary vein isolation and follow-up: An open-irrigation radiofrequency ablation catheter (Celsius®, Biosense Webster, Irvine, CA, USA) was used to ablate the pulmonary vein conduction gaps for all cases using the Rhythmia® mapping system. The ablation settings were as follows: radiofrequency power of 30 W for the anterior wall and 20-25 W for the posterior wall, cutoff temperature of 40°C, and irrigation flow of 17 mL/minute. Following ablation for the gaps, adenosine triphosphate was injected to confirm dormant conduction between the pulmonary vein and left atrium. If we identified a non-pulmonary vein trigger, additional ablation was applied to eliminate the trigger as long as the trigger was mappable.

Antiarrhythmic drugs were discontinued at admission and were not prescribed again for any patient. We followed patients as outpatients in our institute at least every 3 months with 12-lead electrocardiography and every 6 months with Holter monitoring (Fukuda-Denshi, Tokyo, Japan).

Statistical analysis: Continuous data are expressed as the mean ± standard deviation or median. Normally distributed data are given as the mean ± standard deviation, and non-normally distributed data are given as the median and interquartile range. Categorical data are presented as absolute values and percentages. Significance was analyzed using the unpaired t-test for continuous data, and when the data was not normally distributed, a Wilcoxon signed-rank test was used. The data for the two groups were compared using the χ²-squared test or Fisher’s exact test. All analyses were performed using JMP software version 11.0 (SAS, Cary, NC, USA). P-values ≤ 0.05 were considered as statistically significant. This study was approved by the
Results

Patients' characteristics: Of the 34 patients with atrial fibrillation who underwent pulmonary vein isolation, 22 patients had 1 or more pulmonary vein gaps and were assigned to the R group; the remaining 12 patients were assigned to the no reconnection gaps (NR) group. Patients' baseline characteristics are shown in Table I. There were no significant differences in the baseline characteristics of the two groups, nor were there significant differences in the average pulmonary vein diameters measured at the left atrium-pulmonary vein junction on enhanced computed tomographic imaging between the two groups (Table I). Of the 136 pulmonary veins, we excluded 5 pulmonary veins due to inadequate mapping such as an inability to insert the Orion catheter in the pulmonary vein. Therefore, we analyzed 131 pulmonary veins (34 left superior, 32 left inferior, 34 right superior, and 31 right inferior pulmonary veins).

PV reconnection gaps: Among the 131 pulmonary veins, we found reconnection gaps in 41 pulmonary veins (R group), and 90 pulmonary veins had no reconnection gaps (NR group). The mapping parameters are summarized in Table II. There were no significant differences in the mapping parameters between the groups. Reconnection gaps were found in 5 left superior, 7 left inferior, 17 right superior, and 12 right inferior pulmonary veins. The R group had a significantly shorter distance between the earliest activation sites in the pulmonary vein on both activation maps during coronary sinus ostial and LAA pacing compared with the NR group (5.22 ± 0.53 mm versus 17.08 ± 0.36 mm, respectively; \( P < 0.0001 \), Table II). The amplitudes of the potentials in the pulmonary vein recorded by the Orion catheter were higher in the R group than in the NR group (0.61 ± 0.05 mV versus 0.04 ± 0.03 mV, respectively; \( P < 0.0001 \), Table II), and 35/41 (85.3%) reconnected pulmonary vein potentials were recognized by the 20-polar ring catheter, while the remaining 6 pulmonary vein gaps (14.6%) were not identified.

Catheter ablation and Follow-up: All gaps were isolated successfully and elimination of the pulmonary vein potentials was confirmed by the Orion catheter. No patients experienced complications related to the procedure, and all patients remained free of arrhythmias without antiarrhythmic drugs during the short-term follow-up (mean follow-up duration, 8.3 ± 2.4 months).
Discussion

Major findings: The major findings in this study were the following: (1) a significantly shorter distance between the two earliest activation sites in the pulmonary vein with both LAA pacing and coronary sinus ostial pacing with reconnected pulmonary veins compared with isolated pulmonary veins; (2) the amplitude potential in reconnected pulmonary veins was significantly higher than that in the isolated pulmonary veins; and (3) the Rhythmia™ mapping system could identify reconnection gaps in 14% of pulmonary veins that could not be identified by the 20-polar ring catheter.

Mechanism for detecting gaps: LAA far-field potentials are often mistaken as a persistent pulmonary vein potential in the left pulmonary vein; however, pacing from the
LAA and excluding LAA potentials from the WOI makes it easier to recognize pulmonary vein potentials. If a gap is present, the site of the earliest activation inside the pulmonary vein would be the same when pacing from different sites in the left atrium. Figure 2 is an example of a left inferior pulmonary vein gap, showing the earliest activation site as the anterior wall of the left inferior pulmonary vein in both coronary sinus ostium pacing and LAA pacing maps and that the potential in the pulmonary vein moved in the same direction with pacing from the different pacing sites. Figure 3 is an example of no reconnection in the right superior pulmonary vein. The earliest activation site in the right superior pulmonary vein during the coronary sinus ostial pacing was the anteroinferior wall of the carina, but the potential then gradually moved to the anterosuperior wall and did not move to the distal pulmonary vein. In contrast, the earliest activation site in the right superior pulmonary vein during LAA pacing was the distal roof, and the potential gradually moved to the ostium. We cannot define exactly what these potentials reflected, but we recognized the potentials as far-field ones because they were not affected by ablation, and the distance of the earliest activation sites in both maps were long.

The threshold of amplitude may also help determine whether a potential is a pulmonary vein potential. The mean voltage of the pulmonary vein potentials in the NR group in our study was as low as 0.04 ± 0.03 mV. In our findings, if the pulmonary vein potential was lower than 0.07 mV, it was almost always considered “no gap” (Figure 5).

When multiple gaps were seen in the same patient, we used the same protocol to analyze the gaps, and all pulmonary vein gaps were identified and eliminated in our study. Figure 4 is an example of multiple gaps in the right superior pulmonary vein. This method was also applicable to multiple gaps, and there were two different earliest sites (anterior wall and roof of the right superior pulmonary vein) in both the coronary sinus pacing map and the LAA pacing map. We measured the distances between the earliest sites in both maps, which were found to be short, implying reconnection gaps.

**Comparison with previous studies regarding detecting gaps:** In previous studies, several approaches have been proposed to localize reconnection gaps. Eitel et al. identified gaps by excitability during pacing at 10 V/2 ms with the ablation catheter along the previously ablated line.12) Gap identification using this method was successful in 95% of 147 patients. Another group reported a different method of mapping the atrial side of the ablation line during pulmonary vein pacing, resulting in 85% successful identification of pulmonary vein gaps.13) Rhythmia® mapping is useful to precisely detect pulmonary vein gaps. Masuda et al. showed that the Rhythmia® system visualized all pulmonary vein gaps using manual reannotation.14) Conte et al. reported that while the Orion® catheter identified all pulmonary vein gaps, a circular catheter was able to detect only 77% of the pulmonary vein gaps, which was similar to our findings.15)

**Clinical implications:** Clinically, in some patients undergoing redo-ablation, it is difficult to differentiate conduction gaps because pulmonary vein potentials often have low voltage. Ring catheters are usually placed in the pulmonary vein to detect potentials, but ring catheters sometimes fail to identify pulmonary vein potentials, especially

### Table II. Mapping Parameters

| Parameter                              | R group (n = 41 PVs) | NR group (n = 90 PVs) | P value |
|----------------------------------------|---------------------|----------------------|---------|
| Acquired number of points (LAA pacing) | 8748 (2810)         | 6921 (3422)          | 0.45    |
| Acquired number of points (CS ostium pacing) | 7556 (3775.7) | 7752 (4631.3)          | 0.81    |
| Mapping time (LAA pacing), minutes     | 16.3 (7.4)          | 14.1 (6.2)           | 0.58    |
| Mapping time (CS ostium pacing), minutes | 18.4 (8.5) | 14.7 (9.4)            | 0.66    |
| Distance of EAS between LAA and CS map, mm | 5.24 (6.4) | 17.1 (5.8)            | 0.0001 |

All values are expressed as median (interquartile range). LAA indicates left atrium appendage; CS, coronary sinus; EAS, earliest activation site; and RF, radiofrequency.
under atrial fibrillation. Anter et al. reported overestimation of pulmonary vein isolation; 20.8% of pulmonary vein gaps were not identified using the ring catheter but were visible using the Orion catheter. Our study showed that 17% of pulmonary gaps were not identified over the circular catheter, which was a relatively similar percentage reported in previous studies. The Rhythmia mapping system allows visualization of these conduction gaps, but due to its high sensitivity to detect small potentials, it is difficult to differentiate low PV potentials from far-field signals originating from neighboring anatomical structures. Masuda et al. reported that 43% of gaps were not visualized using the Rhythmia mapping system due to incorrect annotation by far-field signals or electric noise, suggesting that a single high-density map can mislead operators. Overdetection of gaps was observed in 36.3% of the cases using the high-density mapping in Garcia-Bolao’s study. Our study helped identify such reconnection gaps by pacing from different sites in the atrium and by excluding the far-field potentials by changing the WOI. Using this simple differential atrial pacing method, we successfully identified and ablated all pulmonary vein gaps. Although our method results in longer procedure time due to its need for creating two maps, our method accurately localizes reconnection gaps and avoids unnecessary ablation by making sure it is not a far-field potential. Furthermore, the mean amplitude of potentials recorded by the Orion catheter in the isolated pulmonary veins was as low as 0.04 ± 0.03 mV versus 0.61 ± 0.05 mV in the reconnected pulmonary veins. Therefore, amplitude potentials inside the pulmonary vein of less than 0.07 mV could be considered potentials in the isolated pulmonary veins. This threshold of pulmonary vein potentials may also help determine whether the potential is a gap. Masuda et al. reported an average gap amplitude voltage of 0.36 ± 0.26 mV, suggesting that approximately 15% of gaps have an amplitude of less than 0.11 mV, which are overlooked using Pappone’s conventional gap voltage cutoff of 0.1 mV.

**Limitations:** There are several limitations in this study. First, this study was a single-center study with limited sample sizes. Nonetheless, consistent findings among all patients verified our hypothesis. Second, we did not compare other mapping devices, and further studies are needed to support our conclusions. Third, we did not evaluate patients’ long-term clinical outcomes. Therefore, it is still unknown whether this mapping system and method provide better outcomes in patients with atrial fibrillation.

**Conclusion**

Differential atrial pacing using a high-resolution mapping system and the voltage of the pulmonary vein potentials may be helpful to identify pulmonary vein reconnection gaps after pulmonary vein isolation.

**Disclosure**

**Conflicts of interest:** None.

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