



## ORIGINAL ARTICLE

# Wide area circumferential ablation for pulmonary vein isolation using radiofrequency versus laser balloon ablation

Jamario Skeete MD<sup>1</sup> | Parikshit S. Sharma MD, MPH<sup>1</sup> | David Kenigsberg MD<sup>2</sup> |  
 Grzegorz Pietrasik MD, PhD<sup>3</sup> | Ahmed F. Osman MD<sup>2</sup> | Venkatesh Ravi MD<sup>1</sup> |  
 Jeanne M. Du-Fay-de-Lavallaz MD, PhD<sup>4</sup> | Zoe Post MD<sup>1</sup> | Jeremiah Wasserlauf MD<sup>1</sup> |  
 Timothy R. Larsen DO<sup>1</sup> | Kousik Krishnan MD<sup>1</sup> | Richard Trohman MD, MBA<sup>1</sup> |  
 Henry D. Huang MD<sup>1</sup>  

<sup>1</sup>Division of Cardiology, Rush University Medical Center, Chicago, Illinois, USA

<sup>2</sup>Florida Heart Rhythm Specialists, Westside Medical Center, Fort Lauderdale, Florida, USA

<sup>3</sup>Division of Cardiology, Cook County Health, Chicago, Illinois, USA

<sup>4</sup>Department of Internal Medicine, University Hospital of Basel, Basel, Switzerland

**Correspondence**

Henry D. Huang, Rush University Medical Center, 1717 W. Harrison St., Suite 317 Kellogg, Chicago, IL 60612, USA.  
 Email: [henry\\_d\\_huang@rush.edu](mailto:henry_d_huang@rush.edu)

**Funding information**

James E. Thompson Fund

**Abstract**

**Background:** Persistent atrial fibrillation (AF) is associated with high recurrence rates of AF and atypical atrial flutters or tachycardia (AFT) postablation. Laser balloon (LB) ablation of the pulmonary vein (PV) ostia has similar efficacy as radiofrequency wide area circumferential ablation (RF-WACA); however, an approach of LB wide area circumferential ablation (LB-WACA) may further improve success rates.

**Objective:** To evaluate freedom from atrial tachyarrhythmia (AFT/AF) recurrence postablation using RF-WACA versus LB-WACA in persistent AF patients.

**Methods:** This was a retrospective multicenter study. Patients were followed for up to 24 months via office visits, Holter, and/or device monitoring. The primary endpoint was freedom from AFT/AF after a single ablation procedure. Secondary endpoints included freedom from AF, freedom from AFT, first-pass isolation of all PVs, and procedural complications.

**Results:** Two hundred and four patients were studied (LB-WACA:  $n = 103$ ; RF-WACA:  $n = 101$ ). Patients' baseline characteristics were similar except patients in the RF-WACA group were older (64 vs. 68,  $p = .03$ ). First-pass isolation was achieved more often during LBA (LB-WACA: 88% vs. RF-WACA 75%;  $p = .04$ ). Procedure ( $p = .36$ ), LA dwell ( $p = .41$ ), and fluoroscopy ( $p = .44$ ) time were similar. The mean follow-up was  $506 \pm 279$  days. Sixty-six patients had arrhythmic events including 24 AFT and 59 AF recurrences. LB-WACA group had higher arrhythmia-free survival ( $p = .009$ ) after single ablation procedures. In the multivariate Cox regression model, RF-WACA was associated with a higher recurrence of AFT compared with LB-WACA (Adjusted HR 3.16 [95% CI: 1.13–8.83];  $p = .03$ ).

**Conclusions:** LB-WACA was associated with higher freedom from atrial arrhythmias mostly driven by the lower occurrence of AFT compared with RF-WACA.

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**KEYWORDS**

atrial fibrillation, catheter ablation, laser ablation, wide area circumferential ablation

## 1 | INTRODUCTION

Catheter ablation has established as a cornerstone approach for the treatment of drug-resistant, symptomatic atrial fibrillation (AF).<sup>1–3</sup> Persistent AF has a more complex pathophysiologic basis than paroxysmal atrial fibrillation (PAF), characterized by extensive left atrial structural and electrical remodeling.<sup>4,5</sup> As such, whereas ostial pulmonary vein isolation (PVI) provides reasonable success in the management of PAF, when used in patients with persistent AF, long-term maintenance of sinus rhythm is often elusive.<sup>6</sup> Consequently, more aggressive techniques for ablation are often employed in this population.<sup>7</sup>

A strategy considers that triggers and drivers perpetuating AF arise not only from the muscular PV sleeves but also from foci extending to left atrial areas before and around the PV ostia is radiofrequency wide area circumferential ablation (RF-WACA) PVI.<sup>8–10</sup> This strategy seeks not only to isolate the individual pulmonary veins (PV) s but also to isolate the adjacent antral surface of the left atrium (LA), including arrhythmogenic aspects of the posterior LA wall.<sup>11,12</sup> In a meta-analysis of 12 trials, a comparison between ostial and WACA PVI strategies using RF demonstrated less recurrence of AF with WACA but a trend toward higher atypical atrial flutter or tachycardia (AFT) recurrence compared with an ostial PVI approach.<sup>13</sup> Recently, a study comparing WACA-RF of ipsilateral PVs to ostial PVI using the laser balloon (LB) catheter system, an emerging technique for PVI, demonstrated similar procedural outcomes of recurrence of any atrial arrhythmias (AFT/AF) at 1-year follow-up.<sup>14</sup>

Although balloon catheters have recently been demonstrated as effective alternatives to RFA for the treatment of PAF and persistent AF, the feasibility of utilizing a WACA strategy with laser balloon catheters has not yet been examined. The LB ablation system has several features which may be favorable for wide-area ablation including a compliant balloon that can be manually adjusted up to a 41 mm diameter size for visualization of a large surface area during ablation. We conducted a multicenter prospective cohort study to assess this hypothesis while comparing the long-term performance and safety of LB versus RF strategies for WACA of ipsilateral PVs in patients with persistent AF.

## 2 | METHODS

### 2.1 | Patient selection

This multicenter study included 204 consecutive patients with drug-refractory persistent AF who underwent first-time catheter ablation from January 1, 2018 to April 30, 2021. Persistent AF was defined as having at least one episode of AF lasting longer than 7 days and failure or intolerance to at least one antiarrhythmic drug (AAD). Exclusion criteria included a history of prior PVI or LA ablation

(surgical or percutaneous), reversible causes of AF (e.g., thyrotoxicosis, electrolyte abnormalities, postoperative), and permanent AF.

This study was conducted at two tertiary medical centers in the United States (Rush University Medical Center, and Westside Medical Center). All operators were experienced in the ablation technique performed (RF-WACA—four operators, LBA-WACA—four operators). The technique of ablation offered was determined at the discretion of the operator. Operators were experienced performing both LB ablation (>100 cases) and RF ablation (>400 cases) for PVI. Institutional review board (IRB) approval was granted by the Rush University Medical Center's and Westside Medical Center's IRB and the study complied with the ethical stipulations set forth by the institutional governing committees. Prior to the procedure, informed written consent was obtained. The data and study materials are available within the article.

### 2.2 | Preprocedural assessment

Patients presented to the procedure in a fasting state. Previously prescribed oral anticoagulation based on the CHA<sub>2</sub>DS<sub>2</sub>-VASC score was continued until the date of the procedure as was any prior antiarrhythmic medications. Evaluation for intracardiac thrombi was performed either on the day prior to the procedure using cardiac computed tomography (CT) or on the day of the procedure using transesophageal echocardiography (TEE) and/or intracardiac echocardiography (ICE).

### 2.3 | Procedure

All ablation procedures were performed under general anesthesia. Bilateral femoral access was obtained with ultrasound guidance using the modified Seldinger technique. Intravenous heparin was administered as boluses and continuous infusion to maintain a target ACT of >300 s. In both groups, esophageal temperature monitoring was performed using a commercial temperature probe (SensiTherm, Abbott). Ablation lesion delivery was halted if the esophageal temperature exceeded 39°C.

Under ICE catheter (AcuNav, Biosense Webster Inc) guidance, a transeptal puncture was made using the modified Brockenbrough technique. An 8.5 F SL1 sheath (Abbott Laboratories) was advanced into the left atrium. For cases undergoing RF-WACA, a second transeptal puncture was performed in a similar fashion.

#### 2.3.1 | Laser balloon ablation

In the LB group, ablations were performed under visual guidance using second-generation (LB2, Heartlight Excalibur, CardioFocus) or

third-generation (LB3, Heartlight X3, CardioFocus) LB catheter ablation systems. Following transeptal puncture, the SL1 sheath was exchanged over an Amplatz super-stiff wire (Boston Scientific) for a 12-Fr steerable sheath-dilator assembly (CardioFocus). Using the deflectable sheath, the LB catheter was positioned to the ostium of the target PV. Balloon inflation, positioning, and ablation were performed using both fluoroscopic and endoscopic visual guidance. Sequential applications of laser energy were delivered between 8.5 W × 20 s and 12.0 W × 20 s in a point-to-point fashion with 20%–30% overlap between contiguous lesions to produce an encircling ablation at the antrum at least 1.5 cm away from the ostium of each PV. If an LB3 catheter was used, laser energy was delivered in RAPID mode (15 W Anterior ridge-side of LPVs and 13 W elsewhere) and/or in a point-by-point fashion in manual mode. In order to complete the WACA lesion set of ipsilateral PVs, an additional linear ablation was performed in manual point-by-point or RAPID mode at the anterior and posterior carina locations to connect the individual circular PV ablation lines (Figure 1). If simultaneous visualization of atrial tissue surrounding ipsilateral PVs was obtained after balloon inflation, then a single encircling lesion set was delivered around both PVs and a single ablation line was still delivered across the PV carina. Ablation of the anterior side of the right PVs was performed during high output pacing of the right phrenic nerve (PN with monitoring of compound motor action potential [CMAP] amplitude and diaphragmatic movement).

After a 30-min waiting period, a high-density multispline or grid catheter (Pentaray, Biosense Webster or HD Grid) was used in all procedures to construct a postablation 3D voltage map (0.2–0.5 mV) of the LA and lesions sets. Pacing maneuvers were performed to confirm whether electrical isolation was achieved across ipsilateral PV lesion sets. If electrical conduction was demonstrated across the WACA line, then the LB2/LB3 catheter was used to deliver lesions in manual or RAPID mode targeting breakthrough sites after repositioning the LB catheter into a different PV branch when necessary.

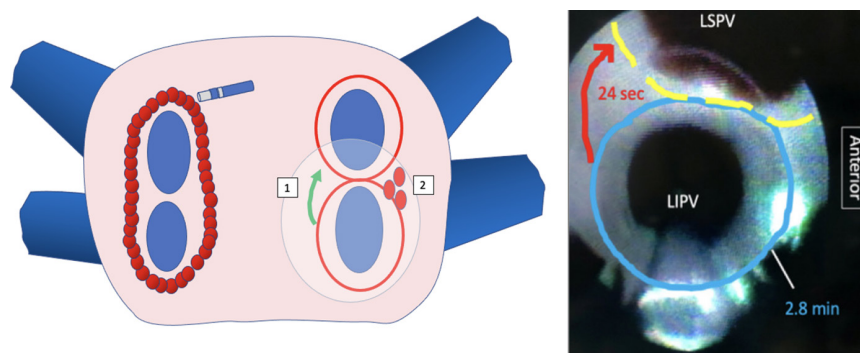
If WACA of ipsilateral PVs was not achievable despite repeated attempts at ablation with the LB catheter, risk of extracardiac injury was felt to be possible, or an epicardial connection remote to the WACA line within the PV was suspected, supplemental RFA was performed at the operator's discretion.

### 2.3.2 | Radiofrequency wide antral circumferential ablation

RF-WACA was performed using an irrigated contact force-sensing RF catheter (ThermoCool Smarttouch/Surround Flow, Biosense Webster or TactiCath, Abbott Laboratories) and a 3D electroanatomic mapping system (Carto 3 V4, Biosense Webster or Precision, Abbott Laboratories).

Following transeptal puncture, the RF ablation catheter was advanced into the LA. Under electroanatomic mapping guidance, circumferential delivery of point-by-point RF energy applications was delivered with guidance by Lesion Index (LSI values: 6.0 for anterior wall/roof; 5.5 for posterior wall) or Ablation Index (AI targets: 500–550 for anterior wall/roof; 400–450 for posterior wall) at a distance of at least 1.5 cm from the PV ostia until both sets of ipsilateral PVs were encircled by a complete ablation line.<sup>13</sup> RF was delivered targeting an interlesion distance of 4–6 mm. All ablation in the RF-WACA group were performed using contact force-sensing irrigated ablation catheters. Ablation of the carina of ipsilateral PVs was performed following attainment of entrance and exit block across the WACA lesion sets.

After a 30-min waiting period, PVs were assessed for electrical isolation by constructing a postablation 3D voltage map (0.2 mV–0.5 mV) and pacing maneuvers using a high-density multispline or grid catheter. If a targeted PV was not isolated after ipsilateral WACA lesion sets and carina ablation or there was an electrical breakthrough across the WACA line after a single pass



**FIGURE 1** Left panel depicts wide area circumferential ablation (WACA) of ipsilateral PVs using RFA and LBA techniques. During the LBA approach, each PV is first circumferentially isolated followed by (1) an ablation line connecting antral lines around superior and inferior PVs or (2) by delivery of point-by-point lesions filling unablated areas of the posterior/anterior carinas. The right panel shows an endoscopic view of the LIPV and the adjacent LSPV at the time of LBA. The blue line shows the line of ablation around the LIPV, whereas the dashed yellow line represents the ablation line for the LSPV. The red arrow demonstrates connecting ablation line to the complete collective encircling of the LSPV and LIPVs (WACA). Estimated times to perform these ablations with the Heartlight X3 ablation system using rapid mode are shown. LIPV: left inferior pulmonary vein; LSPV: left superior pulmonary vein; RFA: radiofrequency ablation; LBA: laser balloon ablation

of ablation around ipsilateral PVs (failure of first-pass isolation), the RF ablation catheter was used to deliver lesions in the area of electrical breakthrough until acute electrical isolation was achieved.

## 2.4 | Postprocedure follow-up

All patients were discharged on anticoagulant therapy. AADs were stopped at 3 months. Follow-up visits occurred at 1-, 3-, 6-, 12-, 18-, and 24-month intervals for the majority of patients and included a 12-lead ECG. A 14-day ambulatory ECG monitor (Ziopatch, iRhythm) was obtained after the 90-day blanking period.

### 2.4.1 | Clinical endpoints

The primary endpoint of the study was freedom from atrial tachyarrhythmia (AFT/AF; defined as the occurrence of atrial fibrillation, atypical atrial flutter, or atrial tachycardia) after the index ablation procedure.

Secondary endpoints included freedom from AF recurrence, freedom from AFT, first-pass isolation of all target PVs (successful isolation of all PVs without the use of supplemental ablation lesions to address gaps or acute reconnection), procedural time, fluoroscopic time, LA dwell time, and the occurrence of procedural complications. Following the 90-day blanking period, atrial tachyarrhythmias (either symptomatic or asymptomatic) were designated as failure events if lasting >30 s and were captured on a 12-lead ECG, continuous telemetry during a healthcare encounter or by implantable cardiac implanted electronic device recordings.

## 2.5 | Statistical analysis

Baseline characteristics by the mode of WACA Laser balloon ablation (LBA) and radiofrequency ablation (RFA) were compared using a two-tailed Student's *t* test for normally distributed continuous variables and Kruskal–Wallis for nonnormally distributed variables. Anderson–Darling test was performed to test for normality. For categorical variables, the chi-square test and the Fisher exact test were used when appropriate. Kaplan–Meier estimates for endpoints, stratified by the mode of WACA (LB-WACA vs. RF-WACA), were determined and statistically evaluated with the log-rank test. The Cox proportional-hazards regression model was used to evaluate the independent contribution of baseline clinical factors to the development of endpoints. Stepwise elimination and backward selections were used to select the most parsimonious set of predictive variables. All *p* values were two-sided, and a *p* value of  $\leq .05$  was considered significant. Analyses were performed with the use of MINITAB software (version 19) and IBM SPSS Statistics software.

## 3 | RESULTS

### 3.1 | Patient characteristics

A total of 204 consecutive patients were included in this study. One hundred and one patients underwent RF-WACA and 103 patients underwent LB-WACA. There were no significant differences in baseline characteristics between the RF-WACA and LB-WACA groups (Table 1), except for age (RF-WACA:  $68 \pm 9$  vs. LB-WACA:  $64 \pm 11$  years;  $p = .03$ ). Usage of AADs after the postprocedure 90-day blanking was higher for the RF-WACA group (RF: 59% vs. 39%;  $p = .01$ ).

### 3.2 | Procedural outcomes

In all patients, acute electrical PVI was achieved during index procedures. The rate of first-pass PV isolation was higher in patients treated with LB-WACA compared to RF-WACA (88.3% vs. 75.2%,  $p = .04$ ) (Table 2). This, however, did not translate to statistically shorter procedural times (129 vs. 135 min;  $p = .32$ ) LA dwell times (92 vs. 97 min;  $p = .48$ ) or fluoroscopy times (10 vs. 11 min;  $p = .56$ ) between LB-WACA and RF-WACA procedures. Notably, procedure time (118 vs. 143 min;  $p = .001$ ) and LA dwell time (78 vs 109 min;  $p = .003$ ) were shorter when using LB3 in comparison with the LB2 catheters. However, fluoroscopy time remained similar (11 vs. 12 min;  $p = .63$ ) using LB3 and LB2, respectively. About 43% of PVs ablated using only RAPID mode using LB3. In the LBA group, touch-up ablation was required in 7/103 (6.8%) patients to obtain complete entrance and exit block of WACA lesion sets during index procedures. Supplemental RFA was used to achieve electrical isolation of WACA lesion sets in 3/103 (2.9%) patients in the LBA group. Anatomic locations requiring touch-up RF ablation were (1) anterior ridge of left PVs ( $n = 1$ ), (2) epicardial connection to LSPV within WACA line ( $n = 1$ ), and (3) anterior and posterior carina of the right PVs due to the wide separation of the RSPV and RIPV ostia ( $n = 3$ ). Two patients (1.9%) required to touch up ablation following acute reconnection during the waiting period which was achieved using the LB catheter. Locations: anterior carina of left PVs ( $n = 1$ ); anterior roof of right PVs ( $n = 1$ ).

In terms of procedural complications in the RF-WACA group, one patient suffered a stroke postprocedure, one patient had phrenic nerve palsy which recovered by 6 months, one patient had a pericardial effusion requiring pericardiocentesis for tamponade, and three patients had small-sized groin hematomas. In the LB-WACA group, two patients had phrenic nerve palsy (both recovered prior to discharge from the index hospitalization), one patient had a stroke postprocedure, and two patients had small groin hematomas.

### 3.3 | Clinical endpoints for the study

The mean follow-up period was  $506 \pm 279$  days. Follow-up duration was similar in both groups (RFA:  $508 \pm 281$  vs. LBA:

	Laser N = 103	RFA N = 101	p value
Age, years (median)	64	68	.02
(mean ± SD)	64 ± 11	68 ± 9	.03
Male gender	61 (60%)	60 (59%)	.89
HTN	75 (73%)	79 (78%)	.28
DM type 2	27 (26%)	26 (26%)	.93
CAD	24 (23%)	28 (28%)	.51
EF % (median)	55	55	.66
(mean ± SD)	49 ± 15	51 ± 16	.47
Prior stroke/TIA	7 (7%)	5 (5%)	.62
Persistent AF onset (days)	155 ± 119	148 ± 91	.71
Duration of AF episode before index ablation procedure (days)	42 ± 22	37 ± 22	.36
Use of β-blocker medications	80 (78%)	72 (72%)	.47
Use of antiarrhythmic medications prior to ablation	63 (61%)	57 (56%)	.73
Use of antiarrhythmic medications after 90 day blanking period	39 (40%)	59 (59%)	<.01
OSA	21 (20%)	27 (27%)	.33
BMI (median)	32	29	.56
(mean ± SD)	32 ± 8	30 ± 7	.39
LA volume index ml/m <sup>2</sup> (median)	42	44	.19
(mean ± SD)	44 ± 17	47 ± 20	.23
LA diameter, cm (median)	4.6	4.4	.59
(mean ± SD)	6 ± 12	4.6 ± 1.1	.31
Time to AFT, days (median)	404	457	.92
(mean ± SD)	470 ± 228	473 ± 261	.93
Time to AF, days (median)	387	308	.27
(mean ± SD)	416 ± 228	387 ± 238	.40
Time to any arrhythmia, days (median)	380	304	.16
(mean ± SD)	415 ± 227	376 ± 233	.25
First-pass isolation	91(88%)	76 (75%)	.04
Procedure time (min)	129 ± 24	135 ± 34	.32
LA dwell time (min)	72 ± 22	77 ± 24	.48
Fluoroscopy time (min)	10 ± 6	11 ± 7	.51
Follow-up duration (days)	504 ± 258	508 ± 281	.84

TABLE 1 Baseline and procedural characteristics of study groups

Abbreviations: AF, Atrial fibrillation; AFT, atypical atrial flutter or tachycardia; BMI, body mass index; CAD, coronary artery disease; DM, diabetes mellitus; EF, ejection fraction; HTN, hypertension; LA, left atrial; OSA, obstructive sleep apnea; RFA, radiofrequency ablation; SD, standard deviation; TIA, transient ischemic attack.

504 ± 258 days;  $p = .8$ ). During this time, there were 66 (32.3%) patients with any arrhythmic events (AFT/AF), consisting of 24 (11.8%) patients who developed AFT and 59 (28.9%) patients with AF recurrences. In the LBA group, there were 25 (24.2%) patients with any AFT/AT events, consisting of 5 (4.9%) patients with AFT and 23 (22.3%) with AF recurrences. In the RFA group, there were 41 (40.6%) patients with AFT/AT events, including 19 (18.8%) with AFT, and 36 (35.3%) with AF recurrences. The rate of AFT/AT recurrence in the 90-day blanking period was 23% in the entire population. There was no significant difference in AFT/AF recurrence

in the blanking period between the RFA and LBA groups (24% vs. 21%;  $p = .74$ ).

Kaplan–Meier curves describing cumulative probabilities of time to occurrence of first postablation arrhythmic events by the modality of WACA are shown in Figure 2. Patients who had LB-WACA were more likely to be free from recurrence of any arrhythmia ( $p = .009$ ), AFT ( $p = .003$ ), and AF ( $p = .046$ ) during the long-term follow-up.

In the multivariate analysis, variables evaluated in the Cox proportional hazard regression stepwise selection model predicting arrhythmic endpoints included: age as a continuous variable, first-pass

pulmonary vein isolation, and use of antiarrhythmic medications after the 90-day blanking period. First-pass pulmonary vein isolation was the only variable that made a significant contribution to the model. As demonstrated in Table 2, after adjustment for the first-pass PV isolation, there was a trend toward a higher risk of postablation occurrence of atrial arrhythmia (AF or AFL) among patients who underwent RF-WACA compared with patients who underwent LB-WACA (HR = 1.62; 95% CI 0.98–2.74;  $p = .07$ ). RF-WACA was associated with threefold increase in risk of AFT (HR = 3.16, 95% CI 1.13–8.83,  $p = .03$ ) but not with an increased risk of AF (HR = 1.34, 95% CI 0.80–2.43,  $p = .25$ ). Following adjustment for age, first-pass PV isolation, and use of antiarrhythmic medications after the 90-day blanking period, the risk of AFT on follow-up remained significantly higher for patients that underwent RF-WACA (Table 2).

In the overall cohort ( $n = 204$ ), successful achievement of first-pass isolation of all target PVs during initial ablation procedures was significantly associated with higher freedom from AF on long-term follow-up ( $p = .004$ ). Figure 3 shows Kaplan–Meier curves

**TABLE 2** Cox regression stepwise model: risks of arrhythmic events in patients with RF-WACA compared to patients with LB-WACA—adjusted for age, first-pass PV isolation, and use of antiarrhythmic medications (age and use of antiarrhythmic medications were forced to the model since  $p$  value was  $>.10$ )

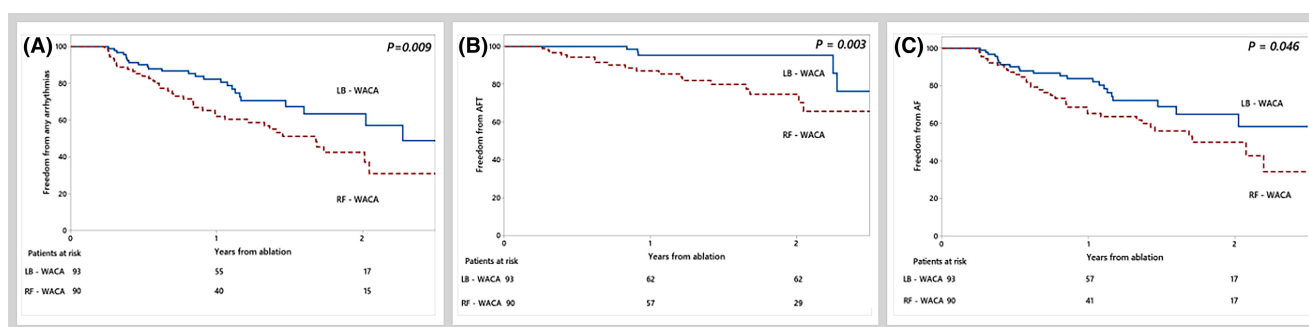
End point	HR	95% CI of HR	$p$ value
Any atrial arrhythmias	1.62	0.98–2.74	.07
Atrial flutter	3.16	1.13–8.83	.03
Atrial fibrillation	1.34	0.80–2.43	.25
Adjusted for first-pass isolation (above)			
Any atrial arrhythmias	1.52	0.88–2.67	.15
Atrial flutter	3.00	1.02–8.82	.04
Atrial fibrillation	1.26	0.73–2.42	.42
Adjusted for first-pass PV isolation, age, and use of AAD medications in a 90-day blanking period (above)			

Abbreviations: AAD, antiarrhythmic drug; HR, hazard ratio; PV, pulmonary veins.

demonstrating cumulative probabilities of time to first AF recurrence based on achievement or absence of first-pass isolation by RF and LB-WACA modalities. Patients who underwent RF-WACA for whom first-pass PV isolation was not achieved had lower freedom from AF on long-term follow-up than other patients in the cohort ( $p < .001$ ).

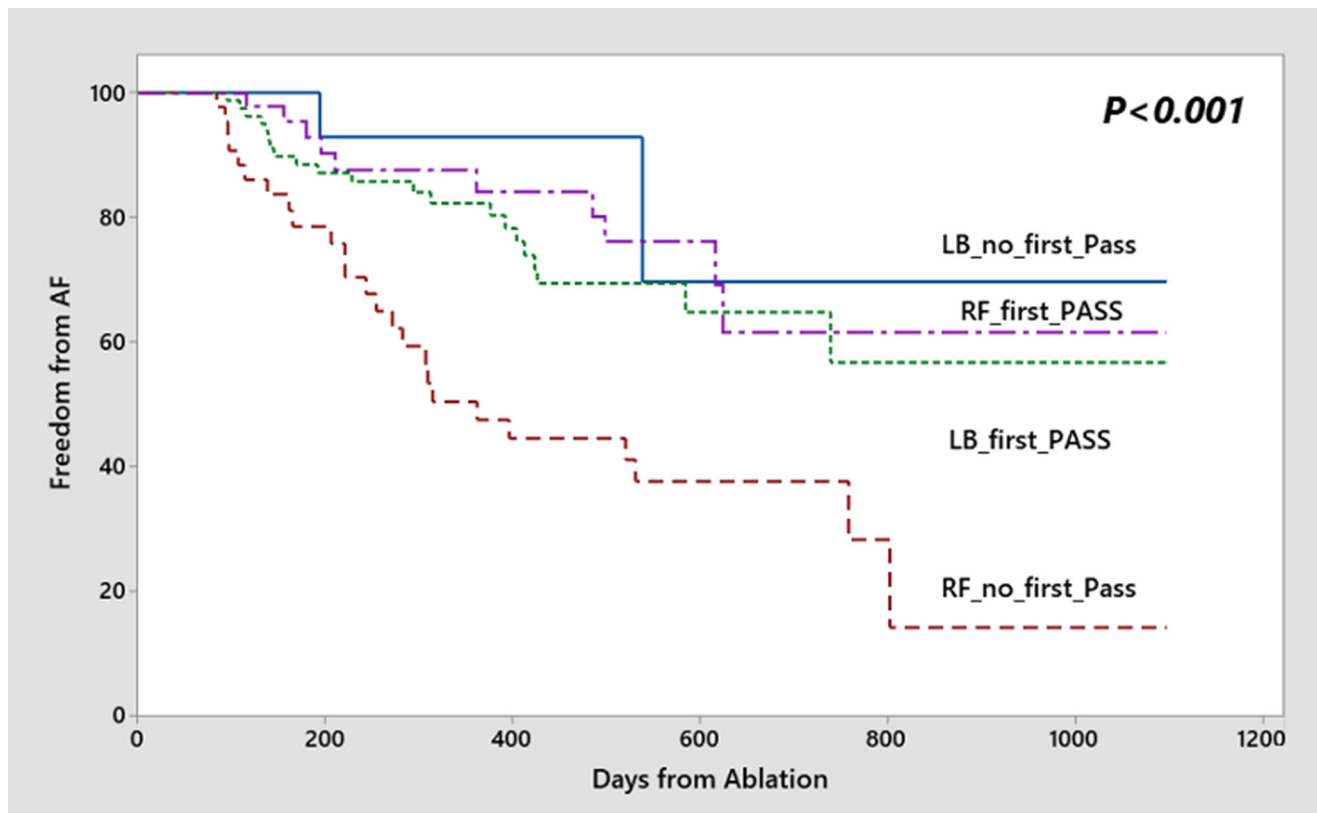
### 3.4 | Localization of AFTs during redo ablation after the 90-day blanking period

There were three patients in the LB-WACA arm with AFT recurrence after the 90-day blanking period who underwent redo-ablation procedures. One of the patients had a low-to-intermediate voltage area (0.2–0.4 mV) on the anterior wall and counterclockwise mitral annular flutter which was successfully ablated with an anterolateral mitral isthmus line. Two other patients had focal atrial tachycardias mapped and ablated on the (1) posterior roof just outside of the left WACA lesion set and on the (2) intraatrial septum within the area of low voltage (scar), respectively. Two patients had durable isolation of all PVs, whereas the third patient had reconnection of the LSPV, LIPV, and RSPV requiring touch-up of the anterior carina and posterior carina/inferior-posterior margin of WACA lesion sets, respectively. In the RF-WACA arm, there were eight patients with AFT recurrence after the 90-day blanking period who underwent redo-ablation procedures. Six patients had atrial flutters localized to the LA which were demonstrated by activation mapping and pacing maneuvers to be: (1) roof dependent ( $n = 1$ ), (2) counterclockwise mitral annular flutters ( $n = 2$ ), and (3) macro-reentrant circuits involving scar areas on the septum ( $n = 1$ ), (4) anterior wall ( $n = 1$ ), and traversing gaps in prior right PV WACA line ( $n = 1$ ). All clinical AFTs were successfully ablated in the redo-RF-WACA group except for one patient who developed incessant peri-mitral flutters refractory to ablation and was eventually cardioverted. Two patients who underwent redo-RF ablation had focal atrial tachycardias mapped to (1) the base of the left atrial appendage and (2) the posterior wall adjacent to the posterior carina region of the right PVs. Foci of atrial tachycardias



**FIGURE 2** (A) Freedom from any atrial arrhythmia. Kaplan–Meier analysis showing arrhythmia-free survival after a single ablation procedure; blue line: laser balloon group. (B) Freedom from atypical atrial flutter or atrial tachycardia (AFT). Kaplan–Meier analysis showing AFT-free survival after single ablation procedure. (C) Freedom from atrial fibrillation (AF). Kaplan–Meier analysis shows AF-free survival after a single ablation procedure





**FIGURE 3** Freedom from AF four groups: first-pass isolation in RF-WACA, first-pass isolation in LB-WACA, no first-pass isolation in RF-WACA, and no first-pass isolation in LB-WACA

for both patients were successfully ablated. In the RF group, four of eight patients were found to have at least one PV chronically reconnected. Patient 1 had reconnection of LIPV requiring ablation underneath the anterior ridge. Patient 2 had chronic reconnection of RSPV and RIPV requiring ablation of the posterior carina, roof, and anterior to the RIPV. Patient 3 had reconnection of the LSPV and LIPV requiring ablation of the anterior ridge and carina for isolation. Patient 4 had reconnection of the RSPV only requiring ablation of the anterior roof and carina for isolation.

#### 4 | DISCUSSION

In this retrospective multicenter study, we assessed the procedural performance of LB-WACA and point-by-point RF-WACA strategies for isolation of ipsilateral PVs in patients with persistent AF and found that the LB ablation strategy was associated with higher long-term freedom from atrial tachyarrhythmias after a single catheter ablation procedure. However, the advantage of the LB-WACA strategy in terms of arrhythmia-free success was driven mostly by lower arrhythmia recurrence caused by atypical atrial flutter or atrial tachycardia compared with the RF strategy. In addition, we also demonstrated a higher risk of AF recurrence after failure to achieve first-pass PV isolation in patients who underwent RF-WACA. These findings highlight the potential added role of LBA as an alternative approach for WACA PVI in patients with persistent AF.

The efficacy of catheter ablation for patients with PAF is well established. However, achieving similar long-term success with the same approaches has been more elusive in patients with persistent AF most likely due to inherent differences in mechanisms underlying AF perpetuation. While various ablation strategies such as linear lesions, electrogram-guided atrial substrate modification, and posterior wall isolation have been examined, the benefit of additional ablation lesion sets beyond PVI has proven unclear.<sup>15</sup> Ouyang and colleagues were the first to describe using a single line of ipsilateral PV encirclement for PVI guided by 3D mapping with a rationale for targeting a larger area of pro-arrhythmogenic tissue while lowering the risk of PV stenosis. In AF cohorts, trials have examined the comparative efficacy of ostial and wide antral PVI approaches and found that WACA is associated with higher freedom from atrial tachyarrhythmia during the long-term follow-up.<sup>13</sup>

In comparison with ostial PVI approaches, a potential pitfall of ablating a wider area of the PV-LA junction is less durable PV isolation after first ablation procedures, given the increased thickness of atrial tissue in areas further away from the PV ostium and higher likelihood of leaving gaps in the intended circular line of ablation. While etiologies of arrhythmia recurrence postablation may be due to non-PV triggers,<sup>16</sup> common mechanisms for failure are the development of macro-reentrant arrhythmias with circuits involving the mitral isthmus, posterior atrial wall, as well as gaps in the lesions encircling PVs themselves, which also allow for PV reconnection and micro-reentrant atrial tachycardia.<sup>17-20</sup> Although

RF-WACA has demonstrated higher clinical efficacy for freedom from AF than ostial PVI, a trend toward more frequent atrial tachycardia recurrence has been observed postablation in subjects undergoing WACA.<sup>13</sup> Furthermore, gaps and nontransmural lesions leading to return of conduction are correlated with higher recurrence postablation.<sup>21,22</sup>

In a previous multicenter trial comparing RF-WACA with LBA using an ostial PVI approach in persistent AF patients, freedom from atrial arrhythmias (AT/AF) was similar (71.2% vs. 69.3% LBA vs. RF-WACA, respectively;  $p = .40$ ) on 1-year follow-up.<sup>14</sup> In the study, AT was observed in 25% of patients in the RF-WACA arm compared with 15% of patients in the LB-ostial PVI arm during 1-year follow-up. In the trial, ablation in the LB arm was performed exclusively with the first-generation LB catheter. The present study demonstrates for the first-time feasibility of a WACA of ipsilateral PVs with LB as an ablation strategy and directly compares single procedural effectiveness and safety of WACA PVI between LB and RF ablation modalities. We found that WACA using an LB strategy was associated with less long-term recurrence of atrial tachyarrhythmias, despite higher usage of AADs beyond the 90-day blanking period in the RF-WACA group after ablation. In addition, our study demonstrated a significantly lower rate of first-pass PV isolation in patients who underwent RF-WACA. However, the advantage of LB-WACA over RF-WACA for the primary endpoint was driven mostly by lower non-AF atrial tachyarrhythmia recurrences in the LB ablation group on the follow-up. In the current study, overall complication rates were similar between RF-WACA and LB-WACA approaches.

Although balloon catheter systems may be less versatile than 3D mapping guided RF techniques when additional LA ablation strategies are desired, the LB system may have several advantages for performing WACA PVI. These include direct tissue visualization during energy applications, ability to deliver overlapping contiguous lesions, which may decrease the likelihood of gaps, and the biophysical characteristics of the laser energy. In our study, ablation was performed using more contemporary second- and third-generation LB catheters. LB2 has a more compliant balloon than the first-generation system allowing for conformation to a wide variety of PV shapes and improving stability during lesion delivery, whereas maintaining steady catheter contact is often a challenge during point-by-point RF ablation affecting the lesion quality. The LB3 catheter has added the ability to continuously deliver laser energy as a single circular lesion using its "RAPID mode", which produces a continuous lesion (avoiding gaps) and significantly shortens overall procedure time and ablation time per PV.

In the current study, the LB strategy was associated with a significantly higher likelihood of achieving first-pass isolation of all target PVs than the RF strategy when performing WACA, which could be a marker of long-term lesion durability. While not associated with higher AFT recurrence, failure to achieve first-pass PV isolation during RF-WACA procedures carried a higher risk of AF recurrence on the long-term follow-up (Figure 3), suggesting possibly inadvertent ablation in the LA or another mechanism may play a role in AFT occurrence postablation. A recent study by Spittler et al. similarly

demonstrated that the occurrence of PV reconnection was not a determinant for ablation-associated atrial tachycardias after RF-PVI.<sup>23</sup> Rather it may be that scarring caused by inadvertent ablation in the LA body due to catheter instability (Video S1) is more likely to create a substrate for future reentrant arrhythmias.<sup>24–26</sup> As for reasons for lower FPI in the RFA group, edema created after point-by-point ablation may be a factor in reducing the depth of energy delivery when addressing gaps in the WACA line. Also, if FPI is not achieved, it may be difficult to tell which areas have a reversible injury and which are destined for permanent necrosis as both areas will have the absence of electrograms. Further RF lesion depth can also be affected by catheter angle during lesion delivery,<sup>27</sup> whereas Laser energy is delivered directly into visualized tissue and overall stability may be higher due to balloon inflation within target PV (Video S2). Mont et al. demonstrated on cardiac MRI that thicker scarring and higher residual gaps were present after antral RFA in comparison with LBA in patients who underwent PVI.<sup>24</sup>

Potentially, a disadvantage of utilizing an LB strategy for WACA is that when the distance between PV ostia is wide (>1.5 cm), achieving a single line of encirclement around ipsilateral PVs using the balloon is more challenging and the possibility of needing supplemental RF to attain isolation may be higher. For the right PVs, in particular, ablation of the carina may be important because of epicardial connections between the PV carina and other atrial areas.<sup>28</sup> While standardized workflows for RF-PVI incorporating multiparametric ablation markers have been shown to improve first-pass isolation rates and 12-month freedom from atrial arrhythmias, those strategies have not yet been examined for RF-WACA in populations with persistent AF.<sup>29,30</sup> Given that tissue thickness may increase with larger targeted areas of ablation, it is plausible that the WACA approach used in the current study's RF arm contributed to a lower rate of first-pass isolation compared with reported rates in prior studies examining LSI- and AI-guided ostial PVI ablation approaches. In a recently published study of 404 patients, FPI was not achieved in a significant proportion of PAF patients who underwent RFA using a WACA approach, and absence of FPI was associated with a higher risk of AF recurrence as well.<sup>31</sup>

## 4.1 | Limitations

This study has several limitations. The most important limitation is the study's retrospective observational design, which could have led to selection bias which may have potentially contributed to differences between treatment groups. Given the modest number of total participants ( $n = 203$ ), it is possible that the failure to detect a difference in the AF recurrence between LB-WACA and RF-WACA may be due to insufficient power. Another important limitation of the study was that due to a small number of redo procedures, we could not uniformly assess the reason/mechanisms for higher AFT/AT in the RF group. A randomized, larger, multicenter study is needed to verify the results of this study. Due to the study's observational nature, continuous implantable loop recorder monitoring was not



routinely performed for purposes of monitoring arrhythmia burden postablation.

## 5 | CONCLUSION

In this multicenter study, an LB-WACA strategy was associated with less atrial arrhythmia recurrence on long-term follow-up than the RF-WACA strategy in patients with persistent AF. The benefit of LB-WACA was mostly driven by the lower recurrence of atrial flutter and atrial tachycardias after the first ablation procedure. First-pass PV isolation occurred less frequently with RF-WACA and may result in an increased risk of AF recurrence. Prospective and randomized studies are needed to confirm these findings.

### ACKNOWLEDGMENTS

This article was supported by James E. Thompson Fund.

### CONFLICT OF INTEREST

Dr. Jeremiah Wasserlauf reports serving as a consultant for Stryker and consultant/speaker for Sanofi; Dr. Richard G. Trohman reports serving as an advisor to Boston Scientific/Guidant, receiving research grants from Boston Scientific/Guidant, Medtronic Inc.; and St. Jude Medical (Abbott), serving as a consultant for St. Jude Medical (Abbott) and receiving speakers fees or honoraria from Boston Scientific/Guidant CRM, Medtronic Inc. and St. Jude Medical (Abbott). Dr. Parikshit S. Sharma has been a speaker for Medtronic and has been a consultant for Abbott, Boston Scientific, and Biotronik. Dr. Kousik Krishnan serves as a consultant to Abbott/St. Jude Medical, Cardiva, and Zoll and research funding from Abbott/St. Jude Medical. Dr. Henry D. Huang reports serving as a consultant for Cardiofocus, receiving research grants from Medtronic. The remaining authors declare that they have no conflict of interest.

### AUTHORS' CONTRIBUTION

Dr. Skeete contributed to drafting the article and data collection, Dr. Sharma contributed to the data collection and critical revision of the article, Dr. Kenigsberg contributed to the concept/design, data collection, and critical revision of the article, Dr. Pietrasik performed data analysis/interpretation, Dr. Osman performed critical revision of the article, Dr. Ravi performed data collection and critical revision of the article, Dr. Du-Fay-de-Lavallaz assisted with data analysis/interpretation and critical revision of the article, Dr. Post, Dr. Wasserlauf, Dr. Larsen, Dr. Krishnan, and Dr. Trohman contributed to critical revision of the article. Dr. Huang contributed to the concept/design, critical revision, and approval of the article.

### ETHICS STATEMENT

The study was approved by the Rush University and Westside Medical Center Institutional Review Boards. Patient consent was not obtained due to the retrospective nature of the study. This study was not a clinical trial so registration was not required.

### ORCID

Henry D. Huang  <https://orcid.org/0000-0002-4103-4317>

### TWITTER

Henry D. Huang  @https://twitter.com/hhuang123

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## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

**How to cite this article:** Skeete J, Sharma PS, Kenigsberg D, Pietrasik G, Osman AF, Ravi V, Wide area circumferential ablation for pulmonary vein isolation using radiofrequency versus laser balloon ablation. *J Arrhythmia.* 2022;38:336–345. <https://doi.org/10.1002/joa3.12722>