Quantitative Analysis of the Isolation Area During the Chronic Phase After a 28-mm Second-Generation Cryoballoon Ablation Demarcated by High-Resolution Electroanatomic Mapping

Shinsuke Miyazaki, MD; Hiroshi Taniguchi, MD; Hitoshi Hachiya, MD; Hiroaki Nakamura, MD; Takamitsu Takagi, MD; Jin Iwasawa, MD; Kenzo Hirao, MD; Yoshito Iesaka, MD

Background—The post–second-generation cryoballoon (CB) ablation isolation area during the chronic phase has not been described. The aim of this study was to quantitatively evaluate the chronic-phase isolation area after 28-mm second-generation CB ablation and compare it to the estimated conventional radiofrequency circumferential pulmonary vein isolation (CPVI) line.

Methods and Results—Thirty-two patients with paroxysmal atrial fibrillation underwent pulmonary vein (PV) isolation using second-generation CB. After a median of 6.0 (4.0–9.0) months, the PV isolation area was evaluated using high-resolution mapping (1-mm electrode, 2-mm interelectrode spacing; 527±99 points per map) and pacing techniques in all patients (17 with and 15 without arrhythmia recurrence beyond blanking period) and compared with estimated conventional radiofrequency CPVI area. PV reconnections were observed in 34 of 126 PVs (27.0%) among 21 of 32 patients (65.6%), which were eliminated by a median of 1.0 (1.0–3.0) focal radiofrequency application. The left- and right-sided PV antrum isolation area and nonablated posterior wall areas were 9.8±1.7, 8.1±2.3, and 17.0±6.1 cm², respectively. The cryoablated areas were significantly smaller than the estimated conventional radiofrequency CPVI areas in all but the right inferior PV. The difference was highest in the left superior PV. In 2 patients (6.3%), recurrent atrial fibrillation originated from the foci identified at the left superior PV antrum outside the CB isolation area but inside the estimated conventional radiofrequency CPVI line.

Conclusions—Although the PV isolation areas during the chronic phase after the second-generation CB ablation were generally wide, they were significantly smaller than the area encircled by the CPVI line except at the right inferior PV antrum. Recurrent atrial fibrillation could originate from the left superior PV antrum and could be isolated by a CPVI but not by a CB. (Circ Arrhythm Electrophysiol. 2016;9:e003879. DOI: 10.1161/CIRCEP.115.003879.)

Key Words: atrial fibrillation • catheter ablation • electrodes

Catheter ablation is recognized as an effective therapeutic option for atrial fibrillation (AF).1-3 Electric pulmonary vein isolation (PVI) is the cornerstone of catheter ablation of AF, and point-by-point radiofrequency (RF) ablation has been the standard means. In RF ablation, the ablation line is designed by the operator, and a larger isolation area is associated with a lower recurrence rate.4 Indeed, several studies confirmed that circumferential PVI (CPVI) including the pulmonary vein (PV) antrum results in a better clinical outcome than segmental PVI.5,6 Recently, cryoballoon (CB) ablation has emerged as an alternative technique for PVI and has gained increasing acceptance as an effective ablation tool.7 The more recently introduced second-generation CB has exhibited a significantly higher performance than the first-generation CB because of the improved cooling effect.8,9 However, CB ablation cannot specifically control the left atrial (LA) lesion size, which means that the isolation area is basically defined by the LA and PV anatomy. Although a previous study showed that the isolation area was wide and antral during the acute phase post 28-mm second-generation CB ablation,10-12 the data during the chronic phase (after disappearance of tissue edema) has not been reported. Moreover, mapping data with small closely spaced electrode catheters, which improves the mapping resolution of low-voltage areas (LVAs),13 has not been reported. The first aim of this study was to quantitatively evaluate the isolation area during the chronic phase using small electrodes with close interelectrode spacing after 28-mm second-generation CB ablation. The second aim was to compare the isolation area post 28-mm CB ablation with the CPVI ablation line in the same patients to clarify the difference in the isolated area between the 2 different technologies.

Received December 23, 2015; accepted March 29, 2016.
From the Cardiovascular Center, Tsuchiura Kyodo Hospital, Tsuchiura, Ibaraki, Japan (S.M., H.T., H.H., H.N., T.T., J.I., Y.I.); and Heart Rhythm Center, Tokyo Medical and Dental University, Tokyo, Japan (K.H.).
Correspondence to Shinsuke Miyazaki, MD, Cardiology Division, Cardiovascular Center, Tsuchiura Kyodo Hospital, 11–7 Manabeshin-machi, Tsuchiura, Ibaraki 300-0053, Japan. E-mail: mshinsuke@k3.dion.ne.jp
© 2016 American Heart Association, Inc.
Circ Arrhythm Electrophysiol is available at http://circep.ahajournals.org DOI: 10.1161/CIRCEP.115.003879
WHAT IS KNOWN

• The isolated area during the chronic phase after the second-generation cryoballoon ablation is generally wide.
• However, when compared to the circumferential pulmonary vein isolation line, the isolated area post-cryoballoon ablation was significantly smaller except the right inferior pulmonary vein antrum. The difference was most prominent at the left superior pulmonary vein antrum, which could be associated with atrial fibrillation recurrence.

WHAT THE STUDY ADDS

• Cryoballoon ablation cannot eliminate atrial fibrillation sources originating from left superior pulmonary vein antra. Additional cryoballoon applications at the left superior pulmonary vein antrum might be an alternative approach to reduce such arrhythmia recurrences.
• Ablation strategy should be discussed based on the pulmonary vein anatomy obtained by preprocedural cardiac computed tomography.

Methods

Study Population

This prospective study consisted of 32 patients with paroxysmal AF who underwent PVI using exclusively 28-mm second-generation CBs with a single 3-minute freeze technique in our institute. Seventeen patients experienced arrhythmia recurrence, and the remaining 15 patients were free from arrhythmia beyond blanking period. All of them consented for the second procedure irrespective of symptomatic recurrence of AF. AF was defined according to the latest guidelines. All patients gave written informed consent. The study protocol was approved by the hospital’s institutional review board. The study complied with the Declaration of Helsinki.

Ablation Protocol During the Initial Procedure

All antiarrhythmic drugs were discontinued for at least 5 half-lives before the procedure. Warfarin and novel oral anticoagulants were stopped 1 day before the procedure. The cardiac anatomy was evaluated preprocedurally using 320-row contrast-enhanced computed tomography. The surface ECG and bipolar intracardiac electrograms were continuously monitored and stored on a computer-based digital recording system (LabSystem PRO, Bard Electrophysiology, Lowell, MA). The bipolar electrograms were filtered from 30 to 500 Hz. A 7-Fr 20-pole 3-site mapping catheter (BeeAT, Japan-Life-Line, Tokyo) was inserted through the right jugular vein for pacing, recording, and internal cardioversion. The procedure was performed under moderate sedation obtained with dexmedetomidine. A 100 IU/kg body weight of heparin was administered immediately after the venous access, and heparinized saline was additionally infused to maintain the activated clotting time at 250 to 350 seconds.

A single trans-septal puncture was performed using an RF needle (Baylis Medical, Inc, Montreal, QC) and 8-Fr long sheath (SL0: AF Division, SJM, Minneapolis, MN). The trans-septal sheath was exchanged over a guidewire for a 15-Fr steerable sheath (Flexcath AF Division, SJM, Minneapolis, MN). A spiral mapping catheter (Achieve, Medtronic) was used to advance the second-generation 28-mm CB (Arctic Front Advance, Medtronic) into the PV for support and to map the PV potentials. No 23-mm CBs were used in any cases. Contrast medium was used to verify the complete occlusion of the PV ostium, which was followed by a freeze cycle of 180 seconds. No additional applications were performed after the isolation. To avoid bilateral phrenic nerve injury, all CB applications were applied under monitoring the ipsilateral diaphragmatic compound motor action potentials during phrenic nerve pacing. The procedural end point was defined as electric PVI verified by a 20-mm circular mapping catheter (Lasso, Biosense Webster, Diamond Bar, CA). Additional touch-up freezes with an 8-mm tip conventional cryocatheter (Freezor MAX, Medtronic) were performed with 2-minute applications. No additional substrate modification was performed.

Mapping During the Second Procedure

Initially, electric PVI was confirmed with a 20-mm circular mapping catheter (same as the initial procedure). In cases with PV reconnections, PVI was achieved by minimal focal ablation where the earliest PV potential was recorded. Then, mapping of the LA was performed in sinus rhythm with a 20-pole steerable mapping catheter arranged with 5 soft radiating wires covering a diameter of 3.5 cm (Pentaray, Biosense Webster; interelectrode spacing 2.6-2 mm) and Carto 3 mapping system after respiration adjustment, and the map was merged onto the cardiac computed tomography rendering. For high-resolution mapping, we recorded bipolar pairs with 2-mm interelectrode spacing resulting in a 3-mm center-to-center interelectrode spacing. Four hundred to 600 LA mapping points per patient were carefully obtained. LVAs were defined as those <0.5 mV according to the published data. After creating voltage maps, pacing was performed from a 3.5-mm irrigated-tip ablation catheter (Smart Touch, Biosense Webster) with a contact force range of 5 to 20 g during sinus rhythm around the entire border of the LVA to confirm the electric isolation area (Figure 1). Bipolar pacing between the 2 distal electrode pairs of the ablation catheter was performed with a pacing output of 10 mA and pulse width of 2 milliseconds. Finally, the estimated ablation line of the ipsilateral CPVI was tagged on the shell using a contact force catheter with a contact force range of 5 to 20 g (Figure 2). The voltage mapping data were blinded to the operator during the CPVI line tagging on the shell to avoid any bias.

Definition of the Isolation Area

The PV ostium was defined as the point of maximal inflection between the PV wall and the LA wall. The cross-sectional area of PV ostia was measured. The isolation area was defined as an LVA (<0.5 mV) evaluated by high-resolution mapping and confirmed by LA capture loss during pacing. The PV antrum area was defined as the antral surface area excluding the PVs. The isolated surface area of each PV antrum, ipsilateral PV antrum, and total PV antrum were calculated. Each area measurement post CPVI was also calculated.

Statistical Analysis

Continuous data were expressed as the mean±SD for normally distributed variables or the median (25th, 75th percentiles) for non-normally distributed variables and were compared using a Student t test or Mann–Whitney U test, respectively. Categorical variables were compared using the χ² test. The isolation areas by 2 different ablation techniques in the same patient were compared using a paired t test or Wilcoxon signed-rank test. The P value presented is for a 2-tailed test. A P value of <0.05 indicated statistical significance. Analyses were conducted using SPSS Statistics version 19.0 (IBM Corp, Armonk, NY).

Results

Patient Characteristics and Procedural Results

The baseline patient characteristics are summarized in Table 1. In 32 patients, a total of 126 PVS including 2 left common PVS were identified. Overall, 121 of 126 PVS (96.0%) were isolated successfully using exclusively 28-mm CBs during the initial procedure. The mean number of CB applications resulting in
PVI was 1.2±0.7, 1.2±0.6, 3.0±1.0, 1.1±0.3, and 1.6±0.8 for the left superior PV (LSPV), left inferior PV (LIPV), left common PV, right superior PV (RSPV), and right inferior PV (RIPV), respectively. Touch-up lesions were created in the remaining 5 PVs (4.0%), and all were RIPVs. In total, all 126 PVs were successfully isolated by cryothermal ablation. Cardiac tamponade requiring pericardiocentesis occurred in 1 patient. This occurred when the 15-Fr sheath was reinserted into LA with a guide of 7-Fr catheter, and we assumed that the size gap between the catheter and sheath was associated with the occurrence.

The time from the first to second ablation procedure was a median of 6.0 (4.0–9.0) months. During the second procedure, PV reconnections were observed in 21 patients (65.6%) but not in the remaining 11 patients (34.4%).

Figure 1. A, After creating the voltage map, pacing was performed with a contact force–sensing catheter around the entire border of the low-voltage area to confirm the isolation area. The blue tags indicate the atrial capture sites, and white tags the loss of atrial capture sites. B, Voltage maps were merged onto the cardiac computed tomography. Please note that the proximal left superior pulmonary vein (LSPV) antrum is intact (red circle area). LIPV indicates left inferior PV; PV, pulmonary vein; RIPV, right inferior PV; and RSPV, right superior PV.

Figure 2. The comparison of the isolation area between post cryoballoon (CB) ablation and after the circumferential pulmonary vein isolation (CPVI). The purple tags indicate the CPVI line. A, The CPVI line was close to the border of the low-voltage area (LVA) created by the CB ablation. B and C, The LVA created by the CB ablation was inside the CPVI line, and this was especially prominent at the left pulmonary vein (PV) antra. LIPV indicates left inferior PV; LSPV, left superior PV; RIPV, right inferior PV; and RSPV, right superior PV.
Among these 21 patients, the first recurrent AF was documented median 3.5 (1–9.3) days after the procedure in 14 patients (66.7%), and recurrence was symptomatic in 12 patients (85.7%). Among 126 PVs, reconnections were identified in 34 PVs (27.0%), including 6, 6, 1, 5, and 16 PVs in the LSPV, LIPV, left common PV, RSPV, and RIPV, respectively. The most frequent site of late reconnection was RIPV bottom, and it was observed in 12 patients. All reconnections were successfully eliminated by a median of 1.0 (1.0–3.0) RF application.

Mapping Data During the Second Procedure
High-resolution mapping was successfully achieved in all 32 patients during the second procedure. The number of electrograms acquired with the multielectrode mapping catheter in the LA was 527±99. The isolation area identified at the antrum of the LSPV, LIPV, RSPV, and RIPV was 5.4±1.2, 4.4±1.1, 4.0±0.9, and 4.1±2.0 cm², respectively (Table 2).

The left-sided isolation area was significantly larger than the right-sided isolation area (9.8±1.7 versus 8.1±2.3 cm²; P=0.002). The mean surface area of the nonablated posterior wall was 17.0±6.1 cm². In total, 48±11% of the posterior LA wall remained electrically intact and unablated. The RIPV antrum isolation area post CB ablation was similar among the 5 PVs, which required touch-up ablation during the initial procedure, and the remaining 27 PVs without touch-up ablation (4.1±1.9 versus 4.1±2.0 cm²; P=0.999). The isolation area of each PV antrum was also similar between the PVs isolated by single applications and those isolated by multiple applications (5.3±1.2 versus 5.7±1.3 cm²; P=0.510 in LSPV, 4.4±1.2 versus 4.6±0.8 cm²; P=0.600 in LIPV, 4.1±1.0 versus 3.6±0.5 cm²; P=0.383 in RSPV, and 4.5±2.0 versus 3.6±1.8 cm²; P=0.181 in RIPV). There was no significant difference in the isolation area of all PV antra (17.3±2.9 versus 16.6±2.6 cm²; P=0.186), the area of intact posterior LA (15.3±5.3 versus 18.8±6.5 cm²; P=0.109), and the ratio of intact posterior LA to total posterior LA (0.46±0.11 versus 0.49±0.11 cm²; P=0.453) between the patients with and without arrhythmia recurrence beyond blanking period.

Comparison of the Isolation Area Between the Different Technologies
The estimated isolation area of each PV antrum after the CPVI was 7.1±1.4, 5.6±1.4, 4.8±1.4, and 4.3±1.5 cm² in the LSPV, LIPV, RSPV, and RIPV, respectively (Table 2).

### Table 1. Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N</th>
<th>Age, y</th>
<th>Paroxysmal AF, n (%)</th>
<th>Female, n (%)</th>
<th>Structural heart disease, n (%)</th>
<th>Hypertension, n (%)</th>
<th>Body mass index, kg/m²</th>
<th>LA diameter, mm</th>
<th>LV ejection fraction, %</th>
<th>Pro-brain natriuretic peptide, pg/mL</th>
<th>PV diameter, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>32</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td>64.8±8.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal AF, n (%)</td>
<td>32 (100)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>10 (31.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Structural heart disease, n (%)</td>
<td>2 (6.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>20 (62.5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.9±2.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA diameter, mm</td>
<td>39.6±5.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>66.3±4.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pro-brain natriuretic peptide, pg/mL</td>
<td>300±478</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Comparison of the Isolation Area After Ablation

<table>
<thead>
<tr>
<th></th>
<th>CPVI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSPV, cm²</td>
<td>5.4±1.2</td>
<td>7.1±1.4</td>
</tr>
<tr>
<td>LIPV, cm²</td>
<td>4.4±1.1</td>
<td>5.6±1.4</td>
</tr>
<tr>
<td>RSPV, cm²</td>
<td>4.0±0.9</td>
<td>4.8±1.4</td>
</tr>
<tr>
<td>RIPV, cm²</td>
<td>4.1±2.0</td>
<td>4.3±1.5</td>
</tr>
<tr>
<td>Left PVs, cm²</td>
<td>9.8±1.7</td>
<td>12.7±2.4</td>
</tr>
<tr>
<td>Right PVs, cm²</td>
<td>8.1±2.3</td>
<td>9.2±2.5</td>
</tr>
<tr>
<td>All PVs, cm²</td>
<td>17.9±2.8</td>
<td>22.0±4.2</td>
</tr>
<tr>
<td>Intact LAPW, cm²</td>
<td>17.0±6.1</td>
<td>12.8±3.5</td>
</tr>
<tr>
<td>Intact LAPW/total LAPW, %</td>
<td>0.48±0.11</td>
<td>0.37±0.06</td>
</tr>
</tbody>
</table>

CPVI indicates circumferential PV isolation; LAPW, left atrial posterior wall; LIPV, left inferior PV; LSPV, left superior PV; PV, pulmonary vein; RIPV, right inferior PV; and RSPV, right superior PV.
The area enclosed by the CPVI line was significantly larger than the isolation area post CB ablation in all PVs except the RIPV. The difference was most prominent at the LSPV antrum (1.7±1.4 cm²), and the isolation area ratio (post CB ablation/post CPVI) at the LSPV antrum was significantly smaller in 10 patients with a funnel-shaped LSPV or common left PV than in the remaining 22 patients (0.67±0.17 versus 0.83±0.15; P=0.017). The left- and right-sided isolation areas after the CPVI were 12.7±2.4 and 9.2±2.5 cm² and were significantly larger than that after the CB ablation (left-sided PVs, P<0.0001; right-sided PVs, P=0.029). On the other hand, the area of the electrically intact posterior LA was significantly

**Figure 4.** A, Four pulmonary veins (PVs) and a short left common PV were identified on preprocedural computed tomography. B, The balloon position during an application to the left superior PV (LSPV) during the initial procedure is shown. C, During the second procedure, atrial fibrillation (AF) initiated from non-PV foci after confirmation of the pulmonary vein isolation. The earliest atrial activation (red arrow) was recorded on the multispline mapping catheter. D, The position of the catheters during non-PV foci mapping is demonstrated. The ablation catheter, multispline mapping catheter, and circular mapping catheter are placed at the posterior left atrium (LA), LA roof, and middle right atrium, respectively. The earliest activation site (red arrow) was identified at the posterior roof close to the left superior PV (LSPV) antrum. E, The white tag (red arrow) indicates the successful ablation site. Voltage mapping showed that the AF foci were located outside the low-voltage area (LVA) created by the cryoballoon but inside the circumferential pulmonary vein isolation line (pink tags). Please also note that the LVA is wide at the right inferior PV (RIPV) antrum. ABL indicates ablation catheter; AP, antero-posterior; CS, coronary sinus; d, distal; os, ostium; p, proximal; PA, postero-anterior; RAm, middle RA; RAs, right atrial septum; RSPV, right superior PV; and SVC, superior vena cava.
smaller after the CPVI than after the CB ablation (12.8±3.5 versus 17.0±6.1 cm²; \(P<0.0001\)).

Among the 32 patients, non-PV foci (site with AF initiation) were identified during the second procedure in 4 patients with arrhythmia recurrence. In 2 patients, arrhythmogenic superior vena cava were identified, and confined superior vena cava fibrillation was observed after the isolation in 1 of 2 patients. In the remaining 2 (6.3%) patients, non-PV foci were identified at the LSPV antrum, which was outside the isolation area created by the CB but inside the CPVI line (Figures 4 and 5). In both patients, no PV reconnections were observed in the LSPV during the second procedure. After the completion of this study, 24 patients (75.0%) were free from recurrent AF without antiarrhythmic drugs during a median follow-up of 7.0 (5.0–9.0) months.

**Discussion**

To the best of our knowledge, this is the first study to assess the isolation area during the chronic phase after a 28-mm second-generation CB ablation using a single 3-minute freeze technique. The isolation area was carefully evaluated.
by high-resolution mapping and also a pacing technique. We found that (1) the isolation area post CB ablation was generally wide (52% of the posterior LA was isolated), (2) the PV antrum isolation area after the CB ablation was smaller than the estimated isolation area after the CPVI in all PVs except the RIPV, (3) the difference in the isolation area was most prominent at the LSPV antrum, especially in patients with funnel-shaped LSPVs or left common PVs, and (4) non-PV foci associated with clinical recurrence were located at the LSPV antrum inside the CPVI line but outside the CB isolation area in 6.3% of the patients.

High-Resolution Isolation Area Mapping With a 3D-Mapping System

With regard to the ablation lesion description and assessment, 3D electroanatomic maps have proven to be useful for measuring ablated areas. However, the mapping resolution is influenced by the electrode size and interelectrode spacing. Anter et al elegantly showed that mapping with small closely spaced electrode catheters could improve the mapping resolution within LVAs and established the normal bipolar voltage criteria in the atria for a multielectrode mapping catheters with 1-mm electrodes. In our study, the isolation area was assessed using the same mapping catheter with small closely spaced electrodes for a precise evaluation. In addition, the electric isolated area was carefully confirmed, especially at the LA borders, by loss of LA capture during pacing from the contact force–sensing catheters.

Isolation Area After PV Isolation

A wide ablation line encircling the entire PV antrum from the LA side targets both AF triggers and the perpetuating substrate. Kiuchi et al elegantly demonstrated that a larger isolation area was associated with a significantly lower AF recurrence rate in RF ablation. On the contrary, the CB catheter is an anatomically based ablation device that allows for a simplified PVI. The isolation line can be designed tailored in point-by-point RF ablation but not in CB ablation. The evaluation of the isolated area during the chronic phase seems to be essential for further discussion of high success rates after second-generation CB ablation in patients with paroxysmal AF.

Recently, a single big-balloon technique has become the standard technique in CB ablation because the large freezing surface area of the second-generation CB enables covering both small and large PVs in addition to the ability to create antral lesion sets and reduces PV stenosis. Furthermore, more recent clinical and experimental studies showed that single 3-minute freeze techniques, without bonus applications, are effective and acceptable approaches in achieving acute PVI and an AF freedom of >80% at 1-year follow-up. Longer applications (4 minutes×2 times) allow a high durability of the PVI (91%); however, they lead to a high incidence of serious complications (3/21 patients). Given the data, a single 3-minute freeze technique seems to be a reasonable strategy when using second-generation CBs. However, further studies are required to discuss the optimal dose of cryoapplication.

Isolation Area of Each PV Antrum After Cryoballoon Ablation

A few studies, which evaluated the isolation area during the acute phase post CB ablation, have been previously reported. Chierchia et al examined 8 patients who underwent 5-minute applications×2 times using 23-mm and 28-mm first-generation CBs. Reddy et al examined 8 patients who underwent 4-minute applications using 23-mm first-generation CBs. More recently, Kenigsberg et al investigated 43 patients who underwent 3-minute applications×2 times using 28-mm second-generation CBs and clarified that the area of the posterior LA wall ablation with CB catheters was wide and antral during the acute phase. The main difference in this study from the published studies is that the isolation area was evaluated (1) during the chronic phase, (2) with high-resolution mapping and pacing techniques, (3) at each PV antrum separately, (4) that ablation was performed with single big (28-mm) balloon 3-minute freeze techniques, and (5) that the isolation area was compared with the conventional CPVI ablation line.

Although the isolation area post CB ablation was wide in our study, the posterior LA isolation rate was smaller than the previously reported data during the acute phase. It might be explained by the hypothesis that the edematous area might appear in the LVA during the acute phase, and by the different study populations between the index and repeat procedures, and different number of CB applications. This study also clarified the different isolation areas of each PV antrum between CB ablation and CPVI. Because of the spherical nature of the CB and size mismatch of the balloon to the PV orifice, the CB ablation area highly depends on the patient LA anatomy. The isolation area was similar at the RIPV antrum, whereas it was significantly smaller post CB ablation than after CPVI at the other 3 PV antra, especially the LSPV antrum. The results are in line with the results of a previous study that when measuring the distance from the PV to the ablation edge, the RIPV had a statistically longer mean distance than the other 3 PVs. Indeed, pushing large balloons deep inside the RIPV is generally challenging. At the LSPV antrum, this different proximity of the isolation area post CB ablation was further emphasized, that is, it was significantly smaller in patients with funnel-shaped LSPVs or common left PVs than the remaining LSPVs. It is likely that CBs are located more distal to obtain a complete occlusion in funnel-shaped LSPVs than other LSPVs. The remaining unablated PV antra could be associated with AF recurrence. Indeed, AF sources associated with clinical recurrences were identified at the LSPV antrum outside the CB isolation area but inside the CPVI line in 2 patients. The 2 cases highlighted the importance of the LA antrum isolation area, and this difference in the isolation area might potentially impact the clinical outcome after the procedure. Although a second-generation CB ablation enables a high success rate presumably because of the high durability of the PVI, it seems important to recognize that CB ablation cannot eliminate AF sources originating from LSPV antra. We think that ablation strategy should be discussed based on the PV anatomy obtained by preprocedural cardiac computed tomography. Additional CB applications at the LSPV antrum might be an alternative approach to reduce such arrhythmia recurrences.
Study Limitations
The study was a single-center nonrandomized study, and the population was relatively small. Prospective randomized study is required to confirm our results in comparing the isolation area between 2 different techniques. However, we performed the comparison in the same population because the anatomy of PVs is highly variable between the patients. The isolation area during the acute phase was not evaluated because additional mapping catheters and 3D-mapping systems are required for this purpose. In cases with PV reconnections, reisolation was performed before creating voltage maps to avoid the risk of mechanical bump during mapping. However, this impact seems to be minimized because the vast majority of the reconnected PVs were isolated by single-point RF applications.

Conclusions
The isolated area during the chronic phase after the second-generation CB ablation with single big-balloon 3-minute freeze techniques is generally wide. However, when compared with the CPVI ablation line, the PV antrum isolated area post CB ablation was significantly smaller except the RIPV antrum. The difference in the isolation area was most prominent at the LSPV antrum, which could be associated with AF recurrence.

Acknowledgments
We thank John Martin and Ashok J. Shah for their help in the preparation of this article.

Disclosures
None.

References


Quantitative Analysis of the Isolation Area During the Chronic Phase After a 28-mm Second-Generation Cryoballoon Ablation Demarcated by High-Resolution Electroanatomic Mapping
Shinsuke Miyazaki, Hiroshi Taniguchi, Hitoshi Hachiya, Hiroaki Nakamura, Takamitsu Takagi, Jin Iwasawa, Kenzo Hirao and Yoshito Iesaka

Circ Arrhythm Electrophysiol. 2016;9:e003879
doi: 10.1161/CIRCEP.115.003879

Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2016 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circep.ahajournals.org/content/9/5/e003879

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Arrhythmia and Electrophysiology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Arrhythmia and Electrophysiology is online at:
http://circep.ahajournals.org//subscriptions/