Recurrence quantification analysis of complex-fractionated electrograms differentiates active and passive sites during atrial fibrillation

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Disclosures: None

Abstract

Objectives: To differentiate electrograms representing sites of active atrial fibrillation (AF) drivers from passive ones.

Background: Ablation of complex-fractionated atrial electrograms (CFAEs) is controversial due to difficulty in distinguishing CFAEs representing sites of active AF drivers from passive mechanisms. We hypothesized that active CFAE sites exhibit repetitive wavefront directionality, thereby inscribing an electrogram conformation (Egm-C) that is more recurrent compared with passive CFAE sites; and that can be differentiated from passive CFAEs using nonlinear recurrence quantification analysis (RQA).

Methods: We developed multiple computer models of active CFAE mechanisms (i.e., rotors) and passive CFAE mechanisms (i.e., wavebreak, slow conduction, and double potentials). CFAE signals were converted into discrete time-series representing Egm-C. The RQA algorithm was used to compare signals derived from active CFAE sites to those from passive CFAE sites. The RQA algorithm was then applied to human CFAE signals collected during AF ablation (n = 17 patients).

Results: RQA was performed in silico on simulated bipolar CFAEs within active (n = 45) and passive (n = 60) areas. Recurrence of Egm-C was significantly higher in active compared with passive CFAE sites (31.8% ± 19.6% vs 0.3% ± 0.5%, respectively, P < .0001) despite no difference in mean cycle length (CL). Similarly, for human AF (n = 39 signals), Egm-C recurrence was higher in active vs passive CFAE areas despite similar CLs (%recurrence 13.6% ± 15.5% vs 0.1% ± 0.3%, P < .002; mean CL 102.5 ± 14.3 vs 106.6 ± 14.4, P = NS).

Conclusion: Active CFAEs critical to AF maintenance exhibit higher Egm-C recurrence and can be differentiated from passive bystander CFAE sites using RQA.

Keywords
ablation, atrial fibrillation, catheter ablation, complex-fractionated electrograms, computational biology, recurrence quantitative analysis, signal analysis
1 | INTRODUCTION

Pulmonary vein isolation remains the cornerstone of atrial fibrillation (AF) ablation, largely because other ablation strategies have not consistently proven to be effective or reproducible. Complex-fractionated atrial electrocardiograms (CFAEs) have been proposed to represent substrates for AF maintenance and their ablation has been associated with AF termination. However, although early studies targeting CFAEs for ablation showed promise, the long-term success of CFAE ablation in follow-up studies has been disappointing. CFAEs may arise due to active mechanisms, such as rapid focal firing or spiral wave re-entry, or from passive mechanisms, such as signal artifact, anisotropy, wavelet collision, double potentials, and slow conduction. A major factor limiting the efficacy of CFAE ablation is inability to differentiate CFAEs that actively drive AF from passive ones that do not play a role in AF maintenance.

The challenge of CFAE analysis relates to the high complexity of signals that not only undergo significant nonlinear spatiotemporal changes but are additionally susceptible to motion artifact and random noise. This renders interpretation using standard signal analysis tools inadequate. Recurrence quantification analysis (RQA), on the other hand, takes a very different approach. Rather than analyzing relative activation timings, morphologies, or frequencies, RQA evaluates the extent of recurring patterns that exist within these highly complex signals. Results from RQA can be quantified via several recurrence variables and displayed visually in a recurrence plot, thereby revealing information about local dynamics that are not evident to the naked eye. Specifically, the wavefront directionality at a site within or near a stable or repetitive driver exhibits a highly repetitive pattern which is reproducibly inscribed on the local bipolar electrogram conformation (Egm-C). Conversely, in passive regions with highly chaotic behavior dependent on multiple inconstant activating wavefronts, repetitive patterns are less likely to be present and would not inscribe a reproducible local Egm-C.

Thus, we hypothesized that RQA of Egm-C would allow differentiation of active from passive CFAE mechanisms. We validated this hypothesis by testing this novel approach in silico on signals from simulated active and passive CFAE models. We subsequently applied these RQA methodologies in vivo to human signals obtained during AF ablation.

2 | METHODS

2.1 | Computer simulations

2.1.1 | Atrial myocyte action potential and myocardial sheet models

We used the Courtemanche model of human atrial action potential with specific changes so several currents to resemble atrial ionic remodeling in heart failure (see Online Supporting Information). Vagal modulation was simulated by adding an acetylcholine (ACh) activated K current ($I_{K(ACh)}$).

Action potential wave propagation was simulated using a two-dimensional (2-D) monodomain finite-difference model, which included anisotropic conduction as well as changes to fiber orientation across the tissue (see Online Supporting Information). Unipolar pseudoelectrograms were generated from a grid of 40 x 40 ring electrodes of 1 mm diameter and an edge-to-edge transverse and longitudinal interelectrode spacing of 4 mm (see Online Supporting Information). All signals were recorded at a sampling frequency of 1 kHz with a bandwidth filter of 30 to 300 Hz. Bipolar electrograms were calculated by subtracting adjacent unipolar electrograms in the transverse direction.

2.1.2 | Computer models of active and passive CFAEs

We simulated active and passive CFAE mechanisms in several scenarios. Given current evidence for both focal sources and stable rotors as AF drivers, active CFAE mechanisms were modeled as either stable rotors (a single rotor, or two stable rotors with different frequencies) or focal areas of ectopy with a similar cycle length (CL) to that of the stable rotors. Rotors were created with standard cross-field stimulations, whereas focal ectopy was simulated by repetitive pacing from a specific site at a regular time interval. Passive CFAE mechanisms were modeled as areas of double potential around a line of block, areas within zones of slow conduction, or areas of multiple wavelets collision. Regional differences in (ACh) within the tissue were used to create dispersion of refractoriness, with higher (ACh) in areas of stable re-entry and focal ectopy, and lower (ACh) in areas of active wavebreak (see Online Supporting Information and Online Figure S1).

We designed four computer models with different combinations of active and passive CFAEs (Figure 1). Each model was simulated for 20 seconds. Details of these models as well as a 6-second movie is included in the Online Supporting Information (Online Videos S1-S4). CFAE maps were then generated using a color display of bipolar electrogram mean CL at each grid point similar to ones generated clinically with 3-D mapping. After allowing AF to stabilize for 10 seconds, mean CLs were calculated over a 5-seconds window and signals with a mean CL of less than 100 ms were considered CFAEs. Electrograms were taken from the active sites within the core of meandering rotors and near the border zones adjacent to passive areas of wavebreak. Electrograms from active sites were compared with those from passive areas, where CFAEs were seen due to wavebreak, slow conduction, or double potentials.

2.1.3 | Clinical active and passive CFAEs

This study was approved by the institutional review boards and the patients provided written informed consent. All patients underwent wide area circumferential pulmonary vein isolation (see Online Supporting Information). No other left atrial ablation was performed.

Patients were eligible if they had spontaneous AF or inducible AF lasting more than 30 minutes following 10-second burst pacing at
maximum output (20 mA) down to atrial refractory period. Detection of CFAEs was based on a clinically utilized automated algorithm\textsuperscript{16} in which mean CL was calculated from 5-second windows using $-\frac{dV}{dt}$ for detection with a 40 ms refractory period and maximum electrogram width of 15 ms. Left atrial signal collection was performed using a circular (Lasso; Biosense-Webster, Diamond Bar, CA) or multispline (PentArray, Biosense-Webster) mapping catheter with 2 or 4 mm electrode spacing. Coronary sinus and right atrial recordings were made using 10 or 20 pole catheters with 2 mm spacing.

All patients demonstrated convincing evidence of active CFAE sites driving the AF as well as passive CFAE sites not related to AF maintenance. Criteria for designation of an active driver CFAE site were: (a) a mean CL less than 120 ms, (b) demonstration of a progressive frequency gradient from the CFAE site to rest of atrium, (c) immediate termination of AF during ablation at the site, and (d) inability to sustain AF after ablation. Passive CFAE sites had a mean CL less than 120 ms but did not necessarily display a frequency gradient to adjacent areas of the atrium. Passive sites were also remote from any ablation lesion, and, thus, were not associated with AF termination or lack of AF inducibility.

### 2.1.4 Recurrence quantification analysis

Signal analysis was performed in MATLAB (MathWorks Inc, Natick, MA) and discretization of bipolar electrograms into series of Egm-C and recurrence quantification was performed as previously described (See Online Supporting Information).\textsuperscript{17,18} RQA variables, such as percent recurrence, determinism, Shannon entropy of the diagonal line length, and maximal diagonal line length were calculated.
2.1.5 Statistical analysis

All values are expressed as mean ± SD. Comparisons of continuous variables between groups were made using the Student t test. A P value less than .05 was considered statistically significant.

3 RESULTS

3.1 Computer simulations

The four models contained five stable drivers of AF (four rotors and one focal source) as well as passive areas with short mean CL due to (a) significant wavebreak and collision, (b) slow conduction, and (c) double potentials recorded near a line of block. Still, frames from the models and CFAE maps are shown in Figure 1; movies are included in the Online Supporting Information. Dominant frequencies of the drivers ranged from 10.4 to 13.0 Hz yielding signals with mean CLs of 69 to 96 ms. All models demonstrated frequency gradients from the stable driver to the rest of the tissue. Forty-five signals were analyzed from these active areas, including signals from the core of each rotor and in the border zone areas at the edge of the driver adjacent to regions with wavebreak. Sixty signals from passive areas were randomly selected from those with mean CL less than 100 ms: 20 each from areas of wavebreak, slow conduction, and line of the block.

RQA was performed on Egm-C. Examples of recurrence plots from active and passive areas of the computer simulations are shown in Figure 2. Plots from active areas were densely populated with recurrent points that tended to occur in long diagonal lines. In comparison, passive areas yielded sparsely populated plots with recurrent points more stochastically distributed and not comprising linear structures.

3.2 Comparison of active and passive sites in computer models

The mean CL of the active and passive signals were similar (84.0 ± 7.4 vs 87.3 ± 9.9 ms; P = NS). However, active areas showed significantly higher %recurrence of Egm-C than the passive areas (31.8% ± 19.6% vs 0.3% ± 0.5%; P < .0001). The active areas also showed significantly higher determinism, entropy, and maximal diagonal line lengths (Table 1). Scatter plots for mean CL and %recurrence for Egm-C are shown in Figure 3. While mean CL did not differentiate active areas from passive areas, these were reliably distinguished by %recurrence of Egm-C. No passive areas demonstrated %recurrence greater than 2.5%, whereas active areas were generally above this cutoff. Several signals located near the periphery of the active site (Figure 3B, green points) and one near the core of a spiral wave (Figure 3B, red point) displayed lower %recurrence.

3.3 Clinical active and passive CFAE discrimination

Active and passive sites were identified in 17 patients undergoing catheter ablation. Ten had paroxysmal AF and seven had persistent AF, all with most recent episode of less than 3 months duration. The full baseline clinical characteristics of the patients are provided in Table 2. In each patient, an active CFAE site was identified based on the four criteria above. Signals from these 17 active CFAE areas were compared with 23 areas with passive CFAEs, which also had mean CL less than 120 ms. All active CFAE sites were located within or near the pulmonary vein antra and were included in the wide area circumferential ablation lesion set. Passive CFAEs were found in the
coronary sinus, left atrial (LA) septum, left atrial appendage, and right atrium along the crista and were remote from any ablation lesions. There was no significant difference between mean CL between active and passive areas (106.6 ± 14.4 vs 102.5 ± 14.3 ms; \( P = \) NS). %Recurrence of Egm-C was markedly higher in active compared with passive areas (%recurrence-Egm-C: 13.6% ± 15.5% vs 0.1% ± 0.3%, respectively; \( P < .01 \)). Similar to results obtained in simulations, determinism, entropy, and length of longest diagonal line were all also significantly higher for active areas (Table 3). No differences were seen in the active or passive areas in patients with paroxysmal vs persistent AF. Representative signals obtained during ablation procedures from active and passive areas along with their recurrence plots are shown in Figure 4 and appear similar to analogous plots derived from simulations.

### 3.4 | Sensitivity and specificity of %recurrence

Figure 5 shows the mean CL and %recurrence-Egm-C from all active and passive sites recorded during ablation procedures. To test the performance of these variables as a predictor of identification of an active site, ROC curves were constructed. Areas under the curve for mean CL and %recurrence-Egm-C were 0.61 and 0.93, respectively. While there was essentially no cutoff for mean CL which separated active from passive sites, a %recurrence-Egm-C of 2.5% predicted active sites with a specificity of 100% and sensitivity of 59%, yielding negative and positive predictive values of 100% and 77%, respectively.

### 4 | DISCUSSION

This is the first study to develop a novel methodology to accurately distinguish CFAE mechanisms that actively maintain AF from those that are completely passive, to validate this methodology in silico, and then to apply it to human AF signals. The following are the main findings: (a) in both computer models and humans, traditional CFAE mapping using mean CL cannot distinguish active from passive CFAE sites. (b) Active CFAE sites demonstrate highly repetitive patterns of Egm-C while passive sites do not. (c) High %recurrence of Egm-C accurately distinguishes active from passive CFAE sites in both computer models and humans. ROC curves were constructed. Areas under the curve for mean CL and %recurrence-Egm-C were 0.61 and 0.93, respectively. While there was essentially no cutoff for mean CL which separated active from passive sites, a %recurrence-Egm-C of 2.5% predicted active sites with a specificity of 100% and sensitivity of 59%, yielding negative and positive predictive values of 100% and 77%, respectively.

### TABLE 1 | Mean cycle length and RQA variables of Egm-C in computer models

<table>
<thead>
<tr>
<th>Simulations</th>
<th>MCL</th>
<th>%Rec</th>
<th>%Det</th>
<th>Ent</th>
<th>( D_{\text{max}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>84.0 ± 7.4*</td>
<td>31.8 ± 19.6**</td>
<td>92.1 ± 13.6**</td>
<td>5.8 ± 1.5**</td>
<td>209.1 ± 124.7**</td>
</tr>
<tr>
<td>Rotor</td>
<td>83.5 ± 7.8</td>
<td>30.7 ± 19.6</td>
<td>91.8 ± 14.2</td>
<td>5.7 ± 1.5</td>
<td>203.5 ± 124.8</td>
</tr>
<tr>
<td>Focal source</td>
<td>87.1 ± 3.9</td>
<td>38.1 ± 20.0</td>
<td>94.0 ± 10.5</td>
<td>6.3 ± 1.7</td>
<td>239.7 ± 129.3</td>
</tr>
<tr>
<td>Passive</td>
<td>87.3 ± 9.9*</td>
<td>0.3 ± 0.5**</td>
<td>21.4 ± 27.5**</td>
<td>0.9 ± 1.3**</td>
<td>10.4 ± 11.0**</td>
</tr>
<tr>
<td>Double potentials</td>
<td>81.7 ± 11</td>
<td>0.1 ± 0.2</td>
<td>12.0 ± 20.2</td>
<td>0.3 ± 0.8</td>
<td>6.4 ± 6.4</td>
</tr>
<tr>
<td>Slow conduction</td>
<td>85.2 ± 8</td>
<td>0.0 ± 0.0</td>
<td>3.9 ± 12.2</td>
<td>0 ± 0</td>
<td>3 ± 3.8</td>
</tr>
<tr>
<td>Wavebreak</td>
<td>95.1 ± 4.6</td>
<td>0.9 ± 0.6</td>
<td>48.4 ± 24.7</td>
<td>2.3 ± 1.2</td>
<td>21.8 ± 10.3</td>
</tr>
</tbody>
</table>

Abbreviations: \( D_{\text{max}} \), longest diagonal line length; Det, determinism; Egm-C, electrogram conformation; Ent, Shannon entropy of the diagonal line length; MCL, mean cycle length; NS, not significant; Rec, recurrence, RQA, recurrence quantification analysis.

* \( P = \) NS.
** \( P < .01 \).
TABLE 2 Characteristics of patients

<table>
<thead>
<tr>
<th></th>
<th>n = 17 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65.1 ± 8.8</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>12 (71)</td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>10 (59)</td>
</tr>
<tr>
<td>LA size</td>
<td>4.3 ± 0.4</td>
</tr>
<tr>
<td>LVEF</td>
<td>53.1 ± 10.9</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td></td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>4 (24)</td>
</tr>
<tr>
<td>Nonischemic cardiomyopathy</td>
<td>2 (12)</td>
</tr>
<tr>
<td>HTN</td>
<td>12 (71)</td>
</tr>
<tr>
<td>DM</td>
<td>3 (18)</td>
</tr>
<tr>
<td>CHADS-VasC score</td>
<td>2.41 ± 1.54</td>
</tr>
<tr>
<td>Failed antiarrhythmic</td>
<td>1.3 ± 0.6</td>
</tr>
</tbody>
</table>

Abbreviations: AF, atrial fibrillation; DM, diabetes mellitus; HTN, hypertension; LA, left atrium; LVEF, left ventricular ejection fraction.

computer models and humans. (d) RQA plots readily identify signals with intermittent active drivers during fibrillation.

Targeting CFAE sites during ablation remains highly controversial with recent studies arguing against routine extensive CFAE ablation. This is invariably due to the difficulty in distinguishing CFAEs due to mechanisms that actively maintain AF from passive CFAEs that do not contribute to AF maintenance. The low specificity in differentiating active from passive CFAEs not only diminishes procedural success but may also increase complication rates due to excessive and unnecessary ablation. A major limiting step in the ability to distinguish active from passive CFAEs relates to the fact that signal complexity per se does not necessarily carry important mechanistic information. As we demonstrate in this paper, the degree of complexity, as measured by a standard clinically used mean CL algorithm, itself does not correlate with driver domains in AF, and, therefore, is a very poor discriminator of active vs passive sites.

Current signal analysis approaches to identify areas critical to the maintenance of AF have increased our current understanding, but all have limitations. While it is true that important areas often display either “fast” or complex-fractionated behavior, time-domain algorithms are nonspecific because they often identify passive areas of double potentials, wavebreak, and slow conduction. Frequency-domain methods have demonstrated that activation gradients often emanate from driver areas but their use has been of limited value in the noisy and nonstationary environment of clinical AF. Methods evaluating electrogram morphology, such as similarity index and cross-correlation coefficients, have provided important insight into the fact that critical areas tend to display similar appearing electrograms. However, in and of themselves, they provide a little insight into the dynamics of the very nonstationary system that is AF. Phase mapping to identify driver rotors or focal sources is another potentially exciting tool; however, the initial clinical results have been difficult to reproduce. Not only are stable rotors not reliably identified, but transient unstable wavefront rotation that is not relevant to AF maintenance can be labeled as a driver. Nonlinear techniques, such as Shannon entropy, have been used to characterize complexity of AF, but the utility of these nonlinear techniques has generally been to characterize the extent of fractionation rather than to provide any meaningful mechanistic insight.

RQA takes a very different approach. Natural patterns are found in dynamical systems, such as AF, and the extent to which they recur is highly indicative of underlying mechanisms. We have previously shown that the continuous bipolar electrogram can be discretized into a series of Egm-C, while maintaining important serial information about the direction of activating wavefronts. CFAEs occur due to a variety of mechanisms. The passive mechanisms, such as double potentials, slow conduction, and wavefront collision that result in a short measured CL are not the result of periodic processes. Recurrent series of wavefront directions do occur in these regions, but diverge quickly. In contrast active driving areas repeat periodically over time creating repetitive patterns of wavefront directions that remain similar to previously observed patterns for longer durations. RQA is a powerful tool to analyze the patterns of these wavefront directions and in doing so, quantify the degree of periodicity, determinism, and stability present. These may be important differentiating characteristics between active and passive areas during AF.

4.1 Dynamics in active and passive areas

In this study, fundamental differences in local dynamics were observed between active and passive areas. Clearly the extent to which recurrences occurred at all (%recurrence) was greater in active compared with passive areas. In addition, the distribution of recurrences within the recurrence plot provides further information about the system. In periodic signals, recurrent points tend to form...

TABLE 3 Mean cycle length and RQA variables for Egm-C in clinical ablations

<table>
<thead>
<tr>
<th>Clinical data</th>
<th>MCL</th>
<th>%Rec</th>
<th>%Det</th>
<th>Ent</th>
<th>D_max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>106.6 ± 14.4</td>
<td>13.6 ± 15.5</td>
<td>59.5 ± 34.8</td>
<td>2.7 ± 2.1</td>
<td>62.1 ± 66.2</td>
</tr>
<tr>
<td>Passive</td>
<td>102.5 ± 14.3</td>
<td>0.1 ± 0.3</td>
<td>7.8 ± 20.1</td>
<td>0.2 ± 0.7</td>
<td>3.8 ± 4.6</td>
</tr>
</tbody>
</table>

Abbreviations: D_max, longest diagonal line length; Det, determinism; Egm-C, electrogram conformation; Ent, Shannon entropy of diagonal line length; MCL, mean cycle length; NS, not significant; Rec, recurrence; RQA, recurrence quantification analysis.

**P = NS.**

**P < .02.**
**FIGURE 4** Representative recurrence plots from active and passive areas during clinical ablation. Recurrence plots generated from 10- to 15-second windows. Five seconds of signals are displayed. A. Electrogram from an active site outside LIPV showing high recurrence of Egm-C. B. Electrogram from a site of passive CFAEs recorded within coronary sinus showing no recurrences. Units for distance in plot is ms. CFAE, complex-fractionated atrial electrogram; D_max, length of longest diagonal line; Det, determinism; Egm-C, electrogram conformation; Ent, Shannon entropy of diagonal line lengths; LIPV, left inferior pulmonary vein; PVAI, pulmonary vein antral isolation; Rec, recurrence.

**FIGURE 5** Scatter plots and ROC curves for mean CL, %recurrence-Egm-C between active and passive sites during clinical ablation. A,B. Data for mean CL %recurrence-Egm-C among active and passive areas. C,D. Respective ROC curves for each of these variables. Areas under the curve were 0.61 and 0.93 for mean CL and %recurrence-Egm-C, respectively. AUC, area under the curve; CL, cycle length; Egm-C, electrogram conformation; ROC, receiver operating characteristic.
long diagonal lines, chaotic signals result in very short lines, and random signals give no lines at all. In signals from both simulations and clinical ablations, points obtained from active areas were more often part of long diagonal lines, while points obtained from passive areas were distributed more stochastically forming only short lines. This indicates that active areas demonstrated greater determinism. Furthermore, the length of the longest diagonal line is another important recurrence parameter, which inversely correlates with the most positive Lyapunov exponent. In nonlinear dynamical systems, the Lyapunov exponent characterizes the rate of separation of two similar trajectories, and, thus, the tendency of a system to diverge into chaos. Maximum line lengths were significantly longer in active areas, demonstrating the relative stability of these areas compared with passive regions.

4.2 | Intermittent nature of AF sources

Previous studies have shown that sources of both paroxysmal and persistent AF are often unstable. Indeed, in this study, multiple patients displayed intermittent burst activity, which when extinguished by ablation, resulted in termination and noninducibility of AF. An electrogram and corresponding recurrence plot from one such patient is shown in Figure 6. The bursts of rapidly activating events with similar electrogram morphology are readily identified as unstable periodic orbits in the recurrence plot. This demonstrates a potential advantage of RQA over currently used methods. Due to the nonstationarity of AF, parameters, such as dominant frequency and similarity index are generally calculated over short windows, and, thus, may miss these intermittent sources due to sampling error. While such parameters may be calculated continuously on a rolling basis, RQA may provide additional information, quantifying the dynamical behavior.

4.3 | Comparisons to previous studies using RQA

Initial attempts at using RQA focused on quantification of the degree of signal complexity. These approaches accurately identify signals without isoelectric baselines as being less recurrent, and, thus, more complex, but they provide limited utility in differentiating...
active from passive mechanisms. Ng et al utilized recurrence analysis to quantify cross correlations of electrogram morphology and calculate a CL of the most predominant waveform. Patients with shortest recurrent CL located in the right atrium were less likely to terminate with pulmonary vein isolation. However, this approach did not clearly identify drivers, as the location of shortest CL did not predict ablation success. Additionally, since this analysis of cross correlations utilized an embedding dimension of only 1, it likely did not maximize the information contained in these complex signals. Zeemering et al applied RQA to high-density epicardial AF recordings during open heart surgery and were able to detect differences in dynamics between patients with paroxysmal and persistent AF. No study to date, however, has been able to differentiate between active and passive areas using RQA. In this paper, we applied a novel approach examining recurrent patterns of electrogram morphology to study CFAE mechanisms. We demonstrated that RQA of Egm-C can accurately distinguish between CFAE signals that arise due to rotors or focal sources with fibrillatory conduction vs passive mechanisms. To the best of our knowledge, this is the first clinical AF paper to methodically develop signal analysis methods of distinguishing active vs passive CFAEs, verify them in silico on the different mechanisms of CFAE formation, and then apply them to human AF. Despite the fact that active and passive CFAE sites were similar in terms of mean CL, RQA was able to accurately distinguish active drivers from passive CFAE sites.

6 | CONCLUSION

The patterns of recurrence of Egm-C provide important mechanistic insight into local dynamics, which are quite different in active and passive areas. RQA is a powerful tool for distinguishing active from passive areas during AF.

AUTHOR CONTRIBUTIONS

AB (MD) contributed in data analysis/interpretation, drafting article, and critical revision of article; BB (BS) contributed in data analysis/interpretation; MF (MD) contributed in data analysis/interpretation; JPM (MD, PhD) contributed in critical revision of article and approval of article; AG (MD) contributed in critical revision of article and approval of article; EC (MD) contributed in critical revision of article and approval of article; CLW Jr (PhD) contributed in concept/design, critical revision of article, and approval of article; JPH (MD) contributed in concept/design, data analysis/interpretation, and statistics; JGA (MD, PhD) contributed in concept/design, data analysis/interpretation, drafting article, critical revision of article, approval of article, statistics, funding secured by, and data collection; AB (MD) contributed in data analysis/interpretation, drafting article, critical revision of article, approval of article, statistics, funding secured by, and data collection.

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REFERENCES


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