

# Characterization of conduction recovery after pulmonary vein isolation using the “single big cryoballoon” technique

Alexander Fürnkranz, MD,\*<sup>†</sup> K. R. Julian Chun, MD,\* Dieter Nuyens, MD, PhD,\* Andreas Metzner, MD,\* Ilka Köster, MD,\* Boris Schmidt, MD,\* Feifan Ouyang, MD,\* Karl-Heinz Kuck, MD\*

From the \*Department of Cardiology, Asklepios Klinik St. Georg, Hamburg, Germany, and <sup>†</sup>Department of Cardiology, Wilhelminenhospital, Vienna, Austria.

**BACKGROUND** Pulmonary vein isolation using the cryoballoon technique (CB-PVI) has evolved into a simple and safe alternative for point-by-point radiofrequency ablation. Systematic analysis of conduction recovery occurring after CB-PVI and causing recurrent atrial fibrillation has not yet been performed.

**OBJECTIVE** The purpose of this study was to analyze conduction recovery after PVI using the single big (28-mm) cryoballoon technique.

**METHODS** Twenty-six patients with recurrent atrial tachyarrhythmia after previous CB-PVI underwent repeat ablation. Pulmonary vein (PV) re-isolation was performed by antral irrigated radiofrequency ablation using electroanatomic mapping. For analysis of the location of conduction gaps, the ipsilateral LA–PV junction was divided into six equally distributed segments.

**RESULTS** PV re-conduction frequently occurred into multiple (>2) PVs (54% patients). Conduction gaps could be abolished by single point ablation in 63% (lateral) and 41% (septal) of patients or by incomplete circular lesions in the remaining patients. A significantly higher number of patients exhibited conduction recovery at inferior segments (85% lateral, 77% septal) compared with superior segments (42% lateral, 31% septal). Furthermore, the ridge between PV ostia and left atrial appendage (LAA) was highly

associated with re-conduction into lateral PVs (81% of patients). Retrospective analysis of the initial CB-PVI-procedure revealed lower freezing temperatures at superior than inferior PVs as well as sharp catheter angulations with loss of central cryoballoon alignment to reach inferior PVs.

**CONCLUSION** Conduction recovery after CB-PVI occurs at a high incidence at inferior sites around ipsilateral PV ostia and the LAA–PV ridge. Modifications of the technique to ensure optimal balloon–tissue contact at predilection sites may improve long-term success rates.

**KEYWORDS** Arrhythmia; Atrial fibrillation; Balloon; Catheter ablation; Cryothermal energy

**ABBREVIATIONS** AF = atrial fibrillation; CB = cryoballoon; LA = left atrium; LAA = left atrial appendage; LAT = left atrial tachycardia; LCPV = left common pulmonary vein; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; PAF = paroxysmal atrial fibrillation; PV = pulmonary vein; PVI = pulmonary vein isolation; RFC = radiofrequency current; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein (Heart Rhythm 2010;7:184–190) © 2010 Published by Elsevier Inc. on behalf of Heart Rhythm Society.

## Introduction

Complete pulmonary vein isolation (PVI) from the left atrium (LA) has become the cornerstone of ablative therapy in patients with paroxysmal atrial fibrillation (PAF).<sup>1</sup> Cryoballoon (CB) ablation is an emerging technology with the potential to simplify this complex procedure and lacks some of the potential serious complications associated with radiofrequency current (RFC) PVI, such as pulmonary vein (PV) stenosis.<sup>2–5</sup> We recently showed that CB-PVI can be performed successfully with exclusive use of a 28-mm balloon.<sup>2</sup> However, as with conventional PVI using RFC,<sup>6</sup> PV

re-conduction may lead to recurrent atrial fibrillation (AF) after CB-PVI.<sup>7</sup> Long-term outcome data of this relatively new technique are lacking.

In contrast to sequential point-by-point ablation by an RFC catheter, the cryoballoon technique consists of simultaneous energy deployment at the LA–PV junction; thus, PVI often can be achieved by a single cryothermal energy application.<sup>2</sup> Although this concept is technically attractive, it also implies that energy deployment cannot be varied along the resulting cryolesion. Such energy variation would be desirable at regions of enhanced muscular thickness, such as the ridge between the lateral PVs and the left atrial appendage (LAA). Moreover, cryoballoon ablation requires continuous tissue contact because convective heating by intervening blood flow or insulating ice formation interferes with tissue freezing.<sup>8</sup>

We hypothesized that areas of re-conduction after CB-PVI are not randomly distributed around the PV ostia but are preferentially located at sites prone to poor balloon–

Dr. Kuck is consultant to CryoCath and has received research grants and honoraria for CryoCath educational lectures. Dr. Chun has received honoraria for CryoCath educational lectures. **Address reprint requests and correspondence:** Dr. Alexander Fürnkranz, Department of Cardiology, Asklepios Klinik St. Georg, Lohmühlenstr. 5, 20099 Hamburg, Germany. E-mail address: a.fuernkranz@gmail.com. (Received September 23, 2009; accepted October 31, 2009.)

tissue contact and/or with enhanced muscular thickness. Knowledge of such areas may be the basis for improved cryoballoon technique and long-term success. The aim of this study was to investigate conduction recovery after CB-PVI using the “single big (28-mm) cryoballoon” technique.

## Methods

### Patients

Between April 2006 and November 2008, 71 patients underwent CB-PVI for highly symptomatic PAF using the single big (28-mm) cryoballoon technique.<sup>2</sup> One bonus cryoballoon application per vein was performed after PVI had been achieved. All patients continued taking the previously ineffective antiarrhythmic drugs, which were discontinued after 1 month if no recurrent AF or left atrial tachycardia (LAT) occurred after the initial ablation procedure.

Thirty-five patients had either recurrent PAF (32 patients [45%]) or LAT (3 patients [4%]) after the initial procedure during a median (Q1;Q3) follow-up of 189 days (68;298) without a blanking period. The first episode of recurrent PAF/LAT occurred 21 days (8;88) after the CB-PVI procedure. Nine patients who had short episodes of AF that were well controlled with antiarrhythmic drugs refused a second procedure.

A repeat procedure was performed in 26 patients with symptomatic recurrent PAF (23 patients) or LAT (3 patients) after a median (Q1;Q3) of 144 (57;217) days following initial CB-PVI. These patients constitute the basis of the current study. The right inferior pulmonary vein (RIPV) could not be isolated at the CB-PVI procedure in 2 of these patients. Patient characteristics are listed in Table 1, and procedural parameters of initial CB-PVI are listed in Table 2.

### Mapping and catheter ablation

The reablation procedure was performed with patients under sedation with continuous propofol infusion.<sup>6</sup> Two 8Fr SL1-sheaths (St Jude Medical, St. Paul, MN, USA) were advanced to the LA via a modified Brockenbrough technique. Intravenous heparin was administered to maintain an activated clotting time of 250 to 300 seconds. One or two decapolar Lasso catheters (Biosense Webster, Diamond Bar, CA, USA) were placed within the left-sided or right-sided ipsilateral PVs to confirm recovery of PV conduction. Three-dimensional electroanatomic mapping (CARTO XP, Biosense

**Table 2** Procedural parameters of initial cryoballoon pulmonary vein isolation

Vein	Diameter (mm)	No. of applications
Left superior pulmonary vein	20 ± 3	2.8 ± 0.9
Left inferior pulmonary vein	19 ± 3	3.2 ± 1.4
Left common pulmonary vein	30 ± 4	5.1 ± 3.6
Right superior pulmonary vein	19 ± 3	2.4 ± 0.8
Right inferior pulmonary vein	18 ± 3	4.1 ± 2.1
Procedural time (min)	219 ± 47	
Fluoroscopy time (min)	46 ± 20	

Webster) of the LA and selective PV angiograms were performed to identify all PV ostia. If discrete PV potentials were recorded in both of the ipsilateral PVs or branches of a common PV, one Lasso catheter was placed in the PV or branch with the earliest PV potential during ablation. Ablation (ThermoCool Navi-Star, Biosense Webster) was started at the antral level of the LA–PV junction at the site of the earliest PV potential. Irrigated RFC energy was delivered with a target temperature of 43°C, maximal power limit of 30 W (posterior LA) or 40 W (anterior LA), and infusion rate of 17 mL/min.

For analysis of the location of conduction gaps, the ipsilateral LA–PV junction was divided into six equally distributed segments (superior, anterosuperior, anteroinferior, inferior, posteroinferior, posterosuperior; Figure 2). The response to ablation at the initial segment was classified as PV reisolation (pattern 1), PV activation sequence change as recorded by the Lasso catheter (pattern 2), or no change (pattern 3). In case of PV reisolation, the ablation region was tagged on the electroanatomic map and the respective segment defined to contain a conduction gap. In case of PV activation sequence change, the respective segment was defined to contain a conduction gap, and ongoing PV conduction was attributed to an additional gap, which was ablated in a similar fashion (Figure 1A). If ablation at the initial segment did not affect PV conduction, ablation was continued in a circular fashion around the ipsilateral PV ostia guided by the earliest PV potential. An effort was made to achieve reisolation with the shortest antral ablation line (Figure 1B). Any of six antral segments around the ipsilateral PVs was defined as contributing to reconnection if PV reisolation necessitated ablation at the respective segment (Figure 2).

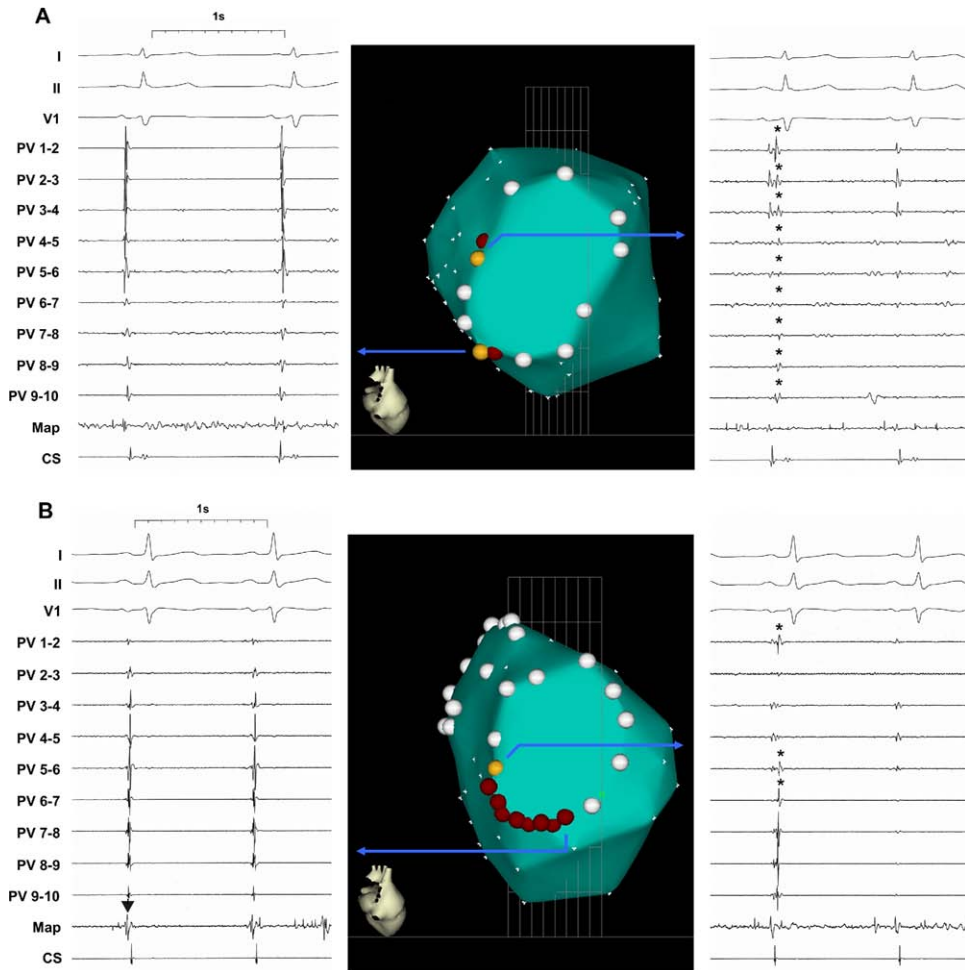
The procedural end-point was defined as (1) the absence of PV potentials documented with the Lasso catheter within all PVs at least 30 minutes after isolation and (2) no inducible atrial tachycardia after ablation in patients who presented with atrial tachycardia after initial CB-PVI.

### Postablation care and follow-up after redo procedure

In all patients, pericardial effusion and pneumothorax were ruled out (transthoracic echocardiogram, chest X-ray film) after the procedure. After ablation, patients were treated

**Table 1** Baseline characteristics of the study patients (n = 26)

Age (years)	59 ± 10
Male (n)	16 (62%)
Paroxysmal atrial fibrillation	26 (100%)
Hypertension (n)	14 (54%)
No. of failed antiarrhythmic drugs (n)	2 ± 1
Duration of atrial fibrillation (years)	8 ± 6
Left atrial diameter (mm)	43 ± 6



**Figure 1** Reisolation of the septal pulmonary veins (PVs) in patients no. 2 and 16. Anatomic CARTO maps in the right lateral view and recordings from surface ECG leads I, II, and V<sub>1</sub>, Lasso recordings from the right inferior pulmonary vein (PV1-2 to PV9-10), and recordings from distal mapping (Map) and coronary sinus (CS) catheters are shown. *Yellow point tags* in the CARTO maps correspond to loci of PV activation sequence change or PV isolation during ablation (*brown point tags*) as indicated by *arrows*. **A:** Sudden activation sequence change in the PV potentials recorded by Lasso catheter (*left*) indicates block of an inferior gap. Subsequent mapping and ablation revealed a second posteroinferior gap with reisolation of the right inferior PV (*right*) during ablation, as indicated by elimination of the PV potential (*asterisk*). **B:** Reisolation of the right inferior PV by linear ablation at the inferior antral segment. At the start of ablation (*left*), early PV activation is recorded by the mapping catheter (*arrowhead*). Reisolation occurred posteriorly (*right*) without prior activation sequence change, as indicated by elimination of the PV potential (*asterisk*).

with intravenous heparin (target partial thromboplastin time 50–70 seconds). Phenprocoumon was started the next day, targeting an international normalized ratio of 2.0–3.0 for at least 3 months. Previous antiarrhythmic therapy was continued for 1 month and then discontinued if patients were free of AF/LAT relapse. Surface ECG and 24-hour Holter ECG recording were performed 1 day after the procedure and repeated after 1, 3, 6, and 12 months or upon symptoms suggestive of recurrent AF/LAT. Recording was performed by the referring physician or in the ablation center. The clinical end-point was defined as the first documented AF/LAT episode  $\geq 30$  seconds in duration.

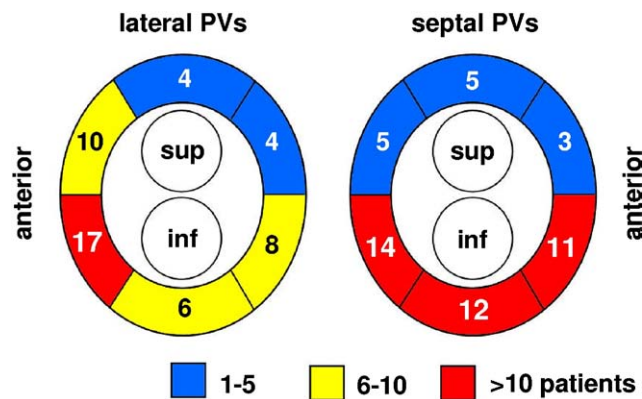
**Temperature monitoring at initial CB-PVI**

Cryoballoon temperature–time curves during each freeze were acquired using CryoConsole software (CryoCath Technologies, Montreal, Quebec, Canada). The temperature sensor is located in the back of the balloon and thus pro-

vides a rough estimate of tissue temperature near the balloon. The minimal temperature for a PV was defined as the lowest balloon temperature achieved during any freeze at that vein. Data from the superior and inferior branches of a left common pulmonary vein (LCPV) were included in the left superior pulmonary vein (LSPV) or left inferior pulmonary vein (LIPV) group, respectively, if the branches were isolated separately (5/7 LCPVs).

**Analysis of balloon catheter positions at initial CB-PVI**

To overcome the force exerted by PV blood flow, the balloon catheter must be pushed onto the PV ostium in order to achieve or maintain tissue contact. This is easiest to accomplish if the sheath, balloon, and guidewire are in direct alignment because the sheath and balloon catheter can be used in concert to create a strong pushing force (Figure 3A). To

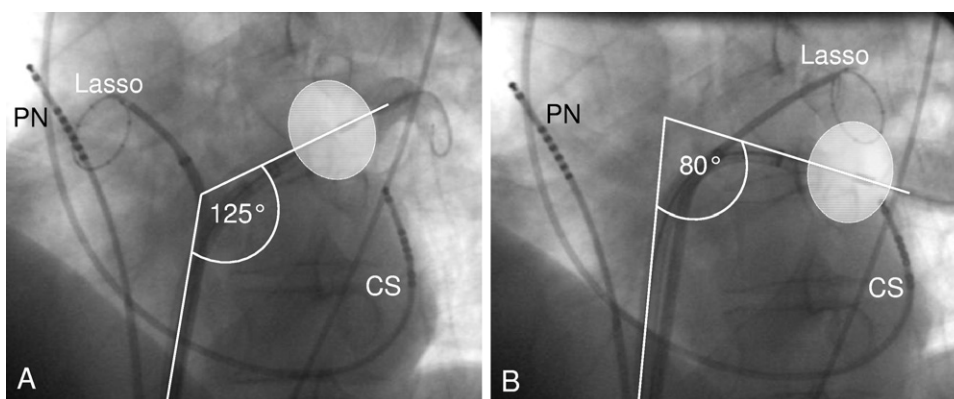


**Figure 2** Location of pulmonary vein (PV) reconduction after cryoballoon PV isolation. Lateral and septal PV ostia are shown in the posteroanterior view. Any of six antral segments around the ipsilateral PVs was defined as contributing to reconduction if PV re-isolation necessitated ablation at the respective segment. Numbers represent number of patients. Significantly more patients exhibited reconduction at inferior than at superior segments for both lateral and septal PVs. In addition, the left atrial appendage–PV ridge was a frequent site of reconduction at lateral PVs.

quantify the degree of deflection of the sheath/balloon system at individual PVs during initial CB-PVI, the angle between the catheter tip bearing the balloon and the proximal transseptal sheath (angle of alignment) was retrospectively analyzed from angiograms recorded before freezing (Figure 3) in the right anterior oblique 30° view for septal PVs or in the left anterior oblique 40° view for lateral PVs (or superior and inferior branches of an LCPV).

### Statistical analysis

Data are given as mean  $\pm$  SD or median and 25th and 75th percentiles (Q1;Q3) where appropriate. The Friedman test and exact method was used to compare predefined segments of septal or lateral PV ostia with respect to reconduction. Continuous variables were evaluated using the Student's t-test.  $P < .05$  was considered significant.



**Figure 3** Analysis of catheter position at cryoballoon pulmonary vein (PV) isolation. Radiographs in the left anterior oblique 40° projection are shown. Contrast medium had been injected via the balloon tip to ensure occlusive position at the PV ostium. **A:** Balloon catheter at the left superior PV shortly before freezing. The angle between the shaft of the transseptal sheath and the balloon center is 125°. The Lasso catheter is in the right superior PV. **B:** Balloon catheter at the left inferior PV before freezing. The angle between the transseptal sheath and balloon is 80°. The Lasso catheter is in the left superior PV. CS = coronary sinus catheter; PN = diagnostic catheter placed at phrenic nerve capture site in superior caval vein.

### Results

Of the 26 study patients, 18 were in sinus rhythm, 3 were in AF, 3 presented with LAT, and 2 presented with common-type atrial flutter at the time of the second procedure. The 2 patients who presented with atrial flutter also exhibited documented episodes of AF. In the patients with AF or atrial flutter, sinus rhythm was restored by external cardioversion or cavotricuspid isthmus ablation at the beginning of the procedure, respectively. In the 3 patients with LAT, mapping and ablation of LATs were performed prior to PV re-isolation.

Among the 3 patients with LAT, three-dimensional and entrainment mapping demonstrated an LA macroreentrant tachycardia around the mitral annulus in 2. RFC energy ( $6.3 \pm 0.6$  applications) was delivered between the left-sided PVs and the mitral annulus, with termination of the tachycardia and bidirectional block of the mitral isthmus. In 1 patient, three-dimensional mapping demonstrated a focal atrial tachycardia originating from the posteroinferior LA 15 mm distant to the LIPV ostium. A single RFC application terminated the tachycardia and resulted in noninducibility.

### Recovered PV conduction during sinus rhythm

In the 26 patients, a total of 97 PVs were identified, with an LCPV in 7 patients. LA–PV conduction was demonstrated in 67 PVs. In most patients, multiple PVs exhibited reconduction: 4 PVs in 5 (19%) patients, 3 PVs in 9 (35%), 2 PVs in 8 (31%), and a single PV in 4 (15%). With regard to individual PVs, recovered PV conduction was present in 19 (79%) of 24 RIPVs (excluding 2 patients in whom the RIPV could not be isolated at initial CB-PVI), 15 (79%) of 19 LIPVs, 12 (63%) of 19 LSPVs, 12 (46%) of 26 right superior pulmonary veins (RSPVs), and 7 (100%) of 7 LCPVs.

At septal PVs, the response to a single ablation at the initial segment was pattern 1 (isolation) in 4 patients and pattern 2 (sequence change and additional gap) in 5 patients.

In the latter patients, a single RFC application abolished the remaining gap (Figure 1A). Thirteen patients exhibited pattern 3 (no change), and short antral linear ablation involving more than one segment was needed in order to achieve reisolation (Figure 1B). In the remaining 4 patients, both septal PVs were isolated. Average RFC lesion length was  $25 \pm 24$  mm.

At lateral PVs, pattern 1 was observed in 12 patients and pattern 2 in 3 patients, with one (2 patients) or two (1 patient) additional gaps abolished by a single RFC application. Nine patients exhibited pattern 3. In the remaining 2 patients, both lateral PVs were isolated. Average RFC lesion length was  $20 \pm 26$  mm.

Total procedural time and radiation time were  $150 \pm 53$  minutes and  $18 \pm 9$  minutes, respectively. No procedure-related complications occurred.

### Location of PV reconnection

In septal PVs, reisolation was most often achieved by antral ablation at inferior locations (Figure 2), involving inferior and anteroinferior segments in 12 (46%) and 11 (42%) of 26 patients, respectively, and posteroinferior segments in 14 (54%) of 26 patients. In contrast, ablation was performed at superior and posterosuperior segments in 5 (19%) of 26 patients and at anterosuperior segments in 3 (12%) of 26 patients ( $P = .001$  for comparison between all segments).

In lateral PVs, the anterior aspect of the LA–PV junction (“ridge”) most often contributed to PV reconnection, necessitating ablation of anteroinferior segments in 17 (65%) of 26 patients and anterosuperior segments in 10 (38%) of 26 patients. Posteroinferior segments were ablated in 8 (31%) of 26 patients, inferior segments in 6 (23%) of 26 patients, and superior and posterosuperior segments in 4 (15%) of 26 patients ( $P = .002$  for comparison between all segments).

In summary, ablation at any inferior segment was performed in 77% (septal) and 85% (lateral) of patients, as opposed to superior segments in 31% (septal) and 42% (lateral) of patients.

### Temperature monitoring at initial CB-PVI

Retrospective analysis of minimal balloon temperatures achieved during initial CB-PVI revealed significantly lower temperatures at superior PVs (or superior branch of an LCPV) compared with inferior PVs (or inferior branch of an LCPV) for both septal ( $-50^\circ\text{C} \pm 7^\circ\text{C}$  vs  $-40^\circ\text{C} \pm 6^\circ\text{C}$ ;  $P < .001$ ) and lateral ( $-49^\circ\text{C} \pm 7^\circ\text{C}$  vs  $-43^\circ\text{C} \pm 4^\circ\text{C}$ ;  $P = .004$ ) PVs. When separating PVs into those with and those without isolation at the reablation procedure, minimal temperatures during initial CB-PVI were as follows: LSPV:  $-50.4^\circ\text{C} \pm 2.9^\circ\text{C}$  (isolated) versus  $-48.6^\circ\text{C} \pm 8.6^\circ\text{C}$  (not isolated,  $P = \text{NS}$ ); LIPV:  $-47.0^\circ\text{C} \pm 3.5^\circ\text{C}$  versus  $-42.1 \pm 3.5$  ( $P = \text{NS}$ ); RSPV:  $-51.9^\circ\text{C} \pm 6.4^\circ\text{C}$  versus  $-46.3^\circ\text{C} \pm 5.8^\circ\text{C}$  ( $P = .038$ ); and RIPV:  $-39.6^\circ\text{C} \pm 4.2^\circ\text{C}$  versus  $-40.7^\circ\text{C} \pm 6.4^\circ\text{C}$  ( $P = \text{NS}$ ). The mean number of cryothermal energy applications at initial CB-PVI according to these groups were as follows: LSPV:  $2.7 \pm 0.8$  (isolated) versus  $3.0 \pm 1.0$  (not isolated,  $P = \text{NS}$ ); LIPV:  $3.3 \pm 1.5$  versus  $3.1 \pm$

$1.5$  ( $P = \text{NS}$ ); RSPV:  $2.5 \pm 0.6$  versus  $2.3 \pm 1.1$  ( $P = \text{NS}$ ); and RIPV:  $3.6 \pm 1.3$  vs.  $4.2 \pm 2.3$  ( $P = \text{NS}$ ).

### Analysis of catheter positions at initial CB-PVI

Retrospective analysis of the angle of alignment representing the degree of deflection of the sheath/balloon system at individual PVs during initial CB-PVI was performed. For inferior PVs this angle was significantly smaller, that is, the degree of deflection was higher compared to that of superior PVs (RIPV:  $85^\circ \pm 18^\circ$  and RSPV:  $121^\circ \pm 23^\circ$ ,  $P < .001$ ; LIPV:  $94^\circ \pm 20^\circ$  and LSPV:  $129^\circ \pm 28^\circ$ ,  $P < .001$ ), resulting in loss of central balloon alignment (Figure 3).

### Follow-up

During a median (Q1;Q3) follow-up of 98 days (39;283) without a blanking period, 18 (69%) of 26 patients remained free of recurrent AF or LAT. Four patients had improved symptoms that were well controlled with antiarrhythmic drugs.

Four patients underwent further ablation due to ongoing episodes of AF: One patient exhibited total PV isolation at the time of the second redo procedure, and a non-PV trigger was identified in the superior caval vein and subsequently isolated. In the remaining 3 patients, AF recurrence was again associated with PV reconnection (intervals between first and second redo: 296, 538, and 283 days). In 2 patients, conduction gaps identified at the second redo procedure were unrelated to those found at the first redo procedure and were located at the anterior ridge at lateral PVs. In the third patient, the second redo procedure was performed at another center (reisolation of RIPV and LSPV), and no information regarding the location of PV conduction gaps was retrievable.

### Discussion

The main findings of this study were as follows. (1) In patients with PAF, the dominant recurrent atrial tachyarrhythmia after CB-PVI was AF. The incidence of LAT following CB-PVI was low. (2) Recurrent AF after CB-PVI was associated with LA–PV reconnection. Conduction gaps after CB-PVI using the single big cryoballoon technique occurred at a high incidence at the inferior LA–PV junction and the anterior ridge between PVs and LAA. (3) These conduction gaps could be eliminated by RFC ablation using electroanatomic mapping, with low procedural and radiation times.

### Recurrent atrial tachyarrhythmia after CB-PVI

The majority of patients in this study presented with PAF as the recurrent arrhythmia. LAT was observed in only 3 patients after initial CB-PVI (4% of total CB-PVI cohort). In these patients, perimitral flutter was found in 2 and a non-PV focal tachycardia in 1. Thus, PV tachycardia was not observed following CB-PVI, whereas PV tachycardia was a common finding in patients with recurrent atrial tachyarrhythmia after PVI using RFC-induced circular linear lesions.<sup>9</sup> The underlying cause of this difference is not

known. Histologic study has shown that cryolesions are well circumscribed with sharp borders, whereas RFC lesions are less clearly demarcated from normal myocardium.<sup>10</sup> This may constitute a difference with respect to creation of a reentrant substrate.<sup>6</sup>

### Predilection sites for LA–PV reconnection

The inferior segments of the LA–PV junction were most often affected by reconnection (Figure 2). For septal PVs, this resulted in reconnection of 79% of inferior PVs compared with 46% of superior PVs. For lateral PVs, the inferior ridge between LAA and PV ostia (anteroinferior segment) was the most common site for PV reconnection, followed by the superior ridge (anterosuperior segment). This may be due to enhanced muscle thickness at this structure. The frequent involvement of the superior ridge may have contributed to the relatively high rate of reconnection (63%) into the LSPV. Moreover, a venous “cross-talk” phenomenon is often observed during CB-PVI at lateral PVs, whereby isolation of ipsilateral PVs occurs simultaneously during freezing at the LIPV when initial freezing at the LSPV failed to achieve PVI due to residual conduction between the veins.<sup>2</sup>

A high incidence of inferior conduction gaps may result from a number of causes. When freezing is performed at inferior PVs, central alignment of the cryoballoon at the PV ostium often is not possible because the sheath/balloon system must be deflected in order to reach the target structure. This results in a smaller angle of alignment during CB-PVI of inferior compared to superior PVs (Figure 3). Consequently, at superior PVs, both sheath and balloon can be used to create a strong push onto the PV ostium to overcome PV blood flow, whereas at inferior PVs only the balloon catheter can be pushed through the deflected sheath, likely impacting on contact force. This may lead to incomplete balloon–tissue contact around inferior PVs. In support of this hypothesis is the observation that more balloon applications were needed to achieve isolation of inferior than superior PVs (Table 2).<sup>2</sup> Residual blood flow has been demonstrated to occur during the course of a cryoballoon application, even when the balloon occluded the PV ostium at the initiation of freezing.<sup>11</sup> It can be assumed that cryolesions created with poor tissue–balloon contact may acutely lead to PV isolation while being prone to later conduction recovery.

Another possible impact of the lack of central alignment of the cryoballoon on lesion quality is a temperature gradient from equator to distal pole of the balloon, with deepest temperatures just in front of the equator caused by injection of the refrigerant to this area. This could preferentially affect inferior sites around ipsilateral PV ostia, because at typical balloon positions for inferior PVs (small angle of alignment) this region is adjacent to the cryoballoon pole (Figure 3B).

The chronic course of cryoballoon-induced lesions is not well known. This study cohort included 2 patients who exhibited consecutive unrelated conduction gaps at the sec-

ond and third ablation procedures. This finding implies that areas of reconnection had been formed after 46 and 149 days (interval between CB-PVI and first redo), respectively, demonstrating that conduction recovery may occur late in the course of a cryolesion.

### Implications for the cryoballoon technique

The study data favor improved techniques to ensure good lesion quality at inferior sites around ipsilateral PVs as well as at the LAA-PV ridge. This can be achieved by repeated freezing with optimal balloon contact to these segments after successful PVI.

In light of the high incidence of inferior conduction recovery, a safety application at inferior PVs with central alignment and perfect contact to the inferior PV circumference should be considered, regardless of possible remaining leakage at the superior PV circumference. This may be of special importance when a “pull-down” maneuver was initially used to isolate an inferior PV, where freezing was started at the superior PV circumference, followed by pulling down the attached balloon to close an inferior gap.<sup>2</sup> During this maneuver, ice formation before pulling down may impact on lesion quality at the inferior PV circumference. Whether such modifications will lead to improved long-term success requires further investigation.

In principle, the cryoballoon technique could be used to close conduction gaps at redo procedures after initial CB-PVI.<sup>4,7</sup> However, the high incidence of multiple reconducting PVs with frequent involvement of the technically more demanding inferior PVs would result in long procedural and, more importantly, radiation times. Moreover, the predilection sites for conduction gaps would also apply for the second procedure. This may explain our observation of a higher success rate after the second procedure compared to reports of repeat CB-PVI.<sup>7</sup> On the other hand, use of conventional RFC energy in conjunction with electroanatomic mapping results in PV reconnection with low radiation exposure. Of note, the procedure times reported for this study include 3 cases of mapping and ablating atrial tachycardia before PV reconnection.

### Relation of initial CB-PVI parameters to reconnection

The minimal temperature measured inside the balloon was shown to be a determinant of chronic PV isolation after CB-PVI in an experimental study.<sup>8</sup> Lower freezing temperatures have been associated with deeper cryolesions.<sup>10</sup> Retrospective analysis of minimal balloon temperatures at initial CB-PVI in our study patients revealed lower temperatures for superior than inferior PVs. This could result from poor balloon–tissue contact at inferior PVs or from local hemodynamic differences, such as covering of the balloon by the LA roof. Moreover, for all but the RIPV, minimal temperatures achieved at CB-PVI were lower at those veins where PV isolation was found at the redo procedure than at reducting veins. However, this difference reached statistical significance only for RSPVs. This may be due to (1) a low

number of patients (e.g., data from RIPV with ongoing isolation represent only 5 cases); (2) a high incidence of “crossover” isolation of lateral PVs,<sup>2</sup> indicating considerable overlap of cryoballoon-induced lesions; or (3) the position of the temperature probe in the back of the balloon, which provides only a rough estimate of tissue temperatures. Thus, the intriguing possibility that modifications of the current technique to achieve lower balloon temperatures will improve long-term success deserves further investigation.

A higher number of cryothermal energy applications at individual PVs was not associated with ongoing PV isolation in this study. Rather, repeat applications necessary to achieve PVI may indicate difficulties in accessing a PV with the cryoballoon, possibly impacting on lesion quality. Whether more than one “bonus” application enhances durability of CB-PVI requires additional study.

### Study limitations

This study has several limitations. Our findings were obtained with the cryoballoon technique using only the 28-mm balloon.<sup>2</sup> Different cryoballoon techniques may exhibit varying predilection sites for conduction recovery. Apart from angiography, no additional visualization of balloon–tissue contact, such as transesophageal ultrasound, was used. Furthermore, no attempt was made to map in detail the level of the previous cryolesions.<sup>12</sup> This may account for the need for more extensive antral ablation to achieve PV re-isolation in many patients in this study. Finally, the study data suggest that use of RFC ablation in conjunction with electroanatomic mapping after initial CB-PVI is associated with a high success rate compared to reports of repeat CB-PVI.<sup>7</sup> However, a randomized study would be necessary to clarify this issue.

### Conclusion

Conduction recovery after cryoballoon PVI using the single big (28-mm) balloon technique occurs at a high incidence at

inferior locations around ipsilateral PV ostia and at the ridge between the lateral PVs and the LAA. Modifications of the cryoballoon technique to ensure optimal wall contact at predilection sites for reconduction and achieve lower balloon temperatures may improve long-term success rates.

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