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Wavefront Field Mapping Reveals A Physiologic Network Between Drivers Where Ablation Terminates Atrial Fibrillation

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Abstract

Background: Localized drivers are proposed mechanisms for persistent atrial fibrillation (AF) from optical mapping of human atria and clinical studies of AF, yet are controversial because drivers fluctuate and ablating them may not terminate AF. We used wavefront field mapping to test the hypothesis that AF drivers, if concurrent, may interact to produce fluctuating areas of control to explain their appearance/disappearance and acute impact of ablation.

Methods: We recruited 54 patients from an international registry in whom persistent AF terminated by targeted ablation. Unipolar AF electrograms were analyzed from 64-pole baskets to

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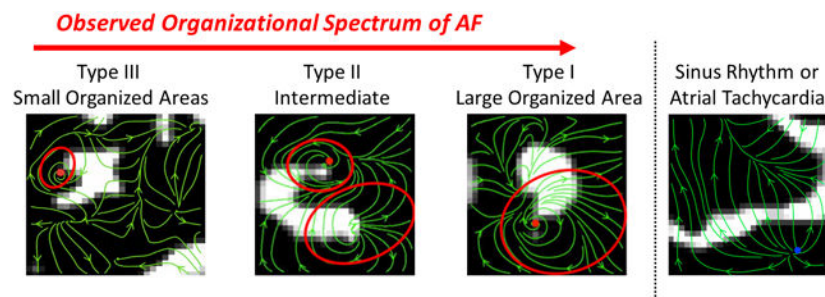
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reconstruct activation times, map propagation vectors each 20ms and create non-proprietary phase maps.

Results: Each patient (63.6 ± 8.5 years, 29.6% women) showed 4.0 ± 2.1 spatially-anchored rotational or focal sites in AF, in 3 patterns. First, a single (type I, $n=7$) or, second, paired chiral-antichiral (type II, $n=5$) rotational drivers controlled most of atrial area. Ablation of 1-2 large drivers terminated all cases of types I or II AF. Third, interaction of 3-5 drivers (type III, $n=42$) with changing areas of control. Targeted ablation at driver centers terminated AF, and required more ablation in types III vs I ($p=0.02$ in LA).

Conclusions: Wavefront field mapping of persistent AF reveals a pathophysiologic network of a small number of spatially anchored rotational and focal sites, which interact, fluctuate and control varying areas. Future work should define whether AF drivers that control larger atrial areas are attractive targets for ablation.

Graphical Abstract



Journal Subject Terms:

Atrial Fibrillation; Electrophysiology; Catheter Ablation and Implantable Cardioverter-Defibrillator; Translational Studies

Keywords

atrial fibrillation; ablation; mapping; rotor; organization; physiological network; multiwavelet reentry

Introduction

It remains unclear what mechanisms must be targeted to treat persistent atrial fibrillation (AF)¹. Pulmonary vein isolation (PVI) is the foundation of AF ablation, yet may not eliminate AF² and has been difficult to improve by targeting other stereotypical anatomical or electrical targets^{3, 4}. AF rotational (rotors) and focal drivers in patient specific locations⁵ have been proposed as therapeutic targets by multiple mapping approaches⁶⁻¹⁵, and have shown promising yet variable success in meta-analyses⁶⁻¹⁵. Controversy remains in part because ablation at drivers may not acutely terminate AF, and because AF drivers may fluctuate over time then reappear due to undefined mechanisms.

We hypothesized that AF drivers may interact dynamically to influence varying atrial areas over time. Our hypothesis was inspired by competing drivers identified in optical maps of human AF^{16, 17} and by recent clinical studies¹⁸ showing fluctuating AF drivers, which have yet to define how drivers interact, sustain AF, or to explain ablation endpoints. Interacting drivers of variable areas of control may explain how drivers fluctuate yet may contribute to AF maintenance, and introduces the concept that the atrial area of influence may determine dominance of an AF driver. In this case, AF may not terminate by ablating a driver that is transiently non-dominant, while terminating AF by ablating a dominant driver may not prevent long-term recurrence if secondary drivers reappear.

We tested our hypothesis using a novel approach to map wavefront fields that describe the underlying propagation of electrical activity during AF¹⁹. This approach enables us to study interactions between orderly activation (potential rotational and focal drivers) and disorder near and remote to atrial regions where targeted ablation did or did not terminate AF.

Methods

Online data, videos, and software code used in this project are available to other researchers for the purposes of reproducing the results or replicating the procedure on <http://narayanlab.stanford.edu> (downloads tab) and also as supplemental material for this manuscript.

Patient Inclusions

We identified 54 patients with persistent AF in the international COMPARE-AF registry (COMPARison of Algorithms for Rotational Evaluation in Atrial Fibrillation,) at 5 centers (Stanford University Hospital, Stanford, CA; University of Colorado, Denver, CO; Indiana University, Indianapolis, IN; Veterans Affairs Medical Center, San Diego, CA; and Klinikum Coburg, Germany) in whom prospective ablation at identified regions terminated persistent AF to sinus rhythm or atrial tachycardia (AT, or atrial flutter (AFL)). In N=44 cases, targeted driver ablation and termination occurred prior to PVI. In the remaining 10 cases, PVI was completed first but AF did not terminate, and subsequent targeted ablation terminated AF. Persistent AF was defined by guidelines (an episode of AF lasting longer than 7 days), and in this study refractory to 1 anti-arrhythmic medication. We excluded patients in whom AF terminated during PVI or any other ablation lesion set. The study was approved by each local IRB.

Electrophysiological Study and Ablation

Patients were studied in the post-absorptive state. Class I and III anti-arrhythmic medications were discontinued for > 5 half-lives (>30 days for amiodarone). Patients who presented in sinus rhythm (50% of cohort) were induced into AF with rapid atrial pacing. Catheters were advanced to the right atrium (RA), coronary sinus and transseptally to left atrium (LA). Basket catheters (64 poles, FIRMap, Abbott) were positioned in RA then LA for 3-dimensional AF mapping referenced to electroanatomic imaging (NavX, St Jude Medical, Sylvar, CA; or Carto, Biosense-Webster, Diamond Bar, CA) (Supplemental figure). Radiofrequency energy was delivered via an irrigated catheter (Thermocool, Biosense-

Webster; or Safire-Blu, St Jude Medical) at 25–35 watts. In all patients, ablation was guided prospectively to regions of interest identified by a clinical system (RhythmView™, Abbott, Inc.), which reveals sites potentially important for AF³. The novel wavefront field approach we describe was not used to guide ablation. Lesions were applied for 15–30 seconds at each site successively, covering areas of $\approx 2 \text{ cm}^2$ as described by Miller et al.¹² PVI was performed per guidelines, comprising circumferential ablation of left and right PV pairs with verification of PV isolation using circular mapping catheters.

Each region of AF ablation was registered to electrodes, e.g. AB23 referencing an ablation site bracketed by electrodes A2, A3, B2, B3 and marked prospectively on atrial shells. Examples of AF termination in such regions are shown in figures 1-3.

Follow-up of patients at each center in the registry followed guideline-defined methods and is ongoing.

Data Export for Analysis

Unipolar electrograms were recorded at 0.05 to 500 Hz at 1 kHz sampling with electroanatomic location turned off to reduce electromagnetic interference. Each data array contained voltage time-series comprising 64 basket electrograms, intracardiac channels such as the coronary sinus, and the 12-lead ECG. AF cycle lengths were measured using custom annotating software as the mean of 15 consecutive coronary sinus bipolar electrograms at least 50 ms apart. Data were exported for analysis from the Bard (LabSystem Pro), Prucka (GE Cardiolab) or Siemens electrophysiological recorder. In all cases, ablation sites were identified in real time by the clinically available mapping system (activation plus phase, RhythmView™). Each site was assigned an atrial location prospectively, prior to ablation.

AF Mapping Methods

We applied 2 approaches recently developed in our laboratory to study organized AF sites ablated prospectively in each procedure. First, we used a non-proprietary phase-based method to map AF. This approach has been validated in human persistent AF, where it reveals rotational sites where ablation may terminate AF that correlate strongly with clinical mapping tools¹⁸, and in animal models of induced AF, where it produced few false rotations ($< 1\%$)^{20, 21}. Non-proprietary phase mapping was thus applied, read by N=6 reviewers blinded to outcome, who identified each termination site 1:1^{18, 22}. Code and data for this method are available online (<http://narayanlab.stanford.edu>). Figures 1-3 show examples of phase maps produced in this way. Because such non-proprietary phase maps correlate closely with clinical maps^{22, 23}, we chose not to analyze clinical maps in this study (Rhythmview™, Abbott).

Second, we used a novel vector mapping method¹⁹ to map propagation and areas of organization and disorganization over time during AF. This new approach recomposes rate-dependent electrograms to compute activation times in AF at each electrode, avoiding both marking of activation times, which has known variability²⁴, and avoiding phase mapping with its limitations²⁵. From these computed activation times, we calculated corresponding activation fronts and used gradient matching to identify the dynamic vector field that describes propagation of these fronts¹⁹. The resulting wave-front field (WFF) was updated

across each episode, and represents the consistent flow of conduction at all points. Results of this analysis were visualized using an animated sequence of images containing activation fronts and stream-lines. The WFF and associated streamlines were applied to original electrograms from each case to compute interactions between sites of rotational and focal activity and surrounding disorder.

Examples of wave-front flow fields are given in figures 1-3, where regions of both rotational and focal activation can be identified by organized wave-front flows over several cycles and may be interpreted more intuitively than either phase or activation maps.

Statistical Analysis

Continuous data are represented as mean \pm standard deviation (SD) or median and interquartile range (IQR) as appropriate. Comparisons between two groups were made with Student's t-tests if normally distributed, or if not normally distributed, with the Mann-Whitney U test. Groups using t-test and chi square test include termination to sinus rhythm versus AT/AFL, ablated sites that lead to termination versus sites that did not lead to termination, and type I/II versus type III AF. Nominal values were expressed as n (%) and compared with chi-square tests, the Fisher exact test when expected cell frequency was < 5 (e.g. gender). Chi square test was used to compare type III versus type I. A probability of < 0.05 was considered statistically significant.

Results

Patient Demographics

Table 1 shows patient demographics. Patients had an average of 4.0 ± 2.1 drivers during AF. Targeted ablation at one of these sites acutely terminated AF in all cases (considered the critical site). Characterization of these sites were central to this study. Patients with termination to AT showed a lower LVEF than those whose AF terminated to sinus rhythm. Presenting rhythm to the electrophysiology lab was AF/AT (50%) or sinus rhythm (Supplemental table). There was no statistically significant difference in CL between patients who presented in AF (168.7 ± 7.8 msec) or sinus rhythm (170.1 ± 8.4 msec) ($p > 0.5$).

Wavefront Field and Phase Mapping

We mapped wavefront fields in AF throughout the atria at sites where ablation did and did not terminate AF to quantify their interactions. Phase maps showed 4.0 ± 2.1 spatially-anchored rotational or focal sites during disorganized AF.

On WFF mapping, AF cases fell into 3 functional patterns. Type I showed a single stable driver with a large area of control. Type II showed a pair of chiral-antichiral drivers in relatively stable locations, each with a large area of control. Type III was less organized with multiple organized sites which appeared, disappeared and interfered with each other over the measured time segment.

Type I: One Predominant AF Driver

Several cases exhibited one stable, spatially anchored AF driver, which typically influenced about one third to one half of the mapped atrium on wavefront field mapping. Other organized sites arising over time were transient and influenced smaller atrial areas. Figure 1 shows persistent AF in a 49-year old man with prior unsuccessful ablation and cardioversions. Panel A shows left atrial anatomy in which ablation at the first targeted region prospectively terminated persistent AF to sinus rhythm. (B) Electrograms show AF termination. (C) Non-proprietary AF phase map^{22, 23} shows stable clockwise (CW) rotational activation at site 1 where ablation terminated AF (H45, marked *), and transient counter clockwise (CCW) rotations at site 2 (D45). On phase mapping, the interaction between these sites is unclear. (D-F) Wave-front flow field maps show CW rotation at site 1 (red dot), that controlled nearly half of the atrium for multiple AF cycles (red circle) shown in cycles 8 (00:16s), 12 (00:27s), 15 (00:31s; panels D-F). Movie 1 shows a stable rotation (phase singularity) at site 1, and movie 2 shows dynamic wave-front flow fields centered around this rotational site for its 4s time segment. Ablation of site 1 terminated AF without ablating site 2.

Overall, 7/54 cases showed this type I pattern. In all 7 cases, ablation of this dominant site terminated AF acutely.

Type II: Stable AF Driver Pair

The second AF pattern (type II) exhibited one pair of chiral-antichiral rotational drivers in relatively anchored spatial locations. Areas controlled by each driver of the pair expanded and contracted reciprocally over time, but combined typically controlled > 50% of mapped atrial areas. Other transient drivers appeared but controlled small atrial areas. Figure 2 shows persistent AF in a 67-year old woman, with atrial anatomy showing the site (CD45, site 1, Fig 2A) where targeted ablation terminated AF to AT (panel B). Open-source AF phase maps (fig 2C) show phase progression around singularity points at site 1 (termination site, marked *) and another site 2 (F34), but again do not explain their interactions. WFF (wavefront field) maps (figures 2D-F) and movies 3,4 show CCW rotation at site 1 and CW rotation at site 2 (red dots) for multiple cycles, each of which controlled fluctuating atrial areas over time (red circles). Ablation at site 1 terminated AF to AT, then completion of ablation at site 2 and touch-up at site 1 terminated AT to sinus rhythm. All stable sources that were identified by mapping were targeted and ablated.

Overall, 5/54 sites showed type II AF maps. While the spatial dominance (area of atrial control) of each driver of the pair varied over time, ablation of one (2 cases) or both (3 cases) of these drivers terminated AF in all cases.

Type III: Multiple, Complex, Interacting AF Drivers

The third AF pattern (type III) was characterized by multiple concurrent drivers (average 3.1 ± 0.8 sites per map) with varying interactions, each having varying areas of atrial control over time, and less organization than types I/II. There was no single dominant site.

Figure 3 shows left atrial anatomy in a 72-year old man in whom ablation at targeted sites (fig 3A) terminated persistent AF (fig 3B). Figure 3C shows an AF phase map indicating 2 rotational activity sites (site 1: CCW phase progression at C2; site 2: CW at E7). Clockwise rotation at a third site AB67 (site 3) is not seen at this timepoint, but arose at other times (Movie 5). WFF (wavefront field) maps (fig 3D-F) reveal dynamic interactions between site 1, where ablation terminated AF (marked '*'), and sites 2 and 3. Rotational activity fluctuated even at the ultimate site of termination (site 1), and was absent at some time points. In figure 3D, frame 00:13s shows CW activation at site 3 with a small area of control and no activity at the other sites. Later at 00:24s (fig 3E), sites 2 and 3 are present, but there is no rotational activity at site 1 (ultimate termination site). At 00:38s (fig 3F), there is clear rotational at site 1 activating a large area of the atrium, site 2 remains active (appearing focal), and site 3 is absent. Movies 5 and 6 show non-proprietary phase and wave-front flow fields movies of these type III maps.

Overall, 42/54 sites showed type III patterns. Table 2 summarizes AF organized site types and characteristics for each AF type.

Acute Impact of Ablation on Each AF Network Type

Persistent AF terminated on ablation of the first targeted AF driver in N=13/53 cases (left atrium, N=9; right atrium N=4), where flow field showed larger areas of control than competing sites ($31\pm 10\%$ versus $20\pm 13\%$, $p < 0.05$). AF terminated at the second targeted site in N=13/53. Overall, AF terminated by ablation in left atrium at the $2.1\pm 1.2^{\text{nd}}$ site out of 2.7 ± 1.3 sites, and overall (both atria) at the $2.9\pm 1.2^{\text{nd}}$ out of 4.0 ± 2.1 sites.

We studied the sequence of sites ablated in the mapped network, and the number of sites ablated prior to AF termination relative to the total number of sites in each case. Figure 4 shows this relationship for all drivers, and figure 5 shows this for left atrial drivers alone. Overall, right atrial driver sites were targeted first (n=33) versus left atrial drivers (n=20). Ablation sequence data was missing for 1/54 patients in the registry.

For type I AF, elimination of the sole driver site terminated AF in all cases. For type II, ablation at one or both of the pair of drivers terminated AF in all cases. Considering only LA drivers, ablation of a solitary or < half of drivers terminated all type I cases but 17/41 type III cases ($p=0.02$ versus type I). Type I AF was more likely to terminate with ablation of a solitary or less than half of drivers than type III ($5/7$ versus $13/41$, $p=0.09$). There was a trend for more organized types I/II AF to terminate earlier in the sequence than type III ($1.5^{\text{th}}/2.4$ versus $2.0^{\text{nd}}/2.7$ LA sites, $p=0.15$). There was no difference in types I, II, III AF depending on whether AF was the presenting rhythm.

These data support the ability of flow field areas to reflect characteristics of that site, rather than prior ablation, particularly for types I,II. However, this concept requires prospective guidance of ablation to 'dominant rotational drivers' identified by flow field, which is planned.

AF type and Demographics

Table 3 breaks down baseline characteristics and driver locations for map types I-III. There was no clear relationship between AF map types (I/II versus III) and the clinical parameters of age, sex, left atrial diameter, left ventricular ejection fraction, CHADS-VASC score, diabetes mellitus type 2, hypertension, presence of coronary artery disease, AF duration, prior ablation, presenting rhythm, left vs right atrial termination, or peri-PV vs non-PV termination.

Discussion

We used a novel approach to map organized wavefront fields during AF, which showed a small number of organized regions controlled by drivers in relatively fixed locations, interacting to cause fluctuating areas of control. We identified three types of AF based on organized driver numbers and their areas of control. Type I AF had a single driver, type II had a chiral-antichiral pair, each of which controlled most of atrial areas and whose elimination terminated AF. Type III AF was less organized, with 3–5 simultaneous sites each controlling smaller areas with more complex interactions, who required more ablation. Clinically, these data could explain lack of AF termination by ablation of a driver that controls small atrial areas or, conversely, why ablation at a driver which controls large atrial area and that terminates AF may not prevent long term recurrence if secondary mechanisms remain. If further validated, these results may provide the basis for improved mapping and ablation of persistent AF.

Driver Stability and Maintenance of AF

While many studies report organized regions in human AF from clinical²², experimental^{6, 8, 12, 26-28} and computational²⁹ studies, there is ongoing debate on how sites that fluctuate over time can drive AF. Rotational and focal AF sites appeared in relatively stable regions, in agreement with optical mapping of human AF³⁰ showing a relationship to microfibrosis on 9T MRI³¹, yet fluctuated temporally due to competing sites. These temporal interactions may explain several previously unexplained clinical observations. For instance, in the type III case of 3 drivers in figure 3, the rotational site where ablation ultimately terminated AF was inapparent at many time points, yet controlled large areas at other times. These data provide a time-dependent interpretation of AF termination – which should be more likely if energy is applied to a site at a time when it controls a greater proportion of atrial area. This hypothesis requires further testing and clinical validation.

These results extend optical mapping in human AF by Li et al.¹⁶, who reported reentrant AF drivers stabilized spatially by atrial structure which fluctuated due to competing drivers, as well as our own previous work¹⁸. To prevent long-term clinical AF recurrence, these data support the approach of ablating all potential AF drivers in the physiological network.

AF Functional Phenotypes and Termination

These data suggest a novel approach to classify AF that extends yet is consistent with prior models, such as those based on numbers of AF wavelets by Konings et al³². We propose that types I and II AF are more organized not just because they exhibit fewer driver regions, but

because these drivers control (organize) a greater atrial area and thus leave less area for collision (fibrillatory conduction). Prospective studies are needed to test if AF types I and II are more amenable to acute termination and long term freedom from AF by eliminating the dominant driver or driver pair.

Type III AF cases (68.3%) required ablation of more than half of drivers to terminate, yet in 10/42 cases AF terminated at the first targeted driver. Consistent with our hypothesis, this could be explained if the first targeted site was dominant at the instant of ablation. Conversely, times when ablation at a targeted site did not terminate AF could be explained if that driver was suppressed at that time. Further studies are needed to further unravel these dynamics, and wavefront field mapping may assist in this goal.

Overall, these concepts could explain why acute AF termination has had mixed results as a long-term predictor of AF recurrence for ablation strategies including PVI³³⁻³⁵. These data strongly support our practice of eliminating all potential AF drivers from multiple mapping epochs¹⁸. Since AF termination during PVI is typically not accompanied by mapping for potential driver sites, such mapping provides an opportunity to improve results from PVI. If mapping is performed, 2–3 basket positions may be necessary to cover most of the atrial surface (Supplemental Figure 1), and potentially it may be of benefit (albeit less practical) to combine endocardial and epicardial mapping³⁶.

Limitations:

This study design used ‘true positives’ – cases in whom ablation terminated AF. While examining non-termination cases must be done, this study is a start by unraveling non-AF-terminating sites in patients in whom AF was ultimately terminated. In theory, AF terminations in the study could be spontaneous, although AF did not terminate prior to ablation and is less likely in persistent AF. Delayed termination of AF after ablation of a driver is sometimes encountered, but would not alter our conclusions that ablation at sites showing organized activity on multiple mapping methods terminated AF. We are in the process of collecting long-term outcomes in this multicenter international registry, and these are not available for this analysis.

Our analyses of ablation lesion site relative to type of AF driver is inevitably limited by the precision of electroanatomic lesion marking in the moving heart, without baskets in place to provide AF maps at the precise timepoint when ablation was delivered. This study is planned. Inclusion of AT termination events may be a limitation, yet transition to AT indicates termination of the fibrillatory process, can be a step towards sinus rhythm (e.g. figure 2) and is included in most prior studies of termination³⁷.

Although prospective ablation was performed based on a proprietary mapping algorithm, this study used only openly-available software analyses (downloadable at our website) without proprietary mapping. The basket contact-mapping catheter has limited resolution, but is sufficient to record organized rotational/focal activity^{38, 39} and has been shown by others to be superior to prior methods⁵. There is a risk of false positive rotations with wider electrode spacing³⁸, and care was taken to equalize spline spacing. Finally, atrial areas of control by wavefront analysis were blinded, estimated visually by analyzing streamlines

surrounding the identified source. We defined this border of the area of control where these streamlines diverge from a coherent pattern (centrifugal lines for focal sources or circumferential lines for rotational sources). This area of control was compared to the entire atrial grid, then quantified using a least-squares approach as a percent of mapped area. Automated methods are being developed which account for dynamic change in flow lines during and between each AF cycle.”.

Finally, the resolution required for AF mapping may follow an inverse principle: global mapping with existing catheters allows detection of macroscopic events but may miss fine detail for which higher resolution is needed. Conversely, small mapping plaques may see high-resolution detail yet miss precessing organized activity and/or reciprocal sites outside the mapping field.

Future improvements in recordings catheters may provide additional mechanistic insights and clinical improvements.

Conclusions

Wavefront field mapping of persistent AF revealed a physiological network of a small number of spatially stable driver regions, each interacting to control variable atrial regions over time. We identified 3 types of AF, with the more organized (type I-II) requiring less ablation to terminate AF. These data may explain why AF may not terminate if ablation targets a transiently non-dominant driver, or why ablation at a transiently dominant driver may terminate AF yet not prevent long term recurrence unless secondary sites are also eliminated. Prospective wavefront field mapping may help improve the mapping and ablation of persistent AF.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is Known:

- Mechanisms that initiate and sustain persistent AF are unclear
- Ablation of potential drivers for persistent AF has had mixed results, in part because it is unclear which are dominant, which are secondary, and why.

What the Study Adds:

- Wavefront fields are a novel approach to reveal organized areas of control during AF, which we used to define 3 types of AF.
- Ablation of dominant driver sites, controlling large areas of the atria, was more likely to lead to acute termination of AF, compared to sites that controlled less of the surrounding atrium;
- Mapping organized areas of control in AF may help classify patients who are more and less likely to benefit from ablation, and may help guide ablation to critical sites.

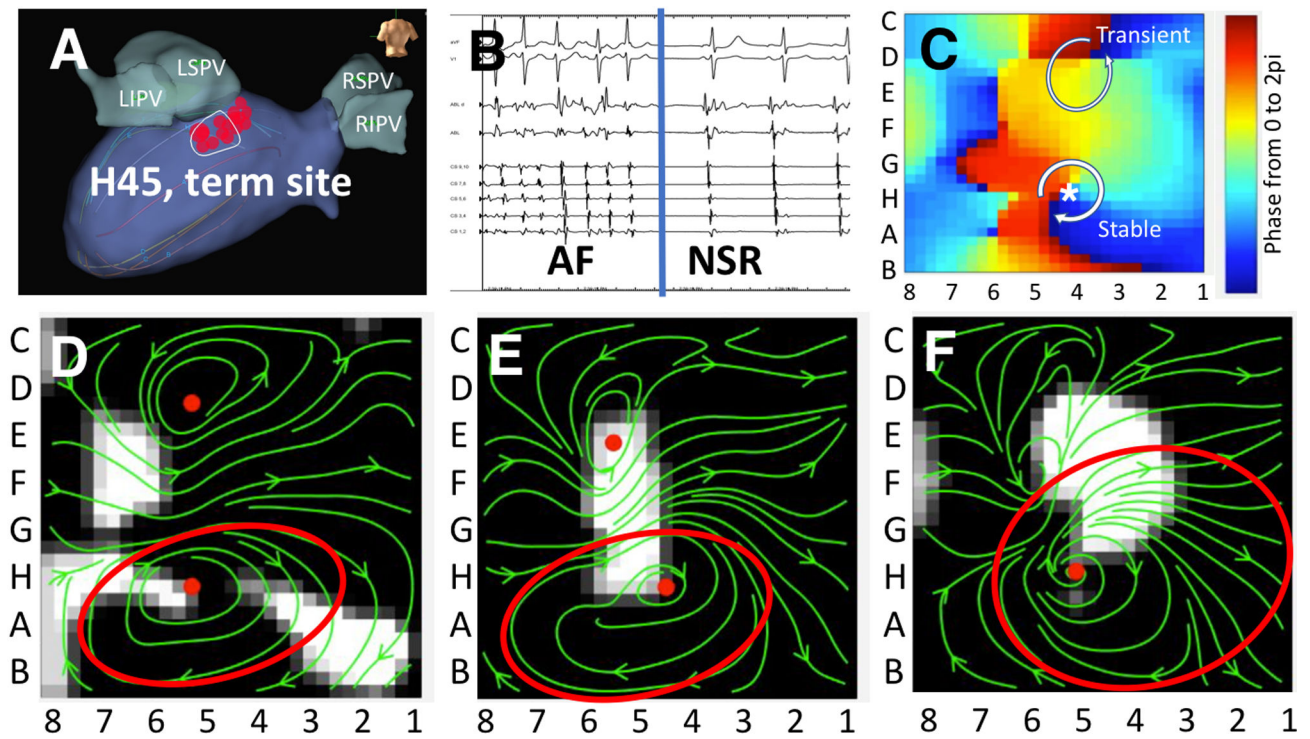


Figure 1.

Persistent AF in a 49-year-old man sustained by one dominant AF driver (type I) (A) Anatomical shell of left atrium (left posterior oblique view) showing solitary site where localized ablation terminated AF to sinus rhythm. (B) Electrograms of AF termination to sinus rhythm. (C) AF phase map identifies stable CW rotation at site H45, the site of termination marked *, and transient counter clockwise rotations at D45. (D-F) Wave-front flow field defines rotational activation at termination site for multiple cycles (Panels D and E). Red dots denote the centers of areas of rotational activity and are determined automatically by the wavefront flow field software. Red circles are manually annotated to show estimated atrial areas controlled by localized sources, based on blinded visual estimates.”.

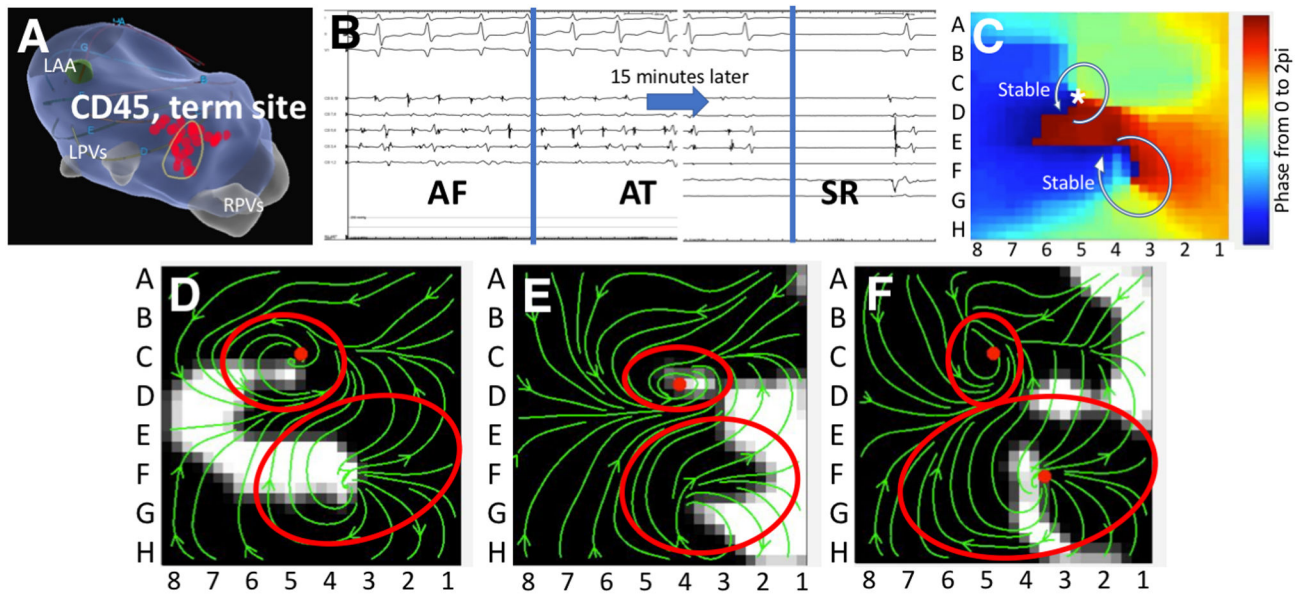


Figure 2. Persistent AF in a 67-year-old woman sustained by a dominant driver pair (type II) (A) Anatomic shell showing two left atrial sites where ablation organized, then terminated AF. (B) Electrograms of termination to AT and sinus rhythm. (C) AF phase map showing counterclockwise rotation at CD45 and clockwise (antichiral) rotation at F34. Site of termination is marked *. (D-F) Wave-front flow field defines a consistent pair of rotational sites over multiple cycles, fluctuating in the areas of mapped atrium emanating from each.

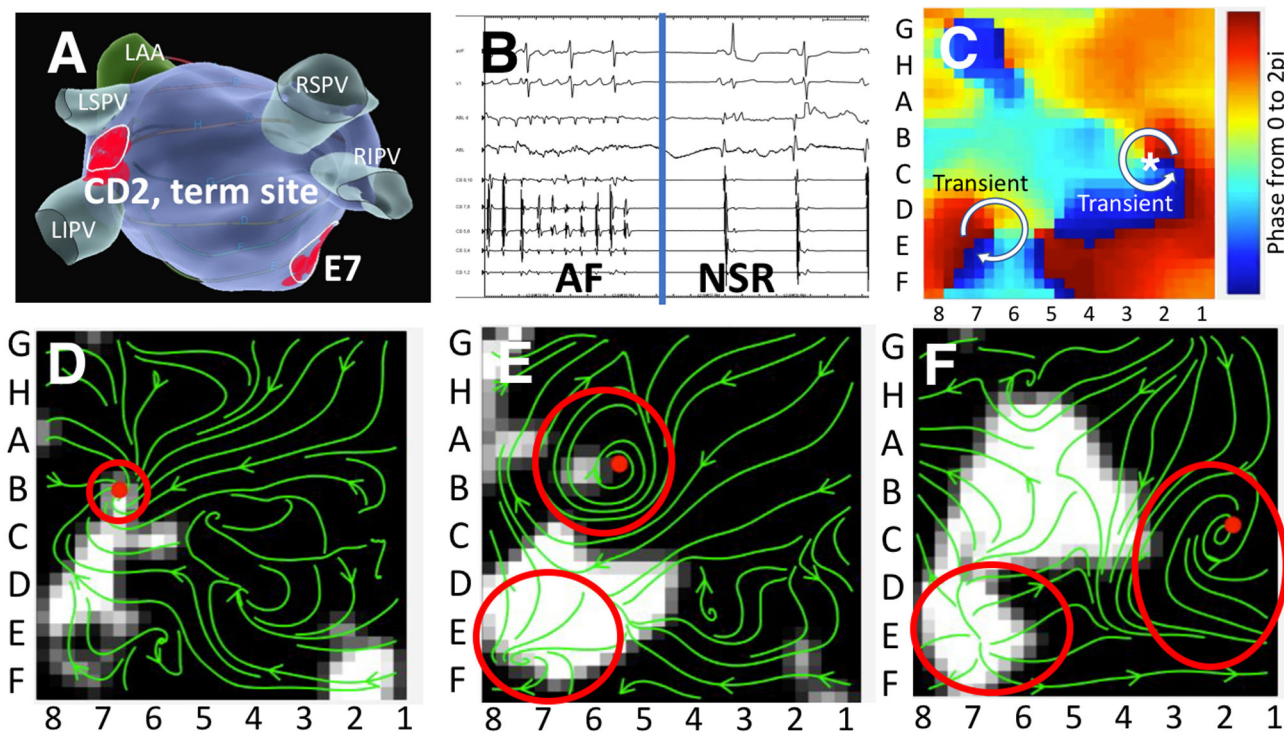


Figure 3. Persistent AF in a 72-year-old man with Dynamically Interacting AF Drivers (type III). (A) Anatomic site of AF termination (C2) showing basket in position; (B) Electrograms of AF termination by ablation; (C) Phase maps show singularity corresponding to CCW phase progression at C2, as well rotations at E7. (D-F) Sequential WFF maps show dynamic back-and-forth interaction between the termination site and other sites at AB67 and E7 with changing spatial domains.

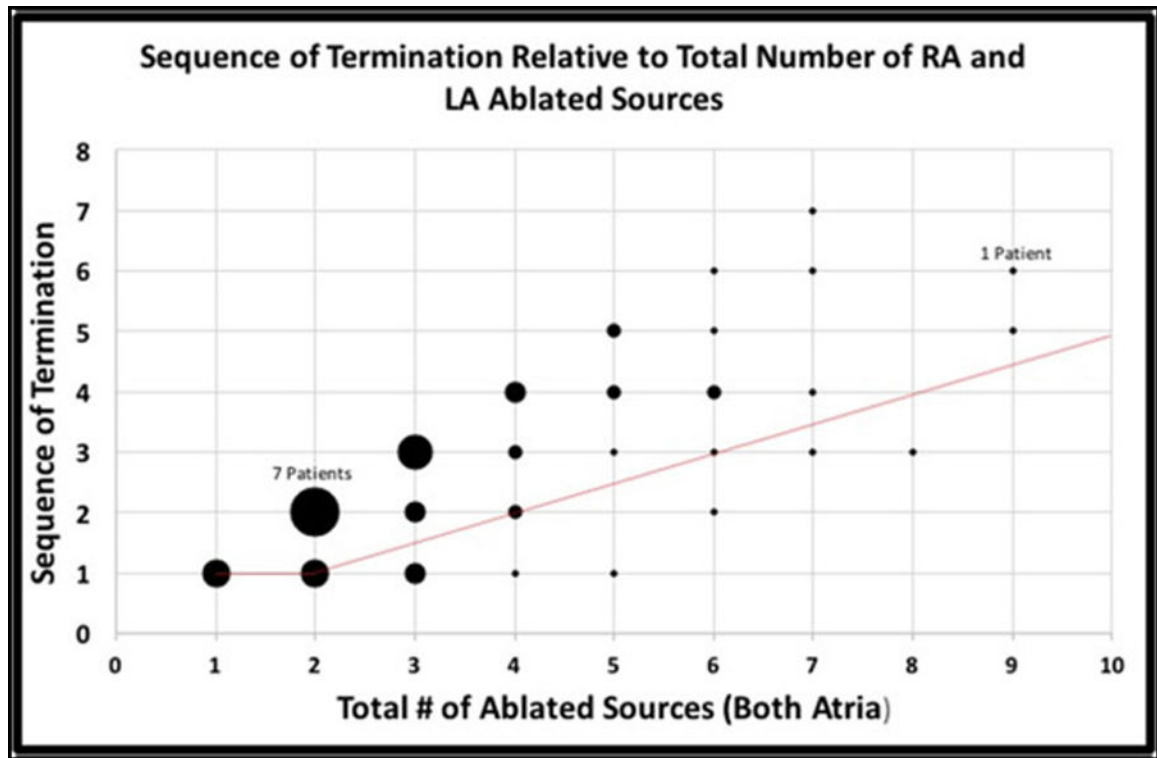


Figure 4. Sequence of ablation of the terminating driver, relative to the total number of LA and RA drivers targeted in the case. The red line shows termination after ablation of 50% of the total drivers seen. Below the line, AF terminated with <50% of drivers ablated; above the line AF terminated after ablation of >50% of drivers.

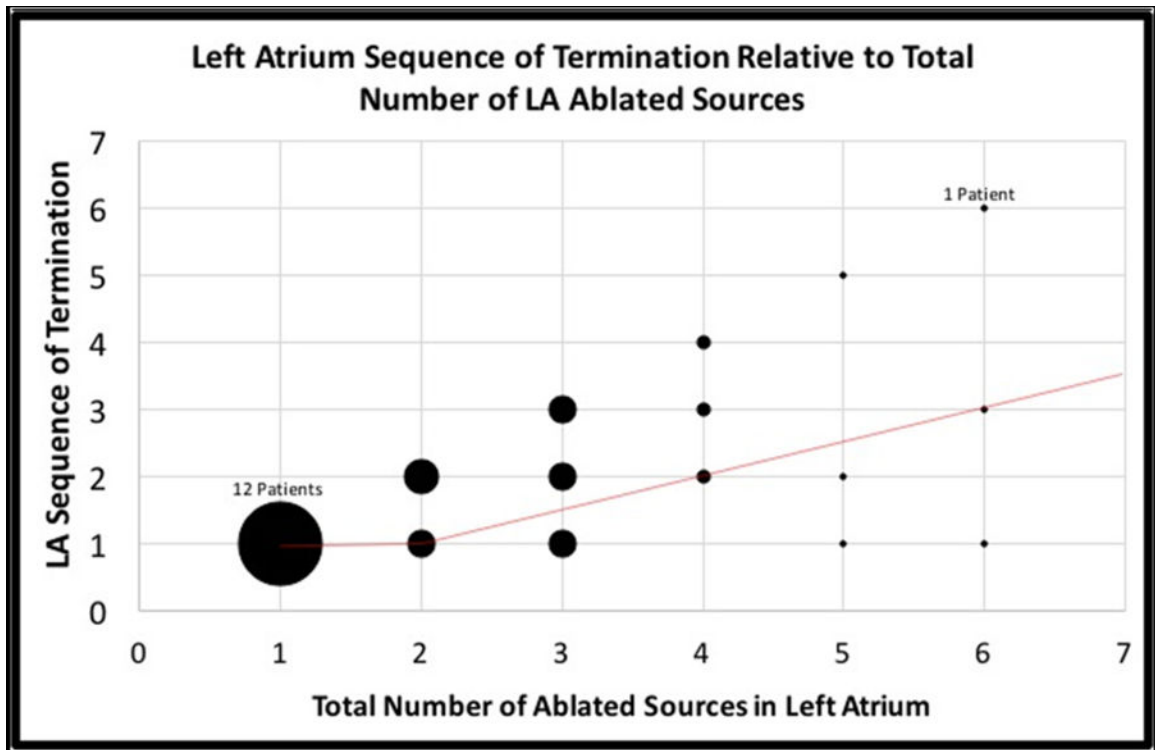


Figure 5. Sequence of ablation of the terminating driver, relative to the total number of left atrial drivers targeted in the case. The red line shows termination after ablation of 50% of the total left atrial drivers seen. Below the line, AF terminated with <50% of drivers ablated; above the line AF terminated after ablation of >50% of drivers.

Patient Demographics

Table 1.

n = 54	Total Sample	Termination to sinus (n=30)	Termination to AT/AFL (n=24)	P-value
Age (Years)	63.6 ± 8.5	63.1 ± 9.1	64.2 ± 7.7	0.6
Male, n(%)	70.4	70.0	70.8	0.9
Prior AF Ablation, n(%)	51.0	51.7	52.4	1.0
AF History (months)	64.7 ± 63.3	69.2 ± 72.9	56.6 ± 41.6	0.5
Left Atrial diameter (mm)	46.7 ± 7.4	47.5 ± 8.0	45.6 ± 6.8	0.4
LVEF (%)	54.1 ± 11.8	58.0 ± 8.0	48.3 ± 14.3	0.01
CHADSVASe score	2.3 ± 1.5	2.2 ± 1.7	2.4 ± 1.3	0.6
Hypertension, n(%)	70.2	65.5	77.8	0.6
DM2, n(%)	19.1	17.2	22.2	1.0
Prior stroke or TIA, n(%)	10.6	13.8	5.6	0.6
CAD, n(%)	26	20.7	35	0.4
Body Mass Index (kg/m ²)	30.8 ± 6.3	30.8 ± 6.5	31.0 ± 6.1	0.9

Table presents n(%) for categorical variables and mean (±SD) for continuous variables. AF, atrial fibrillation; AT, atrial tachycardia; AFL, atrial flutter; CAD, coronary artery disease; DM2, diabetes mellitus type 2; LVEF, left ventricle ejection fraction; TIA, transient ischemia attack;

Table 2.

Characteristics of AF in Types I/II versus Type III AF

Characteristic	Total Sample	Type I or II maps (n=12)	Type III maps (n=42)	P-Value
<i>Characteristics of Localized drivers (n=54)</i>				
LA/RA Termination Site (% in LA)	46 / 8 (85.1)	11 / 1 (91.7)	35 / 7 (83.3)	0.7
PV/NPV Termination Site (% near PV)	28 / 26 (51.8)	8 / 4 (66.7)	20 / 22 (47.6)	0.4
No. drivers (LA/RA) (% LA)	136 / 79 (63.3)	29 / 18 (61.7)	107 / 61 (63.7)	0.9
<i>Activation at AF Term Site</i>				
Rotational	47	11	36	
Focal	7	1	6	

AF, atrial fibrillation; LA, left atrium; NPV, non-pulmonary vein; PV, pulmonary vein; RA, right atrium.

Table 3.

Patient Characteristics between Types I/II and Type III AF

Characteristic	Total Sample (n=42)	Type I or II AF (n=12)	Type III AF (n=42)	P-Value
Age (years)	63.8 ± 8.5	65.0 ± 7.0	63.5 ± 8.1	0.7
Male, n(%)	71.2	63.6	73.2	0.8
LA diameter (mm)	46.7 ± 7.4	47.1 ± 4.8	46.4 ± 8.1	0.7
LVEF (%)	54.1 ± 11.8	54.6 ± 7.9	53.8 ± 12.8	0.8
CHADS-VASC score	2.3 ± 1.5	1.9 ± 1.7	2.4 ± 1.4	0.4
DM2, n(%)	19.1	10.0	21.6	0.7
HTN, n(%)	70.2	60.0	73.0	0.7
Prior stroke or TIA, n(%)	10.6	10.0	10.8	1.0
CAD, n(%)	26.0	10.0	30.8	0.3
AF History (months)	66.1 ± 64.5	83.1 ± 74.5	62.2 ± 64.5	0.5
Prior LA ablation, n(%)	51.0	50.0	52.5	0.9
Presented for ablation in AF/AT, n(%)	50.0	50.0	50.0	1.0

Table presents n(%) for categorical variables and mean (±SD) for continuous variables. AF, atrial fibrillation; AT, atrial tachycardia; CAD, coronary artery disease; DM2, diabetes mellitus type 2; HTN, hypertension; LA, left atrium; LVEF, left ventricular ejection fraction; TIA, transient ischemia attack.