Background  The limited efficacy and complications of segmental ostial pulmonary vein isolation (PVI) for treating atrial fibrillation (AF) have been discussed so, in the present study the feasibility and efficiency of performing segmental pulmonary vein (PV) antrum isolation to treat AF were assessed.

Methods and Results  A total of 187 patients with drug-refractory AF (paroxysmal 120, persistent 67) underwent segmental PVI guided by circumferential 20-electrode catheters (Lasso). Radiofrequency (RF) current was delivered either at the ostium using a regular Lasso (15–20mm in diameter, 70 patients: Group 1) or at the antrum using a larger Lasso (25–30mm in diameter, 117 patients: Group 2). A significantly wider region had to be ablated, with a longer RF application time, to isolate all 4 PVs in Group 2 patients than in Group 1 patients. Although the rate of recurrence of AF after the initial session was equal in both groups, a significantly greater number of patients were free from AF after a mean of 1.4 procedures in Group 2 than in Group 1 (93% vs 76% for paroxysmal AF, 78% vs 48% for persistent AF).

Conclusions  Segmental antral PVI using large-sized Lasso catheters was found to be more effective and safer than ostial PVI for the treatment of AF. (Circ J 2007; 71: 753–760)

Key Words: Antrum isolation; Atrial fibrillation; Catheter ablation; Pulmonary veins

Table 1  Comparison of Patient Characteristics in the 2 Groups

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=70)</th>
<th>Group 2 (n=117)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52±10.3</td>
<td>53±9.8</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>52/18</td>
<td>92/25</td>
<td>NS</td>
</tr>
<tr>
<td>Paroxysmal/persistent AF</td>
<td>44/26</td>
<td>79/38</td>
<td>NS</td>
</tr>
<tr>
<td>Organic heart disease</td>
<td>16</td>
<td>29</td>
<td>NS</td>
</tr>
<tr>
<td>LA diameter (mm)</td>
<td>38.5±4.2</td>
<td>39.5±6.0</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up (days)</td>
<td>1,015±257</td>
<td>647±197</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Group 1 represents patients who underwent ostial pulmonary vein isolation; Group 2 represents patients who underwent pulmonary vein antrum isolation.

AF, atrial fibrillation; LA, left atrial.
Informed consent was given by each patient before the procedure, according to the protocol approved by the hospital’s Human Research Committee.

**Mapping Techniques**

Mapping and ablation was performed as described previously. Briefly, the procedures were performed 7 days after the withdrawal of antiarrhythmic drugs (no patient took amiodarone). The LA and PVs were explored through either a patent foramen ovale (19 patients) or transseptal catheterization with 1–2 catheters: 1–2 for circumferential PV mapping, and a quadripolar mapping/ablation catheter. The direct visualization of all 4 PVs was performed using selective venography through a long sheath (8F (SR-0, DAIG company, USA) for superior PVs; 8F percutaneous transseptal introducer sheath (Medtronic, USA) for inferior PVs) after manual injection of contrast medium. Heparin was titrated to maintain a partial thromboplastin time of 60–90 s (control = 30 s).

The PV ostium and antrum were identified on the angiographic image (Figs 1A, B). As has been previously described, the PV ostium was angiographically defined as the region where the outline from the LA to PV curves with a maximum angle, whereas the PV antrum was defined as the intervening area between the venous tube and the widely opened LA, which was identified angiographically as the gradually widening region around the PV ostium. PV mapping was performed using a steerable circular catheter with a diameter of either 15, 20, 25 or 30 mm equipped with 20 1-mm electrodes in a loop made of shape-retaining material orthogonal to the shaft (Lasso, Biosense Webster, Diamond Bar, CA, USA). In the Group 1 patients, we mapped and ablated the PV ostium according to the conventional method, using a standard Lasso catheter (15 or 20 mm in diameter), whereas larger sized Lasso catheters (diameter of 25 or 30 mm) were used for mapping the PV antrum in the Group 2 patients. In practice, we chose the Lasso catheter based on the roughly measured diameter of the PV ostium or antrum according to the angiographic image (Figs 1A–D). In order to improve the contact between the large-sized Lasso catheter and the surrounding wall of the PV antrum (outside of the PV ostium) for better mapping, we used a catheter holder stabilizer (custom-made) which helps to maintain the position of the ring catheter against the LA wall and thus minimize its movement. The close contact of the ring configuration of the Lasso catheter with the PV antral wall was confirmed in 3 patients of Group 2 by intracardiac echocardiography (USE-1200, Tom Tec Imaging Systems, Germany) (Fig 1E). In both groups, the local potentials (PV muscle potentials in OPVI or PV antral potentials in PVAI) were recorded in the bipolar mode from 10 bipole (1–2, 3–4, ..., up to 19–20 with the initial electrode as the anode and the next electrode as the cathode) through bandpass filters of 30–500 Hz and an amplification of 1–2 cm/mV on a polygraph (EPMed Systems, Inc, West Berlin, NJ, USA).
Ablation Procedure

In each case, all 4 PVs were electrically disconnected from the LA, except if the PV had a diameter less than 12mm and no arrhythmogenicity. In cases with SR, the segments of the PV perimeter demonstrating the earliest activation and the polarity reversal were preferentially targeted. In patients who underwent PVI during ongoing AF, the segments demonstrating either fractionated electrograms during disorganized local potential activation, or electrogram polarity reversal, or the earliest activation during the transient or sustained organization of the local potential activation, were preferentially targeted (Figs 3A, B). RF energy was delivered at the distal electrode (8-mm tip) of the thermocouple-equipped ablation catheter (Fantasista, Japan Lifeline, Tokyo, Japan, or Blazer II, Boston Scientific, CA, USA) with a target temperature...
of 50°C and a power limit of 30–35 W for 30–60 s each site. In order to avoid char formation on the circular mapping catheter, we ablated not on the mapping catheter directly, but proximally to the electrodes of the Lasso catheter.

The endpoint of ablation in both groups was the establishment of a bidirectional conduction block between the LA and PV. After elimination of PV muscle conduction distal to the ablation site(s), indicated either by the abolition or dissociation of distal PVPs, the absence of conduction from the PV to LA was also confirmed by pacing inside the PV by the mapping catheter or the Lasso catheter during SR.11,12 After electrical disconnection of the targeted PVs, provocative maneuvers (isoproterenol and burst pacing) were performed to reveal other remaining foci in the ostium proximal to the ablation sites or in other atrial tissues. Additional RF ablation was performed, targeting these remaining foci if necessary.

The position of the esophagus behind the LA was monitored throughout the ablation procedure in approximately half of Group 2 patients (64 patients), in order to avoid esophageal damage from the RF energy applications. As described previously, direct esophagography was performed by infusing water-soluble contrast medium (approx. 4–8 ml amidotrizoic acid, Schering AG, Germany) through a nasogastric tube under deep sedation and retaining it in the esophagus throughout the procedure to reveal its silhouette. Real-time monitoring of the esophageal location enabled ablation to be carried out safely.

No continuous ablation lines were produced in this patient population, except for 2 atrial tachycardias in 2 patients in Group 2, which appeared after the PVAI procedure (described in Results).

Patient Follow-up After Ablation

All patients remained in hospital for at least 4 days after the procedure, with continuous monitoring of the ECG. After being discharged, the patients underwent careful observation (2 weeks after discharge, then monthly) at the cardiology clinic, without taking any antiarrhythmic agents. The outcome of PVI was evaluated by patient symptoms, ECG at periodical follow-up, and also by periodically performing 24-h ambulatory monitoring (at 1 day, and 1, 3,
Segmental PV Antrum Isolation With Large Lasso

6, 9, and 12 months after the procedure). If the patients complained of any symptoms suggestive of tachycardia, a cardiac event recorder (CG-6106, Card Guard Scientific Survival, Rehovot, Israel) was used for 5 successive days to define the cause of symptoms. In the case of early AF recurrence during admission, either a drip-infusion of antiarrhythmic drugs was administered or electrical cardioversion was performed. In general, the patients were discharged on warfarin anticoagulation (continued for 6 to 12 months after the procedure), but without any antiarrhythmic therapy.

The outcome of the procedure was generally evaluated 3 months after the procedure. AF recurrence within the first month after ablation was not counted in the analysis and those who did not have any evidence of tachycardia after more than 1 month of follow-up were considered to be “successful”. In cases of AF recurrence with severe symptoms, antiarrhythmic drugs, which had been ineffective before the procedure, were used either temporarily or continuously.

Survival, Rehovot, Israel) was used for 5 successive days around their antrums. RF applications targeting these regions became organized, we could easily identify the potentials, which would reflect delayed conduction along the LA–PV electrical breakthrough. In the LIPV, an additional RF application at the anterior wall was necessary to eliminate the remaining PV–LA conduction and to attain a bidirectional conduction block. These residual PV–LA potentials at the successful ablation sites in both veins showed fragmented electromgrams between the atrial and PV potentials, showing fragmented activity between the atrial and PV potentials. RF applications (Fig 2B). It is notable that most of the local potentials at the successful ablation sites in both veins showed fragmented electromgrams between the atrial and PV potentials, which would reflect delayed conduction along the LA–PV electrical breakthrough. In the LIPV, an additional RF application at the anterior wall was necessary to eliminate the remaining PV–LA conduction and to attain a bidirectional conduction block. These residual PV–LA conduction in the absence of LA–PV conduction were observed in 27.4% (79/274) and 25.0% (114/458) of the targeted PVs in Group 1 and 2, respectively (p=NS).

Fig 3 is a typical example of PVAI in a patient from Group 2 who had persistent AF. At baseline, both superior and inferior PVs showed localized fragmented activity around their antrums. RF applications targeting these regions eliminated the fragmentation, thus resulting in organization of the PV antral potentials (Fig 3A). Once the local potentials became organized, we could easily identify the residual breakthrough point from the LA to the PV antrum, even during ongoing AF. As shown in Fig 3B, we next targeted the region with the earliest activation and the electrical polarity reversal (inset of Fig 3B) at electrode #1–2, which slowed down the activation frequencies in this vein, as well as the alteration of the activation sequence. Another RF application (4th ABL) adjacent to electrodes #9–12 further slowed down the activation frequency of this vein and then terminated the AF (before the complete disconnection of this vein). In total, RF applications at the segments of fragmented activities around the PV antrum during AF were attempted in 56 cases from Group 2, which resulted in organization of local activity and termination of the AF in 22 cases (39%). RF application around the PV ostium targeting the fragmented activities during AF in 28 cases of Group 1 resulted in AF termination in only 6 cases (21%, a significantly lower rate than that observed in Group 2, p<0.05).

The results of ablation are shown in Table 2. A total of 736 PVs were ablated among 187 patients in both groups of this study, including 187 LSPV, 187 RSPV, 177 LIPV, and 185 RIPVs. Nine left PVs with a common trunk were counted as LSPV (2 in Group 1, 7 in Group 2). Although there was no significant difference between the 2 groups regarding the success rate of isolating target PVs (99% in each group), PVAI required a significantly longer RF application time during a longer procedure time compared with OPVI (Table 2). The extent of the regions where RF energy was effectively applied was also compared between the 2 groups. When we divided the PV-ostial or PV-antral perimeter into 8 segments, 4.2±1.5 sectors and 6.1±1.1 sectors of the superior PVs had to be ablated in Groups 1 and 2, respectively (p<0.01). Similarly in the inferior PVs, significantly more sectors needed to be ablated with PVAI than with OPVI (3.5±1.1 vs 4.3±1.4 sectors in Groups 1 and 2, respectively, p<0.05). All the circumferential RF energy applications were required in 8% and 15% of PVs in Group 1 and 2 patients, respectively (p<0.05).

Fig 4 demonstrates the AF-free survival curve after the initial and final PVI in both groups. In the Group 1 patients, the AF-free ratio after the first procedure was 58% and 32% in paroxysmal and persistent AF patients, respectively.

Table 2 Comparison of Ablation Results in the 2 Groups

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=70)</th>
<th>Group 2 (n=117)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of isolated PV</td>
<td>99%</td>
<td>99%</td>
<td>NS</td>
</tr>
<tr>
<td>RF numbers/4-PVI</td>
<td>24±7</td>
<td>38±11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RF duration (min)</td>
<td>22±7</td>
<td>36±9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Procedure time (h)</td>
<td>4.8±1.2</td>
<td>5.2±1.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Fluoroscopic time (h)</td>
<td>49±18</td>
<td>56±21</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>No. of ablated sectors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior PVs</td>
<td>4.4±1.5</td>
<td>6.1±1.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Inferior PVs</td>
<td>3.5±1.3</td>
<td>4.3±1.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Drug use (temporary)</td>
<td>7 (10%)</td>
<td>8 (7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Drug use (continuous)</td>
<td>11 (16%)</td>
<td>14 (12%)</td>
<td>NS</td>
</tr>
<tr>
<td>No. of ABL procedures</td>
<td>1.4±0.4</td>
<td>1.4±0.5</td>
<td>NS</td>
</tr>
<tr>
<td>Non-PV focus in repeat ABL</td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Around PV ostium</td>
<td>12 (17%)</td>
<td>4 (3%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>SVC</td>
<td>6 (8%)</td>
<td>12 (10%)</td>
<td>NS</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PV stenosis</td>
<td>3</td>
<td>0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LA flutter</td>
<td>1</td>
<td>4</td>
<td>NS</td>
</tr>
</tbody>
</table>

Group 1 represents patients who underwent ostial pulmonary vein isolation; Group 2 represents patients who underwent pulmonary vein antrum isolation.
PV, pulmonary vein; RF, radiofrequency; ABL, ablation; SVC, superior vena cava. Other abbreviation see in Table 1.
(p=0.048), whereas 62% and 36% of Group 2 patients, respectively, were free from AF after the first procedure (p=0.0008, Fig 4A i&ii). After the first procedure, no significant difference was observed in the AF-free ratio between the 2 groups. Repeat ablation sessions were performed in 39% (27/70) and 37% (43/117) of patients with a mean procedure number of 1.4±0.4 and 1.4±0.5 times in Group 1 and 2, respectively (p=NS). A third procedure was performed in 2 and 5 patients in Group 1 and 2, respectively. Regarding the final outcome, in Group 1 76% and 48% of the patients with paroxysmal and persistent AF became free from AF (p=0.016) compared with 93% and 77.5% of the respective patients in Group 2 (p=0.028). Significant difference between the 2 groups was observed in the AF-free ratio after the final procedure regardless of the type of AF (Group 1 vs 2: 75.6% vs 92.7% for paroxysmal AF, †p=0.015; 47.7% vs 77.5% for persistent AF, ‡p=0.032). Other abbreviations see in Figs 1,3.

It is noteworthy that there was a significant difference between the 2 groups in the cause of AF recurrence after the first procedure (Fig 4A i&ii). After the first procedure, no significant difference was observed in the AF-free ratio between the 2 groups. Repeat ablation sessions were performed in 39% (27/70) and 37% (43/117) of patients with a mean procedure number of 1.4±0.4 and 1.4±0.5 times in Group 1 and 2, respectively (p=NS). A third procedure was performed in 2 and 5 patients in Group 1 and 2, respectively. Regarding the final outcome, in Group 1 76% and 48% of the patients with paroxysmal and persistent AF became free from AF (p=0.016) compared with 93% and 77.5% of the respective patients in Group 2 (p=0.028). The AF-free ratio after the final procedure was significantly higher in Group 2 than in Group 1, regardless of the type of AF (93% vs 76% for paroxysmal AF, p=0.015; 78% vs 48% for persistent AF, p=0.032).

It is noteworthy that there was a significant difference between the 2 groups in the cause of AF recurrence after the first procedure (Table 2). Ectopic firing from residual tissue around the PV ostium occurred more frequently in Group 1 than in Group 2 during the second session (17% and 3%, respectively, of patients in Groups 1 and 2 who underwent the second session (p=0.05)). However, recurrent conduction of previously isolated PV was similarly found in both groups (100% of patients who underwent the 2nd session in both Groups 1 and 2). The average number of re-conducted PVs was also similar in both groups (2.4±1.1 vs 2.3±1.4 PVs in the 2nd procedure, 2.0±0.0 vs 2.0±0.7 PVs in the 3rd procedure, in Groups 1 and 2, respectively, p=NS). There were no life-threatening complications in the study population, except 3 cases of PV stenosis (single vein in each patient) in Group 1. Left atrial flutter, which newly appeared after the procedure, was observed in 1 and 4 patients in Group 1 and 2, respectively (p=NS). All instances of LA flutter were successfully eliminated during repeat ablation sessions, 3 cases of which were related to recurrent PV conduction and a peri-mitral reentry was documented in 2 patients, both of which were successfully eliminated by left isthmus ablation.14 No continuous ablation lines were produced in this patient population, except for the above 2 cases of peri-mitral reentrant tachycardia in Group 2.

Discussion

Segmental PVI using a circular mapping catheter was originally developed by Haissaguerre et al11 in order to disconnect arrhythmogenic PVs from the LA at their ostia. Because the diameter of PV at its ostium has been estimated to be approximately 15–20mm,115 Lasso catheters with equivalent diameters are generally used for OPVI.1,2 Although the efficiency of OPVI in suppressing the occurrence of paroxysmal AF has been well established, several problems relating to the technique have also been identified, such as residual ectopic foci arising from arrhythmogenic tissue remaining around the PV ostium16 or because of PV
ostial narrowing? On the other hand, wide-area circumferential ablation around both ipsilateral superior and inferior PVs, which has been developed and used widely, also results in de novo complications from linear RF application in the LA, such as atrioesophageal fistula and LA flutter. In the present study, we aimed to isolate each of the 4 PVs at its antrum under the guidance of activation-mapping using large-sized Lasso catheters and we compared the results of this approach with those for the conventional PV ostial isolation. We showed that (i) segmental PVAI is feasible using the large-sized Lasso catheter, although a significantly wider region is required to ablate compared with OPVI, and (ii) segmental PVAI is safer and more effective than OPVI, especially in cases of persistent AF. As far as we are concerned, there has not been a previous report describing the feasibility, efficiency and safety of segmental PVAI using large-sized Lasso catheters.

Häissaguerre et al reported that nearly half of the PV perimeter must be ablated for electrical isolation of a PV at its ostium; whereas Marrouche et al reported that almost the entire PV perimeter must be targeted for proximal isolation of a PV. One of the major new findings of the present study is that proximal isolation of a PV at its antrum can be achieved in an EP-guided segmental manner, thus following the same strategy as for the OPVI, but without making linear ablation lesions. Large-sized Lasso catheters with a diameter of either 25 or 30 mm can fit well at the antrum of each PV and reveal those segments of the PV perimeter that demonstrate the earliest activation or electrical polarity reversal, which suggest the location of LA-PV breakthroughs. Although isolation of a PV at its antrum required a significantly longer period of RF application and greater density of lesions than conventional OPVI, it had a higher AF-free survival ratio and a lower incidence of serious complications such as PV stenosis. Debate remains over the anatomical substrate of the electrical breakthrough between the LA and PVs. There have been only a few anatomical reports of the complex architecture of the prolonged myocardial sleeves extending into the PVs. Ho et al described that, in addition to the circular or spirally oriented bundles of fibers, there are adjacent longitudinal or obliquely oriented fibers in an intricate and mesh-like arrangement. Such longitudinal fascicles have been reported to be broader proximally and to then branch or become thinner distally, which may thus explain the greater number of RF applications required in Group 2 than in Group 1.

Nademane et al recently reported that areas with complex fractionated electrograms represent a defined electrophysiologic substrate of AF that is an ideal target for ablation. They found that the region around each PV was on of the areas where fractionated electrograms are frequently observed. Häissaguerre et al also demonstrated that ablation of regions displaying rapid or heterogenous activation could often prolong the AF cycle length and terminate AF. In the present study, we preferentially targeted segments of the PV antrum with fractionated electrograms when we ablated during AF, which frequently organized these electrograms or terminated the ongoing AF (Fig 3). Regions with fragmented activity around the ipsilateral superior and inferior PV antrum could be identified simultaneously using the large-sized Lasso catheter, thus suggesting its usefulness for not only for the isolation of PV at its antrum but also for identifying and eliminating AF substrate around the PV antrum.

PVAI with a roving Lasso technique has been recently developed by Verma et al who mapped and ablated each PV at its antrum under the guidance of a standard 20-mm Lasso catheter and intracardiac echocardiography. Because the area of the PV antrum is larger than the 20-mm Lasso, they sequentially repositioned the Lasso along each segment of the antral circumference, resulting in an excellent outcome for cure of AF. Although our method of PVAI has some similarities to their method, it is unique because the entire PV antral circumference can be mapped at once with the larger-sized Lasso catheter. In both Verma et al’s report and the present study, there were no complications involving the esophagus, even though the ablation target regions in PVAI are sometimes very close to it. Thus, it might be beneficial to segmentally apply RF energy with/without titrating it under microbubble monitoring! Real-time monitoring of the esophagus with either intracardiac echocardiography or continuous esophageal would further improve the safety of PVAI.

There may be discussion about the evaluation of the ablation outcome after multiple procedures. Because it is now well recognized that resumption of conduction in previously isolated PVs can occur in most cases with AF recurrence and that re-isolation of these PVs leads to marked improvement in ablation outcome, repeat procedures might be regarded as a part of a stepwise approach to more complete isolation of targeted PVs.

Study Limitations
This study was not randomized with 2 groups of patients treated during different periods. Although the basic patient characteristics were similar in both groups, operator learning experience might contribute in some degree to the better outcome for Group 2 (more operator experience) compared with Group 1. Because the recurrences were quantified according to patient symptoms and serial ECGs and Holter monitoring, our criterion of AF recurrence may thus have underestimated the true recurrence rate by not identifying asymptomatic AF recurrence.

Conclusions
Segmental antral PVI with electrophysiological guidance is feasible using the large-sized (25–30 mm) Lasso catheters. Antral PVI was found to be more effective and safer than the conventional ostial PVI for the treatment of paroxysmal and persistent AF.

References