

# Individualized ablation strategy to treat persistent atrial fibrillation: Core-to-boundary approach guided by charge-density mapping

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**BACKGROUND** Noncontact charge-density mapping allows rapid real-time global mapping of atrial fibrillation (AF), offering the opportunity for a personalized ablation strategy.

**OBJECTIVE** The purpose of this study was to compare the 2-year outcome of an individualized strategy consisting of pulmonary vein isolation (PVI) plus core-to-boundary ablation (targeting the conduction pattern core with an extension to the nearest nonconducting boundary) guided by charge-density mapping, with an empirical PVI plus posterior wall electrical isolation (PWI) strategy.

**METHODS** Forty patients (age  $62 \pm 12$  years; 29 male) with persistent AF ( $10 \pm 5$  months) prospectively underwent charge-density mapping-guided PVI, followed by core-to-boundary stepwise ablation until termination of AF or depletion of identified cores. Freedom from AF/atrial tachycardia (AT) at 24 months was compared with a propensity score-matched control group of 80 patients with empirical PVI + PWI guided by conventional contact mapping.

**RESULTS** Acute AF termination occurred in 8 of 40 patients after charge-density mapping-guided PVI alone and in 21 of the

remaining 32 patients after core-to-boundary ablation in the study cohort, compared with 8 of 80 (10%) in the control cohort ( $P < .001$ ). On average,  $2.2 \pm 0.6$  cores were ablated post-PVI before acute AF termination. At 24 months, freedom from AF/AT after a single procedure was 68% in the study group vs 46% in the control group ( $P = .043$ ).

**CONCLUSION** An individualized ablation strategy consisting of PVI plus core-to-boundary ablation guided by noncontact charge-density mapping is a feasible and effective strategy for treating persistent AF, with a favorable 24-month outcome.

**KEYWORDS** Catheter ablation; Conduction pattern core; Driver; Maintainer; Noncontact charge-density mapping; Persistent atrial fibrillation

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## Introduction

Mechanisms that sustain persistent atrial fibrillation (perAF) remain the subject of ongoing research and discussion. Focal activation from the muscle sleeves within the pulmonary veins (PVs) is a common trigger.<sup>1</sup> Pulmonary vein electrical isolation (PVI) alone delivers modest success in treating perAF. Additional ablation beyond PVI has not improved

clinical outcomes.<sup>2,3</sup> A better understanding of perAF is sought through new mapping technologies, but these efforts have not yet established a consensus on the best ablation strategy.<sup>4</sup>

A noncontact charge-density mapping (CDM) system (Acutus Medical, Carlsbad, CA) provides ultrasound-acquired anatomy and localized electrical assessment of

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cardiac activation across the whole chamber.<sup>5</sup> Charge density represents a continuous, tissue-level distribution of the actual sources of electric charge that exist at the cellular level. CDM has been reported to provide better resolution of localized portrayal of activation than voltage-based mapping. This potentially helps to identify patient-specific mechanisms that can initiate or perpetuate perAF.

The aim of this study was to compare the outcome of an individualized approach to PVI plus core-to-boundary ablation (C-to-B) targeting repetitive activation pattern guided by CDM (study group) vs empirical PVI plus posterior wall isolation (PWI) (control group) in patients with perAF.

## Methods

### Patients

Patients undergoing *de novo* radiofrequency (RF) catheter ablation of perAF from Royal Brompton Hospital, London, and John Radcliffe Hospital, Oxford, from November 2016 to April 2018 were prospectively enrolled. A personalized ablation strategy consisting of PVI encompassing antral conduction pattern cores (CPCs) followed by ablation of remaining CPCs guided by noncontact CDM in steps of map-ablate-remap until atrial fibrillation (AF) termination or CPC depletion was adopted for the study group. The CPCs were “anchored” to the nearest nonconducting boundary (C-to-B ablation). In a 1:2 ratio, a propensity score-matched cohort from a database of 2435 patients who underwent *de novo* empirical PVI + PWI ablation for perAF were selected as a control group. Ablation was guided by conventional 3-dimensional (3D) contact anatomic mapping and consisted of empirical PVI with roof and inferoposterior linear ablation between the contralateral antral PVI lesion sets. The study was approved by the National Ethics Committee (NHS Health Research Authority). The research reported in this paper adhered to Consolidated Standards of Reporting Trials (CONSORT) guidelines.

### Noncontact CDM

In brief, the methodology includes static and dynamic 3D maps of electrical activation across an ultrasound-acquired cardiac chamber surface.<sup>6</sup> A 10F, 48-pole noncontact mapping catheter (AcQMap, Acutus Medical) was used to collect the electroanatomic data. The AcQMap methodology applies an algorithm to determine and organize local activation time as a moving window of isochronal color bands, generating a “propagation history map.”<sup>5</sup> CDM of human atria has been described and validated in previous studies.<sup>7,8</sup>

### Electrophysiological procedure

All procedures were performed with patients under general anaesthesia. Heparin was administered by intravenous bolus to maintain an activated clotting time  $\geq 350$  seconds. Following transseptal access, the noncontact mapping catheter was introduced into the left atrium (LA) over a 0.032-inch guidewire via a 12F deflectable sheath (AcQGuide sheath, Acutus Medical) for chamber reconstruction and

CDM. The technical aspects of clinical data acquisition using noncontact CDM have been previously described.<sup>6</sup>

### CPC identified by CDM

CPCs identified in propagation maps during perAF were characterized into three types as described previously: (1) focal centrifugal activation (FCA): a discrete site of early activation with radial propagation to the periphery; (2) localized rotational activation (LRA): a spiral wave centered on a confined zone, with propagation sweeping through  $\geq 270^\circ$ ; and (3) localized irregular activation (LIA): isthmuslike conduction, with multidirectional entry and exit through or pivoting around a confined zone.<sup>8</sup>

PerAF maps were generated from 30-second recordings taken before and after PVI to assess potential changes in the number, locations, and occurrence of CPCs. To assess the stability and repetitiveness of CPCs before ablation, at least three, 5-second segments of perAF were mapped and analyzed from each recording. If the centers of CPCs were  $\geq 1$  cm apart, they were considered spatially distinct.

### Individualized ablation strategy (PVI + C-to-B)

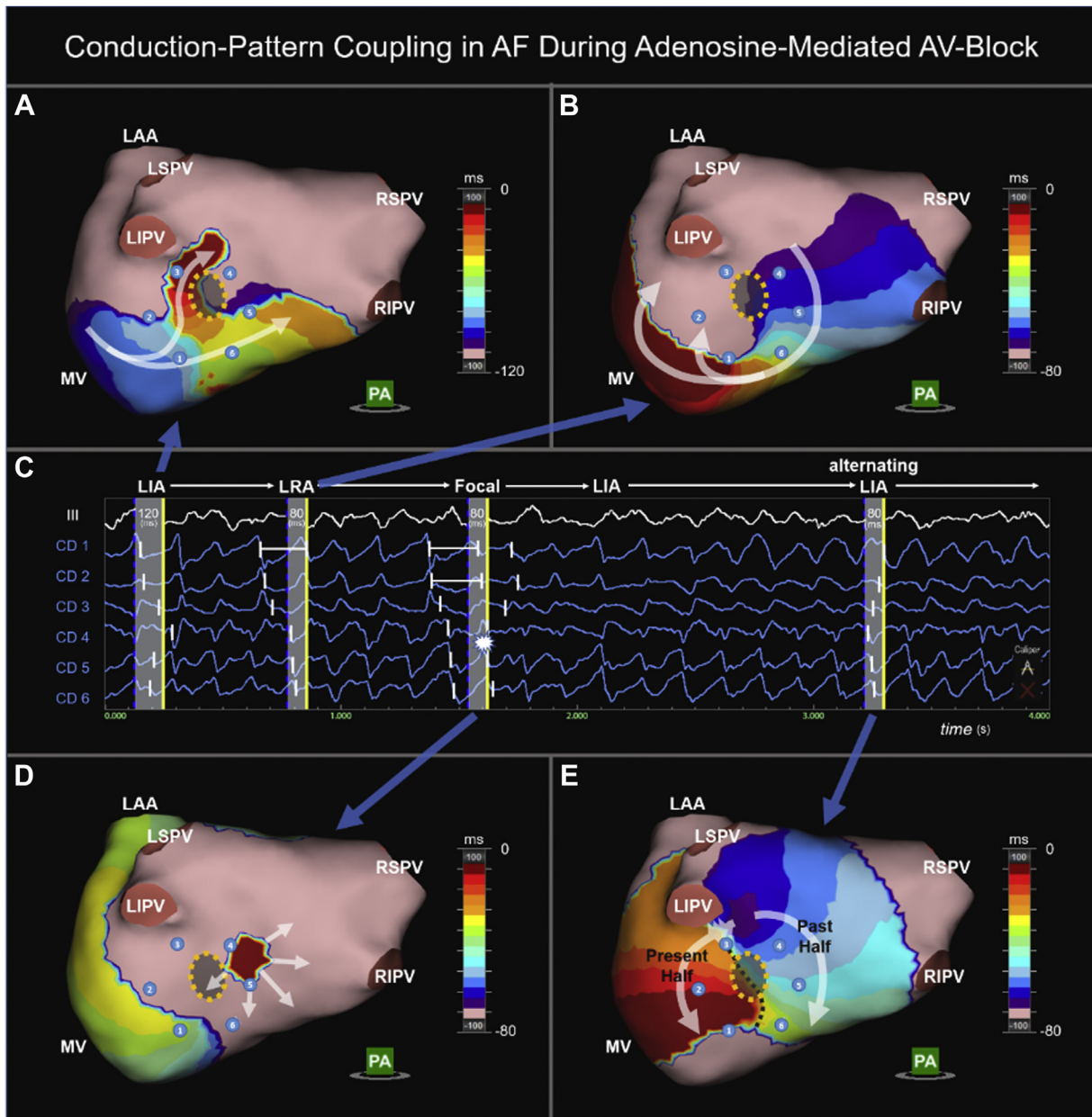
The individualized strategy targeted CPCs identified by CDM. Following the initial propagation mapping of perAF, circumferential PVI was performed to incorporate CPCs identified within 1 cm of PV ostia. CDM of perAF was repeated after PVI to confirm treatment effect and/or identify any new or altered CPC sites. The remaining CPCs with repetitive patterns of FCA, LRA, and LIA were ablated with core ablation lesions that were then “anchored” to the nearest nonconducting boundary such as the PVI lesion set or the mitral annulus. This strategy is defined as C-to-B ablation.<sup>9</sup> The map-ablate-remap steps were repeated until AF termination or depletion of CPCs.

CPCs with coexistence of LIA and LRA were preferentially targeted given an observed common spatiotemporal association with periodic activity of LIA and LRA.<sup>8</sup> Then, the sites with LIA/LRA/focal repetitive patterns in isolation ( $\geq 2$  cycles) were targeted (Figure 1).

If AF persisted after confirmation of CPC depletion in the LA, then the right atrium (RA) was mapped. In the RA, the ablation strategy guided by CDM was at the discretion of the operator, with either the same C-to-B strategy or core-only strategy if the target site was in the vicinity of the intrinsic conduction system or phrenic nerve.

In cases in which AF converted to atrial tachycardia (AT), the tachycardia was mapped and ablated accordingly. If AF persisted after all CPCs were eliminated, a synchronized cardioversion was performed to restore sinus rhythm (SR). Bidirectional block at the PVs and across the linear ablation lines was confirmed with either differential electrical stimulation maneuvers and/or CDM. The individualized ablation strategy is illustrated by the flow chart in Figure 2.

In the study group, an irrigated RF ablation catheter (ThermoCool, Biosense Webster, Diamond Bar, CA; or TactiCath,



**Figure 1** Example of a preferentially targeted conduction pattern core (CPC) site with coexistence of different conduction patterns. Preferentially targeted CPC on the lower left atrial posterior wall with coexistence of localized irregular activation (LIA) (A, E), localized rotational activation (LRA) (B), and focal centrifugal activation (D) in a patient with persistent atrial fibrillation (AF). C: Continuous electrograms from 6 locations around the CPC in this AF segment. Yellow dotted circle represents confined zone of preferential conduction that spatially defines this CPC. White arrows indicate propagation directions of conduction patterns. LAA = left atrial appendage; LIPV = left inferior superior pulmonary vein; LSPV = left superior pulmonary vein; MV = mitral valve; PA = posteroanterior; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

Abbott) with power delivery of 30–40 W was used for ablation.

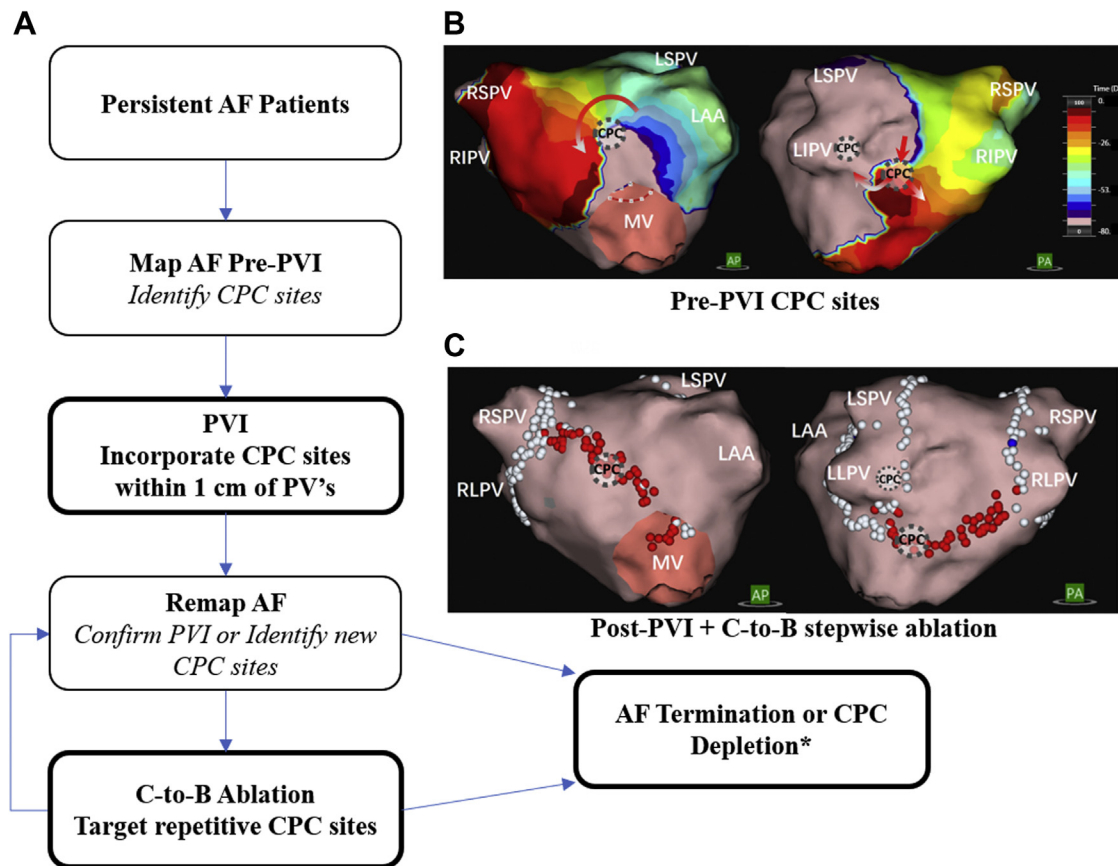
### Empirical ablation strategy (PVI + PWI)

In the propensity score-matched control group, a conventional 3D electroanatomic contact mapping system (CARTO, Biosense Webster) was used to guide ablation. Ablation was delivered through a contact force-sensing ablation catheter (ThermoCool, SmartTouch, Biosense Webster) using the same power delivery of 30–40 W. Empirical PVI was

performed, followed by linear ablation across the roof and inferoposterior wall connecting the contralateral PVs antral lesions achieving PWI. If the patient remained in perAF, direct current cardioversion was performed to restore SR. Empirical cavotricuspid isthmus ablation was also performed in the RA at the discretion of the operator.

### Follow-up

Patients were monitored for 24 hours for any acute complications. Follow-up was at 3, 6, and 12 months and then at



**Figure 2** Stepwise individualized approach (PVI + C-to-B) to treat persistent AF guided by charge-density mapping (CDM). \*Mapping and ablation workflow is repeated in the right atrium. If persistent AF continues after CPC depletion in the right atrium, cardioversion is performed to restore sinus rhythm. **B:** Example of 3 CPCs located on the middle anterior wall (anteroposterior [AP] view) and on the lower posterior wall (PA view) pre-PVI. **C:** PVI + C-to-B ablation strategies guided by CDM. After PVI, a new map was created. CPCs at the anterior wall (AP view) and low posterior wall (PA view) of LA were targeted, followed by connecting the lesion sets to the left and right circumferential lesions, respectively. C-to-B = core-to-boundary; LAA = left atrial appendage; PVI = pulmonary vein isolation; other abbreviations as in Figure 1.

6-month intervals thereafter. Any occurrence of AF or AT (>30 seconds) after a 3-month blanking period following the procedure detected on electrocardiogram or continuous heart rhythm monitoring was considered as arrhythmia recurrence. The cardiac monitoring follow-up of the study group was akin to the control group. The 24-hour Holter recording was adopted to confirmed patients' heart rhythm in both symptomatic and asymptomatic patients at regular intervals. Detection of arrhythmia recurrence was reported via a research/clinical network of initiatives consisting of dedicated patient phone lines/e-mails, community primary care physician reporting, arrhythmia specialist nurse reporting, and interval secondary/tertiary care outpatient reviews.

### Statistical analysis

To estimate the propensity score, we applied logistic regression on the following covariates: age, gender, body mass index, duration of perAF, diabetes mellitus, hypertension, left ventricular ejection fraction, and LA diameter. Based on their propensity score, patients who underwent individualized PVI + C-to-B ablation and empirical PVI + PVI ablation were matched 1:2, using a nearest-neighbor algorithm

(nonreplacement type with calliper width = 1/5 logit of the standard deviation [SD]). Analyses were conducted on the matched cohorts, with cutoff  $P = .05$ . Difference in freedom from AF/AT between the 2 cohorts was assessed using the Gehan-Breslow-Wilcoxon method. Data distributions are expressed as mean  $\pm$  SD or median (interquartile range [IQR]). Continuous variables were compared using the Student  $t$  test where data distribution met the criteria for normality; otherwise, the Wilcoxon and Mann-Whitney  $U$  tests were used. Categorical variables were compared using the  $\chi^2$  or exact test. All analyses were performed using SPSS Version 22.0 (SPSS Inc, Chicago, IL).  $P < .05$  was considered significant.

### Results Patients

Forty patients (age  $62 \pm 12$  years; 29 male) with perAF (duration  $10 \pm 5$  months) composed the study group (PVI + C-to-B). Six patients (15%) had long-standing perAF (duration  $18 \pm 3$  months). AF was induced with high-frequency intra-atrial pacing in 3 patients who were in SR at the beginning of the procedure (previously electively cardioverted).



**Table 1** Patient characteristics

	Study group (n = 40)	Control group (n = 80)	P value
Age (yr)	62 ± 12	64 ± 9	NS
Male	29 (73)	61 (76)	NS
Duration of perAF (mo)	10 ± 5	9 ± 5	NS
Hypertension	16 (40)	30 (38)	NS
Diabetes mellitus	8 (20)	18 (23)	NS
Heart failure (New York Heart Association functional class ≥II)	14 (35)	25 (31)	NS
Previous failed DCCV	37 (93)	72 (90)	NS
Mean BMI (kg/m <sup>2</sup> )	28 ± 4	27 ± 4	NS
CHA <sub>2</sub> DS <sub>2</sub> -VASc score >2	23 (58)	44 (55)	NS
LA diameter (mm)	43 ± 6	43 ± 6	NS
Mean LVEF (%)	53 ± 12	53 ± 11	NS
Antiarrhythmic medication			
Beta-blocker	32 (80)	63 (79)	NS
Amiodarone	10 (25)	19 (24)	NS
Flecainide	4 (10)	10 (13)	NS
Anticoagulation			
Warfarin	7 (18)	16 (20)	NS
Apixaban	15 (38)	27 (34)	NS
Dabigatran	4 (10)	6 (8)	NS
Rivaroxaban	12 (30)	20 (25)	NS

Values are given as mean ± SD or n (%).

BMI = body mass index; DCCV = direct current cardioversion; LA = left atrium; LVEF = left ventricular ejection fraction; perAF = persistent atrial fibrillation.

Mean LA diameter was 43 ± 6 mm, and left ventricular ejection fraction was 53% ± 12%. Eighty patients with perAF with *de novo* AF (empirical PVI + PWI) ablation were propensity matched in the control group. Patient characteristics are summarized in Table 1.

## CDM characteristics

### CPC "burden" before PVI

In the study group (n = 40), a mean of 3.7 ± 1.0 CPCs per patient was observed before PVI. In 80% of patients (32/40), ≥3 CPCs were identified in the LA. The anatomic distributions were anterior wall in 37 patients; posterior wall in 34; septal wall in 26; PV/ostia in 25; and LA roof in 9. On the anterior wall, the most prevalent conduction pattern was a combination of LIA and LRA at the same core (38%). On the posterior wall, the most prevalent pattern was a combination of FCA, LRA, and LIA at the same core (29%).

### Impact of PVI on perAF conduction pattern

In the study cohort, PVI was adjusted to incorporate a total of 56 CPCs identified within 1 cm of the PV antra (1.4 ± 0.8 sites per patient). Of these 56 cores, despite coexistence of different conduction patterns, FCA was the dominant pattern near the PV/ostia (62%). In 8 of 40 patients, PVI (average 1.1 ± 0.6 CPCs enclosed) terminated perAF to either SR (5/8) or isthmus-dependent macroreentrant AT (3/8). In the remaining 32 patients, the majority (86%) still had ≥3 CPCs

following PVI (mean 3.6 ± 1.0). The anatomic distributions in these 32 patients were posterior wall in 32; mid-anterior wall in 30; septal wall in 23; and roof in 11. The most prevalent CPC had a combination of LRA and LIA coexisting at the same core on the posterior wall (36%) and the anterior wall (36%). A majority of CPCs (77%) identified in the pre-PVI maps were still present after PVI. The distribution of LA CPCs pre- and post-PVI are illustrated in Figure 3.

### Impact of C-to-B ablation

On average, an additional 2.2 ± 0.6 CPCs were ablated, followed by anchorage to anatomic boundaries after PVI. The number of CPCs targeted per patient correlated with the duration of perAF (Figure 4). The 3 perAF patients who presented in SR (electively cardioverted before procedure and maintained SR for 3 ± 1 weeks) before ablation had an average of 1 targeted CPC.

The result of ablation following each workflow step is shown in Figure 5. Ablation was more commonly targeted on the anterior wall (81%), the posterior wall (81%), and the roof (19%). In total, perAF terminated to isthmus-dependent macroreentrant AT or SR in 68% patients (27/40) after targeting CPCs in the LA. The termination site was most commonly observed at the posterior wall (57%), followed by the anterior wall (33%) and the roof (10%).

CPCs on the anterior wall consisted primarily of a combination of LIA and LRA (31%), or LIA alone (27%). CPCs on the posterior wall consisted of a combination of LIA and LRA (38%), or a combination of FCA, LIA, and LRA (19%).

### RA CPC ablation

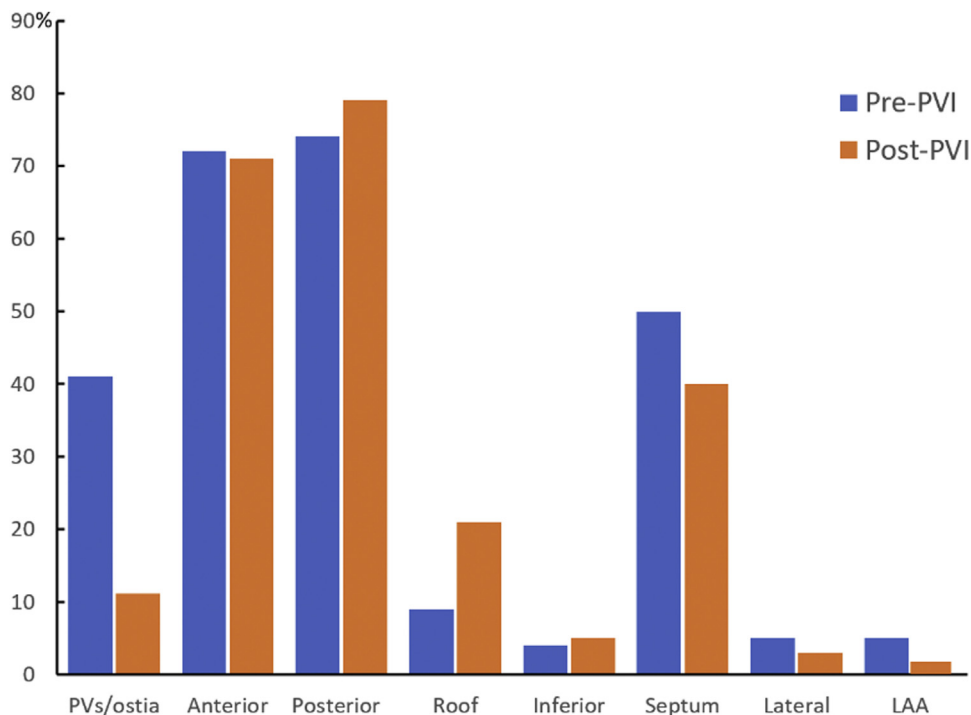
Eleven patients had RA mapping, with ablation of CPCs in 4 patients. On average, 1.6 ± 0.5 sites in the RA were targeted. PerAF terminated in 2 of 4 patients (1 terminated following focal ablation on the septum only; 1 terminated after targeting CPCs on the septum and posterior wall). The remaining 2 patients were cardioverted to SR after CPC depletion in both atria.

## Outcomes: Study vs control

In the study group, mean ablation time was 33 ± 12 minutes for PVI and 32 ± 22 minutes for CPCs after PVI. Four patients (10%) underwent RA CPC ablation in the study group, and 48 patients (60%) in the control group had empirical CTI ablation. In the study group, median skin-to-end procedural time was 210 minutes (IQR 181–268 minutes), and the median skin-to-AF conversion to SR time (29/40) was 180 minutes (IQR 106–237 minutes). Median RF time was 59 minutes (IQR 40–92 minutes) and from AF conversion to SR (29/40) was 44 minutes (IQR 30–84 minutes) (Supplemental Table 1). No major complications occurred during or after the procedure in the study group and the control group.

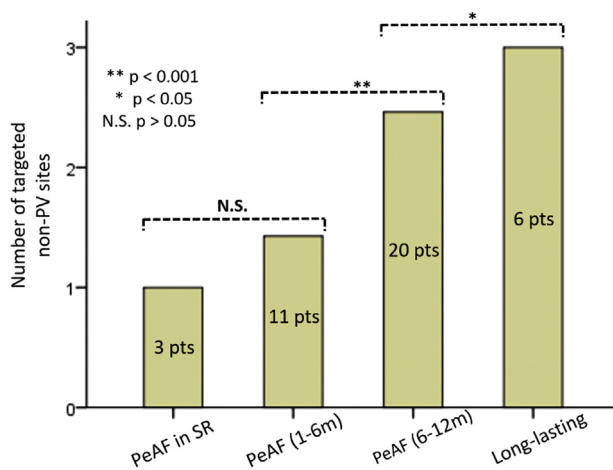
### Acute termination of perAF

The incidence of acute perAF termination by ablation was significantly different between the ablation strategies of the study and control groups (73% vs 10%; *P* < .001). In the



**Figure 3** Distribution of sites with CPCs in the left atrium pre- and post-PVI. The dominant cores were on anterior and posterior walls. PV = pulmonary vein; other abbreviations as in Figures 1 and 2.

study group, acute perAF termination occurred in 29 of 40 patients (73%) after PVI and C-to-B ablation. Of the 29 patients, perAF directly terminated to SR in 22 patients and indirectly via conversion to macroreentrant AT in 7 patients. The most common CPCs ablated when AF terminated were LIA coupled with LRA (33%), followed by LIA (24%). Eleven patients in whom no further CPCs were identified after ablation were cardioverted to SR.



**Figure 4** Average number of targeted CPCs before AF termination increased with the duration of persistent atrial fibrillation. The average number of CPCs increased with the duration of persistent atrial fibrillation (PeAF). AF was induced with high-frequency intra-atrial pacing at the beginning of the procedure in patients who were electively cardioverted before the procedure. N.S. = not significant; SR = sinus rhythm; other abbreviations as in Figures 1 and 3.

#### Freedom from AF/AT during follow-up

At 24-month follow-up, 68% of patients in the study group and 46% in the control group were free from AF/AT in the absence of antiarrhythmic medications (amiodarone, sotalol, sodium channel blockers) following a single procedure (Figure 6). Atrial arrhythmia recurrence was seen in 13 of 40 patients (AF 5/40; AT 8/40) in the study group. Median time from procedure to first recurrence of AF/AT was 6 months (IQR 5–12 months).

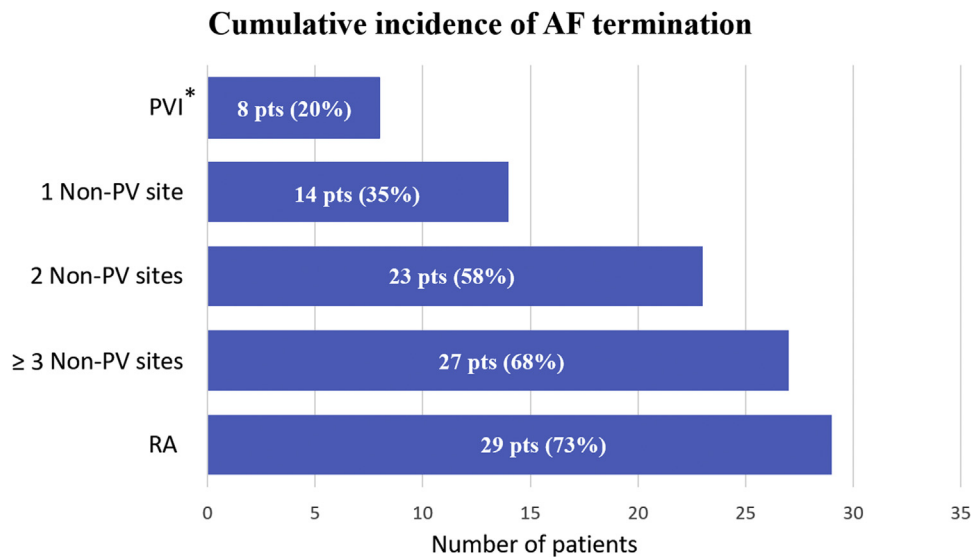
## Discussion

### Main findings

This study characterized conduction patterns in perAF identified by a novel CDM technology and tested a mapping-guided individualized ablation strategy of targeting CPCs with PVI plus C-to-B ablation. The main findings are as follows. (1) The number of CPCs correlated with the duration of perAF. (2) Spatiotemporal stability and occurrence of CPCs did not change significantly after PVI. (3) Compared to empirical PVI + PWI ablation strategy, the individualized ablation strategy targeting CPCs had a high rate of acute procedural perAF termination (73%) and a favorable 24-month outcome, with 68% patients free from AF/AT in the absence of antiarrhythmic medications after a single procedure.

### Mechanisms of perAF

Mechanisms sustaining perAF are likely to vary between individuals and with the duration of arrhythmia. Existing hypotheses propose that perAF is a disorder with varying spatiotemporal activation resulting from single or multiple



**Figure 5** Acute outcome from the individualized ablation strategy (PVI + C-to-B). \*Persistent AF terminated in 8 patients after PVI (7/8 patients; CPCs located close to PV ostia were incorporated as part of the PVI ablation). Total number of patients was 40. RA = right atrium; other abbreviations as in Figures 1, 2, and 3.

localized stable (focal/reentrant) sites or multiple unstable wavelets.<sup>10</sup> An AF driver site has been defined as either a focal or localized source demonstrating fast, repetitive activity that propagates outward from the source, breaking down into disorganized (fibrillatory) conduction as it moved further away from its origin, or as one at which termination occurs during ablation.<sup>11</sup> These sites have attracted considerable research interest and have been demonstrated in various clinical studies using different mapping technologies.<sup>12,13</sup>

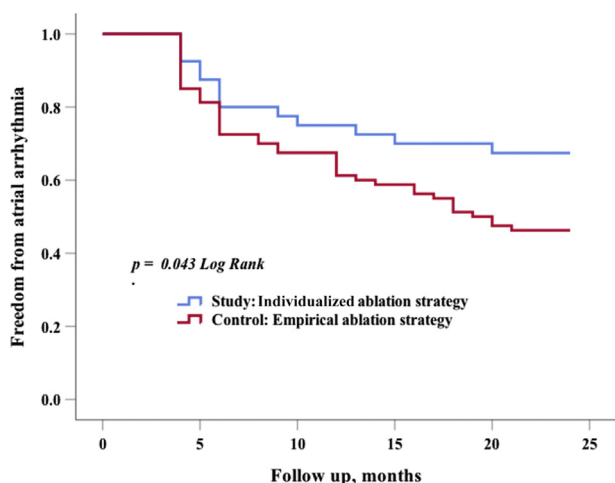
Instantaneous global noncontact mapping may help to elucidate the underlying patient-specific mechanisms of atrial arrhythmias.<sup>7,14,15</sup> CDM is designed to provide a more localized delineation of complex and irregular conduction patterns than voltage-based mapping. It acquires anatomic representation using high-resolution, M-mode ultrasound with

simultaneous assessment of cardiac activation and is not affected by the same limitations as contact mapping.<sup>6</sup> Hence, it may help to identify differing characteristics of perAF activation to provide a better understanding of the hierarchy or the combination of the conduction mechanisms responsible for perpetuation of perAF among different individuals.<sup>6</sup>

Although we identified local rotational activation patterns among our cohort, we did not observe these patterns to be stable and continuous. They coexisted with other CPCs, albeit sometimes at certain preferential sites. This is in keeping with the findings of other perAF studies using noninvasive 3D mapping and high-resolution epicardial mapping.<sup>13,16</sup> The higher percentage of acute perAF termination and more favorable medium-term outcome by targeting these CPCs with RF ablation suggest they may contribute to the mechanisms maintaining perAF. A better understanding of the coexistence of different conduction mechanisms in perAF (focal, rotational, and irregular) and their spatiotemporal relations may explain the variability of clinical outcomes and further promote individualized ablation strategies to treat perAF.

### Characteristics of CPCs

Electrical and structural remodeling is fundamental to the perAF disease process. Atrial substrate heterogeneity increases and spreads with prolongation of perAF duration, raising susceptibility of initiating and probability of maintaining perAF. The present study observed a correlation between the number of targeted CPCs required to achieve perAF termination with the duration of perAF. This is consistent with reports by Cuculich et al<sup>17</sup> and Haissaguerre et al<sup>13</sup> using noninvasive activation mapping. In addition, two-thirds of the CPCs observed in the pre-PVI maps were noted in the post-PVI maps. This reduction may be partly explained by the elimination of CPC within the circumferential PVI



**Figure 6** Cumulative freedom from persistent atrial fibrillation/ tachycardia after a single procedure in the study group (68%) and control group (46%) at 24 months ( $P = .043$ ).

lesion line. There also may be an organizing effect imposed by PVI, which had been observed in some studies.<sup>18,19</sup>

The frequency and sequence of conduction patterns around and through a CPC differed in each perAF segment, yet the conduction core was preferentially anchored to a spatially consistent location that was commonly at the mid-anterior and mid-posterior walls.<sup>8</sup> Given the frequency of CPCs on the anterior wall in these patients, an empirical PVI + PWI ablation strategy would have missed these potentially important sites. This may underlie the higher rate of arrhythmia recurrence in the control group. However, the relationship between different activation patterns and characterization of the atrial substrate needs to be clarified in further studies with histologic and functional data.

### Clinical implications: CPC ablation guided by global mapping in treating perAF

Recent randomized trials have demonstrated that PVI alone achieves outcomes similar to those of more extensive ablation strategies in treating perAF. However, the outcomes achieved in perAF remain suboptimal compared to those for paroxysmal AF, generating continued interest in research to better understand what trigger/driver sites outside the PVs should be ablated.

In the present study, the acute procedural perAF termination rate during ablation guided by noncontact CDM was noteworthy. Although acute termination of perAF by ablation may not be a definitive endpoint for long-term freedom from AF, a recent meta-analysis of studies adopting AF “driver” ablation demonstrated a correlation between acute termination and long-term outcome.<sup>20</sup> The 24-month single procedure outcome (freedom from AF/AT) from the present study compared favorably with the 12-month outcomes of the UNCOVER AF (Utilizing Novel Dipole Density Capabilities to Objectively Visualize the Etiology of Rhythms in Atrial Fibrillation) trial using the same mapping system and other studies that targeted AF drivers in addition to PVI using other contact/noncontact mapping systems.<sup>20,21</sup> The present study is the first to show a real-world application of AF ablation guided by noncontact CDM compared with empirical PVI + PWI ablation strategy guided by conventional contact mapping. The 12-month outcome in the control group is comparable to that of other randomized studies that used such an empirical ablation approach to treat persistent/paroxysmal AF.<sup>22</sup>

### Study limitations

The study bears the inherent limitation of a prospective observation study. Longer-term continuous cardiac monitoring would be more effective than the intermittent monitoring strategy for identifying AF. The significance or hierarchy of each conduction pattern type was not compared. Further studies are needed to demonstrate the spatiotemporal relations of different activation patterns and to characterize the respective contribution of each activation pattern in human AF. Contact force-sensing catheters were used in all patients in the control group. This might have introduced bias in

favor of the control group, yet the clinical outcome was better in the study group.

### Conclusion

An individualized ablation strategy consisting of PVI plus C-to-B ablation guided by noncontact CDM is a feasible and effective strategy for treating persistent AF, with a favorable 24-month outcome. A larger randomized control study is required to confirm this finding.

### Appendix Supplementary data

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.hrthm.2021.02.014>.

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