CLINICAL RESEARCH
Ablation for Atrial Fibrillation

The distance between the vein and lesions predicts the requirement of carina ablation in circumferential pulmonary vein isolation

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Aims
Additional ablation in the pulmonary vein (PV) carina region is sometimes required to achieve electrical isolation following circumferential pulmonary vein isolation (PVI). This study investigated the procedural predictors for the requirement of additional carina ablation to achieve complete electrical isolation with PVI.

Methods and results
Eighty patients with drug-refractory paroxysmal AF underwent circumferential PVI. After the first round of PVI, we placed circular catheters inside the veins to identify the residual PV potentials, and also performed electroanatomic mapping to observe the earliest activation sites during sinus rhythm. The requirement of an additional gap and carina ablation, and the optimal distance that predicted an incomplete PV block were assessed. In the first 40 patients, 43% of the ipsilateral PVs were electrically isolated after the initial PVI. Subsequent ablation of the gaps and ablation of the carina were required in the remaining 57% PVs. The only predictor of the requirement of carina ablation was the mean distance between the lesion-related scar and the ostia (P = 0.03). The longer the distance from the isolating lesions to the PV ostia (>8 mm) predicted an incomplete PV isolation after the first round of circumferential isolation. In the next 40 patients, a fixed distance of 8 mm to the PV ostia decreased the requirement of a carina ablation and resulted in a shorter procedure time (P < 0.05).

Conclusions
This study indicated the importance of complete linear lesions and additional carina ablation when the wide area circumferential PV isolation was applied.

Keywords
Atrial fibrillation • Catheter ablation • Left atrium • Pulmonary vein

Introduction
Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia.1 The pulmonary veins (PVs) are a dominant source of triggers initiating AF. In recent years, circumferential PV isolation has become the mainstream catheter ablation technique for AF.2,3 According to the consensus document, complete electric isolation of the PVs should be the goal when targeting PVs and/or the PV antrum.3 However, the elimination of PV potentials could be achieved with varying degrees of success after creating the initial anatomic-guided circumferential lesions.4–7 Immediate and late relapses of atrial arrhythmias were related to the conduction gaps on the incomplete circumferential PV isolation (PVI) lines.4 Recent studies also indicated that additional ablation at the PV carina region is sometimes required to achieve electrical isolation.5,7 However, the carina ablation may increase the risk of PV stenosis. Currently, the predictors for the requirement of additional carina ablation are not clear. The purpose of this study was first to evaluate the requirements and predictors of
the need for a carina ablation to achieve a complete electrical isolation of the PVs. Secondly, we validated the findings from the initial data set, i.e. the requirement of a carina ablation and the long-term outcome in the next 40 patients with an optimal and fixed distance from the isolation line to the defined PV ostia.

Methods

Patient characteristics
This study enrolled 80 symptomatic drug refractory (mean, 2 ± 1 drugs, range 1–3) paroxysmal AF patients undergoing AF mapping and radiofrequency (RF) ablation guided by a NavX mapping system (NavX, with CFE software, 7.0, St Jude. Medical, Inc., USA). The first 40 consecutive patients (Group I) underwent circumferential PV isolation. In the Group I patients, we investigated the factors that were related to requiring a carina ablation aimed at achieving the elimination of all PV potentials. The second 40 consecutive patients (Group II) received circumferential PVI with a fixed distance to the angiographically determined PV ostia, based on the analysis results of the Group I patients. In this study, the patients with persistent AF, paroxysmal AF who required a left atrial (LA) linear ablation, or those undergoing repeat procedures were excluded from this study. Patients with a common PV ostium were also excluded in this study.

Electrophysiological study
Each patient underwent an electrophysiological study and catheter ablation in the fasting state, after informed consent was obtained. All antiarrhythmic drugs except for amiodarone were discontinued for at least five half-lives before the procedure. None of these patients received any amiodarone therapy during the electrophysiological study. The method of the three-dimensional (3D) electroanatomic mapping has been described previously.\(^8,9\) Mapping was performed with an irrigated 4-mm tip deflectable catheter (EPT, Boston Scientific Corporation, USA) inserted into the LA alongside the transseptal sheath without the need for an additional puncture site. A 3D geometry of the LA was then created using the NavX mapping system.

Signal recording and the analysis
Bipolar atrial electrograms were collected from all recording sites in the LA with a point-by-point approach sequentially by the ablation catheter during sinus rhythm (SR) under the guidance of a NavX system and conventional mapping system. The peak-to-peak bipolar voltage of each site was measured. The total activation time was measured in the left atrium. In all patients, a voltage analysis was performed before the catheter ablation and after the first round of circumferential PVI.

A baseline multidetector computed tomography (MDCT) was acquired in all subjects for reconstructing and merging the 3D reconstructed geometry during the procedure. The delineation of the anatomical regions was performed with a 3D merged epicardial view and endocardial in real time. In Group II, the distance between the lesion set and PV ostia was fixed, based on the statistical results in the Group I patients. The distance from the isolating lesions to the PV ostia was confirmed by the electroanatomic maps after PVI in both groups. The mean distance from the centre of the PVI-related low-voltage zone to the PV ostia was calculated by averaging the distance of the roof, anterior carina, posterior carina, and bottom PV regions (Figures 1 and 2), based on the voltage mapping after the first round of PVI in both groups.

Catheter ablation
After a successful transseptal procedure, continuous circumferential lesions were created, encircling the right and left PV ostia guided by a NavX system using an irrigated-tip 3.5 mm ablation catheter. A power control mode with a temperature setting of 40–43°C and maximal power of 25–30 W was used. The energy and temperature were reduced while delivering energy to sites near the oesophagus (20–25 W). The ipsilateral PVs were encircled as a single unit. Circumferential ablation was performed on the anterior and posterior walls at >0.5 cm (Group I) and 0.8 cm (Group II) away from the defined PV ostia, defined by the angiographically reconstructed 3D geometry of the CT scan. Successful circumferential PVI was demonstrated by the absence of any PV activity or dissociated PV activity. A circular catheter was alternately placed in the superior and inferior PVs on each side to look for attenuation and elimination of the PVPs. The intracardiac

Figure 1  Electroanatomic map in a patient after the first round of circumferential pulmonary vein (PV) isolation (blue lesion). The left panel shows the activation during sinus rhythm (SR). The wavefront propagated through the anterior pulmonary vein isolating lesion into the pulmonary vein. The right panel shows the peak-to-peak bipolar voltage, and the preferential conduction was bordered by the low-voltage area (voltage < 0.3 mV). An incomplete isolating lesion could be identified by the activation map and voltage map. Linear ablation targeting the gaps was performed parallel to the original line (brown lesion).
tracings recorded by the circular catheter (with and without atrial pacing) and electroanatomic maps were analysed to search for the presence of any gaps in the circumferential lesions around the PVs. The earliest signals recorded by the spiral catheter were targeted initially, which also coincided with the gap in the electroanatomic map. The activation map and voltage map after the first round of PVI revealed the location of any conduction preferentially through the prior line (Figure 1). Subsequent re-isolation of the conduction gaps was performed on the prior ablation line, if the circumferential lesions could not eliminate the PV potentials recorded from the circular catheter inside the PVs. Subsequently, RF energy was delivered in the carina between the superior and inferior PVs if the endpoint of the PVP elimination was not achieved after the circumferential ipsilateral lesions were created. The requirement of additional linear ablation was assessed based on the AF inducibility.

The endpoint for the electrical isolation of the PVs was the elimination of the PVP potentials from the ipsilateral PVs or a decrease in the PVP amplitude of <0.1 mV in both the superior and inferior PVs on each side. The endpoint for the procedural success was defined as the non-inducibility of sustained AF lasting >60 s. After the PVI, the mapping and ablation were only applied to spontaneously initiating focal atrial tachycardias and non-PV ectopy that initiated AF. The methods of the identification of the non-PV ectopy have been described in our previous publications.

Follow-up of the atrial fibrillation recurrences

After discharge, the patients underwent follow-up (2 weeks after the catheter ablation, then every 1–3 months thereafter) at our cardiology clinic or with the referring physicians where routine ECGs were obtained during each follow-up, and antiarrhythmic medications were prescribed for 8 weeks to prevent any early recurrences of AF. During the clinical follow-up, 24-h Holter monitoring and/or cardiac event recording with a recording duration of 1 week were performed to define the cause of the clinical symptoms. A follow-up MDCT was performed 3 months after the procedure in all patients to evaluate any possible procedure-related PV stenosis. Recurrence of an atrial arrhythmia was defined as an episode lasting >1 min and that was confirmed by ECGs 2 months after the ablation (blanking period). The endpoint for the follow-up was the clinically documented the recurrence of atrial arrhythmias or repeat ablation procedures.

Statistical analysis

Data were presented as the mean value ± standard deviation (SD) if normally distributed. A χ² test with a Fisher’s exact test was used for the categorical data. Normally distributed continuous variables were compared using the Student’s t-test, whereas not normally distributed variables were compared using the Mann–Whitney U test. Various clinical and electrophysiological factors were used to assess the requirement of carina ablation and the recurrence of atrial arrhythmias after the first procedure. Variables selected to be tested in the multivariate analysis were those with a P-value of <0.2 in the univariate models. Receiver-operating characteristic (ROC) curves were constructed to identify the distance from the PV isolating lesions to the PV ostia for the prediction of a PVI after the first round of circumferential PVI, and were defined as the value on the ROC curve with the best sensitivity–specificity trade-off. Statistical significance was considered when the two-sided P-value was <0.05.
Results

First round of circumferential pulmonary vein isolation in the Group I patients

The baseline characteristics in Groups I and II were similar (P > 0.05, Table 1). In Group I (n = 40), after one round of encircling lesions around a total of 80 ipsilateral PVs, a total of 34 (43%) of the ipsilateral PVs were electrically isolated (15 right PVs and 19 left PVs). In a total of 10 patients (25% of 40), electrical isolation of all PVs was achieved after the first round of circumferential PVI. In 16 (35%) patients, electrical isolation of at least one PV was achieved, and in 24 (40%) patients, no electrical isolation of any of the PVs was achieved.

Subsequent electroanatomic mapping, re-isolation, and carina ablation

The mean distance from the ablation-related lower voltage zone to the PV ostia was 1.2 ± 0.6 cm for the right PVs and 1.0 ± 0.5 cm for the left PVs. Activation maps during SR revealed that there was preferential conduction into the PV (75%, with 25 right PVs and 21 left PVs in 30 patients). Post-PVI voltage maps showed the preferential conduction into PV was bordered by a low-voltage area during SR (Figure 1). We intended to re-isolate the PVs parallel to the circumferential lesions according to the voltage maps and the recordings of circular catheters, rather than applying energy inside (Figure 1). After the re-isolation, complete electrical isolation was achieved in an additional five (20%) of the right PVs and four (19%) of the left PVs. In the remaining 37 PVs, activation maps showed that the earliest activation sites were located within the isolation lines. Voltage mapping showed a reduction in the local bipolar electrogram in the original circumferential lesions (Figure 2). Owing to the persistent presence of PV potentials recorded by the circular catheter, carina ablation was required in the remaining 20 (80%) right PVs and 17 (81%) left PVs to achieve complete electrical isolation of all PVs (100%).

Table I Baseline and clinical characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group I (n = 40)</th>
<th>Group II (n = 40)</th>
</tr>
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<tbody>
<tr>
<td><strong>Baseline characteristics</strong></td>
<td></td>
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</tr>
<tr>
<td>Age (years)</td>
<td>49 ± 12</td>
<td>50 ± 12</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>31/9</td>
<td>31/9</td>
</tr>
<tr>
<td>Hypertension (n, %)</td>
<td>8 (20%)</td>
<td>8 (20%)</td>
</tr>
<tr>
<td>Diabetes (n, %)</td>
<td>2 (5%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Structure heart disease (n, %)</td>
<td>7 (24%)</td>
<td>7 (24%)</td>
</tr>
<tr>
<td>Coronary disease (n, %)</td>
<td>6 (16%)</td>
<td>6 (16%)</td>
</tr>
<tr>
<td><strong>Echocardiography</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td>37 ± 5.5</td>
<td>38 ± 3.9</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>58 ± 6.5</td>
<td>60 ± 5.6</td>
</tr>
<tr>
<td><strong>Electrophysiological characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-PV triggers (n, %)</td>
<td>5 (13%)</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>SVC = 1</td>
<td>SVC = 4</td>
<td></td>
</tr>
<tr>
<td>LOM = 1</td>
<td>LA septum = 1</td>
<td></td>
</tr>
<tr>
<td>LA septum = 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Electrophysiological characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total left atrial activation time (ms)</td>
<td>116 ± 25</td>
<td>125 ± 32</td>
</tr>
<tr>
<td>Mean LA voltage (mV)</td>
<td>1.63 ± 0.67</td>
<td>1.53 ± 0.54</td>
</tr>
</tbody>
</table>

LA, left atrium; LOM, ligament of Marshall; PV, pulmonary vein; SVC, superior vena cava.

Table 1. Baseline and clinical characteristics.

*P < 0.05 when compared with the Group I patients.

Prediction of the requirement of a carina ablation in the Group I patients

A univariate analysis showed that the requirement of a carina ablation in conjunction with circumferential PVI was not related to any clinical or atrial substrate factors (sex, age, left atrial diameter, left ventricular ejection fraction, LA mean peak-to-peak voltage, or LA total activation time, P > 0.05). The only predictor was the mean distance between the ipsilateral isolating lesions and the PV ostia (P < 0.001 for right PVs, and P = 0.001 for left PVs). The distance from the PV ostia was shorter in those with a conduction block pattern after the first round of PVI for both the right and left side PVs (P < 0.05, Figure 3A). Receiver-operating characteristic curves were constructed to identify the threshold for an incomplete block after the first round of the PVI in each PV (left and right PVs). The cut-off value of the mean distance to the PV ostia to predict an incomplete PVI was >8 mm for all PVs [n = 80 for all PVs, Figure 3B, with a sensitivity of 0.85 (95% CI = 0.72–0.94) and a specificity of 0.77 (95% CI = 0.63–0.88)].

The requirement of carina ablation in the Group II patients

In the next 40 patients (Group II), we validated the optimal distance from the PV ostium to the line according to the results of the ROC curve analysis. The first round of circumferential PVI was applied with a fixed distance of 8 mm to the defined right and left PV ostia (Figure 3B). In Group II, a right carina ablation was required only in 10 (25%) patients and left carina ablation in 8 (20%). The mean distance from the ablation-related low-voltage zone to the PV ostia was 0.8 ± 0.2 cm for the right PVs and 0.8 ± 0.1 cm for the left PVs. The requirement of a carina ablation in Group II was less than that in the Group I patients (P = 0.018 and 0.026 for the right and left PVs, respectively). The procedural time for the PVI in the Group II patients was shorter than that in the Group I patients (88 ± 31 vs. 77 ± 23 min, in the Group I and II patients, respectively, P = 0.047). The number of RF applications was 87 ± 23 vs. 76 ± 17 in Group I and II, respectively, P = 0.06.

Repeat procedure and long-term follow-up

In the Group I patients, with a mean follow-up of 16 ± 6 months (range 10–22 months), recurrences of atrial arrhythmias were observed in nine patients (23%, six with paroxysmal AF, two with atrial tachycardia, and one with non-PAF). Pulmonary vein CT scanning 3 months after the procedure did not demonstrate any PV stenosis in any of the patients (0% in both groups). The
The success rate of a single procedure without any drug was 77% (31 of 40), and the final success rate after multiple procedures without any drug was 88% (35 of 40). In Group II, with a follow-up of 11 ± 4 months (range 4–14 months), recurrences of atrial arrhythmias were observed in eight patients (20%, six with paroxysmal AF, two with atypical atrial flutter). The success rate of a single procedure without any drugs was 80% (32 of 40), and the final success rate after multiple procedures without any drugs was 90% (36 of 40). The single procedure success rate was similar between the two groups (77 vs. 80% and 88 vs. 90%, in the Group I and II patients, respectively, \( P \approx 0.05 \)).

Beyond a blanking period of 2 months, a Kaplan–Meier analysis showed that the AF-free survival without any drugs was similar between the two groups (long-rank test: \( P = 0.74 \)).

In Table 2, a univariate analysis showed the mean voltage of the LA, LA diameter, mean distance from the isolation lesions to the PV ostium, and carina ablation did not predict the outcome of a single-procedure success (\( P > 0.05 \)). A multivariate analysis showed that longer the distance from the circumferential lesion to the PV ostia in the carina region (\( n = 80 \)) significantly predicted the single procedure efficacy (\( P = 0.04 \)).

### Discussion

#### Main findings

Incomplete PVI was common after the first round of the circumferential PVI. Additional carina ablation was required to obtain electrical isolation when the distance of the isolating lesions was >8 mm from the defined PV ostia. Wider circumferential lesions indicated a requirement of an additional carina ablation to achieve a complete electrical isolation with a longer procedural time.

#### Different techniques of pulmonary vein ablation

Currently, circumferential PV ablation is the most widespread ablation technique in patients with paroxysmal AF. With the approach
first described by Pappone et al., wide encircling lesions were placed outside the ostia of the ipsilateral PVs with the endpoint of a reduction in the local bipolar voltage of >80% or 0.1 mV within the isolation line.4,13 In other centres, the PVI approach is a conjunction of circumferential PVI and ostial PVI by using circular catheters to confirm complete electrical isolation.12,14 In clinical practice, it has been demonstrated that only 45–80% of the encircled PVs are electrically isolated after the first round of PVI.6,16 The single procedure efficacy of circumferential isolating lesions was shown to be better than small ostial lesions.16 However, it remains unclear whether larger isolating lesions are necessary or whether small isolating lesions might be sufficient. This study demonstrated that patients with wider area isolating lesions are less likely to have the PVs electrically isolated after the first round of circumferential lesions. Carina ablation remained necessary in some patients with wide circumferential lesions. The endpoint of a reduction in the local bipolar voltage on the prior isolating lines may not be equivalent to complete electrical isolation of the PVs.

The importance of the pulmonary vein carina in the catheter ablation of atrial fibrillation

Many laboratories have reported an increased success of PVI by targeting the carina in those patients with persistent conduction into the PVs after the circumferential ablation.6,7 suggesting the important role of the carina in the circumferential PVI. In this study, a wider antral lesion may produce subepicardial conduction due to a non-transmural ablation. Re-isolation on the prior lines with the elimination of the local bipolar electrograms could not electrically isolate all the PVs in patients who received wider PV antral lesions. Several recent studies could explain these phenomena. Cabrera et al. recently demonstrated the histological evidence in humans showing the intermuscular connections between contiguous PV orifices where fascicles meet and they are interwoven.17,18 The longitudinal pattern of activation conducting into the PV requires an energy application to electrically isolate the PVs, and this study suggested the limitation of being able to achieve a full thickness ablation lesion when using larger isolation lesions.13 Secondly, the earliest LA breakthrough sites could change and were located within the isolation lines after the first round of circumferential PVI.14 Finally, Tan et al. also reported an epicardial connection between the PVs and LA with a complete electrical isolation of the PVs.

Clinical implications

Wide circumferential PVI has become modified with wide area circumferential lesions to minimize the risk of PV stenosis, and to encircle the non-PV triggers near the PV ostia.19 However, this study demonstrated that wider area PVI lines were associated with a higher incidence of conduction gaps and epicardial breakthroughs into the carina. This study demonstrated that a simplified approach with a fixed distance from the isolation lines to the defined PV antra reduced procedure time and risk to achieve electrical isolation of the PVs. This study also showed that a wider lesion in the carina region may improve the long-term efficacy. However, a larger prospective trial may be required to confirm this result.

Limitations

First, the predictors of a carina ablation and the long-term efficacy of wide circumferential lesions may not be extrapolated to patients with non-paroxysmal AF patients. Secondly, several factors may affect the efficacy of circumferential catheter ablation, including the stability of the catheter during ablation and contact force at each location. This study only evaluated the effect of wide circumferential isolation on the efficacy of PVI. Thirdly, endocardial bipolar voltage mapping during SR may be inadequate to identify all the gaps in the PV ostium. This is the universal limitation of endocardial bipolar recording to identify the conduction gaps intramurally or in the epicardium. Finally, owing to the limitation of anatomy, we could not extend the left PV isolation lesion of the

**Table 2** Univariate and multivariate analyses of AF recurrences after a single ablation procedure (n = 80)

<table>
<thead>
<tr>
<th>Factors predicting recurrence after a single ablation procedure</th>
<th>AF recurrence (+)</th>
<th>AF recurrence (-)</th>
<th>Univariate analysis P-value</th>
<th>Multivariate analysis OR (95% CI) P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male, %)</td>
<td>93%</td>
<td>70%</td>
<td>0.155</td>
<td>0.98 (0.91–1.03) 0.33</td>
</tr>
<tr>
<td>Age (years)</td>
<td>53 ± 18</td>
<td>51 ± 19</td>
<td>0.258</td>
<td>– –</td>
</tr>
<tr>
<td>Left atrial enlargement (mm)</td>
<td>37 ± 5.3</td>
<td>38 ± 4.5</td>
<td>0.528</td>
<td>– –</td>
</tr>
<tr>
<td>Left ventricular EF (%)</td>
<td>55 ± 6.7</td>
<td>59 ± 6.3</td>
<td>0.452</td>
<td>– –</td>
</tr>
<tr>
<td>LA total activation time (ms)</td>
<td>121 ± 30</td>
<td>114 ± 23</td>
<td>0.22</td>
<td>– –</td>
</tr>
<tr>
<td>Mean distance from the lesion to the PV antra (cm)</td>
<td>0.9 ± 0.3</td>
<td>1.0 ± 0.4</td>
<td>0.27</td>
<td>– –</td>
</tr>
<tr>
<td>Distance from the lesion to the PV carina (cm)</td>
<td>1.0 ± 0.4</td>
<td>1.5 ± 0.6</td>
<td>0.03</td>
<td>0.19 (0.039–0.925) 0.04</td>
</tr>
<tr>
<td>Right carinal ablation (+)</td>
<td>56%</td>
<td>38%</td>
<td>0.25</td>
<td>– –</td>
</tr>
<tr>
<td>Left carinal ablation (+)</td>
<td>19%</td>
<td>38%</td>
<td>0.22</td>
<td>– –</td>
</tr>
</tbody>
</table>

* Averaging the distance between the roof, anterior carina, posterior carina, and bottom

* Averaging the distance between the anterior and posterior carina of the PVs.
segment of the anterior ridge and left anterior carina region outside the ridge area. A very wide circumferential lesion of this segment could not be performed and was not assessed.

**Conclusion**

An additional gap ablation and carina ablation was required to obtain electrical isolation when wider circumferential isolating lesions were applied for PVI in patients with paroxysmal AF. A wider circumferential PVI indicated the requirement of a carina ablation and a longer procedure time, and a fixed distance of 0.8 cm from the isolation line to the PV ostia decreased the requirement of a carina ablation and the procedure time to achieve PV isolation with an equivalent outcome.

**Conflict of interest:** None declared.

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