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One-year outcomes of a conformable single-shot pulsed-field ablation catheter for the treatment of paroxysmal atrial fibrillation

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ABSTRACT

BACKGROUND Most single-shot pulsed-field ablation (PFA) catheters require extensive repositioning for pulmonary vein isolation (PVI), posing a challenge for obtaining contiguous, durable lesions.

OBJECTIVE To determine 1-year outcomes of a single-shot, all-in-one mapping and ablation PFA catheter for treating paroxysmal atrial fibrillation (PAF).

METHODS After PVI with the large-lattice catheter with expandable tip (Sphere-360), follow-up included Holter monitoring at 180 and 365 days and scheduled/symptomatic trans-telephonic monitoring (TTM) or modeled insertable loop recorder (ILR) data. Efficacy outcomes were acute PVI and 12-month freedom from atrial arrhythmias (AA), after 90-day blanking. Optional invasive remapping at 75 days facilitated waveform refinement from PULSE1, PULSE2, to the optimized PULSE3.

RESULTS At 3 centers, 100 PAF patients underwent PFA with PULSE1 ($n = 30$), PULSE2 ($n = 20$), or PULSE3 ($n = 50$). Procedure, left atrial dwell, and fluoroscopy times were 57.9 ± 20.6, 22.2 ± 11.8 and 6.8 ± 5.7 minutes, respectively. All 395 targeted PVs were acutely isolated, with a transpired PVI time of 11.5 ± 6.0 minutes, using 4.0 ± 1.3 lesions/PV. There were no primary safety events (serious device-related events within 7 days post-PFA). PVI durability with PULSE3 ($n = 40$) was 98% (per-vein) and 93% (per-patient). One-year freedom from AA recurrence was 82.0% (95% CI:73.0%–88.3%) overall, and 88.0% (95%CI, 75.2%–94.4%) for PULSE3 patients. Of the ILR sub-cohort (n = 15 PULSE3 patients), 3 patients (20%) had recurrences, with an AA burden reduction from 26% (baseline) to 1.6% (post-ablation).

CONCLUSION The large lattice PFA catheter was efficient, safe, and effective in treating PAF. The observed high PVI durability translated to clinical effectiveness, even in continuously monitored patients.

KEYWORDS Pulsed-field ablation; Mapping; Atrial fibrillation; Catheter ablation; Burden

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Introduction

Pulmonary vein isolation (PVI) is the cornerstone for treating patients with atrial fibrillation (AF).[1,2] However, achieving reliable PVI durability with current technologies continues to be a challenge in spite of the recent innovation of pulsed-field ablation (PFA)[3,4]; PFA uses irreversible electroporation (IRE), a technique that uses rapid, high-voltage electrical pulses to destabilize cell membranes and induce cell death—resulting in myocardial tissue destruction with minimal to no collateral damage.[5–8] Most currently available commercial PFA

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catheters require users to employ a segmental approach or require multiple re-positioning to achieve electrical pulmonary vein (PV) isolation, which may be limited by inadvertent gaps between lesion sets.[9–13] Gaps may lead to electrical PV reconnection, resulting in subsequent AF recurrence with the need for repeated treatment, or may create new atypical atrial flutter (AFL) circuits that may be even more symptomatic than the index AF.[14] Delivery of IRE with a wide surface area electrode increases the likelihood of forming a contiguous (gap-free) lesion encircling each PV.

To address these limitations, a true single-shot PFA catheter was crafted with a large-lattice, expandable tip (up to 34 mm) to be able to conform to the shape of the PVs. This design may facilitate the successful ablation of assorted left atrial and PV anatomies without the need for catheter rotation in each location and limited re-positioning. Pulsed-field (PF) energy is delivered from most of the lattice, enabling circumferential, transmural lesions around the PVs.[15–17] Furthermore, by being an all-in-one-mapping and ablation catheter that is connected to an electro-anatomical mapping (EAM) system, this novel catheter brings efficiency to the PVI procedure, with previously reported PVI procedure times being < 1 hour.[17] As evidenced in an interim analysis of this study, patients with paroxysmal AF (PAF) treated with this catheter had high long-term PVI durability on invasive remapping.[17] Herein, we report the full long-term results of treating PAF with this single-shot PFA catheter, including efficiency, safety, chronic efficacy, lesion durability on remapping, as well as atrial arrhythmia (AA) burden in a sub-cohort of patients who received insertable loop recorders (ILRs) for continuous cardiac rhythm monitoring.

Methods

Study design

This prospective, single-arm, multicenter trial aimed to assess the safety and efficacy of a novel conformable, single-shot PFA catheter (Sphere-360; Medtronic, Minneapolis, Minnesota) with a dedicated EAM system (Prism-1 Affera, Medtronic) for the treatment of PAF through PVI. This analysis pools data from 2 nearly-identical Affera-sponsored trials (NCT05144503, NCT05115214). Patient enrollment occurred at 2 centers in Czechia and 1 center in Lithuania. The list of centers and investigators can be found in the Supplemental Material. Before enrollment, each center obtained approval from the local ethics review board/competent authority and secured informed consent from all participants. The study adhered to the principles of the Declaration of Helsinki. The authors were responsible for ensuring integrity of data collection, analysis, and dissemination.

Abbreviations

AAD: anti-arrhythmic drug

AA: atrial arrhythmia

AF: atrial fibrillation

AFL: atrial flutter

AT: atrial tachycardia

EAM: electro-anatomical mapping

PAF: paroxysmal atrial fibrillation

PFA: pulsed-field ablation

PV: pulmonary vein

TTM: trans-telephonic monitoring

Study participants

The study enrolled patients aged 18 to 75 years with symptomatic PAF who had not previously undergone cardiac catheter ablation and had either failed or were intolerant to at least 1 class I-IV anti-arrhythmic drug (AAD). Eligibility required documented PAF within the past 12 months confirmed by at least 2 episodes of AF on electrocardiography (ECG). Within 30 days prior to the initial ablation procedure, patients underwent a screening process to confirm eligibility and collect baseline data. The evaluation included a review of medical and arrhythmia history, current medications, physical exam, transthoracic echocardiogram, thrombus screening, 12-lead ECG, and a pregnancy test if applicable. Thrombus screening, performed within 24 hours of the procedure, was conducted using either transesophageal echocardiography or intracardiac echocardiography at the time of the procedure. Major exclusion criteria included a body mass index > 40 kg/m^2, left ventricular ejection fraction < 40%, New York Hear Association class III or IV heart failure classification, and a left atrial diameter > 50 mm. However, patients were not excluded based on PV anatomy or a history of AFL or atrial tachycardia (AT). Comprehensive inclusion and exclusion criteria are detailed in Supplemental Table 1.

Large-lattice PFA mapping and ablation system

The ablation system has been described in detail previously.[17] There are 3 main components: (1) the expandable large-lattice circumferential ablation catheter (single-shot PFA catheter), (2) the PF generator, and (3) the EAM system. The 8-Fr single-shot PFA catheter has an electrode array comprised of a compressible nitinol lattice framework (expandable up to 34 mm in diameter) that is divided into 6 (equal area) sections through which a biphasic, monopolar waveform is sequentially distributed. The lattice also encompasses radiopaque markers which permits viewing the catheter on fluoroscopy. In conjunction with the EAM system (including the HexaMap catheter interface unit and Prism-1 mapping software; Medtronic), the PFA catheter allows for the simultaneous collection of PV/left atrium (LA) anatomy and creation of voltage and activation maps using electromagnetic tracking. Six mini-electrode pairs, which are uniformly distributed across the lattice surface, can be employed for cardiac stimulation, bipolar electrogram (EGM) recording, and impedance measurements to help assess cardiac tissue-to-catheter proximity. For PFA, the PF generator (HexaPulse; Medtronic) delivers trains of biphasic microsecond pulses up to 2.0 kV through the 6 sections of the electrode array that are separately and sequentially energized. The durability data observed with the initial waveforms provided the opportunity for improved optimization of the pulse waveform and system hardware, resulting in the development of 3 patient cohorts: PULSE1, PULSE2 and PULSE3.

PFA procedure

The PFA procedure has been thoroughly detailed in a previous publication.[17] Briefly, procedures were performed under continuous anticoagulation with heparin to maintain a target activated clotting time of > 300 seconds. Under general anesthesia and paralytics, the PFA catheter was introduced over a guidewire into the LA via transseptal puncture, using an 8.5-Fr steerable sheath (Agilis; Abbott, St. Paul, MN). Employing the EAM system and catheter, the geometric shell of the PV anatomy was rendered. The advancement of the collapsed single-shot PFA catheter in the targeted PV was facilitated by a mildly curved shape and guided by fluoroscopy and/or intra-cardiac echocardiography imaging, with the lattice framework progressively withdrawn and expanded between each PF energy application. To achieve full PV isolation, approximately 4 applications (5–6 seconds per application) were delivered per PV, with the study device maneuvered to deliver successively proximal applications toward the antrum. Protocol-mandated entrance block was confirmed after either a 20-minute wait period or an adenosine infusion. At investigator discretion, adjunctive linear lesions were implemented with a focal 9-mm lattice-tip catheter (Sphere-9 catheter; Medtronic) when needed to treat AT or AFL.

Catheter usability

The ease of use of the PFA catheter was determined with an operator survey in which the catheter was graded from 0–4 on the following parameters: (1) ease of insertion/removal of catheter into/from intra-vascular sheath, (2) ability to reach targeted veins, (3) ability to manipulate the catheter tip within the heart, (4) catheter tip visualization on fluoroscopy, (5) geometric shell created with the catheter, and (6) ability to generate acceptable acute ablation lesions with the catheter. A score of 0 indicated the least satisfaction, whereas a score of 4 indicated the highest.

Study follow-up

Patients underwent monitoring over a 12-month follow-up period, including in-person or virtual visits at 10 days, 75 days, 6 months, and 12 months following ablation. Cardiac medications, including AADs, that were prescribed at investigator's discretion throughout the study were recorded at each visit. Continuous 48-hour Holter monitoring was conducted at 180 and 365 days. Trans-telephonic monitoring (TTM) was performed weekly through 21 weeks (including the 90-day blanking period), monthly thereafter, and when patients were symptomatic throughout the study. Alternatively, a subset of PULSE3 patients (n = 15) were continuously monitored with an ILR (LINQ II; Medtronic); these patients also manually triggered ILR recordings according to the TTM regime. Optional esophagogastroduodenoscopy (EGD) and brain magnetic resonance imaging (MRI) were conducted 24 to 48 hours following the procedure; these were performed routinely, and not due to symptoms.

At the discretion of the patient and investigator, an optional invasive remapping procedure was performed at 75 ± 15 days post-ablation. Remapped patients underwent an additional virtual visit at 10 ± 3 days after the remap procedure. During the remapping procedure, a commercially available catheter was used to reisolate any reconnected PVs or linear lesions.

Study efficacy and safety outcomes

The primary efficacy outcome was acute electrical isolation of all PVs using the study device. The secondary efficacy outcomes were (1) chronic efficacy, defined as freedom from >30 second AA recurrence excluding a 90-day blanking period, and (2) PVI durability on a per-vein (veins that remain isolated) and per-patient (patients with all PVs isolated) basis. For the 12-month efficacy outcome, either TTM and Holter data or EGM data from the ILR that simulated the TTM (patient-triggered recordings—both symptomatic and scheduled) and Holter (48 hours of continuous monitoring) schedule were used. In a separate analysis of the PULSE3 ILR sub-cohort, the full continuous EGM recording data including all automatic recordings were also employed in determining AA recurrence and burden.

An independent clinical events committee/data safety and monitoring board (Supplemental Material) reviewed all adverse events and complications. The primary safety outcome was the occurrence of study device-related serious adverse events within 7 days of the index ablation, including the following: death, myocardial infarction, persistent phrenic nerve palsy, transient ischemic attack, stroke, thromboembolism, major vascular complications/ bleeding, heart block, gastroparesis, severe pericarditis, hospitalization (initial and prolonged) because of cardiovascular or pulmonary AEs, cardiac tamponade/perforation (up to 30 days), PV stenosis (up to 180 days), and atrio-esophageal fistula (up to 180 days). The secondary safety outcome was the percentage of patients with device- or procedure-related serious adverse events that were evaluated at each follow-up visit.

AA burden analysis

Patients that received ILRs had them implanted a median of 43 days before the index ablation to capture pre-ablation data. The ILR's algorithm continuously monitors and detects AA, allowing for precise determination of arrhythmia recurrence timing and measurement of AA burden (hours in AF per day and percentage of total time in AF). AA episodes were adjudicated and confirmed by review of stored EGMs.

Statistical analysis

To enhance lesion durability, propriety adjustments to pulse waveform parameters, and hardware/software updates were implemented throughout the enrollment process, resulting in PULSE1/PULSE2/PULSE3 waveforms, with PULSE3 being the most optimized waveform. The analysis cohorts comprised the total cohort (a combination of PULSE1, PULSE2, and PULSE3 data) and the PULSE3 sub-cohort. Because this was originally designed as a first-in-human study, there was no formal hypothesis testing or power calculation.

Post hoc analyses were conducted to compare PULSE3 against the combined PULSE1/PULSE2 data to highlight any clinical differences resulting from waveform evolution and PFA system optimization.

Continuous variables are presented as mean ± standard deviation. Categorical variables are expressed as numbers and percentages. Freedom from secondary efficacy failure (recurrence of AT/AF/AFL after the 90-day blanking period) was estimated using Kaplan-Meier methods. A log-rank test was used to compare secondary efficacy between PULSE3 and PULSE1/PULSE2. AA burden pre-ablation is defined as the average AA total daily burden in the 30 days prior to the ablation procedure. Post-ablation AA burden is the average AA total daily burden post the 90-day blanking period (days 91–365).

Results

Study population and baseline characteristics

At 3 European centers, including 7 operators, 100 PAF patients (60% men, aged 58.4 ± 10.6 years, diagnosed with PAF for 3.4 ± 3.7 years) underwent PFA using the PULSE1 (n = 30), PULSE2 (n = 20), or PULSE3 (n = 50) waveform (Figure 1). Other than the percentage of men, the total and PULSE3 cohorts did not differ significantly in baseline characteristics, including LA diameter (41.0 ± 4.4 vs 41.0 ± 4.5 mm), left ventricular ejection fraction (59.7 ± 5.7% vs 60.0 ± 6.0%), CHA_2DS_2-VASc scores (1.8 ± 1.3 vs 1.8 ± 1.2), and history of stroke or transient ischemic attack (3% vs 2%) (Table 1). Over 90% and 80% of patients in both groups received anticoagulants and class I/III AADs, respectively.

Procedural characteristics

As shown in Table 2, the procedure time (which included the protocol-mandated 20-minute waiting period and/or adenosine challenge that was employed in 68.9% of PVs) was 57.9 ± 20.6 minutes in the total cohort. The LA dwell times for the single-shot catheter (encompassing both mapping and ablation) were 22.2 ± 11.8 and 27.6 ± 12.1 minutes, and fluoroscopy times were 6.8 ± 5.7 and 8.2 ± 6.4 minutes, for the total cohort *vs* PULSE3 cohorts, respectively. Overall, 26 procedures were performed with ≤ 3 minutes of fluoroscopy, and with zero fluoroscopy.

Overall, 1.5 ± 0.5 and 1.8 ± 0.4 minutes of PF energy were delivered to accomplish PVI in the total and PULSE3 cohorts, respectively. Using 4.0 ± 1.3 applications per PV, PVI was achieved with transpired ablation times (time elapsing between the beginning of the first lesion to the end of the last lesion) of 11.5 ± 7.1 and 13.4 ± 7.8 minutes in the total and PULSE3 cohorts, respectively. Employing the study device, acute PVI was successfully achieved in 100% of the 395 targeted PVs, including 7 right middle PVs and 12 left common PVs.

EGD and brain MRI were performed 24–48 hours post the index ablation in 18% and 40% of patients, respectively. The results of these optional assessments are presented in Supplemental Tables 2 and 3.

The PFA catheter received a median score of 4 (with 4 being the highest score for a range of 0–4) for all 6 catheter usability parameters (Supplemental Table 4). Furthermore, 91% of the scores were ≥ 3.

Safety

No primary safety events occurred, including no death, persistent phrenic nerve palsy, PV stenosis, or atrio-esophageal fistula. Overall, only 1 serious procedure/device-related adverse event occurred: transient diplopia and vertigo at discharge. There were no acute findings via an immediate cerebral CT and an MRI performed 9 days after symptom commencement; the event was deemed to be non-specific as adjudicated by the independent clinical events committee. Since the interim results publications,[18] no additional serious procedure/device-related adverse events occurred. Supplemental Table 5 depicts a list of all 59 adverse events, including 1

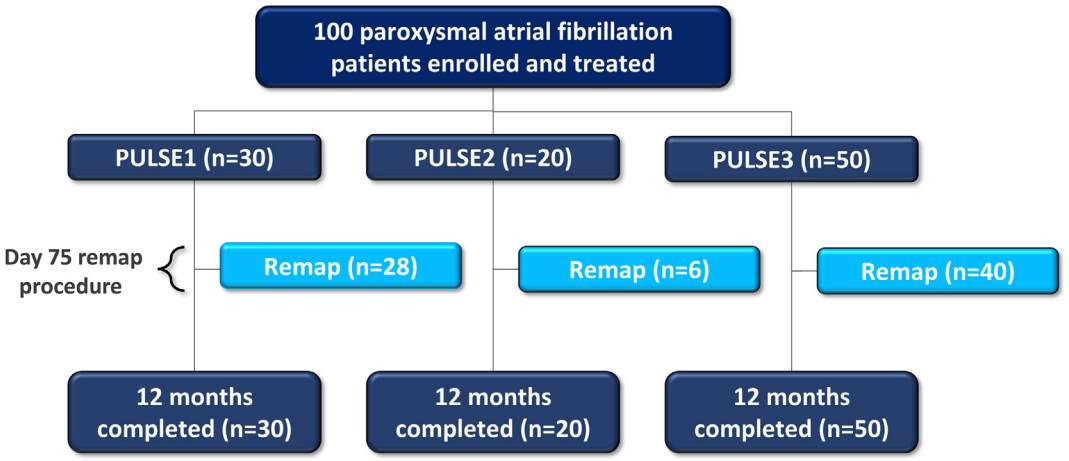

Figure 1
Patient flow diagram. The overall patient population undergoing PFA treatment includes the PULSE1 (n = 30), PULSE2 (n = 20) and PULSE3 (n = 50) cohorts. Also shown are the numbers of patients in each cohort that underwent the optional remapping procedure, and who reached 12-month follow-up. PFA = pulsed-field ablation.

Table 1 Baseline patient characteristics

Characteristic	Total cohort (n = 100)	PULSE3 (n = 50)	*P*-value*
Age (yrs)	58.4 ± 10.6	58.4 ± 12.3	.96
Men	60 (60)	37 (74)	<.01
Time from AF diagnosis to enrollment (yrs)†	3.4 ± 3.7	2.9 ± 3.6	.15
Body mass index (kg/m^2)	29.1 ± 4.2	28.7 ± 3.9	.33
LA diameter (mm)	41.0 ± 4.4	41.0 ± 4.5	.91
LVEF (%)‡	59.7 ± 5.7	60.0 ± 6.0	.58
CHA_2DS_2-VASc	1.8 ± 1.3	1.8 ± 1.2	.81
Prior DC cardioversion for AF	47 (47)	22 (44)	.69
Medical characteristics			
Hypertension	70 (70)	34 (68)	.83
Diabetes (type 2)	7 (7)	5 (10)	.44
Stroke or TIA	3 (3)	1 (2)	1.0
Coronary artery disease	12 (12)	8 (16)	.36
Sleep apnea	3 (3)	1 (2)	1.0
Atrial tachycardia	10 (10)	7 (14)	.32
Atrial flutter	18 (18)	9 (18)	1.0
Prior CTI ablation§	1 (6)	0 (0)	1.0
Medications			
Anticoagulant use ≥3 weeks pre-ablation	93 (93)	48 (96)	.44
Warfarin	2 (2)	0 (0)	.49
DOAC	90 (90)	47 (94)	.32
Other	1 (1)	1 (2)	1.0
Prior AADs¶			
Class I–IV	99 (100)	49 (100)	NA
Class I or III	80 (81)	40 (82)	1.0

Values are reported as mean ± standard deviation, incidence number (percentage).
AADs = anti-arrhythmic drugs; AF = atrial fibrillation; DC = direct current; DOAC = direct oral anticoagulant; LA = left atrium; LVEF = left ventricular ejection fraction.
*P < .05 when compared to PULSE1/PULSE2 arm (n = 50).
†95 patients with time from AF diagnosis to enrollment reported; 95 total cohort, 50 PULSE3.
‡99 patients with LVEF reported; 99 total cohort, 49 PULSE3.
§Percentage out of patients with atrial flutter.
¶99 patients with prior AADs reported; 99 total cohort, 49 PULSE3.

Table 2 Procedural characteristics

Characteristic	Total cohort (n = 100)	PULSE3 (n = 50)
Total procedure time (mins)*	57.9 ± 20.6	61.3 ± 18.1
Total fluoroscopy time (mins)†§	6.8 ± 5.7	8.2 ± 6.4
Single-shot PFA LA dwell time (mins)‡	22.2 ± 11.8	27.6 ± 12.1
PVI transpired time (mins)§	11.5 ± 7.1	13.4 ± 7.8
Number of applications per PV	4.0 ± 1.3	4.7 ± 1.1
Single-shot PFA PVI application time (mins)¶	1.5 ± 0.5	1.8 ± 0.4
General anesthesia use	99 (99)	49 (98)
Acute PVI success	395 (100)	194 (100)
RSPV	100 (25)	50 (26)
RIPV	100 (25)	50 (26)
LSPV	88 (22)	42 (22)
LIPV	88 (22)	42 (22)
RMPV	7 (2)	2 (1)
LCPV	12 (3)	8 (4)
Non-PVI ablation	16 (16)	6 (12)
CTI	10 (10)	5 (10)
Acute non-PVI success using focal lattice-tip catheter	20 (100)	6 (100)
Pre-ablation map#	100 (100)	50 (100)
Performed with single-shot PFA catheter	95 (95)	49 (98)
Performed with focal lattice-tip catheter	9 (9)	4 (8)
Post-ablation map	67 (100)	42 (84)
Performed with single-shot PFA catheter	43 (43)	37 (74)
Performed with focal lattice-tip catheter	27 (27)	8 (16)
Endoscopic evaluation of esophagus post-ablation	18 (18)	0 (0)
Brain MR imaging post-ablation	40 (40)	19 (38)

Values are reported as mean ± standard deviation, incidence number (percentage).
CTI = cavotricuspid isthmus; LA = left atrium; LCPV = left common pulmonary vein; LIPV = left inferior pulmonary vein; MRI = magnetic resonance; PFA = pulsed-field ablation; PV = pulmonary vein; PVI = pulmonary vein isolation; RIPV = right inferior pulmonary vein; RMPV = right middle pulmonary vein; RSPV = right superior pulmonary vein.
*Total procedure time is defined as first sheath inserted to last sheath pulled out and includes the protocol-mandated 20-minute wait period or infusion of adenosine.
†Total fluoroscopy time is defined as fluoroscopy time through total procedure, vein access to sheath removal.
‡Single-shot PFA left atrial dwell time is defined as first single-shot PFA catheter inserted to last single-shot PFA catheter pulled out and includes mapping time. Note: More post-ablation maps were performed in the PULSE3 cohort.
§PVI transpired time is defined as first PV ablation to last PV ablation (last PV ablation excludes any PV touch-up after any linear lesions).
¶Single-shot PFA PVI application time is defined as the time the generator is delivering PF energy during PVI with the single-shot PFA catheter.
#Some patients were mapped with both the single-shot PFA catheter and the focal lattice-tip catheter.

new instance of groin bleeding, sore groin, and headache for procedure/device-related events occurring since the interim analysis.[17]

Anti-arrhythmic medications post-ablation

At baseline, the class I/III prescription rate was similar in the total and PULSE3 cohorts (81% vs 82%, Supplemental Table 6). Overall, class I/III AAD usage reduced from baseline to 90 days in the total (81%–31%) and PULSE3 cohorts (82%–35%). By day 365, only 24% of patients from the total cohort and 29% of patients from PULSE3 were receiving class I/III AAD medication. On day 90 and day 365, no new class III AADs were initiated for PULSE3 patients; for class I AADs, 4 PULSE3 patients not on AADs prior to the procedure began taking class I AADs during follow-up.

Lesion durability

The optional invasive remapping procedure was performed in 74 patients (of which, 40 patients received the PULSE3 waveform) at 90.3 ± 64.2 days post-ablation (Figure 1). Voltage maps representing PV electrical activity before and after

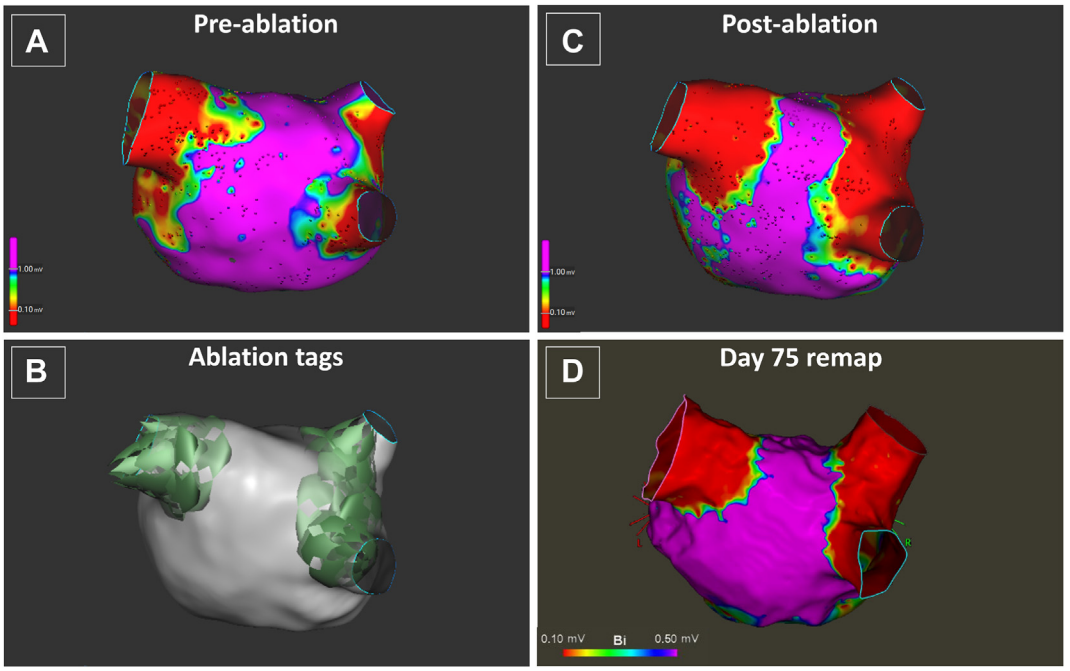

Figure 2
Representative electro-anatomical maps. Shown are bipolar voltage amplitude maps from a single representative patient **A:** before and **C:** after PFA treatment and from **D:** Day 75 remap procedure. In **B:** the green ablation tags denote the locations of PFA applications. The color range is 0.1 (*red*)–1.0 mV (*purple*).

ablation and at remap for a single representative patient are depicted in Figure 2.

A total of 292 PVs were evaluated during remapping, with 26 (9%) veins found to be reconnected (Supplemental Table 7). Of these 26 PVs, only 3 were from the PULSE3 cohort versus 23 from PULSE1/PULSE2 group (P <.01). The 3 PV reconnections in the PULSE3 cohort (encompassing 4 gaps) occurred in the anterior/superior aspect of 3 left superior PVs (LSPVs) (Figure 3). The single gaps found in the LSPVs of patients 1 and 3 were re-isolated with just 1 PFA application, with the gaps occurring on the LSPV ridge and on the proximal portion of the vein, respectively; the clear distal reconnection with 2 discrete gaps found in the LSPV of patient 2 were also easily re-isolated.

On a per-vein basis, the overall PVI durability rate was 91%, leading to 78% of patients having all veins durably isolated (Figure 4). However, waveform optimization significantly enhanced per-vein durability from 83% to 98% and per-patient durability from 62% to 93% with PULSE1/PULSE2 and PULSE3 treatment, respectively (P <.01 for both).

One-year efficacy

The mean follow-up for the total cohort was 360.1 ± 15.7 days, with 100% reaching the 12-month end point (Figure 5). Strong adherence to the monitoring protocol resulted in 96.3% TTM and 100% Holter monitoring compliance rates. Following the 90-day blanking period, 82.0% (95% CI: 73.0%|–88.3%) of the total cohort and 88.0% (95% CI: 75.2%–94.41%) of the PULSE3 cohort were free from AF/AFL/AT recurrence at 365 days post index ablation (Figure 5).

Efficacy and AA burden in the ILR patient sub-cohort

Utilizing the full continuous ILR data (including all recorded patient-triggered and automated recordings) from a subset of PULSE3 patients (n = 15) resulted in a 1-year freedom from AF/AFL/AT recurrence of 80.0% (95% CI: 50.0%–93.1%). Of the 15-patient PULSE3 ILR sub-cohort, a total of 3 patients had AA recurrence detected by the ILR. Two of these patients had recurrences that were detected using the traditional simulated TTM/Holter regimen, whereas the third patient had recurrences detected when the fully automatic recordings were included from the continuous ILR recordings.

The pre- and postAA burden plots for these 3 patients and an example of 1 patient without recurrence are depicted in Supplemental Figure 1. For the 3 patients with AA recurrence, 30 days before the index ablation, the daily burden was 26 ± 23%, translating to 369 ± 337 minutes per day. Following the ablation procedure, these patients experienced a 94% reduction in daily AA burden, with a postablation burden of 1.6 ± 1.8%, equaling 23 ± 26 minutes per day (Figure 6). All 3 patients were remapped, with only 1 having a left superior PV re-ablated because of connection and the other 2 having all PVs to remain isolated.

Discussion

In this single-arm trial, we evaluated the 1-year outcomes of conducting PVI with a single-shot large-lattice PFA catheter in a PAF population. The primary efficacy outcome of acute isolation in all PVs was achieved via approximately 4 applications per PV in 11.5 minutes with relatively low fluoroscopy (6.8 minutes). No (0.0%) primary safety events occurred.

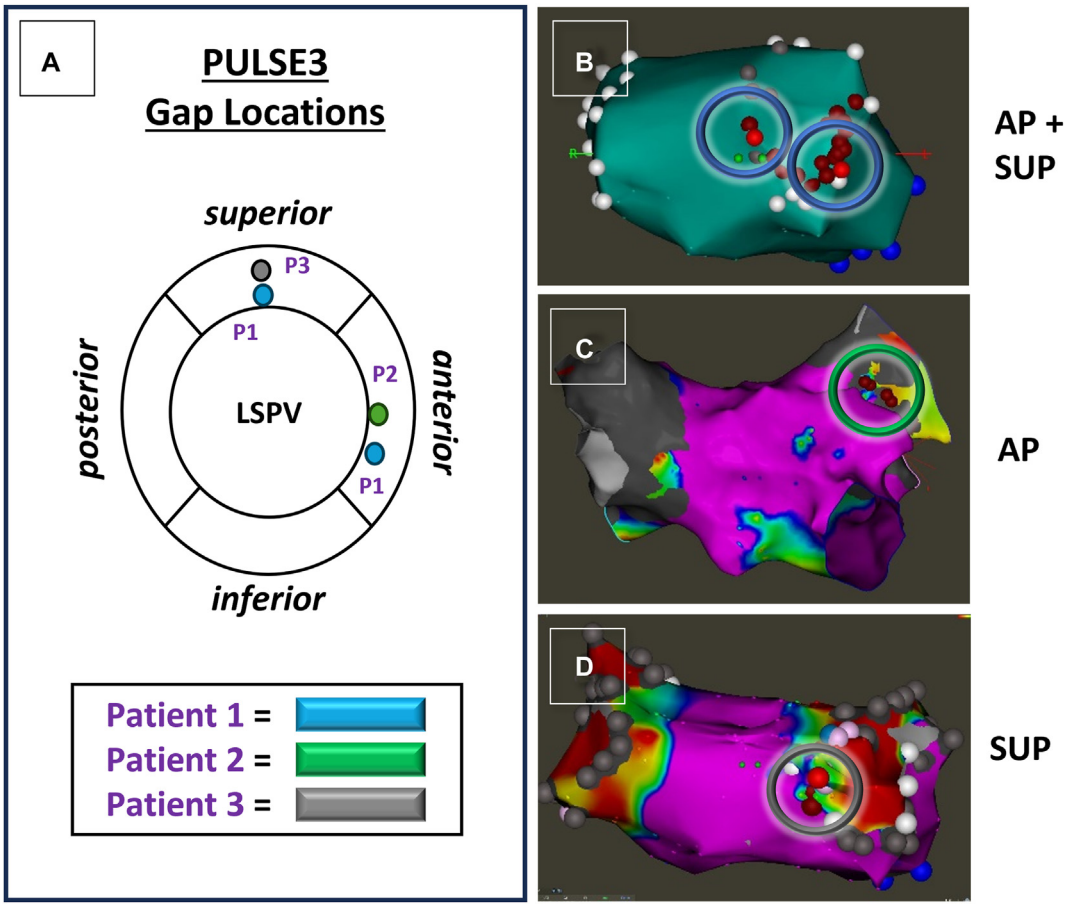

Figure 3
PVI Lesion Gaps During Remapping Procedures. **A:** Diagram of gap locations in 3 LSPVs in 3 PULSE3 patients: patient 1 (*blue dots*), patient 2 (*green dot*) and patient 3 (*gray dot*). Electro-anatomical maps of these reconnected LSPVs showing **B:** 2 discrete gaps (*blue circles*) located in the distal end (anterior and superior), **C:** 1 gap (*green circle*) on the LSPV ridge (anterior), and **C:** 1 gap (*gray circle*) in the proximal portion (superior) of the PV. AP = anterior; LSPV = left superior pulmonary vein; SUP = superior.

Optimization of the waveform (PULSE3) resulted in 98% lesion durability, with only 3 PV reconnections observed on invasive remapping. For the PULSE3 cohort, 1-year freedom from AA recurrence was 88.4% (and 80.0% in patients that were continuously monitored). Finally, even in the subset of PULSE3 patients with recurrences documented by continuous monitoring, PVI lead to a daily AA burden reduction of 94%. These results demonstrate that the all-in-one mapping and ablation PFA catheter is an efficient, safe, and effective solution for PVI in PAF patients.

Workflow and procedural efficacy

Unlike several other PFA catheter technologies, this large-lattice PFA catheter does not require catheter rotation to achieve circumferentially homogeneous peri-ostial tissue ablation. Instead, the approach was to start by positioning the catheter within the PV for the first PF application—a reasonable approach since PV stenosis is not a concern with these PF waveforms. Then, a total of 3 additional PF applications were delivered with the catheter withdrawn ~3 to 5 mm between successive applications—thereby allowing for longitudinal redundancy of the isolating lesion set. Given that the lattice framework is conformable, catheter positioning was relatively simple. The facile nature of catheter positioning and ablation workflow is underscored by the 11.5 ± 7.1 minutes of transpired ablation time.

The facile integration with the mapping system had high special accuracy since the catheter has 3 magnetic sensors to precisely discern location, rotation, and shape/deployment. Furthermore, the seamless integration allows rapid rendering of the LA-PV anatomy and tagging of ablation zones with each PV and antrum, with relatively minimal fluoroscopy use. Indeed, 26% of cases were performed with < 3 minutes of fluoroscopy use, of which 4 cases were performed with zero fluoroscopy (and the operator and EP staff not wearing lead protection). These latter cases provide proof-of-principle that completely fluoroless AF ablation is feasible with this PFA catheter technology.

Lesion durability and 1-year effectiveness

PVI lesion durability with this large-lattice PFA catheter was high: even the initial PULSE1/PULSE2 waveforms had reasonable lesion durability (83% per-vein, 62% per-patient), but the

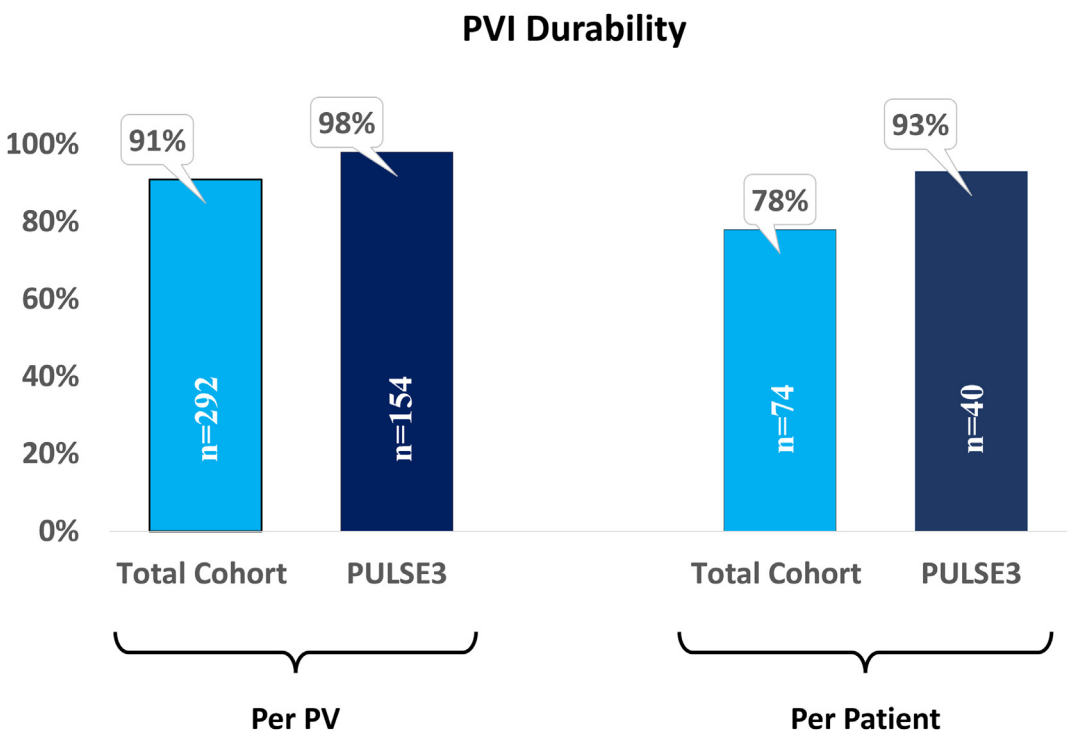

Figure 4
Durability of pulmonary vein isolation. The durability of PVI is shown for 74 patients in the total cohort (*blue bars*) and for 40 patients in the PULSE3 cohort (*dark blue bars*), with 292 and 154 veins remapped, respectively. PVI durability is shown on a per-vein (*left*) and per-patient basis (*right*). The P-values comparing PULSE1/PULSE2 (n = 34) versus PULSE3 (n = 40) are <0.01 for both per-vein and per-patient durability. PV = pulmonary vein; PVI = pulmonary vein isolation.

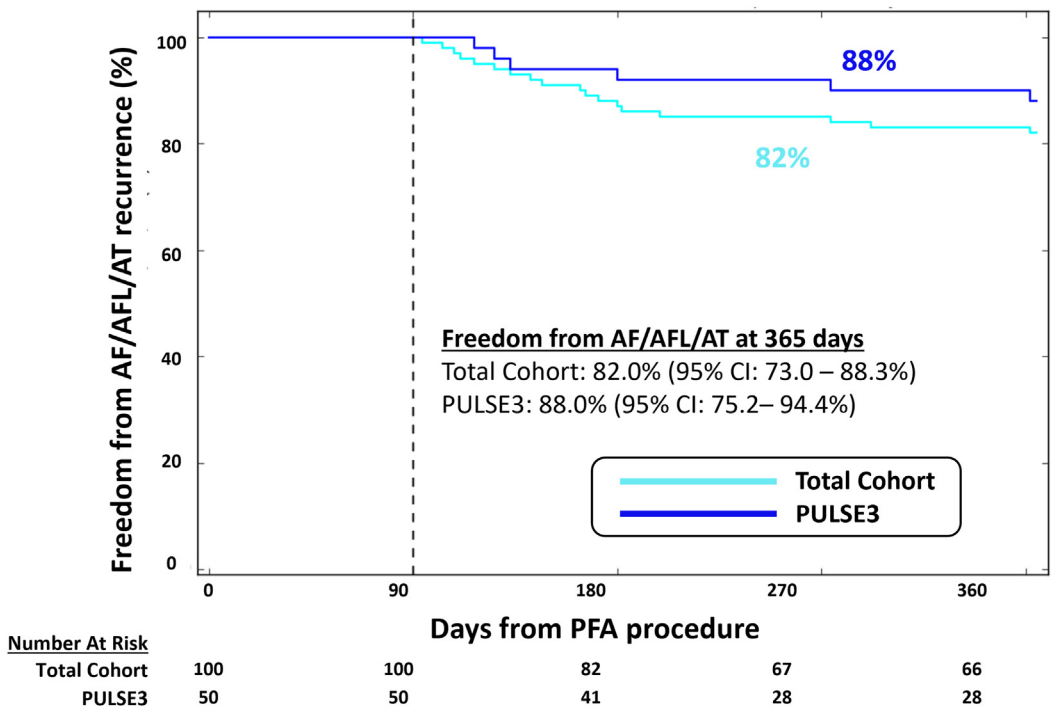

Figure 5
Freedom from atrial arrhythmia recurrence at 12-month follow-up. Displayed are the Kaplan-Meier estimates of freedom from AF/AFL/AT recurrence lasting ≥30 seconds at 365 days for the total cohort (*light blue line*) and the PULSE3 cohort (*blue line*) monitored via TTMs and Holter monitoring, or EGM data from an ILR modeled to replicate the same TTM/Holter regimen. When comparing the PULSE1/PULSE2 group (n = 50) to the PULSE3 group (n = 50), the *P*-value is 0.11 (log-rank test). The dotted line indicates the conclusion of the 90-day blanking period. AF = atrial fibrillation; AFL = atrial flutter; AT = atrial tachycardia; ILR = insertable loop recorder; TTM = trans-telephonic monitoring.

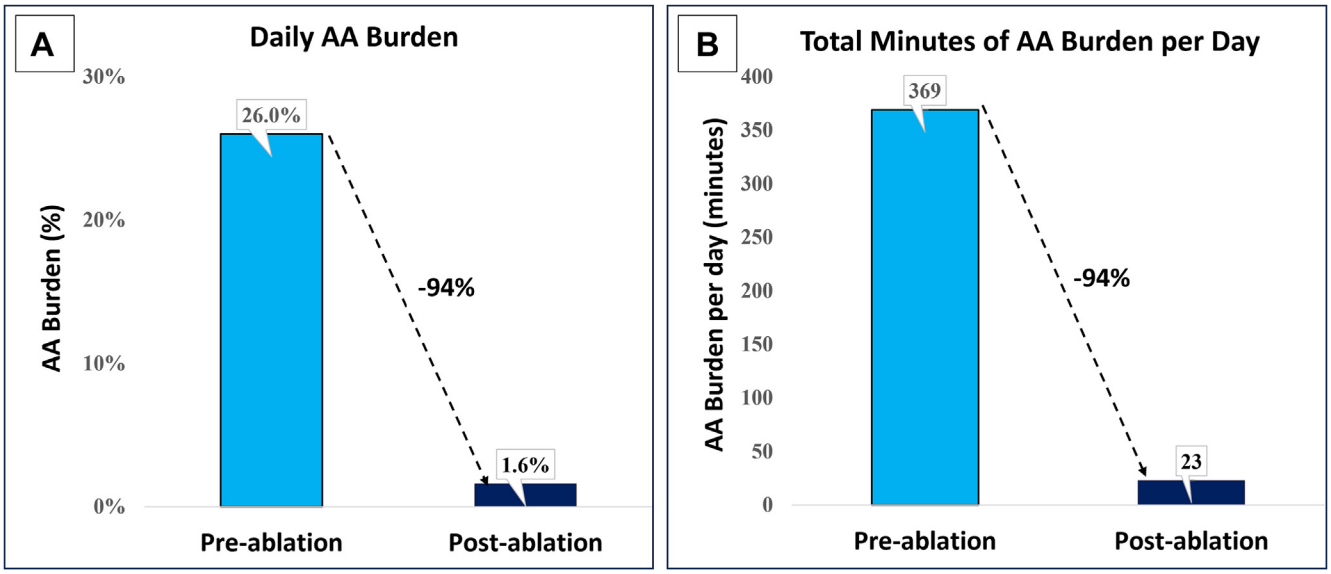

Figure 6
Atrial arrhythmia burden of the PULSE3 ILR cohort with recurrence. The average daily AA burden in **A:** percentage and **B:** total minutes 30 days before PFA and day 91–365 post-PFA in 3 PULSE3 patients that received an ILR and had confirmed AA recurrence. The *black arrow* depicts 94% reduction in daily AA burden. AA = atrial arrhythmia; ILR = insertable loop recorder; PFA = pulsed-field ablation.

optimized PULSE3 waveform demonstrated superior durability (98% per-vein, 93% per-patient). It was interesting that the only PULSE3 cases with PV reconnection all had reconnections in the anterior or superior aspects of the LSPV. Although definitive reasons for this localization of reconnections are unknown, there may be a causal relationship to the anterior takeoff of the LSPV—this anatomical relationship may result in less longitudinal redundancy of ablation. If this speculation is correct, it is possible that initial positioning of the lattice catheter somewhat deeper within the LSPV to allow better longitudinal lesion redundancy might mitigate this reconnection issue.

In any event, the 98% per-vein lesion durability translated to superior clinical outcomes. The 1-year freedom from recurrent AAs with the optimized PULSE3 waveform of 88.0% is as good as or higher than that observed in other single-arm European PFA trials with similar monitoring schedules and efficacy end point in a PAF population.[9,19,20] Indeed, the very high PVI durability raises the possibility of potentially high clinical effectiveness even in patients with persistent AF with this lattice PFA catheter.

This clinical study is also one of the few trials to incorporate the use of ILRs with continuous ECG monitoring in follow-up after PFA to treat PAF. Although only 15 patients received ILRs (all after ablation using the PULSE3 waveform), the clinical success using this continuous ECG data revealed a 1-year freedom from AF/AFL/AT recurrence of 80.0%—a success far superior to that observed in *CIRCA-DOSE*, the largest trial using ILRs in follow-up after thermal ablation of PAF using radiofrequency or cryotherapy (53.9% and 52.2% success, respectively).[21] Our results with the ILR cohort (although in a small number of patients) also surpassed those observed in the SINGLESHOT CHAMPION study in which PAF patients that were monitored via ILR were randomized to PFA (n = 105) and cryoablation (n = 105) and experienced a 62.9% and 49.3% rate of freedom from all AAs, respectively.[18] Furthermore, the 80% efficacy rate among the 15-patient ILR cohort is a reflection of a 1-year complete absence of any recurrence despite continuous monitoring with ILR compared to the traditional recurrence definition used in other trials. It is also worth noting that only 1 additional patient with AA recurrence was detected by continuous ILR monitoring—thus increasing somewhat one's confidence in even the standard intermittent follow-up data of the remaining patients.

AA burden

From the very first clinical trial of catheter ablation for AF, the gold standard for a recurrence has been $\geq$ 30 seconds of continuous AA; however, this metric itself has not been associated with any clinically relevant patient outcomes.[1,22–24] In fact, even among patients labeled as failed procedures, there can be significant reductions in AA burden translated into measurable clinical benefits. Thus, there is now broad consensus that the 30-second metric is a poor reflection of patient clinical benefit, and other metrics are necessary.

Alternatively, in a number of AF ablation studies, post-ablation residual AA burden, defined as the proportion of time a patient spends in an AA over a monitoring period, has proven to be a good metric correlating to patient clinical status. Indeed, the residual AA burden tracks well with both the improvement in quality-of-life and decrease in health care utilization such as cardioversion, hospitalization, and redo ablation. This has proven true in studies involving both thermal ablation—radiofrequency and cryotherapy—and PFA.[22,24–29] However, the PFA studies that have investigated AA burden have all used intermittent

methods of monitoring—TTM plus periodic Holter monitoring—and not continuous insertable monitors which provide a more comprehensive assessment of therapeutic efficacy.[13,26,27]

So it is in this context that the use of continuous monitoring in a subset of patients in our study is of interest. In the 3 PULSE3 patients with AA recurrences, and hence deemed "ablation failures" using the traditional 30-second definition, there was a 94% reduction in AA burden. Furthermore, in 2 of these patients with recurrence all of their PVs remained isolated on remapping; this further points to a gap in knowledge about the relationship between AA recurrence and PV isolation. Thus, the exact definition of AF ablation success continues to evolve, but these ILR data from the 15-patient cohort indicate that the large-lattice PFA catheter delivers excellent outcomes regardless of the ultimate definition.

Limitations

Given that patients were consecutively enrolled in the study, the PULSE3 cohort procedures have a slight increase in heterogeneity because of more operators being added later in the study. The 1-year efficacy rates could be influenced by AADs, with 24% of the total cohort and 29% of the PULSE3 cohort still taking class I/III drugs at 12-months. However, this aligns with outcomes in other single-arm European PFA trials, with 13%–33% of patients remaining on AAD medication 1-year following ablation.[9,19,20] Furthermore, patients remained on AADs at physician discretion. The burden calculations are limited to a small subset of patients (n = 15); clinically significant threshold of AA burden decrease may differ in patients with persistent AF.

Conclusion

The all-in-one mapping and ablation large-lattice, expandable, single-shot PFA catheter provides an efficient, safe, and effective treatment for PAF with a predictable limited set of applications and high, long-term PVI durability. Among a subset of patients who had continuous ILR monitoring, the effectiveness rate was high; even among the patients who had AA recurrence, there were substantial reductions in AA burden following PFA.

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Appendix
Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2025.04.031.

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