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Independent Mapping Methods Reveal Rotational Activation Near Pulmonary Veins Where Atrial Fibrillation Terminates Before Pulmonary Vein Isolation

Rachita Navara, MD^{*,1}, George Leef, MD^{*,1}, Fatemah Shenasa¹, Christopher Kowalewski^{1,2}, Albert J. Rogers, MD¹, Gabriela Meckler, BS¹, Junaid A. B. Zaman, MD¹, Tina Baykaner, MD, MPH¹, Shirley Park, MD¹, Mintu Turakhia, MD, MAS¹, Paul Zei, MD, PhD¹, Mohan Viswanathan, MD¹, Paul J. Wang, MD, PhD^{‡,1}, and Sanjiv M. Narayan, MD, PhD^{‡,1}

¹Division of Cardiology, Stanford University, Stanford, CA, USA

²Friedrich-Alexander-Universitaet Erlangen-Nürnberg, Germany

Abstract

OBJECTIVE—To investigate mechanisms by which atrial fibrillation (AF) may terminate during ablation near the pulmonary veins before the veins are isolated (PVI).

INTRODUCTION—It remains unstudied how AF may terminate during ablation before PVs are isolated, or how patients with PV reconnection can be arrhythmia-free. We studied patients in whom PV antral ablation terminated AF before PVI, using 2 independent mapping methods.

METHODS—We studied patients with AF referred for ablation, in whom bi-atrial contact basket electrograms were studied by both an activation/phase mapping method and by a second validated mapping method reported not to create false rotational activity.

RESULTS—In 22 patients (age 60.1±10.4, 36% persistent AF), ablation at sites near the PVs terminated AF (77% to sinus rhythm) prior to PVI. AF propagation revealed rotational (n=20) and focal (n=2) patterns at sites of termination by mapping method 1 and method 2. Both methods showed organized sites that were spatially concordant (p<0.001) with similar stability (p<0.001). Vagal slowing was not observed at sites of AF termination.

DISCUSSION—PV antral regions where ablation terminated AF before PVI exhibited rotational and focal activation by two independent mapping methods. These data provide an alternative mechanism for the success of PVI, and may explain AF termination before PVI or lack of arrhythmias despite PV reconnection. Mapping such sites may enable targeted PV lesion sets and improved freedom from AF.

Keywords

catheter ablation; atrial fibrillation; rotors; focal activation; FIRM mapping

Correspondence: Sanjiv M. Narayan, MD PhD, 780 Welch Road, MC 5773, Stanford CA 94305, **Voice:** +1 650-7246131; **Fax:** +1 650-7246131; sanjiv1@stanford.edu.

^{*}R. Navara & G. Leef contributed equally to this work as first authors.

[‡]PJ Wang & SM Narayan contributed equally to this work as senior authors.

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Introduction

Ectopic activity from the PVs (pulmonary veins) is thought to initiate or drive AF, explaining why PVI (pulmonary vein isolation) is a central component in treating atrial fibrillation¹. However, it is unclear why some patients remain in sinus rhythm despite PV reconnection on repeat mapping², or how AF may terminate *before* veins are isolated³.

We hypothesized that PV antral sites where ablation terminates AF before PV isolation may harbor AF-sustaining mechanisms that can be identified by mapping. AF mechanisms in such cases may comprise focal or rotational drivers^{4,5} ablation of which has recently shown promising acute outcomes with distinct modes of termination in recent studies⁶⁻⁹, although not all¹⁰⁻¹² studies. We were particularly interested in whether any mapping characteristics could explain acute termination of AF.

To test our mechanistic hypothesis, we examined patients at our institution in whom prospective ablation in the PV antra terminated AF prior to PVI, using 2 independent methods to map mechanisms at sites of AF termination. In parallel, we studied alternative mechanisms for AF termination prior to PVI including ablation of autonomic ganglia or ablation at sites of ectopic activity near the Ligament of Marshall.

Methods

Study Design

Two hundred thirty patients >21 years of age underwent ablation of drug-refractory paroxysmal or persistent AF at Stanford University via basket mapping by 6 operators between October 10, 2014 and August 1, 2016, which yielded 80 terminations of AF. We identified 22 patients in whom targeted ablation near the PVs terminated AF prior to commencing PV isolation. Electroanatomic shells were studied by 3 independent reviewers to determine whether sites of termination were in the peri-PV region, defined as along or within 1-2 cm of a wide-area PV isolation lesion set. Reviewers had high agreement ($\kappa = 0.87$, $p < 0.01$). The presence of comorbid conditions, echocardiographic parameters, and lab values were obtained from each patient's electronic medical record. This study was approved by our Institutional Committee on Human Research.

Electrophysiology Study and AF Mapping

Each EP (electrophysiology) study was performed after discontinuing antiarrhythmic medications for 5 half-lives, except for n=2 patients on amiodarone (1 discontinued 30 days prior, and 1 case not discontinued). Catheters were advanced transvenously to right atrium and coronary sinus, and transseptally to the left atrium. A 64-pole basket catheter (FIRMap, Abbott, CA) was used to map both atria and was moved to multiple positions to ensure adequate coverage¹³. Electroanatomic atrial shells were created in NavX (St Jude Medical, Sylmar, CA) or Carto (Diamond-Bar, CA) to relate basket electrode positions to anatomy. If AF was not present at the beginning of the procedure, it was induced with rapid atrial pacing.

Ablation in all cases in this study was targeted using mapping method 1 (Rhythmview™, Abbott), which uses activation and phase^{4,6,14}. Briefly, unipolar AF signals (0.05-500 Hz) were recorded using basket catheters, deactivating the localization signal of the electroanatomic mapping system to minimize electronic noise. Electrograms were analyzed using algorithms to filter far-field using monophasic potential data to estimate repolarization¹⁵ and conduction^{16,17} and create activation maps (grayscale).

AF activation and propagation maps were analyzed to guide ablation, assisted by phase information, in which a phase singularity (red regions) radiating spiral waves that drives surrounding disorganized activity suggested a rotational driver. Focal impulses were defined by centrifugal activation from an origin driving surrounding activity. Rotational and focal sites were considered AF drivers and used to guide ablation if they lay within regions < 2-3 cm² (<1 electrode) over >1 minute of recordings.

Ablation

Ablation commenced at organized sites identified prospectively, via radiofrequency energy delivered by an irrigated catheter at 25-35 watts. Successive lesions were each applied for 15-30 seconds to cover a total area of ~1-2 cm² of organized zones identified by mapping method 1. After this step, wide area circumferential ablation (WACA) was performed with verification of PV entrance block.

Second AF Mapping Method

Validation of AF mapping using a second independent method was blinded to results of activation/phase mapping and sites of termination. Unipolar AF electrograms were exported from the precise segments used by method 1 for analysis by an independent method 2. Our implementation of method 2 is described¹³ and follows the steps of Kuklik et al. Briefly, the QRS complex is removed on each channel by computing an average QRS complex and subtracting it from electrograms. Next, we applied a 1–30 Hz fourth-order Butterworth band pass filter and computed the dominant cycle length of each electrogram from the Welch Power Spectrum Density estimate of the signal, with a window size of 2,000 milliseconds, overlap of 1,000 milliseconds, and a cycle length cutoff between 130 and 280 milliseconds. Finally, the recomposed signal was constructed as a sum of single-period sinusoidal waves with frequency equal to the computed dominant frequency and amplitude equal to the negative slope of the electrogram. For display we interpolated these recomposed signals to a grid, and applied the Hilbert Transform to compute phase maps (Figs. 1–2, movies 2,4). We have made raw basket datasets and code available online at <http://narayanlab.stanford.edu>, downloads tab.

Method 2 differs from method 1 (the prospective clinical method) in several respects. First, method 2 does not create activation maps of AF, unlike the gray scale activation maps that are the principal output from the clinical method 1. Second, method 2 does not apply proprietary algorithms¹⁸ to filter far-field timing data using action potential duration or conduction restitution, unlike the clinical method. Third, method 2 reconstructs AF signals using sinusoids, unlike the clinical system. We selected method 2 because it did not create

false rotational activation in Kuklik et al.¹⁹, which showed <1% rotational sites using 1-2 cm² electrode plaques in clinical studies and in sheep models of AF.

Phase maps were analyzed by 3 blinded operators. The location and stability of organized sites were then compared to sites identified prospectively from method 1. In two cases, digital data from the procedures was corrupted and could not be examined by mapping method 2. Rotational activity determined by both techniques was considered spatially concordant if locations differed by 1 electrode.

Statistical Analysis

Continuous data is represented as mean $\pm$ SD (standard deviation). Comparisons between groups were made with independent-samples t-tests or with Mann-Whitney U test if non-Gaussian. Gaussian distribution of continuous variables was verified by Shapiro-Wilk test. Correlation between two continuous variables (i.e., number of rotations observed with the two methods) was calculated with Pearson's correlation coefficient. Nominal values were expressed as n (%) and compared with chi-square test or Fisher's exact test if expected cell frequency was < 5. Agreement on rotor locations between 3 raters was assessed with Fleiss kappa score. A probability of < 0.05 was considered statistically significant throughout all analyses. Statistical analysis was performed using Excel and STATA version 12.1 (College Station, TX).

Results

Baseline Characteristics

Patients were aged 60.1 $\pm$ 10.4 years, 72.7% male (Table 1). AF was persistent in 36%. Full patient level characteristics are presented in Supplemental Table 1. Comparing patients in whom AF terminated to AT (n=5) versus sinus rhythm (n=17), we found no significant difference in the incidence of HTN, CAD, DM, reduced EF, or prior ablation procedures.

The baseline characteristics of the 22 peri-PV termination patients were also compared to the characteristics of all other patients who underwent ablation using activation/phase mapping during the same timeframe, with results in Table 2. The peri-PV termination patients were slightly younger (60.0 $\pm$ 0.2 vs 65.0 $\pm$ 11.1 years, $p = 0.05$), but had similar CHADS₂-VASc scores, and similar rates of other comorbidities HTN, CAD, DM2, male sex, prior ablation, and depressed EF to all activation/phase mapped patients ($p = \text{NS}$ for all). In the PV termination cohort, there was less LA enlargement ($p < 0.001$) and a trend toward less persistent AF ($p = 0.06$) compared to all patients.

AF Termination by Ablation Near PVs Before PVI

AF terminated acutely during targeted ablation in each case, before PVI was performed and when the PVs remained electrically connected to the left atrium. Termination was to sinus rhythm in 77% of cases (Supplemental Table 2).

Figure 1 illustrates a 61-year-old man with persistent AF and no prior ablation. Ablation at the LPV carina (Figure 1A) terminated AF to sinus rhythm (Figure 1B). At this time, PVs were still connected and AF was non-inducible. Mapping method 1 revealed

counterclockwise rotational activation at the site of termination (Figure 1C) around a phase singularity (colored region, Figure 1C). Movie 1 shows 5 rotational cycles at this site in a 1.8 second excerpt, with spatial precession (“wobble”) and surrounding disorder. Mapping method 2 confirmed rotational activation at the termination site (Figure 1D) which also exhibited 5 cycles of rotation over 1.8s (Movie 2). PVI via WACA was then performed to bisect this site. After this single procedure, the patient has remained in sinus rhythm off medications at 14 month follow-up.

Figure 2 illustrates a 60-year-old woman with paroxysmal AF and prior ablation in whom ablation near the LIPV (Figure 2A) terminated AF to sinus rhythm (Figure 2B). At the time of termination, PVs were connected despite prior PVI. Counterclockwise rotational activity was seen at the site of termination by method 1 (Figure 2C) and confirmed by method 2 (Figure 2D). Movies 3–4 show AF maps from each method, demonstrating 8 rotations in 1.8s at these sites with some fluctuation and precession. WACA touch-up was subsequently performed. After this procedure, the patient has no clinical recurrence of AF after 2 years without antiarrhythmic drugs.

Overall Locations and Validation of Rotational and Focal Sites

Overall, sites of termination revealed rotational activation in $n=20$ and focal activation in $n=2$ cases. Analysis by 3 observers revealed a high degree of agreement on the location of drivers between methods 1 and 2, with $\kappa = 0.86$ ($p<0.001$; 3 observers: GL, GM, AR). Rotational activation at the terminating source was sustained and the number of cycles observed was highly correlated between methods. Rotational circuits were interrupted by colliding wavefronts and meander, as we recently reported²⁰. However, the number of cycles detected at the site of termination over 4 seconds was similar between methods: 13.4 ± 4.2 versus 12.4 ± 5.3 (method 1 vs 2, $R^2 = 0.66$, $p<0.001$). Thus, the driver was present for a greater percentage of the 4s time segment when visualized using method 1 vs 2, but the difference was small (64.0% vs 59.1%, $p=0.02$). The AF driver tended to migrate by 1 electrode more often with mapping method 2 vs method 1 (38.9% versus 11.1%, $p=0.12$). There were also more drivers visualized using method 2 vs method 1 (2.8 ± 0.8 vs 2.2 ± 0.8 , $p<0.001$).

Figure 3 presents a montage of electroanatomic maps of termination sites in all patients. In each case, PVs were still connected after AF termination by ablation at these sites. Termination sites are summarized in Supplemental Table 2.

Locations and Ablation Sequence of Rotational Activation in These Patients

Patients in this series had 5.1 ± 2.4 AF sources identified during activation/phase mapping in multiple basket segments (epochs). Each of these identified sites was fully ablated, except when proximity to sensitive structures precluded ablation, yielding 4.9 ± 2.2 total ablated sites. Peri-PV locations comprise 33.1% of these sources. Other left atrial locations comprised 33.9%, and right atrial locations comprised 33.0%. In $n=2$ patients, the site of termination was the first to be addressed. Overall, the termination site was the 1.8 ± 1.1 th to be ablated out of 3.4 ± 1.8 in the left atrium, and the 3.2 ± 1.4 th out of 4.9 ± 2.2 overall.

Alternative Mechanisms for AF termination at Peri-PV sites

Touchup of prior PVI was an alternative mechanism for AF termination. However, ablation at peri-PV organized sites did not isolate the PVs in any patient. Of n=10 patients who presented with recurrent AF after prior PVI, all had reconnection of 1 PV and required additional 'touch-up' to isolate the veins.

We observed similar mapping patterns, i.e., drivers and signal characteristics at the site of termination using both mapping methods in patients with and without prior ablation (driver stability in prior vs no prior PVI by method 1: $p=0.13$; method 2: $p=0.31$).

We considered whether AF termination sites co-localized with GPs (ganglionated plexi) or the Ligament of Marshall. Peri-PV sources co-localized with GPs in 31.8% of cases (7/22) by anatomical criteria (reader agreement; $\kappa = 0.94$, $p<0.001$). However, we did not observe vagal slowing in any case at the time of AF termination. Seven cases demonstrated termination near the Ligament of Marshall region (Figure 3, panels 5,6,8,9,10,11,19). None of these sites showed focal activation – rotation was seen by both mapping methods. Epicardial ablation was not required to ablate or terminate these sites.

Finally, we considered whether AF terminations might be random. Prior to termination, 5 out of 8 patients with persistent AF had continuous AF for 158 ± 52 minutes. Six out of 14 patients with paroxysmal AF had continuous AF for 148 ± 62 minutes until ablation at the site of termination. AF terminated within 1.8 ± 3.3 minutes of prospective ablation at sites demonstrating rotational or focal activation, before any further ablation including PVI was attempted.

Patients in this series were enrolled under different study protocols, and the long-term success of each is being collected. There were no deaths, no cardiac tamponade, no phrenic nerve palsy, no groin complications requiring surgical repair and no stroke/TIA.

Discussion

We studied and mapped mechanisms for termination of persistent or paroxysmal AF by ablation near the PVs but prior to PV isolation. Two independent mapping methods revealed sustained, organized and predominantly rotational activation during AF at sites of termination. As described in the preceding section, other potential mechanisms including touchup of previous ablation, GP co-localization, and random termination were not supported. To the best of our knowledge, this is the first study in which 2 independent AF mapping approaches were used to map AF, using the presence and site of AF termination to interpret both.

If rotational or focal activation near the PVs is confirmed in wider populations, identification of such sites *a priori* may help to tailor the location of PVI lesion sets to improve outcomes.

Localized sources of AF

These data add to evidence that human AF is maintained by localized sources, although the debate continues. Optical mapping of human atria show stable AF drivers on the

endocardium that may co-localize with clinically identified AF sources²¹. Some clinical studies support rotational and focal sources^{4,5} with promising ablation results⁶⁻⁸, although other studies disagree. It is unclear if conflicting results reflect patient selection, mapping methodology for AF, or inter-center variations with any approach to AF ablation²². It also remains controversial how ablation at a rotational source may terminate AF. For instance, it is unknown if such sites reflect microreentry around scars, functional obstacles including conduction block or slowing, or other undescribed effects. Such mechanistic studies are of great importance, and may be clarified by human studies such as this where mapping systems are compared in patients with AF termination by ablation.

One unexplained issue in the driver literature to date is why ablation at some rotational drivers is associated with termination, while in others it is not. One possibility is that focal or rotational sites where ablation does not acutely terminate AF act as primary drivers at other times²⁰. Another possibility is that non-terminating sites may intrinsically differ; for instance, they may be slower or be associated with co-factors such as fibrosis, which may prevent acute termination even if eliminated. Another possibility is that ablation is incomplete at sites where AF does not acutely terminate, supported by our study of recurrent AF demonstrating at least one 'conserved' AF drive from prior mapping in each case²³. Finally, it is also possible that some of these sites are false positive detections, although they were confirmed by a second mapping system.

Utility of Two Separate Mapping Techniques

The two mapping methods compared in this study revealed similar results despite their different approaches. Method 1 (activation/phase) creates AF activation maps via repolarization and conduction data to filter far-field signals, with phase as a secondary analysis¹⁸. Conversely, method 2¹⁹ avoids proprietary algorithms and is phase-based yet does not appear to create false rotations in prior studies. Both methods revealed similar spatiotemporal dynamics in AF, which may speak to the robustness of our findings. AF maps by both methods resemble optical maps of human AF, i.e., stable endocardial rotations interrupted by competing waves²⁴. In preliminary studies, method 1 correlates with human optical maps²¹ of AF.

It is not clear why other AF mapping studies produce different results. Known epicardial-endocardial differences in AF from optical imaging of human atria²¹ may explain less stable activity on body surface mapping⁵ or surgical²⁵ epicardial maps. Recent work shows that traditional surgical mapping by marking electrograms may encounter difficulties in the face of complex electrograms²⁶, and that computational-guidance may assist activation marking of AF in such cases²⁷.

Other differences may reflect patient populations, differences between animal models (e.g., sheep) and human AF, or algorithmic implementation.

Further studies are needed to compare AF mapping methodologies in the same patients with an endpoint such as AF termination by ablation, as in this study. For this reason, we have made basket data and software available for download: <http://narayanlab.stanford.edu> (downloads tab).

Alternative Mechanisms

There are other potentially localized mechanisms that cannot be definitively excluded but are not supported by our data: the majority of AF source locations did not colocalize near GPs, and no case exhibited vagal slowing during ablation that terminated AF.

Inspection of AF termination sites shows that seven sites were near the Ligament of Marshall, although localized rotational sources rather than ectopy were observed. In the remaining 15 cases, termination sites were remote from the Ligament of Marshall. We did not prospectively guide ablation sites by presence of complex fractionated electrograms (CFAEs) or high dominant frequency (DF). Previous work is unclear on whether CFAE are strongly⁵ or less strongly²⁸ associated with drivers. Recent work by Chen et al. suggest that specific electrogram patterns of dominant frequency and kurtosis²⁹, or electrogram dispersion³⁰ may mark AF driver sites.

It is quite possible that the effects of AF driver ablation are additive. In all cases, limited ablation terminated AF prior to commencing PVI. In N=2 patients with persistent AF, ablation at the first site near the PVs terminated AF prior to PVI. In remaining patients, ablation of earlier sites did not terminate AF, the targeted site was the second site in the left atrium and the third site ablated overall. These points and the small total of area of ablated LA and RA tissue (<5-10%) prior to PVI argues in favor of a localized mechanism of ablation, rather than by limiting critical mass for multiwavelet reentry. To further establish mechanisms, animal or clinical studies could be performed in which ablation is delivered selectively to drivers presumed to be primary, e.g., those with high dominant frequency surrounded by gradients of stepdown³¹, versus ablation of all presumed driver sites. Another approach would be to transiently stun tissue via cryocooling to assess the impact of interrupting each driver in turn to identify 'primary' from 'secondary' drivers.

Terminations could in theory be related to isolation of PVs in patients with prior PVI. However, PV isolation was not seen at the point of termination, and this would not explain the 12/22 of patients without any prior LA ablation in whom AF terminated prior to beginning PVI. In patients with previous unsuccessful PVI, PV reconnection required subsequent touch-up lesions after AF termination in each case.

Finally, it is unclear how many AF terminations would have occurred by chance. Over one-third of patients had persistent AF and over 40% of the paroxysmal AF patients sustained AF continuously during the procedure for an average of 2.5 hours until the organized AF area was ablated, making chance termination less likely. After ablation at PV drivers, cases of paroxysmal AF no longer self-initiated spontaneously and were no longer inducible. Given that paroxysmal AF will typically need induction, we feel that these data have value even in patients with paroxysmal AF.

Clinical Relevance

PVI may prevent AF recurrence in some patients by eliminating AF drivers near the PV antra. Such drivers would typically go unnoticed and may be missed by PVI lesion set that is slightly too wide or too lateral unless AF is mapped. We have observed that such AF drivers/sources may even arise just beyond or at the edge of wide lesion sets from the second

generation cryoballoon. On the other hand, lesions that pass through such mechanisms may explain AF-freedom despite PV reconnection or incomplete isolation, or acute AF termination before PVI (as in this study). A prior study in a different cohort of patients showed that PVI may be unsuccessful if sites of rotational and focal activation were left unablated³.

AF termination is a debated long-term endpoint³². However, we used AF termination as a clear way to judge acute efficacy of AF ablation. We included AF termination to atrial tachycardia (AT) as well as to sinus rhythm, since both represent termination of the fibrillatory process. Indeed, both rhythms are included in the vast majority of studies of AF termination. Termination of AF to sinus rhythm was more common in this series (75% to sinus) than in prior studies³³ (15% sinus) prior to PVI, albeit in different populations.

Limitations

This study has several limitations. This is a study of procedures performed by different operators. We are unable to draw conclusions about the frequency of AF termination due to PV rotational sources in general practice without consistent mapping in all patients, and without a protocol in which targeted ablation is completed prior to PVI. This study examined only “true positive” cases – in whom ablation terminated AF – and does not comment on potential driver sites where ablation did not terminate AF.

Patients with prior ablation were included by design to assess whether sources differed between groups. Including patients with prior ablation may introduce a limitation in terms of patient heterogeneity, but is also a strength of this study. We observed similar mapping patterns, i.e., drivers and signal characteristics at the site of termination in both groups, using both mapping methods. Moreover, optical mapping studies of human atria^{24,34,35} suggest that AF drivers may relate to scar/fibrosis which may be present whether in unablated or previously ablated patients.

We did not perform concurrent epicardial mapping. Clinical data was obtained from case records rather than from a core lab. Stochastic termination of AF cannot be excluded, but is uncommon in persistent AF, and unlikely even in patients with paroxysmal AF due to their long duration in AF prior to acute termination.

The use of AF induction is a limitation, although will be needed to study paroxysmal AF in most patients. Nevertheless, termination of persistent AF by limited ablation prior to PVI is uncommon even in patients who present in sinus rhythm, yet was seen in all patients in this study.

Conclusions

Two independent mapping methods revealed sustained rotational (and focal) activation patterns in AF at PV sites where ablation terminated AF prior to PVI. These data may explain how patients can be arrhythmia-free post-PVI despite PV reconnection, or why AF may terminate before PVs are isolated. Identification of such activation patterns may enable PVI to be tailored to individual mechanisms to improve ablation outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviation List

AF	Atrial fibrillation
CFAE	Complex Fractionated Electrogram
FIRM	Focal Impulse and Rotor Modulation
GPs	Ganglionated Plexi
LA/RA	Left/Right Atrium
NPAF	Non-paroxysmal AF
PAF	Paroxysmal AF
PV	Pulmonary Veins
PVI	Pulmonary Vein Isolation
SR	Sinus Rhythm
WACA	Wide Area Circumferential Ablation

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Figure 1. Termination of AF by prospectively ablating a left pulmonary vein carina rotational site prior to PVI in a 61-year-old male (panel 16 from Figure 3) with persistent AF
 (A) Electroanatomic shell showing ablation site (outlined in white, red arrow). (B) Electrograms show acute AF termination during ablation and ongoing PV connection to LA. (C) Still panels from movie 1 (activation/phase mapping) show counterclockwise rotational activation at the termination site. Red-green region is Rotational Activity Profile (RAP), i.e., the automatically identified site of phase singularity clustering (rotational activity). (D) Still panels from movie 2 (method 2) also shows counterclockwise rotational activation at the same site.

Figure 2. Termination of AF by ablating at a LIPV rotational site in a 60-year-old female (panel 19 from Figure 3) with paroxysmal AF

(A) Electroanatomic shell identifying ablation site (outlined in white) leading to AF termination. (B) Electrograms show acute AF termination during ablation and ongoing PV connection to LA. (C) Still panels from activation/phase mapping in movie 3 showing counterclockwise rotational activation at the termination site. Again, red-green region is Rotational Activity Profile (RAP), algorithmically identified area of highest rotation. (D) Still panels from method 2 in movie 3 also show counterclockwise rotational activation at the same site.

Figure 3. Montage of Peri-PV ablation sites that terminated AF prior to PV isolation
 Panels indicate electroanatomic (NavX or Carto) shells for all 22 patients with ablation site labeled (by white outline or red arrow).

Table 1

Demographics of the patient population:

	Paroxysmal AF (n = 14)	Persistent AF (n = 8)	p-value
Age	58.3±10.7	63.3±9.6	0.38
Male Sex, % (n)	64.3% (9/14)	87.5% (7/8)	0.35
CHADS ₂ VASc Score	2.1±1.5	1.8±1.5	0.64
Hypertension, % (n)	57.1% (8/14)	62.5% (5/8)	1.0
Diabetes Mellitus, % (n)	21.4% (3/14)	37.5% (3/8)	0.62
Coronary Artery Disease, % (n)	14.3% (2/14)	0% (0/8)	0.51
Left Atrial Enlargement, % (n)	38.5% (5/13)	62.5% (5/8)	0.39
Reduced LVEF, % (n)	7.1% (1/14)	37.5% (3/8)	0.12
AF Duration, months	88.6±74.8	88.1±79.5	0.99
Prior PVI, % (n)	42.9% (6/14)	50.0% (4/8)	1.0

Table 2

Demographics of patient population compared to all FIRM activation/phase-mapped patients:

	PV terminations (n=22)	All others (n = 208)	p-value
Age	60.0±10.6	64.5±11.1	0.05
Male Sex, % (n)	72.7% (16/22)	67.8% (141/208)	0.67
Paroxysmal AF, % (n)	63.6% (14/22)	42.3% (85/201)	0.06
CHADS ₂ VASc Score	1.95±1.40	2.26 ±1.51	0.37
AF Duration, months	88.7±74.8	76.2±72.4	0.39
Hypertension, % (n)	59.0% (13/22)	60.0% (123/205)	0.93
Diabetes Mellitus, % (n)	27.3% (6/22)	12.7% (26/205)	0.10
Coronary Artery Disease, % (n)	9.1% (2/22)	17.6% (36/205)	0.55
Left Atrial Enlargement, % (n)	47.6% (10/21)	80.0% (128/160)	< 0.001
Reduced LVEF, % (n)	18.2% (4/22)	32.6% (57/175)	0.17
Prior PVI, % (n)	45.5% (10/22)	34.8% (69/198)	0.32