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Characterization of acute residual pulmonary vein connections using electroanatomic mapping during pulsed-field ablation of atrial fibrillation

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ABSTRACT

BACKGROUND Single-shot pulsed-field ablation (PFA) catheters show promising safety and efficacy for achieving pulmonary vein isolation (PVI) in atrial fibrillation (AF). However, additional PFA applications are sometimes required after standard PFA delivery to achieve PVI.

OBJECTIVE This study aimed to evaluate the real-world frequency and location of acute residual pulmonary vein (PV) connections using 3-dimensional electroanatomic mapping (3D-EAM) during index PFA.

METHODS Patients undergoing index PVI with a single-shot PFA catheter and receiving postablation 3D-EAM were prospectively studied. First-pass isolation (FPI) rates and distribution of residual PV connections were assessed.

RESULTS A total of 535 patients from 48 international centers (89 operators) were included (paroxysmal AF 375; persistent AF 160). Mean procedure time was 75.9 ± 31.9 minutes, and mapping time was 8.4 ± 5.2 minutes. Ablation was performed with a pentaspline, variable conformation PFA catheter in 72.7% of cases and a fixed-loop PFA catheter in 27.3%. Bilateral FPI was achieved in 75.1% of patients (paroxysmal AF 77.1% vs persistent AF 70.6%; $P = .126$). The individual PV FPI rate was 92.7% (1834 of 1978 PVs). Excluding common PVs, residual PV connections were more frequent in superior PVs (superior 8.9% vs inferior 3.8%; $P < .001$), specifically in the left superior PV (10.1%). Predictors of FPI included standard 4-vein anatomy (odds ratio, 1.83; 95% confidence interval, 1.09–3.07; $P = .021$) and the pentaspline catheter (odds ratio, 3.53; 95% confidence interval, 1.81–6.87; $P < .001$).

CONCLUSION Using 3D-EAM, an acute residual connection of at least 1 PV was observed in a quarter of patients after standard PFA delivery and was most common in the left superior PV. Potential mechanisms include reversible electroporation, highlighting the potential need for additional lesions and the value of a mandatory post-PFA "waiting period."

KEYWORDS Atrial fibrillation; Pulsed-field ablation; Electroporation; Catheter ablation; Pulmonary vein isolation; Reconnection; Mapping

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Introduction

Pulmonary vein isolation (PVI) forms the cornerstone of atrial fibrillation (AF) catheter ablation. Historically, PVI has been achieved using thermal ablation modalities, namely radiofrequency (RF) and cryoablation.[1] More recently, pulsed-field ablation (PFA) has emerged as an alternative nonthermal

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ablation modality, inducing selective myocardial cellular injury through electroporation. Clinical studies suggest that PFA offers comparable efficacy with thermal ablation, with potential safety and efficiency advantages.[2,3]

Several single-shot PFA devices are commercially available.[2,4,5] Although electrode configuration, electrical waveforms, and ablation protocols differ between single-shot PFA catheters, they are characterized by the delivery of multiple electrical pulses to each pulmonary vein (PV). Although electrogram silence is often observed after the first application, further applications are delivered, as prescribed by each device manufacturer, to achieve irreversible electroporation. After this "standard" set of PFA delivery, isolation of each PV can be confirmed through demonstration of entrance and exit blocks. An acute residual PV connection still observed at the end of the procedure suggests reversible electroporation, and additional PFA can be delivered to achieve durable PVI.

PFA using a single-shot catheter is commonly performed under fluoroscopic guidance,[3,6,7] but postablation 3-dimensional (3D) electroanatomic mapping (3D-EAM) is increasingly used to assess acute PVI success.[8,9] The long-term durability of PFA using 3D-EAM has been reported in patients undergoing redo AF ablation.[10,11] However, data regarding the frequency and location of *acute* PV gaps after index PFA remain limited.

This study aimed to characterize the anatomic distribution and predictors of residual PV conduction using post-PFA 3D-EAM in a large, multicenter population to identify opportunities for procedural refinement.

Methods

Study design

Acute observational data from patients undergoing index PVI with a single-shot PFA catheter and postablation 3D-EAM in an open architecture platform (EnSite X, Abbott Medical) were prospectively collected. The 2 single-shot PFA catheters included in the analysis were the pentaspline, variable conformation PFA catheter (FARAWAVE, Boston Scientific) and the fixed-loop PFA catheter (PulseSelect, Medtronic). Both patients with paroxysmal (pAF) and persistent AF (persAF) were eligible for inclusion.

A total of 89 operators from 48 centers (across Europe, the United States, and Australia) contributed cases as part of the initial evaluation of the novel mapping software between February and October 2024. All patients provided an informed written consent for their clinical procedure. No patient identifiable information was collected, and no specific protocol was implemented; as such, ethical approval was not sought. The study adhered to the principles of the Declaration of Helsinki and is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Abbreviations

3D-EAM: 3-dimensional electroanatomic mapping

AF: atrial fibrillation

FPI: first-pass isolation

ICE: intracardiac echocardiography

pAF: paroxysmal atrial fibrillation

persAF: persistent atrial fibrillation

PFA: pulsed-field ablation

PV: pulmonary vein

PVI: pulmonary vein isolation

PWI: posterior wall isolation

Mapping and ablation

A preablation 3D model of the left atrium and PVs was created in EnSite X (software version 3.0.2, PFA catheter visualization license, Abbott) using either a high-density grid-like mapping catheter (Advisor HD Grid or Advisor HD Grid X mapping catheter, Abbott Medical), a high-density 20-pole circular mapping catheter (LASSO Circular Mapping Catheter, Johnson & Johnson MedTech), or the PFA catheter used for ablation itself (Figure 1A). By connecting the FARAWAVE or PulseSelect catheter to the catheter interface module, movement of the PFA catheter was visualized in real time within the model to aid ablation.

PFA was performed using the FARAWAVE or PulseSelect catheter as per manufacturer recommendations. The "standard delivery" included a minimum of 8 PFA applications per PV (FARAWAVE, 4 in the "basket" and 4 in the "flower" configuration; PulseSelect, 4 at the PV ostium and 4 at the antrum). Additional PV applications (beyond the 8 "standard" applications) were permitted before remapping, at the operator's discretion. Adjunctive non-PV PFA was also permitted (eg, posterior wall isolation [PWI], left atrial roof or mitral isthmus line, and cavotricuspid isthmus [CTI] ablation).

Surrogate PFA lesion markers were displayed within the EnSite X map at the sites of delivery from the FARAWAVE or PulseSelect electrodes, using a modified local activation time map. These appeared as red circles on the 3D model and enabled visual evaluation of PV coverage (Figure 1B).

After ablation, a 3D voltage or activation map was created with the mapping catheter used for preablation mapping (Figure 1C). Operators assessed postablation maps for acute residual PV connections, and if observed, their location was recorded and further PFA applications were delivered as deemed necessary. Pacing maneuvers to differentiate true PV reconnection from far-field signals—such as those originating from the left atrial appendage—were used at the operator's discretion.

As an observational analysis designed to capture real-world clinical practice, no formal procedural protocol was implemented across centers. The use of fluoroscopy, the choice of anesthetic method (general anesthesia, deep sedation, or conscious sedation), and the use of transesophageal echocardiography and/or intracardiac echocardiography (ICE) to guide transeptal puncture and/or to assess for PV contact during PFA delivery were recorded. Accordingly, the order of PV ablation and the use or duration of a "waiting period" after PFA delivery and before remapping were left to the discretion of the operating electrophysiologist. Procedural-related complications were not systematically recorded as part of the dataset.

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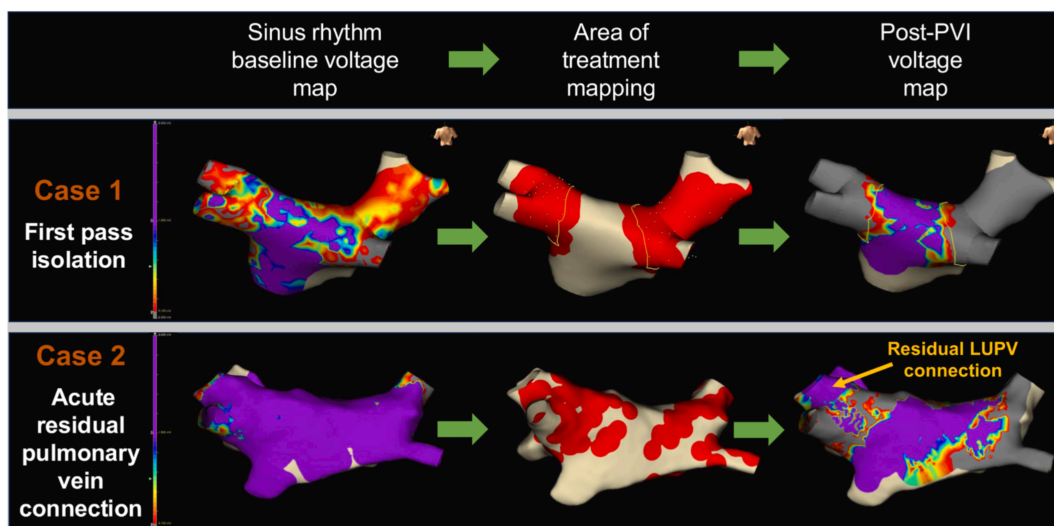


Figure 1
Electroanatomic mapping-guided PFA. Two cases demonstrating first-pass isolation (case 1) and an acute residual pulmonary vein connection in the LUPV after standard PFA applications with the pentaspline PFA catheter (case 2). *Left-hand images:* Preablation voltage map of the left atrium in sinus rhythm. *Middle images:* Surrogate lesion markers (*red*) enabling visualization of pulmonary vein coverage immediately after PFA delivery. *Right-hand images:* Post-PVI voltage map. LUPV = left upper pulmonary vein; PFA = pulsed-field ablation; PVI = pulmonary vein isolation.

Outcomes

The primary outcome was bilateral first-pass isolation (FPI) on a per-patient level. FPI was defined as the isolation of a PV on the first check after ablation, as assessed by the operator on 3D-EAM. Secondary outcomes included individual PV acute residual connection rates and distribution, classified according to an 18-point PV diagram as per previous reports.[12]

Statistics

Statistical distribution was determined using the Shapiro-Wilk test. Continuous variables were normally distributed and expressed as mean ± standard deviation. For comparisons between groups, continuous variables were compared using *t* tests. Outliers were removed from the procedure time analysis; these were predominantly caused by data entry errors owing to incorrect "AM" and "PM" timestamps. Categorical variables were expressed as counts and percentages and compared using χ^2 or Fisher's exact test, as appropriate.

FPI was reported as a binary "Yes" or "No" for all patients. If "Yes," all PVs were assumed to be isolated. If "No," all veins were assumed to be isolated except those recorded in the dataset; if no residual connections were recorded, patients were included in the overall subject-level FPI assessment, but excluded from the PV-specific FPI analysis as gap location could not be determined. A logistic regression was performed to ascertain the effects of clinical variables on FPI. Univariable associations with $P \leq .25$ were included in a multivariable logistic regression model. The number of PFA applications was not populated in more than 100 subjects, and the number of PFA applications was not always provided for all PVs; patients with missing PFA application data were excluded in this section of the analysis, with the resulting sample sizes reported. Only the total number of PFA applications per PV was recorded; no distinction was made between applications delivered before vs after remapping.

Two-sided *P* values of $< .05$ were considered statistically significant. Statistical analysis was performed in SAS (version 9.4, SAS Institute).

Results

Procedural characteristics

A total of 535 patients were studied (pAF 375; persAF 160). The procedural setup is presented in Table 1. Procedures were mostly performed under general anesthesia (79.2%), with deep sedation with propofol used in 20.4% and conscious sedation in 0.4%. Transesophageal echocardiography was performed in 22.2% of cases, whereas ICE was used to guide transeptal puncture in 89.7% of cases and assess PV contact during PFA delivery in 80.7%.

A pentaspline, variable conformation PFA catheter was used in 72.7% of cases (389/535) and a fixed-loop PFA catheter in 27.3% (146/535). Postablation 3D-EAM was most commonly performed with the Advisor HD Grid or HD Grid X (45.8%), followed by the LASSO (15.3%), the FARAWAVE catheter itself (9.2%), and the PulseSelect catheter itself (13.0%) (Table 1).

Procedural characteristics are presented in Table 2. Most patients (76.3%) had a standard 4-vein anatomy, with 20.0% having a left common PV with standard right PV anatomy. Mean procedural duration was 75.9 ± 31.9 minutes and comparable between AF types (pAF 76.3 ± 31.4 minutes vs persAF 75.0 ± 33.1; $P = .70$). Left atrial dwell time was 59.6 ± 24.5 minutes, mapping time 8.4 ± 5.2 minutes, and fluoroscopy time 15.8 ± 10.9 minutes. A zero-fluoroscopy approach was used in 22.2% of cases and more frequently in persAF (pAF 18.2% vs persAF 31.9%; $P = .002$).

Additional non-PV ablation was performed with the PFA catheter in 64.1% of patients and was more common in patients with persAF (pAF 52.8% vs persAF 90.6%; $P < .001$). This included PWI in 60.2%, a roof line only in 16.4%, CTI line in 12.0%, and mitral isthmus line in 8.8%. Additional RF ablation was delivered in 9.2% of patients, most commonly an RF CTI line (7.5%) or mitral isthmus line (1.3%). In 1 patient with pAF (0.3%) undergoing PVI only, additional RF ablation was required to achieve PVI (Table 2).

FPI and residual PV connections

Bilateral FPI was achieved in 75.1% of patients (402/535) and was numerically higher in the pAF cohort than in the persAF cohort, although this did not reach statistical significance (pAF 77.1% [289/375]; persAF 70.6% [113/160]; $P = .126$) (Table 3). Bilateral FPI was higher in the FARAWAVE cohort than the PulseSelect cohort (FARAWAVE 79.9% [311/389] vs PulseSelect 62.3% [91 of 146]; $P < .001$).

In patients included in the PV-specific analysis, 77.9% (406/521) had no acute residual PV connections when mapped after standard PFA delivery, 17.5% (91/521) had 1 connection, 4.0% (21/521) 2 connections, 0.2% (1/521) 3 connections, and 0.4% (2/521) 4 connections (Figure 2). Across all anatomies, the FPI rate per individual PV was 92.7% (1834/1978 PVs). Excluding common PVs, acute residual connections were most frequently observed in the left superior PV (LSPV) (10.1% [43/424]), followed by the right superior PV (7.8% [40/512]), the left inferior PV (4.5% [19/424]), and the right inferior PV (3.3% [17/512]). Overall, acute residual PV connections were more common in the superior than inferior PVs (superior PVs 8.9% [83/936] vs inferior PVs 3.8% [36 of 936]; $P < .001$). These trends were observed across both pAF and persAF cohorts and FARAWAVE and PulseSelect cohorts (Table 3). In common PVs, acute residual connections were observed in 25.8% of left common PVs (25/97), whereas none were detected in the right common PVs (0/9).

Sites of acute residual PV connections within the 18-point PV diagram are presented in Figure 3. The 2 most common sites were the anterosuperior portions of the LSPV (7.1% [37/521 PVs]) and right superior PV (5.6% [29/521 PVs]).

By procedure end, patients received 42.9 ± 13.0 PFA applications across all PVs and 15.1 ± 12.8 non-PV applications. Patients treated with PulseSelect received more PFA applications than those treated with FARAWAVE (FARAWAVE 41.1 ± 12.9 applications vs PulseSelect 47.2 ± 12.1 applications; $P < .001$), with more applications in all individual PVs. No difference in the number of PFA applications was observed between the pAF and persAF cohorts (pAF 42.6 ± 13.8 applications vs persAF 43.5 ± 10.7 applications; $P = .486$). The number of PFA applications per patient is presented in Table 3.

Table 1 Procedural setup

Characteristic	Total (N = 535)
Anesthesia type	
General anesthesia	79.2% (373/471)
Deep sedation with propofol	20.4% (96/471)
Conscious sedation	0.4% (2/471)
Transesophageal echocardiography	22.2% (106/477)
Intracardiac echocardiography	
Used for transeptal access	89.7% (429/478)
Used to assess PV contact during PFA	80.7% (432/535)
PFA catheter	
FARAWAVE	72.7% (389/535)
PulseSelect	27.3% (146/535)
Catheter used for postablation 3D-EAM	
Advisor HD Grid or HD Grid X	45.8% (204/445)
Circular mapping catheter	15.3% (68/445)
FARAWAVE	9.2% (41/445)
PulseSelect	13.0% (58/445)
Other	0.7% (3/445)

3D-EAM = 3-dimensional electroanatomic mapping; PFA = pulsed-field ablation; PV = pulmonary vein.

Factors associated with FPI

On univariable logistic regression, factors associated with FPI included standard 4-vein anatomy (odds ratio [OR], 2.11; 95% confidence interval [CI], 1.33–3.35; $P = .002$) and the FARAWAVE catheter (OR, 2.41; 95% CI, 1.59–3.66; $P < .001$), whereas general anesthesia (OR, 1.57; 95% CI, 0.97–2.55; $P = .068$), pAF (OR, 1.40; 95% CI, 0.92–2.12; $P = .115$), use of ICE to assess PV contact during PFA (OR, 0.84; 95% CI, 0.51–1.40; $P = .509$), and use of the PFA catheter to create the postablation 3D-EAM (OR, 1.59; 95% CI, 0.97–2.63; $P = .068$) were not associated (Supplemental Table 1). On multivariable analysis, standard 4-vein anatomy (OR, 1.83; 95% CI, 1.09–3.07; $P = .021$) and the FARAWAVE catheter (OR, 3.53; 95% CI, 1.81–6.87; $P < .001$) were the only factors associated with FPI (Table 4).

Discussion

This study offers novel insights into the real-world acute efficacy of 2 single-shot PFA catheters using 3D-EAM (Central Illustration). To the best of our knowledge, this is the largest study to systematically assess residual PV connections after index PFA. The key findings are the following:

(i) An acute residual connection in at least 1 PV was observed in a quarter of patients after standard (manufacturer-recommended) PFA delivery.
(ii) Residual PV connections were more common in superior than inferior PVs, with the LSPV most frequently affected.
(iii) Within the superior PVs, the anterosuperior segments were the most frequent sites of reconnection.
(iv) An acute residual connection was observed in a quarter of left common PVs.
(v) Predictors of FPI included standard 4-vein anatomy and the use of the pentaspline catheter.

Overall, these findings highlight specific anatomic sites of vulnerability associated with 2 widely-used single-shot PFA catheters and underscore the potential utility of acute post-PFA mapping in enhancing procedural efficacy. These data

Table 2 Procedural characteristics

Characteristic	Paroxysmal AF (n = 375)	Persistent AF (n = 160)	Total (N = 535)
PV configuration			
Standard 4-vein anatomy	77.0% (244/317)	74.8% (107/143)	76.3% (351/460)
Left common PV, standard right PV anatomy	19.2% (61/317)	21.7% (31/143)	20.0% (92/460)
Right common PV, standard left PV anatomy	0.6% (2/317)	1.4% (2/143)	0.9% (4/460)
Bilateral common PVs	0.6% (2/317)	2.1% (3/143)	1.1% (5/460)
Other	2.5% (8/317)	0.0% (0/143)	1.7% (8/460)
Procedure duration (min)	76.3 ± 31.4 (323)	75.0 ± 33.1 (143)	75.9 ± 31.9 (466)
Left atrial dwell time (min)	59.2 ± 24.4 (300)	60.5 ± 24.8 (133)	59.6 ± 24.5 (433)
Mapping time (min)	8.3 ± 5.6 (211)	8.5 ± 4.2 (103)	8.4 ± 5.2 (314)
Fluoroscopy time (min)	16.2 ± 10.2 (266)	14.5 ± 12.8 (92)	15.8 ± 10.9 (358)
Zero-fluoroscopy approach	18.2% (59/325)	31.9% (43/135)	22.2% (102/460)
Non-PV ablation performed with PFA catheter			
Yes	52.8% (198/375)	90.6% (145/160)	64.1% (343/535)
Posterior wall isolation	48.5% (182/375)	87.5% (140/160)	60.2% (322/535)
CTI line	8.8% (33/375)	19.4% (31/160)	12.0% (64/535)
Mitral isthmus line	5.3% (20/375)	16.9% (27/160)	8.8% (47/535)
Roof line	15.5% (58/375)	18.8% (30/160)	16.4% (88/535)
Other	0.8% (3/375)	4.4% (7/160)	1.9% (10/535)
Ablation performed with RF			
Yes	10.4% (39/375)	6.3% (10/160)	9.2% (49/535)
PVI	0.3% (1/375)	0.0% (0/160)	0.2% (1/535)
CTI line	9.3% (35/375)	3.1% (5/160)	7.5% (40/535)
Mitral isthmus line	1.3% (5/375)	1.3% (2/160)	1.3% (7/535)
Roof line	0.3% (1/375)	0.0% (0/160)	0.2% (1/535)
Focal lesion	0.8% (3/375)	1.3% (2/160)	0.9% (5/535)
Other	0.0% (0/375)	1.9% (3/160)	0.6% (3/535)

3D-EAM = 3-dimensional electroanatomic mapping; AF = atrial fibrillation; CTI = cavotricuspid isthmus; PFA = pulsed-field ablation; PV = pulmonary vein; PVI = pulmonary vein isolation; RF = radiofrequency.

Table 3 First pass isolation rates and number of PFA applications

	Total (N = 535)	Paroxysmal AF (n = 375)	Persistent AF (n = 160)	*P* value	FARAWAVE (n = 389)	PulseSelect (n = 146)	*P* value
Bilateral FPI, % (n/N)	75.1% (402/535)	77.1% (289/375)	70.6% (113/160)	.126	79.9% (311/389)	62.3% (91/146)	<.001*
Acute residual PV connections, % (n/N)							
LSPV	10.1% (43/424)	10.2% (31/303)	9.9% (12/121)	>.999	7.7% (25/324)	18.0% (18/100)	.007*
LIPV	4.5% (19/424)	4.0% (12/303)	5.8% (7/121)	.439	3.1% (10/324)	9.0% (9/100)	.023*
LCPV	25.8% (25/97)	23.8% (15/63)	29.4% (10/34)	.629	20.4% (11/54)	32.6% (14/43)	.243
RSPV	7.8% (40/512)	6.6% (24/362)	10.7% (16/150)	.147	5.4% (20/371)	14.2% (20/141)	.002*
RIPV	3.3% (17/512)	3.3% (12/362)	3.3% (5/150)	>.999	1.6% (6/371)	7.8% (11/141)	.001*
RCPV	0.0% (0/9)	0.0% (0/4)	0.0% (0/5)	>.999	0.0% (0/7)	0.0% (0/2)	>.999
Number of PFA applications per patient, mean ± SD (n)							
All PVs	42.9 ± 13.0 (379)	42.6 ± 13.8 (262)	43.5 ± 10.7 (117)	.486	41.1 ± 12.9 (270)	47.2 ± 12.1 (109)	<.001*
LSPV	10.6 ± 3.4 (301)	10.6 ± 3.4 (214)	10.5 ± 3.5 (87)	.844	10.0 ± 3.1 (229)	12.6 ± 3.8 (72)	<.001*
LIPV	9.8 ± 2.8 (301)	9.8 ± 3.0 (214)	9.6 ± 2.2 (87)	.503	9.4 ± 2.4 (229)	11.0 ± 3.6 (72)	<.001*
LCPV	23.2 ± 10.5 (68)	23.2 ± 12.6 (41)	23.1 ± 6.1 (27)	.950	23.7 ± 13.3 (37)	22.5 ± 5.6 (31)	.642
RSPV	10.4 ± 3.4 (373)	10.2 ± 3.3 (260)	10.8 ± 3.6 (113)	.137	9.8 ± 3.0 (264)	11.7 ± 4.0 (109)	<.001*
RIPV	9.7 ± 2.7 (373)	9.8 ± 2.8 (260)	9.6 ± 2.5 (113)	.702	9.2 ± 2.3 (264)	10.9 ± 3.2 (109)	<.001*
RCPV	16.4 ± 0.9 (5)	16.0 ± NA (1)	16.5 ± 1.0 (4)	NA	16.4 ±0.9 (5)	NA	NA
Other	15.1 ± 12.8 (51)	17.4 ± 16.0 (27)	12.6 ± 7.5 (24)	.171	14.1 ± 13.4 (42)	20.0 ± 8.3 (9)	.103

One case had an acute residual connection reported only in the left carina.
AF = atrial fibrillation; FPI = first-pass isolation; LCPV = left common pulmonary vein; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; LUPV = left upper pulmonary vein; NA = not available; PFA = pulsed-field ablation; PV = pulmonary vein; RCPV = right common pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein; RUPV = right upper pulmonary vein; SD = standard deviation.
*Statistically significant.

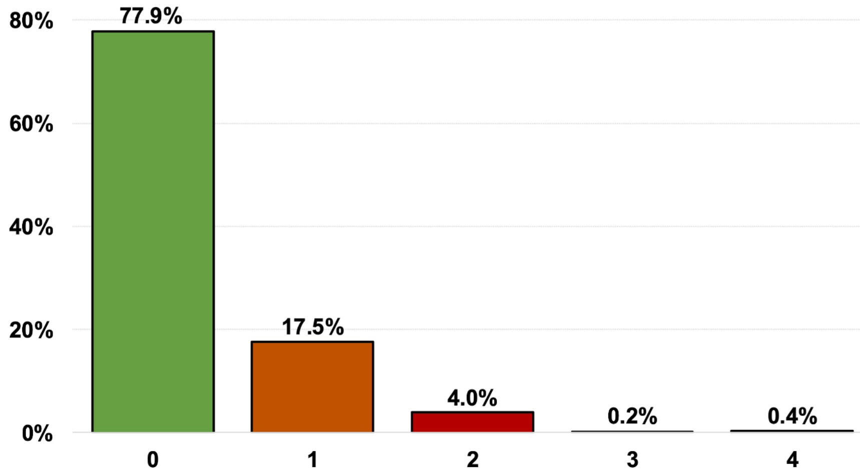


Figure 2
Acute residual PV connections per patient. PV = pulmonary vein.

also reinforce the importance of procedural standardization and lesion validation techniques to ensure durable isolation.

Mapping after PFA

Early clinical studies of single-shot PFA systems demonstrated rapid and effective PVI, with promising lesion durability confirmed on mandated remapping 1 to 3 months after ablation.[5,13] In the IMPULSE/PEFCAT study, all patients (18/18) treated with the FARAPULSE system using an optimized biphasic waveform demonstrated durable bilateral PVI at 3 months.[13] Notably, although index cases included acute postablation mapping to guide the need for additional PFA applications, FPI rates were not specifically reported.[13] Similarly, in the PULSED AF trial evaluating the PulseSelect catheter, acute postablation mapping was performed in more than 90% of patients, yet details regarding FPI rates and the anatomic distribution of residual PV conduction were not reported.[5]

Emerging real-world data indicate that PV reconnections are not uncommon after index PFA.[10,11,14–16] Much of this evidence comes from patients undergoing repeat ablation owing to atrial arrhythmia recurrence. In the MANIFEST-REDO registry, which assessed 427 patients undergoing repeat ablation after FARAPULSE PVI, at least 1 PV reconnection was observed in 55% of cases.[11] Similarly, in the EUPORIA registry, reconnection was observed in 63% of patients (90/144) undergoing redo procedures.[10] Together, these studies reinforce that PV reconnections remain a dominant mechanism of atrial arrhythmia recurrence, even in the era of PFA. Although such studies offer valuable insights into PVI durability, they are inherently limited by selection bias, focusing exclusively on patients with clinical recurrence.

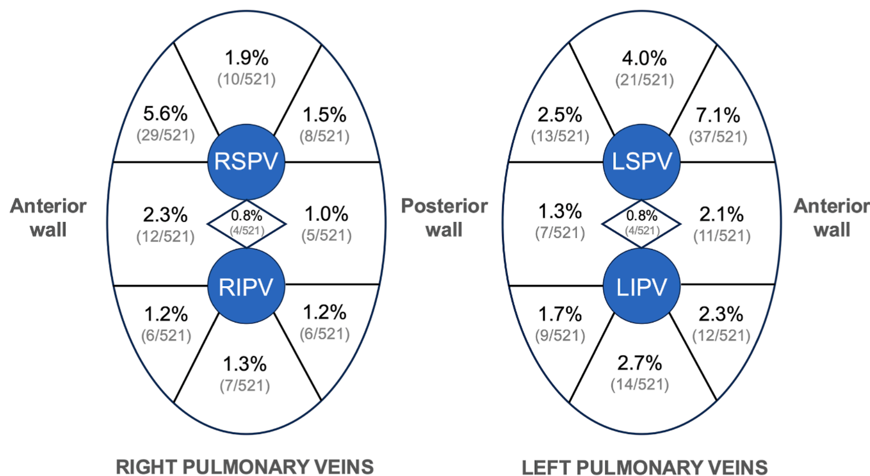


Figure 3
Location of acute residual pulmonary vein connections during index pulsed-field ablation. LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

Table 4 Factors associated with first-pass isolation on multivariable logistic regression

Variable	Odds ratio	95% confidence interval	*P* value
Paroxysmal atrial fibrillation	1.62	0.97–2.69	.064
Pentaspline catheter used for ablation	3.53	1.81–6.87	<.001*
Standard 4-vein anatomy	1.83	1.09–3.07	.021*
General anesthesia	0.57	0.26–1.26	.167
Pulsed-field ablation catheter used for 3D electroanatomic mapping	1.58	0.86–2.91	.139

3D = 3-dimensional.
*Statistically significant.

In contrast, in the present study, acute residual PV connections were detected in 25% of patients after standard PFA delivery (Table 3). Potential mechanisms for this observation include reversible electroporation, from either suboptimal dosing or poor catheter-tissue contact, and tissue edema masking conduction—factors increasingly recognized in the context of PFA.[17–19] These phenomena may transiently suppress PV signals, leading to an overestimation of acute efficacy when relying solely on electrogram-based endpoints (without 3D-EAM). Although the overall FPI rate per individual PV was relatively high (92.7%), the bilateral FPI rate of 75.1% underscores the frequency with which at least 1 vein demonstrates acute reconnection. This distinction is important, given that durable isolation of all PVs is essential for long-term procedural success.

The utility of acute mapping post-PFA has been highlighted in several small-scale studies. In a 2-center study of 138 patients undergoing FARAPULSE PVI, 6% of PVs (29/546) required more than the standard 8 PFA applications owing to PV reconnection or catheter malposition. In another single-center study of 121 patients treated with FARAPULSE, insufficient antral PVI was observed in 20% of patients using a high-density mapping catheter.[20] In our study, we used a combination of high-density catheters and PFA catheters for mapping, observing a similarly high rate of acute PV reconnection. These reconnections may result from islands or tongues of viable myocardial tissue or reconnections of entire PVs. Similarly, using a multielectrode, variable loop PFA catheter (VARIPULSE, Johnson & Johnson MedTech), acute remapping after standard PFA delivery identified persistent conduction in at least 1 PV in 13.3% of patients (16/45).[16] In another study evaluating a focal, monopolar PFA system (CENTAURI, CardioFocus), FPI was achieved in 92% of PVs (297/322).

Taken together, these data support the adoption of a mandatory check of all PVs at the end of the procedure—something not always adopted in clinical practice—and a "waiting period" after PFA to allow recovery of potentially masked PV signals, preferably using systematic postablation mapping. Immediate, targeted touch-up ablation in this context may improve long-term PVI durability, although it requires prospective assessment.

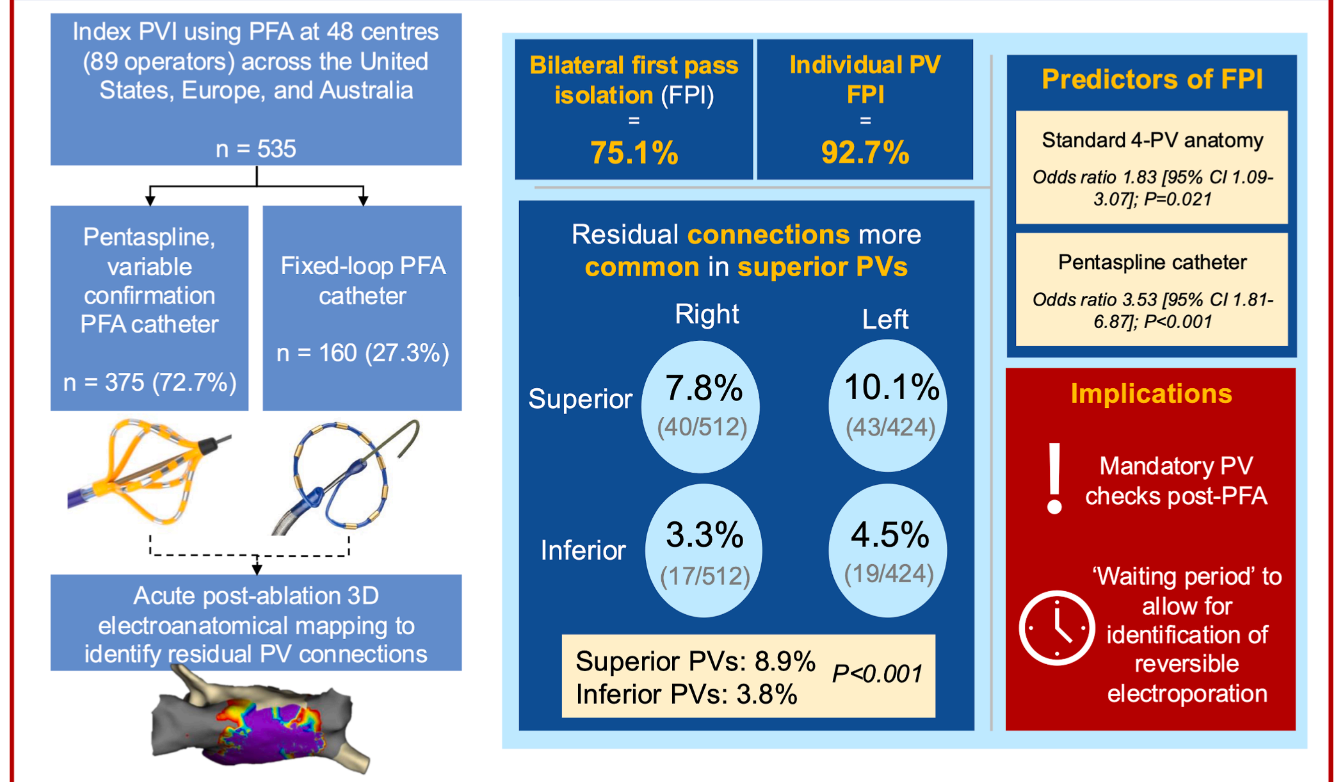
Distribution of PV connections

In the present study, acute residual PV connections were most frequent in the superior PVs, particularly in the LSPV (Figure 3). This distribution likely reflects a combination of anatomic and procedural factors. The superior PVs tend to have wider ostia and more variable angulation than inferior PVs, potentially hindering optimal catheter positioning and tissue contact.[19] As a result, these areas may be more susceptible to catheter instability from respiratory and cardiac motion or may experience incomplete field coverage during standard PFA delivery, a recognized contributor to suboptimal lesion formation.[21]

In addition, the ridge between the LSPV and the left atrial appendage is relatively thick and may require more extensive ablation, whereas the angular left-sided carina presents further challenges for achieving adequate tissue contact with single-shot ablation devices. Notably, the predominance of residual connections in the LSPV mirrors observations from thermal ablation studies.[22] Furthermore, the LSPV is almost universally the first vein treated during single-shot PFA. As a result, it benefits from the longest interval for potential recovery of conduction before reassessment at the end of the procedure—possibly explaining why it is the most frequently reconnected vein in the present study. Whether other PVs would exhibit similarly high reconnection rates if a comparable "waiting period" were introduced after the final PFA application remains to be determined and warrants further investigation, including the determination of the optimal duration for such a "waiting period." Notably, the greater use of adjunctive non-PV ablation (eg, PWI) in patients with persAF in our study likely extended the interval between PVI and remapping, which may have increased the likelihood of detecting acute reconnections in this group. This observation supports, although does not confirm, the potential value of a standardized "waiting period."

Standard 4-vein anatomy was associated with a higher likelihood of FPI in our cohort, suggesting that anatomic variants—such as a left common PV—may pose additional challenges for achieving PVI using single-shot PFA catheters. Larger vessel diameter and complex ostial geometry in left common PVs may reduce catheter contact, contributing to the observed 25.8% rate of acute residual conduction. This highlights the potential limitations of fixed-configuration PFA systems in conforming to variable anatomies.

Finally, PFA catheter configuration may play a critical role in acute- and long-term efficacy. In a study by Schaack et al,[23] the addition of 2 extra "olive" configuration PFA applications using the FARAWAVE catheter was associated with significantly



Central Illustration
Characterisation of acute residual pulmonary vein connections using electroanatomical mapping during pulsed-field ablation of atrial fibrillation

improved PVI durability compared to conventional (4 flower, 4 basket) applications. This highlights the importance of optimizing both catheter design and deployment technique to overcome anatomic challenges and enhance lesion durability.

Predictors of FPI

Although not the primary objective of this study, FPI was more frequently achieved with the FARAWAVE catheter than the PulseSelect catheter (79.9% vs 62.3%, respectively). The FARAWAVE catheter has been commercially available for a longer duration, and greater cumulative operator experience may have contributed to its superior performance.

In addition, general anesthesia was associated with a trend toward a higher likelihood of achieving FPI on multivariate analysis (OR, 1.57; 95% CI, 0.97–2.55; $P = .068$) (Table 4). This association is plausible: general anesthesia may reduce patient motion and respiratory variability compared with conscious sedation, potentially improving catheter stability and tissue contact and minimizing mapping shifts. This highlights procedural factors that may influence acute efficacy and merits further prospective evaluation.

Limitations

First, although large and multicenter, this was an observational analysis, and procedural decisions were at the operator's discretion. Second, to preserve anonymity, patient identifiable data (eg, age, sex, comorbidities) were not collected, limiting the analysis to recorded procedural characteristics. Third, the presence and location of acute residual PV connections were operator determined and not verified centrally. The lack of a standardized waiting period and missing data on the exact timing between ablation and remapping are important limitations, because these factors may have influenced the acute PV reconnection rates. Fourth, certain patients had missing data; the most important of these were missing numbers of PFA applications, which were not populated in more than 100 subjects (with resulting sample sizes reported). Fifth, only the total number of PFA applications per PV was recorded, without specific pre- and postremapping applications. Furthermore, operator experience with PFA prior tos registry participation was not captured and was therefore unavailable for analysis. Finally, long-term PVI durability was not assessed; correlation of

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acute mapping after PFA with clinical outcomes will be essential in future studies.

Conclusion

This real-world, large, prospective, multicenter study demonstrates that acute residual PV connections remain common after standard single-shot PFA delivery, particularly in the superior PVs and left common PVs. These findings reveal consistent anatomic sites of vulnerability and emphasize the utility of acute 3D-EAM in verifying and optimizing acute efficacy. Further procedural refinements—including implementing a structured post-PFA assessment strategy involving a mandatory "waiting period" followed by systematic PV mapping to confirm PVI and enable additional touch-up ablation—may enhance procedural success. Whether such improvements in acute PVI translate into superior long-term clinical outcomes remains to be determined.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2025.06.037.

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