Evaluation of different ablation strategies verifying the optimal overlap ratio in point-by-point laser balloon ablation for patients with atrial fibrillation

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BACKGROUND Optimal overlap ratio remains unclear in point-by-point laser balloon (LB) ablation.

OBJECTIVE This study sought to determine the optimal overlap strategy with target energies on the acute and chronic outcomes in LB pulmonary vein (PV) isolation (PVI).

METHODS Consecutive 38 patients (148 PVs) with atrial fibrillation underwent the first-generation LB PVI with the following protocols based on the overlap ratios for each PV anterior/posterior wall: 50%/50% (13 patients [49 PVs], group A), 50%/25% (15 patients [60 PVs], group B), and 25%/25% (10 patients [39 PVs], group C). High energies (240–255 J: 12 W / 20 seconds, 8.5 W / 30 seconds), moderate energies (200–210 J: 10 W / 20 seconds, 7 W / 30 seconds), and low-to-moderate energies (low, 165–170 J: 5.5 W / 30 seconds, 8.5 W / 20 seconds) were targeted for left PV anterior walls, right PV anterior walls, and bilateral PV posterior walls, respectively. First-pass PVI, the other procedure-related data, and atrial tachyarrhythmia recurrences were analyzed.

RESULTS First-pass PVI rate per PV was higher in group A (94%) than in group B (88%) and group C (62%) (P < .001). All PVs were finally isolated. First-pass time, total LB PVI time, complications, and atrial tachyarrhythmia recurrences during a mean follow-up of 11 ± 5 months did not differ between the groups. A few residual gaps after first-pass LB ablations were found for PV anterior walls even in group A and group B.

CONCLUSION Sufficiently overlapped LB ablation promises a high rate of first-pass PVI without adverse outcomes. High energy could be required for PV anterior walls.

KEYWORDS Atrial fibrillation; Optimal energy; Optimal overlap ratio; Point-by-point laser balloon ablation; Pulmonary vein isolation

In point-by-point LB ablation, 30%–50% overlapped ablation with high power (8.5 W or more) is recommended for high rate of first-pass PVI (ie, successful PVI after the initial circular [first-pass] LB ablation) using the attached software (LightTrack; CardioFocus). However, no specific overlap ratio for acute and durable PVI has been clarified. Additionally, it has been reported in an experimental study that lesion size and continuity depend not only on power (W), but also on laser energy (J). Hence, we performed this study verifying optimal overlap ratio with target energy for successful acute and chronic outcomes in point-by-point LB PVI.

Methods

Study subjects and design

From January 2019 to July 2020, consecutive 38 patients underwent LB1 PVI for nonvalvular symptomatic drug-refractory AF and were enrolled. The inclusion criteria were as follows: (1) paroxysmal AF or persistent AF with a duration of 1 year or less, (2) patients aged 18–80 years,
(3) left atrial diameter ≤50 mm, and (4) left ventricular ejection fraction >30%. The exclusion criteria were as follows: (1) contraindication to oral anticoagulants or PVI, (2) previous PVI attempts, and (3) moderate or severe valvular heart disease. All ablations were performed with the following protocols based on the overlap ratio for each PV anterior/posterior wall: 50%/50% (group A), 50%/25% (group B), and 25%/25% (group C), respectively (Figures 1 and 2).

Target energy (J) per application for each PV region is described below. The allocation of the patients into the groups was performed by the physicians’ discretion considering alternation and randomness.

The primary endpoint was first-pass PVI. First-pass time (ie, initial circular LB ablation time), total LB PVI time (ie, the time from the first laser deployment to the final laser deployment, including the gap ablation phase), complications, and rate of atrial tachyarrhythmia recurrences lasting for more than 30 seconds after the blanking period of 90 days after the index procedure were evaluated as the secondary endpoints. PV stenosis was examined as one of the secondary endpoints by computed tomography (CT). The study was approved by the local institutional review board (local ethics committee number: 19-034) and conducted according to the principles of the Declaration of Helsinki. All patients provided informed consent.

**Different overlap protocols and target energies**

PVs were divided into the following regions: left PV anterior wall, left PV posterior wall, right PV anterior wall, and right PV posterior wall (Figure 2). We used fixed overlap ratios of 25% or 50% for bilateral PV anterior/posterior regions (Figure 3A). Overlap ratio was visually confirmed during the procedures by experienced investigators other than the operators. Laser titrations for the tissue hidden under the balloon shaft (blind spot) were attempted after tissue exposure by LB rotation. However, when LB rotation was difficult, zero rotational maneuver was performed, as described previously.\(^4\)\(^-\)\(^6\) In zero rotational maneuver, the marks marked every 45° on the handle of the LB catheter were manually rotated by a half and one-third turn for 25% and 50% overlap ratios, respectively (Figure 3B).

Laser energies were classified according to the total energy per application into the following 3 ranges: (1) high (240–255 J), 12 W / 20 seconds and 8.5 W / 30 seconds; (2) moderate (200–210 J), 10 W / 20 seconds and 7 W / 30 seconds; and (3) low (165–170 J), 5.5 W / 30 seconds and 8.5 W / 20 seconds (Figure 3C). High energy, moderate energy, and low-to-moderate energies were targeted for left PV anterior wall, right PV anterior wall, and bilateral PV posterior walls, respectively. A higher power (W) setting for the selected energy range was generally used (eg, 12 W / 20 seconds in case of high energy). A lower power setting in an individual range or a setting of 5.5 W / 30 seconds was locally selected in case of laser titration near blood, esophageal temperature rise, or strong pain, while an overlap ratio was the same. Regarding PV posterior walls, moderate energy was preferentially used. However, low energy or a setting of 5.5 W / 30 seconds was applied in the above-mentioned situations.

**KEY FINDINGS**

- The optimal overlap ratio with target energy (J) for each pulmonary vein (PV) region for successful PV isolation (PVI) in point-by-point laser balloon (LB) ablation is related to the key principle of LB PVI in all the generations of LB.
- LB ablation with a sufficient overlap ratio (50%) facilitated higher rate of first-pass PVI (ie, successful PVI after the initial circular [first-pass] LB ablation) than LB ablation with a lower overlap ratio (25%).
- There were no differences in first-pass time, total LB PVI time, complications, and atrial tachyarrhythmia recurrences after the index procedure between the different overlap protocols.
- LB ablation with a 50% overlap ratio showed no residual PV gaps after first-pass LB ablation for PV posterior walls; however, high energy was required for PV anterior walls even with 50% overlapped ablation.

**Figure 1** Study design. LB1 = first-generation laser balloon; PV = pulmonary vein; PVI = pulmonary vein isolation.
Anticoagulants were continued for at least 1 month before ablation and were discontinued only on the day of the procedure. A total of 6 experienced physicians attended the procedures as operators or assistants. All the procedures were performed by 2 or more physicians under deep sedation. A transseptal puncture was performed using an 8.5F transseptal sheath (SL0; Abbott, St Paul, MN). Heparin was repeatedly administered to maintain the activated clotting time at 300–350 seconds. The transseptal sheath was exchanged with a 12F steerable sheath (CardioFocus). LB was inflated at the left atrial antrum. Laser energy was deployed according to the above-mentioned protocols. The degree of PV occlusion was defined as PV occlusion grade according to the previous reports, as follows: (1) 360°; (2) 270–359°; (3) 180–269°; and (4) <180°.4,7 If the temperature was >39°C on an esophageal temperature probe (Esophaster; Japan Lifeline, Tokyo, Japan), energy delivery was stopped. During ablation of right-sided PVs, we stimulated the right phrenic nerve using a diagnostic

**Figure 2**  Ablation protocols with different overlap ratios. LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

**Figure 3**  Selected overlap ratios and target laser energies. A: Ablation with 50% (upper) and 25% (middle) overlap ratios. Schema of consecutive laser titrations with the 2 overlap ratios (lower). B: The marks marked every 45° on the handle of the laser balloon catheter were used as the index of overlap ratio for zero rotational maneuvers. C: Target energies (J) for each pulmonary vein (PV) region. LIPV = left inferior PV; LSPV = left superior PV; RIPV = right inferior PV; RSPV = right superior PV.
catheter for early detection of phrenic nerve injury. If PV potentials remained after first-pass LB ablation, additional LB ablation was performed using a circumferential mapping catheter. The gap site was recorded by dividing each PV into 4 quadrants (eg, anterosuperior). If balloon PVI could not be achieved, radiofrequency current touch-up was allowed. Ablation for typical atrial flutter, left atrial tachycardia, or non-PV foci was performed as needed. Isoproterenol was infused for detection of non-PV foci, as previously described.10

Follow-up
Anticoagulants were resumed in the early postoperative period and continued for at least 3 months. Antiarrhythmic drug therapy was basically discontinued at least 90 days after ablation. Patients attended outpatient visits every 3 months, and 24-hour Holter monitoring was performed at 3–6 and 12 months after the procedure. A contrast-enhanced CT (SOMATOM Drive; Siemens Healthineers, Erlangen, Germany) was performed for the detection of PV stenosis after 6 months or more after the procedure in patients without allergy for contrast medium, bronchial asthma, renal dysfunction, or refusal to CT. PV stenosis was evaluated as previously mentioned previously.11,12 PV ostium was identified as the intersection of the tangents extending from the long axis of the PV wall and the left atrial free wall. PV ostial diameters were measured in the anterior-posterior and cranial-caudal views. PV stenosis was categorized by a reduced rate of PV ostial diameter in either view as mild (30%–50%), moderate (51%–70%), and severe (>70%).

Statistical analysis
Categorical variables are expressed as number and percentage. Continuous variables with normal distribution and nonparametric variables are presented as means ± standard deviation and the median and interquartile range, respectively. Comparison among 3 groups was performed using 1-way analysis of variance or Kruskal–Wallis test.

Results
Patient characteristics
There were no significant differences between the groups regarding age, sex, CHA2DS2-VASc score, left atrial diameter, or left ventricular ejection fraction (Table 1). Group A, group B, and group C were composed of 12 of 13 (92%), 14 of 15 (93%), and 9 of 10 (90%) patients with paroxysmal AF, respectively (P = .863). Structural heart disease included nonischemic cardiomyopathies and hypertensive heart disease.

Acute procedural data
All PVs were successfully isolated at the end of the index procedure in all groups (Table 2). The rate of first-pass PVI for all PVs was higher in group A than in group B and group C (group A vs group B vs group C, P = .029). Radiofrequency current touch-up was required in 0 of 13 (0%) patients in group A, 3 of 15 (20%) patients in group B, and 3 of 10 (30%) patients in group C, respectively (P = .340). Acute PV reconduction after successful PVI was observed.

First-pass time and total LB PVI time were not significantly different between the 3 groups (group A vs group B vs group C, first-pass time, 75 ± 16 minutes vs 71 ± 15 minutes vs 64 ± 13 minutes, P = .251; total LB PVI time, 82 ± 14 minutes vs 85 ± 19 minutes vs 92 ± 25 minutes, P = .474) (Figure 4A). No significant differences were found between the 3 groups regarding procedure time, fluoroscopy

Table 1 Baseline clinical characteristics

|                         | Group A (13 patients) | Group B (15 patients) | Group C (10 patients) | P value |
|-------------------------|-----------------------|-----------------------|-----------------------|---------|
| Male                    | 9 (69)                | 11 (73)               | 7 (70)                | .945    |
| Age (years)             | 66 ± 11               | 66 ± 10               | 61 ± 8                | .435    |
| Paroxysmal AF           | 12 (92)               | 14 (93)               | 9 (90)                | .863    |
| History of AF (years)   | 2 (0–3)               | 1 (1–3)               | 1 (0–1)               | .979    |
| Hypertension            | 10 (77)               | 4 (27)                | 5 (50)                | .127    |
| Diabetes                | 0 (0)                 | 1 (7)                 | 0 (0)                 | .884    |
| Stroke                  | 0 (0)                 | 1 (7)                 | 0 (0)                 | .884    |
| Coronary artery disease | 3 (23)                | 3 (20)                | 0 (0)                 | .159    |
| Structural heart disease| 1 (8)                 | 2 (13)                | 3 (30)                | .987    |
| CHA2DS2-VASc score      | 2 (1–2)               | 3 (1–3)               | 1 (0–2)               | .163    |
| No. of antiarrhythmic drugs | 1 (0–1)              | 1 (0–1)               | 1 (0–2)               | .166    |
| Left atrial diameter (mm) | 38 ± 5               | 37 ± 5                | 39 ± 3                | .804    |
| Left ventricular ejection fraction (%) | 62 ± 4             | 57 ± 8                | 57 ± 8                | .070    |
| LCPV                    | 3 (23)                | 0 (0)                 | 1 (10)                | .234    |
| RMPV                    | 0 (0)                 | 0 (0)                 | 1 (10)                | .174    |

Values are presented as n (%), mean ± standard deviation, or median (interquartile range).
AF = atrial fibrillation; LCPV = left common pulmonary vein; RMPV = right middle pulmonary vein.
time, and X-ray dose. Regarding complications, right phrenic nerve injury occurred in 1 patient in group B. The phrenic nerve injury fully recovered 6 months after the procedure. No symptomatic gastric hypomotility or esophageal mucosal injury was observed.

**Procedural details per PV**

The median PV occlusion grade was almost perfect (1) in all the groups (Table 3). There were no differences in the rate of zero rotational maneuvers between the groups. The mean application number for all PVs at the completion of first-pass LB ablation decreased in the order of group A, group B, and group C (group A vs group B vs group C, 46/49 [94%] PVs vs 53/60 [88%] PVs vs 24/39 [62%] PVs, \( P < .001 \)) (Figure 4B). Regarding the comparison on first-pass PVI between all 2 groups, a significant difference was found between group A and group C (\( P < .001 \)) and between group B and group C (\( P = .002 \)).

Only moderate energy was used for 40%–60% of bilateral PV posterior walls, without any statistical difference between the groups. More total energy was titrated for bilateral PV anterior walls in group A and group B (group A vs group B vs group C, left PV anterior walls, \( P < .001 \); right PV anterior walls, \( P = .011 \)). The mean application number for all PVs at the completion of PVI was higher in group A (group A vs group B vs group C, \( P < .001 \)).

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**Figure 4** Differences in the ablation time and first-pass pulmonary vein isolation (PVI) between the different overlap protocols. A: First-pass time and total laser balloon (LB) PVI time. B: First-pass PVI rate.
Residual PV gap after first-pass LB ablation

A total of 28 PV gaps were confirmed after first-pass LB ablation (Figure 5). Regarding PV anterior walls, there were PV gaps in 3 of 49 (6%) PVs in group A, in 4 of 60 (7%) PVs in group B, and in 8 of 39 (21%) PVs in group C ($P = .037$). Most of the PV anterior wall gaps in group A and group B were found after ablations with a setting of 5.5 W / 30 seconds because of inadequate PV occlusion. Only a few PV anterior wall gaps were observed even after ablation with moderate-to-high energies with a 50% overlap ratio. No PV posterior wall gaps were detected after 50% overlapped ablation.

Atrial tachyarrhythmia recurrence and PV stenosis

Atrial tachyarrhythmia recurrence was found during a mean follow-up of 11 ± 5 months in 3, 1, and 1 patients in group A, group B, and group C, respectively ($P = .630$). Two patients in group A and 1 in group B underwent the second procedure. In group A, there were PV reconnections in the anteroinferior region and posteroinferior region of a right superior PV in 1 patient and in the posteroinferior region of a right superior PV and posterosuperior region of a right inferior PV in another patient. In group B, PV reconnections were revealed in the posteroinferior region of right superior PV and anteroinferior region of right inferior PV. All PVs were reisolated by radiofrequency current catheters.

At a mean of 10 ± 3 months after the index procedure, CT revealed PV stenosis in 2 PVs (left superior PV and right inferior PV) in a patient in group A and a right superior PV in a patient in group B. Those patients had no symptoms. There was no statistical difference in the incidence of PV stenosis per PV between the groups ($P = .115$).

Discussion

Major findings

The optimal overlap ratios with target energy (J) have not been determined for point-by-point LB ablation. Many PV orifices are oval rather than round.13 The overlap ratios are also semi-quantitative, although it was confirmed in real time by 2 or more experienced examiners. Based on these conditions, we pursued the best ablation strategy for clinical practice.

This study determined the following findings: (1) LB ablation with a sufficient overlap ratio (50%) showed higher first-pass PVI rate than 25% overlapped ablation. First-pass
time and total LB PVI time did not differ between the groups. (2) There were no significant differences in the complication rates between the groups. (3) Regarding PV gaps after first-pass LB ablation, there were a few gaps on PV anterior walls even after 50% overlapped ablation, while no gaps were found on PV posterior walls after 50% overlapped ablations. (4) Atrial tachyarrhythmia recurrence rate did not differ between the groups.

Factors for continuous and deep lesion formation
With radiofrequency current, ablation index incorporating stability, contact force, time, and power in a weighted formula has been used as an index for predicting quantified lesion size using a contact force sensing catheter (ThermoCool SmartTouch; Biosense Webster, Diamond Bar, CA) and 3-dimensional mapping system (CARTO System; Biosense Webster).14 Taghji and colleagues14 proposed “CLOSE protocol” as optimal ablation index (ablation index ≥400 on the posterior wall and ≥550 on the anterior wall) with a specified interlesion distance (≤6 mm). They reported that PVI with this protocol enabled high first-pass PVI ratio per PV pair (98%), with high rate of freedom from atrial tachyarrhythmia recurrence at 12 months after the index procedures (92.3%) in patients with paroxysmal AF. Hoffmann and colleagues15 also described that ablation with a smaller interlesion difference facilitated higher first-pass PVI rate than ablation with a larger interlesion difference in ablation index—guided PVI. Additionally, there are differences in the wall thickness between left atrial anterior and posterior walls.16 Impedance changes, which indicate lesion size,17 may compensate for the variability in left atrial wall thickness. However, impedance changes are not available for LB PVI. Therefore, optimal overlap ratio with target energy could be a simple index for acceptable clinical outcomes in point-by-point LB PVI.

Clinical implications of selection of optimal overlap ratio
LB1 requires longer procedure time than cryoballoon (ie, 1-shot device).2,3,18,19 LB2 facilitated more favorable PV occlusion and fewer repositioning maneuvers by more compliant balloon characteristics and arc marks on the balloon shaft.4,5 However, those improvements are not directly linked with shorter procedures than LB1.4,5 Additionally, Heeger and colleagues6 reported that RAPID mode—only ablation was possible in only 41% of all PVs in LB3 PVI. Therefore, point-by-point laser titration is still required.

We hypothesized that high energy might enable laser ablation with low overlap ratio and minimal laser applications, leading to the reduction of procedure time, complications, and burden on the operators. In contrast, this study revealed that 50% overlapped LB ablation facilitated high first-pass PVI rate without any adverse procedural or chronic outcomes. From this study, sufficiently overlapped laser ablation was thought to be preferable for point-by-point LB ablation.

Limitations
First, this was a retrospective single-center study comparing 3 ablation strategies in a relatively small number of patients. More patients might be preferred regarding the evaluation of the incidence of PV stenosis and atrial tachyarrhythmia recurrences. Second, atrial tachyarrhythmia recurrences after the index procedure were evaluated only by 24-hour Holter monitoring along with outpatient visits every 3 months. Longer Holter monitoring or external event monitor may
have been preferred to detect atrial tachyarrhythmia recurrences. Third, we did not assess the effect of LB PVI with a 30%–40% overlap ratio on efficacy or safety. Fourth, lesion formation could have depended on the differences in the left atrial wall thickness between the individuals. Fifth, no esophageal endoscopic examination was performed after the index procedures. Therefore, esophageal injury remains unclear. Sixth, as compared to ablations with radiofrequency current catheters or cryoballoons, laser balloon ablation lacks real-time electrogram data to guide ablation endpoint. Therefore, the target laser energies may have to be estimated by real-time monitoring of PVI if possible. Finally, we did not verify dragging ablation. Especially, LB3 enables automated dragging ablation with higher power (13 W or 15 W), leading to the shorter procedure time than LB2.20 Dragging ablation is possible even with LB1 and LB2.

Conclusion
Point-by-point LB ablation with sufficient overlap ratio facilitates high first-pass PVI rate without any adverse acute or chronic outcomes. High energy is required for PV anterior walls in some cases.

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Authorship
All authors attest they meet the current ICMJE criteria for authorship.

Patient Consent
Informed consent was obtained from all patients.

Ethics Statement
The research reported in this study was conducted according to the principles of the Declaration of Helsinki. The study was approved by the Institutional Review Board of Sakakibara Heart Institute.