Spatial relationship between high-dominant-frequency sites and the linear ablation line in persistent atrial fibrillation: its impact on complex fractionated electrograms

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Aims Complex fractionated electrograms (CFEs) and high-dominant-frequency (DF) sites theoretically represent abnormal substrates and targets for atrial fibrillation (AF) ablation. The relationship between the high-DF sites in the left atrium (LA) and commonly used linear ablation line to the distribution of the CFEs in patients with persistent AF is unknown.

Methods and results This study enrolled 62 persistent AF patients who underwent construction of LA CFE and DF maps (>350 points/map). Circumferential pulmonary vein isolation and linear ablation including that at the septum, roof, mitral-annulus, and ridge of the appendage were performed. Multipolar catheter mapping identified sites with high DFs (≥8 Hz) in all patients (9.8 ± 4.6/patient). In 47 patients in whom AF persisted despite ablation, there was a significant reduction in the continuous CFE (≥50 ms) burden after the linear ablation (62 vs.11%; P < 0.0001), with a decrease in both the DF within the coronary sinus (6.9 ± 0.9 vs. 5.9 ± 0.8 Hz; P < 0.0001) and CFE surface area (42.8 ± 18.8 vs. 12.6 ± 10.5 cm²; P < 0.0001). Comparing the high-DF sites with the ablated lesions, 64% of the high-DF sites (324 of 507) were on or adjacent to the ablation lines. Residual CFEs were observed in the infero-posterior regions in 83% of the patients. Almost half of the high-DF sites away from the linear ablation line were identified in the inferior (34%) and posterior (14%) LA regions.

Conclusion Linear ablation resulted in the localization of the continuous CFE regions and reduced the global LA DF in patients with persistent AF. This may be related to the proximity relationship between the linear ablation lines and high-DF sites except for in the infero-posterior regions.

Keywords Atrial fibrillation • Catheter ablation • Complex fractionated electrograms • Dominant frequency analysis

Introduction

Catheter ablation of persistent atrial fibrillation (AF) remains a challenging procedure and the success rates vary significantly between the different centres.1 The atrial substrates with complex fractionated atrial electrograms (CFEs) have been recognized as the maintainers of AF.2–4 Notably, the ablation of continuous CFE sites has a higher likelihood of prolonging the AF cycle length and termination.5 Thus, combined with pulmonary vein isolation (PVI), ablation of CFEs is widely used and is associated with higher acute and long-term success rates in patients with persistent AF.6 However, CFE ablation does not always have an impact on the AF cycle length.6 In some series, CFEs are targeted first, followed by PVI,7,8 and this may lead to an extensive amount of left atrial (LA) ablation accompanied with inadvertent collateral injury.

Previous studies showed that linear LA ablation is effective for LA substrate modification and improved the clinical outcome.9–11 Another study also showed that PVI resulted in a significant decrease in the CFEs associated with both pulmonary vein (PV) and non-PV areas in patients with persistent AF.12 Despite the evolution of the
What’s new?

- We demonstrated the detailed spatial relationship between the substrate sustaining atrial fibrillation (AF) and the commonly used linear left atrium (LA) ablation lines designed to limit the amount of extensive LA ablation in patients with persistent AF.
- Multipolar catheter mapping, allowing >350 points per map, identified the sites with high dominant frequencies (DFs) (≥8 Hz) (9.8 ± 4.6 sites/patient). Linear LA ablation resulted in the localization of the continuous complex fractionated electrogram (CFE) regions (62 ± 11%) and reduced the global LA DF (6.9 vs. 5.9 Hz) beyond the pulmonary vein isolation lines.
- A noteworthy finding is that 64% of the high-DF sites were on or adjacent to the linear ablation lines. Residual CFEs were observed in the infero-posterior regions in 83% of the patients, and almost half of the high-DF sites away from the ablation lines were identified in those regions.
- These findings may be related to the proximity relationship between the linear ablation lines and high-DF sites except for in the infero-posterior regions.

Electrophysiological study

Duodecapolar catheters were placed in the coronary sinus via the right internal jugular vein for a positional reference. The proximal electrode pairs were positioned around the superior vena cava (SVC)–right atrial (RA) junction to identify any non-PV foci originating from the SVC. A circular mapping catheter (20-pole, 15-to 25-mm Lasso, 6-mm bipole spacing; Biosense Webster, Diamond Bar, CA, USA) and a 3.5 mm irrigated-tip catheter (Biosense Webster) were introduced into the LA. Intravenous heparin was infused throughout the procedure to maintain an activated clotting time of 350–400 s. All patients presented to the electrophysiology laboratory in AF. Following the creation of a detailed LA geometry (Ensite, NavX, St. Jude Medical, St. Paul, MN, USA) using a circular catheter and ablation catheter, electrograms (EGMs) were acquired with a high density using a double-loop multipolar catheter (20-pole, 20 mm AFocus II, 4 mm bipole spacing; St. Jude Medical Inc.), registered at multiple LA sites.

Catheter ablation strategy

After the high-density mapping, continuous circumferential lesions were created encircling the right and left PV ostia guided by the 3D-LA geometry created by the NavX system. We did not use image integration of the 3D-CT using NavX Fusion. Successful circumferential PVI was demonstrated by the absence of any PV activity or dissociated PV activity. When AF did not terminate during the PVI, additional linear LA ablation applications were performed, including those at the (i) septum, (ii) roof, (iii) mitral annulus, and (iv) ridge between the left atrial appendage (LAA) and left superior PV (Figure 1).

Linear ablation was guided by the NavX system with the creation of split potentials or an EGM voltage reduction of 50% after each application of radiofrequency (RF) energy. The entire course of the oesophagus was depicted and superimposed on the LA to avoid any oesophageal injury.

Signal recording and analysis

During AF, high-density frequency and fractionation mapping was performed. The NavX settings were the same for all CFE maps, except for the sensitivity, which was adjusted for each patient on the basis of the background electrical noise level. At each point, deflections above baseline were automatically detected by the NavX algorithm, and the mean CFE cycle length (MCL) was calculated by averaging the intervals between the deflections over a 5 s window. The MCL algorithm had a refractory period set at 40 ms to minimize any double counting of EGMs, and width criterion set at 10 ms to minimize counting ventricular far-field signals. For both maps, the CFE points were only included if they were within 5 mm of the geometry shell, thus minimizing the acquisition of points that were not in contact with the LA. In accordance with the criteria proposed by Nademanee et al., regions with a mean cycle length of ≤120 ms were considered CFE positive. Sites with continuous CFEs indicated the most fractionated sites with a local mean fractionation interval of ≤50 ms over a 5 s duration.

The consistency of the DF value and fractionated EGMs over time has been validated previously. The Ensite system allows for a colour display of both the CFE and DF maps through the use of integrated software. The details of the DF analysis are also described in detail elsewhere. In brief, the signals were truncated to 5 s at a sampling rate of 1200 Hz providing 4096 points for analysis (resolution 0.14 Hz). The signals were rectified and processed by a Hanning window and filtered from 4 to 13 Hz. A fast-Fourier transformation was performed and the point DF was determined as the frequency associated with the maximum peak power in the spectrum. That DF value could be projected onto the LA shell as a colour-coded display. We compared the CFE regions to those with a direct inverse DF of 4–13 Hz. The CFE regions (40–120 ms) were outlined on the LA...
shell using annotation markers in the Ensite system. The map was then switched to the ‘DF mode’ and the DF regions (4–13 Hz) were similarly outlined in a different colour (see Figures 2 and 3). According to previous studies, we defined a high-DF region as that with a radius of 5 mm and the cut-off value was set to 8 Hz.19 To avoid any inclusion of spurious values, all acquired signals were visually inspected and those signals with clear noise/artifact were excluded from analysis.

Analysis of complex fractionated electrograms/dominant frequencies and coronary sinus electrograms

After the ablation, a qualitative analysis of the CFE maps was performed by visually assessing the distribution of the CFEs for the pre- and post-ablation maps (Figure 2). Predefined LA regions were used to determine the regional distribution of the CFEs.20 The LA surface area with CFEs was identified in the PV antrum, septum, roof, posterior, inferior, anterior, lateral, and LAA and its base. For every map, the presence or absence of CFEs and high-DF sites was assessed visually in each of these eight regions. The surface areas of the CFE, DF, and overlapping CFE + DF regions could then be analysed from the system.

The spatial contiguity between the high-DF sites and linear ablation line were examined. The distance between the high-DF sites and linear ablation lesions was determined by the 3D coordinates provided by the NavX system. Considering the cardiac and respiratory movement during RF applications, we speculated that the periphery of high-DF sites included a 1 cm margin extending into the surrounding area.

Electrograms in the coronary sinus (CS) were recorded for 10 s during AF before and after the ablation. Baseline EGMs were recorded immediately before the first application of RF energy. In patients who remained in AF after ablation, the EGMs were recorded during AF upon completion of the linear ablation. The EGMs were processed and analysed off-line for an evaluation of the effectiveness of the linear ablation. As described previously, the DF and MCL were calculated by using the software.

Statistical analysis

All data are reported as the mean ± standard deviation for continuous variables and the number of subjects for categorical variables unless otherwise indicated. Normally distributed continuous variables were compared using Student’s t-test; non-normally distributed variables were compared using a Mann–Whitney U test. A one-way analysis of variance (ANOVA) was used to compare the continuous variables among multiple groups with a Scheffe’s post hoc multiple-comparison analysis. A P value of < 0.05 was considered significant for all statistical determinations.

Results

Patient characteristics

The baseline patient characteristics are shown in Table 1. The average number of mapping sites in the LA was 383 ± 118 points per patient. In 15 patients (24%), AF terminated during the linear ablation. Thus, both pre- and post-ablation mean cycle length CFE and DF maps were obtained and analysed in the 47 remaining patients.
Figure 2 (A) Electroanatomical maps of the left atrium seen from the anteroposterior (left side panel) and posteroanterior (right sided panel) views of the pre-linear (upper panel) and post-linear (lower panel) left atrium ablation mean cycle length complex fractionated electrogram maps. Sites with a mean complex fractionated electrogram cycle length of ≤120 ms are colour-coded red/white, and sites with a mean complex fractionated electrogram cycle length of >120 ms are colour-coded purple. There is a marked reduction in the complex fractionated electrogram burden between the two maps in the pulmonary vein as well as non-pulmonary vein areas, with the complex fractionated electrogram regions after ablation localized to the mid-septum, left atrium appendage, and infero-posterior wall (indicated by the white arrows). The yellow tic marks represent the electrogram detection by the NavX algorithm. The complex fractionated electrogram detection settings were a width = 10, refractory period = 50 ms, and sensitivity = 0.05 mV. MA, mitral annulus. (B) Posteroanterior (left side panel) and right anterior oblique (right side panel) views in another patient with the same settings as in (A). Note the diffuse presence of complex fractionated electrograms on the posterior wall before ablation. After a linear left atrium ablation using the same map settings, the complex fractionated electrograms were localized to the roof and inferoposterior wall; there were no longer any complex fractionated electrograms present in the midposterior wall, despite the absence of ablation in this region. The red dots represent the linear left atrium ablation lesions. LSPV, left superior pulmonary vein; RSPV, right superior pulmonary vein.
Distribution of the complex fractionated electrograms and high dominant frequencies in the left atrium

Multipolar catheter mapping identified sites with continuous CFEs (>50 ms) in all patients. Continuous CFEs were found in the following locations: PV antrum (32 of 62 patients, 52%), septum (45 of 62 patients, 73%), posterior wall (47 of 62 patients, 46%), inferior region (36 of 62 patients, 58%), lateral region (36 of 62 patients, 58%), anterior region (34 of 62 patients, 55%), roof (43 of 62 patients, 69%), and LAA and its base (45 of 62 patients, 73%).

Multipolar catheter mapping identified sites with high DFs (>8 Hz) in 9.8 ± 4.6 sites per patient. High-DF sites were found in the following locations: PV antrum (56 of 62 patients, 90%), septum (47 of 62 patients, 76%), posterior wall (50 of 62 patients, 81%), inferior region (43 of 62 patients, 69%), lateral region (21 of 62 patients, 34%), anterior region (26 of 62 patients, 42%), roof (34 of 62 patients, 55%), and LAA and its base (17 of 62 patients, 27%).

Figure 2 shows typical high-density CFE maps in patients with persistent AF. Almost half (53%) of the high-DF sites were overlapped with the CFE surface area, and 34% of the high-DF sites were located immediately contiguous to the CFE surface area. The total high-DF surface area in the LA was 10.4 ± 6.4 cm². The CFE surface area was significantly greater than the high-DF surface area (40.4 ± 18.3 cm², P < 0.0001).

Catheter ablation results

All four PVs were successfully isolated in all patients. Procedural AF termination [conversion to atrial flutter/atrial tachycardia

Table 1 Patient characteristics

<table>
<thead>
<tr>
<th>Study subjects (n = 62)</th>
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<tr>
<td>Age (years)</td>
<td>61 ± 11</td>
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<tr>
<td>Gender (male/female)</td>
<td>50/12</td>
</tr>
<tr>
<td>Longstanding (&gt;1 year), n (%)</td>
<td>46 (74%)</td>
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<tr>
<td>Left atrial diameter (mm)</td>
<td>45 ± 5</td>
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<tr>
<td>LA volume indexed (mL/m²)</td>
<td>85.6 (69.0, 102.1)</td>
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<tr>
<td>Left ventricular ejection fraction</td>
<td>0.56 ± 0.08</td>
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<tr>
<td>Structural heart disease, n (%)</td>
<td>2 (3%)</td>
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<tr>
<td>Duration of continues AF duration (years)</td>
<td>3.1 ± 2.4</td>
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The values are expressed as the mean ± SD, or median (quartiles).
(AFL/AT) or sinus rhythm] was observed in 15 patients (24%). Five patients (8%) developed AFL/AT during linear ablation, including two patients with mitral isthmus-dependent flutter, one with an anterior wall focal AT and one with cavotricuspid isthmus-dependent flutter. These AFLs/ATs were all successfully mapped and ablated accordingly. Bidirectional conduction block of the roofline was achieved in 58 (93.5%) of 62 patients after ablation. Mitral isthmus block was also confirmed in all patients in whom mitral isthmus-dependent flutter was induced.

Atrial fibrillation termination during catheter ablation occurred in sites with high-DF regions that were contiguous to continuous CFE regions. At these termination sites, the mean DF was 11.1 ± 0.9 Hz (range 9.8–12.5 Hz). The total number of high DFs in the LA (6.7 ± 2.9 vs. 10.6 ± 4.7 sites; P < 0.05) and the LA volume index (median 69.0 vs. 89.9 mL/m²; P < 0.01) were significantly smaller in the patients with, vs. those without AF termination during the linear ablation. The total procedural duration, fluoroscopy time, and RF time were 186 ± 38, 55 ± 16, and 56 ± 12 min, respectively. With a follow-up period of 14.9 ± 5.6 months, the freedom from AF with and without drugs after the primary procedure was 71% (N = 44).

**Relationship between high-dominant-frequency sites and linear ablation lines**

The relationship between the high-DF sites (≥ 8 Hz) and ablation line was analysed in 47 patients in whom AF persisted despite the ablation. Each high-DF site and the linear ablated lesions were compared and the distance between those locations were measured manually offline as described before. Figure 3 shows the high-DF maps in a patient with long-lasting AF. A total of 64% (324 of 507) of the high-DF sites were on or adjacent (<1 cm) to the linear ablation line. The percentage of overlap between the high-DF sites and linear LA ablation lines in each anatomic LA region are demonstrated in Figure 4 (blue bar). All high-DF sites recorded at the PV antrum were encircled by the circumferential PVI line. Almost half of the high-DF sites (88 of 183, 48%) that were >1 cm outside of the linear ablation line were identified in the inferior (62 of 183, 34%) and posterior regions (26 of 183, 14%). Of those, 90% (81 of 88) of the high-DF sites were located close to the oesophagus (Figure 3).

**Qualitative and quantitative complex fractionated electrogram analysis**

A qualitative and quantitative analysis of the CFEs was performed in 47 patients still in AF after catheter ablation. For the LA regions remote from the distal PVs, there was a dramatic reduction in the percentage of CFE-positive regions after the linear ablation for both the regions with a frequency of <120 ms (97% vs. 60%; P < 0.0001) and <50 ms (62 vs. 11%; P < 0.05; Figure 4). However, there was a trend toward a lesser effect on the continuous CFE burden in the inferior and posterior regions with the linear ablation (P = 0.08). There was a significant reduction in the CFE surface area after the linear ablation (42.8 ± 18.8 cm² pre-ablation vs. 12.6 ± 10.5 cm² post-ablation; P < 0.0001) (Figure 5A). Residual CFEs in the inferior or posterior LA were observed in...
4.9 cm² post-ablation; 9.8 patients (9.8 with multi-electrode catheters identified sites with high DFs in all consistent AF. We observed that (i) high-density mapping achieved line to the distribution of continuous CFEs in the patients with per-
This study is the first to demonstrate the spatial relationship between high-DF sites and the commonly used linear LA ablation. Major findings
Figure 5 Effect of the linear left atrium ablation on the complex fractionated electrogram surface area (A), dominant frequency in the coronary sinus (B), and complex fractionated electrogram mean in the coronary sinus (C). The complex fractionated electrogram surface area is shown at baseline and after the linear left atrium ablation. There was a significant decrease in the complex fractionated electrogram surface area after the linear ablation (*P < 0.0001). The complex fractionated electrogram mean and dominant frequency recorded in the coronary sinus are shown at baseline, after pulmonary vein isolation, and after linear left atrium ablation. There was a significant decrease in the dominant frequency (P < 0.001) within the coronary sinus, and increase in the complex fractionated electrogram mean (P < 0.001) in the coronary sinus after the linear ablation. *P < 0.05 compared with baseline; †P < 0.05 compared with after pulmonary vein isolation.

83% (39 of 47 patients) of the patients in whom AF could not be terminated. Both the inferior (9.7 ± 5.0 cm² pre-ablation vs. 5.8 ± 4.9 cm² post-ablation; P < 0.0001) and posterior (7.7 ± 4.4 cm² pre-ablation vs. 2.7 ± 3.2 cm² post-ablation; P < 0.0001) CFE surface areas were significantly reduced after the linear ablation.

Effect of catheter ablation on the complex fractionated electrogram cycle length and dominant frequency in the coronary sinus
Among the 47 patients still in AF after catheter ablation, the DF in the CS significantly decreased during catheter ablation (ANOVA; P < 0.0001) (Figure 5B), from 6.9 ± 0.9 Hz (95% confidence interval, CI 6.6–7.1) at baseline to 6.3 ± 0.7 Hz (95% CI 6.1–6.5) after the PVI (P < 0.05), and from 6.3 ± 0.7 Hz (95% CI 6.1–6.5) after the PVI to 5.9 ± 0.8 Hz (95% CI 5.6–6.1) after the linear ablation (P < 0.05). The percentage decrease in the CS DF was 15 ± 9%. The MCL (mean CFE) also significantly increased during catheter ablation (ANOVA; P < 0.0001) (Figure 5C), from 76.2 ± 25.8 ms (95% CI 69.0–83.4) at baseline to 92.9 ± 32.3 ms (95% CI 83.9–101.9) after the PVI (P < 0.05), and from 92.9 ± 32.3 ms (95% CI 83.9–101.9) after the PVI to 110.2 ± 32.7 ms (95% CI 101.0–119.3) after the linear ablation (P < 0.05).

Discussion
Major findings
This study is the first to demonstrate the spatial relationship between high-DF sites and the commonly used linear LA ablation line to the distribution of continuous CFEs in the patients with persistent AF. We observed that (i) high-density mapping achieved with multi-electrode catheters identified sites with high DFs in all patients (9.8 ± 4.6 sites/patient); (ii) the distribution of high DFs was non-uniform in the entire LA body, with a higher incidence of neighbouring linear LA ablation lines; (iii) linear LA ablation, without targeting CFEs, resulted in the localization of the continuous CFEs and a reduction in the global LA DF beyond the PVI; and (iv) residual CFEs were detected in 83% of the patients in the infero-posterior LA region, and almost half of the high-DF sites away from the ablation lines were identified in those regions. These findings could be a consequence of the proximity relationship between the linear LA ablation lines and high-DF sites excluding the infero-posterior region.

The substrate mapping and catheter ablation of AF incorporated an analysis of the DF (frequency domain substrate) and CFEs (time domain substrate).21–23 As high-frequency EGMs have been suggested to indicate sites close to a rotor,24,25 high-DF mapping in the LA has been demonstrated in patients with paroxysmal26 and persistent18 AF. However, identifying rotors as the drivers of AF directly in patients is very difficult with the existing mapping techniques.27 In our study, we demonstrated that high-DF sites are distributed sporadically, and most of the high-DF sites are overlapped or located immediately contiguous to the CFE surface area in the entire LA body. This is in keeping with the results from both previous animal28 and clinical studies reporting the distribution of high-DF sites.13,18 As the high-DF region could be <5 mm in radius,18 the application of simultaneous high-density mapping achieved with multi-electrode catheters is required to increase the sampled density and allow for simultaneous recording of multiple high-DF sites. Simultaneous recording of the AF in the entire LA would be the methodology to get a deeper understanding of the fibrillatory mechanism and to distinguish the instantaneous local cycle length during AF. By using the 20-polar, double-loop catheter, similar LA regions were mapped through different bipolar orientations, hence the probability that particular LA sites were only mapped in a single-bipole orientation could be reduced. Furthermore, the ability to allow >350 points to be acquired per map in our study, strengthened the use the DF
mapping both clinically and as a research tool. The exclusion of points with an EGM projection distance of >5 mm to the LA geometry prevents registration of points with poor contact and farfield signals. In addition, the accuracy of each map was improved by a manual assessment of all EGMs.

The CFE mean is a widely used algorithm that is integrated into the NavX system. The method has been evaluated with regard to the temporal stability of CFE sites in AF. A previous report demonstrated that a standardized and validated algorithm for the identification of fractionation, using an fractionation index <120 ms, refractory window of 49 ms, and signal width of 10 ms, could achieve a sensitivity of 0.75 and specificity of 0.80. In this study, by using the settings (CFE mean, up to 50 ms; refractory window of 40 ms) according to a recent study by Lin et al., to detect continuous CFAE sites, we were able to demonstrate that the core of the CFAE sites had higher fractionated EGMs during AF, and exhibited an attenuation of the surrounding intermittent fractionated sites (CFE mean, 50–120 ms). Those continuous CFE sites had a spatial contiguity with the high-DF sites and those were also associated with the termination of AF. Thus, the setting we used appears to be favourable for the delineation of the substrate sustaining AF.

Previous studies reported the effectiveness of the linear LA ablation approach for the clinical outcome and substrate modification of persistent AF. In our study, we demonstrated that AF termination during the ablation occurred in sites where high-DF sites were contiguous to the CFE regions. These findings are consistent with the previous studies which demonstrated that the sites with high-DF regions adjacent to areas of CFEs were related to the procedural termination in patients with paroxysmal and persistent AF. In this study, a smaller number of high-DFs and a smaller size of the LA were noted in patients with AF termination during the procedure. This observation implies that the sites with higher-frequency sources may be localized in a smaller sized LA in these patients, and those sites are successfully eliminated by a linear ablation approach. In contrast, multiple high-DF sites were observed in larger LAs in patients with AF that persisted despite the linear ablation. This finding indicated that multiple drivers existed for the maintenance of the AF in those patients. These observations strengthen our assertion that the present mapping technique is useful for electroanatomic substrate delineation in patients with persistent AF.

The DF and CFEs seem to represent important substrates in the context of AF ablation and may be spatially related in some way. A critical decrease in the DF of >11% has been proposed to be associated with the maintenance of sinus rhythm after ablation of persistent AF. It is therefore apparent that sites containing the maximal DF could play a role in maintaining AF and that an ablation to reduce the global DF may confer a long-term benefit. In our study, among the patients in whom AF persisted after the ablation, linear LA ablation without targeting CFEs resulted in eliminating the majority of the CFE areas and a decrease in the DF (>15%) within the CS (indicating the DF in the global LA) beyond the PVI. A previous study showed that PVI resulted in a significant decrease in both PV and non-PV CFE areas in patients with persistent AF. Only limited data are available on the relationship of a comprehensive linear LA ablation approach to a substrate modification for persistent AF treatment. A noteworthy finding from our study was that the linear ablation lines overlapped with the majority of the high-DF sites, despite their sporadic distribution. Some possibilities may explain how eliminating the majority of the CFE areas with only a linear approach can occur. First, PV isolation and linear ablation could impact the ganglionic plexi adjacent to both the PV antrum and entire LA body, respectively. A recent paper assessed the influence of the autonomic nervous system on the prevalence of CFAEs in both atria during AF. The regions presenting with CFEs which were significantly decreased even in the remote regions, might have been due to the impact of the autonomic nervous system brought on by the linear ablation. Second, the isolation of the PVs and linear ablated lesions prevented PV firing from existing and collisions with the LA wavefronts, which may have reduced the passive LA CFEs. Another possibility is that this lesion set may eliminate wave breaks and fibrillatory conduction at the rotor or its periphery. Furthermore, during energy deliveries to the atrial tissue, slight catheter movement resulting from either cardiac systole or the respiratory cycle also may contribute to unintentional ablation involving the periphery of those substrates. Although little is known with regard to whether high-DF sites and continuous CFE regions bear any relationship to each other during ablation, a close spatial relationship between them demonstrated by our high-density mapping method may also support our speculation. Taken together, these results suggest that a systematic linear LA ablation approach may unintentionally eliminate the higher-frequency sources ‘driving AF’ or the points of the wavelet curvature critical for the AF maintenance in the patients with persistent AF.

Another important observation from this study is that residual CFEs were detected in 83% of the patients in the infero-posterior LA regions, and almost half of the high-DF sites away from the ablation lines were identified in those regions. Although the surface area of the CFEs in those regions could be shrunk to more than half of its baseline level by only linear ablation, a higher propensity of residual high-frequency sources in those regions may be related to the low procedural termination rate in this series of patients. To eliminate the high-frequency sources in those regions, safe approaches are indispensable for avoiding collateral injury. These observations have important implications for ablation strategies that employ hybrid approaches for treating patients with persistent AF. In addition, our data demonstrated that the surface area of the CFEs was larger than that of the high DFs, and those partially overlapped, and we infer that if CFEs are targeted first, this may lead to an extensive amount of LA ablation. Thus, the total RF applications required for the EGM-based (CFE targeted) ablation might be reduced by linear ablation. Although further randomized and prospective studies will be needed, the linear ablation seems to be favourable to be performed prior to the EGM-based ablation.

**Limitations**

First, mapping of the higher-frequency sources was limited to the LA, and did not include the RA in this study. A previous study documented that abolition of the LA to RA DF gradient predicts the long-term success in AF patients. However, it has been shown by other studies that the LA plays a greater role in driving AF as it usually contains sites with higher-frequency
activation in persistent AF. Second, the automatic CFE algorithm may not be the optimal tool for quantifying continuous CFEs. However, the automatic algorithm has been confirmed by the catheter ablation results in many laboratories. Finally, CFE regions were not targeted for ablation in this study; therefore, we cannot determine how ablation of those regions would affect the procedural outcome.

Clinical implications

The findings of this study suggest that linear LA ablation designed to limit the amount of extensive LA ablation around the oesophageal region could eliminate most of the continuous CFEs in patients with persistent AF. Although a lesser effect upon the CFE burden in the infero-posterior regions was documented, the surface area of the CFEs in those regions could be shrunk to more than half of its baseline level. The clinical efficacy of additional ablation of residual CFEs after the linear LA ablation remains to be determined in future studies.

Conflict of interest: none declared.

References


