Electrogram morphology recurrence patterns during atrial fibrillation

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BACKGROUND Traditional mapping of atrial fibrillation (AF) is limited by changing electrogram morphologies and variable cycle lengths.

OBJECTIVE We tested the hypothesis that morphology recurrence plot analysis would identify sites of stable and repeatable electrogram morphology patterns.

METHODS AF electrograms recorded from left atrial (LA) and right atrial (RA) sites in 19 patients (10 men; mean age 59 ± 10 years) before AF ablation were analyzed. Morphology recurrence plots for each electrogram recording were created by cross-correlation of each automatically detected activation with every other activation in the recording. A recurrence percentage, the percentage of the most common morphology, and the mean cycle length of activations with the most recurrent morphology were computed.

RESULTS The morphology recurrence plots commonly showed checkerboard patterns of alternating high and low cross-correlation values, indicating periodic recurrences in morphologies. The mean recurrence percentage for all sites and all patients was 38 ± 25%. The highest recurrence percentage per patient averaged 83 ± 17%. The highest recurrence percentage was located in the RA in 5 patients and in the LA in 14 patients. Patients with sites of shortest mean cycle length of activations with the most recurrent morphology in the LA and RA had ablation failure rates of 25% and 100%, respectively (hazard ratio 4.95; $P = .05$).

CONCLUSION A new technique to characterize electrogram morphology recurrence demonstrated that there is a distribution of sites with high and low repeatability of electrogram morphologies. Sites with rapid activation of highly repetitive morphology patterns may be critical to sustaining AF. Further testing of this approach to map and ablate AF sources is warranted.

KEYWORDS Atrial fibrillation; Electrograms; Mapping; Signal processing

ABBREVIATIONS AF = atrial fibrillation; **CL** = cycle length; **CL_R** = cycle length of the most recurrent morphology; **CFAE** = complex fractionated atrial electrogram; **DF** = dominant frequency; **FIRM** = focal impulse and rotor modulation; **LA** = left atrium/atrial; **PV** = pulmonary vein; **RA** = right atrium/atrial; **Rec%** = recurrence percentage

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Introduction

A successful ablation strategy tailored to the specific mechanism of a patient's atrial fibrillation (AF) is considered one of the "holy grails" of AF treatment. Because of the complexity of the electrical activity of the atria during AF and the limitations of the technology available to identify electrograms for "mapping" the atria, the ability to characterize the activation patterns during electrophysiologic testing in patients with AF is extremely difficult. AF has been traditionally thought to be maintained by either rapid firing foci,[1,2] reentrant wavefronts,[3–5] or rotors.[6,7] The pulmonary veins (PVs) have been shown to be a common location for AF triggers and drivers.[8] However, ablation strategies that isolate the veins are effective in only a subset of patients with AF.[9] The rapid and seemingly chaotic electrogram activity that is characteristic of AF cannot currently be used to determine whether AF in a particular patient has a PV origin or is maintained by other foci/mechanisms.

Attempts have been made to use catheter-based electrogram recordings in ablation procedures. Frequency domain measures have been used to estimate the rate and regularity of AF electrograms.[10,11] It has been hypothesized that high-frequency sources could represent drivers of AF. However, the difficulty in using this technique is that the variability of these measurements may be almost as great as the difference between recording sites.[12] Sanders et al[11] showed that sites of high-frequency activation could be located and ablated in patients with paroxysmal AF. However, mapping of activation rates in persistent AF could not identify the culprit sources.[11,13] Complex fractionated atrial electrograms

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(CFAEs)[14] and focal impulse and rotor modulation (FIRM) mapping have also been proposed as strategies for mapping foci or sources of AF that can be targeted by ablation.[15]

In arrhythmias with regular activation patterns, the bipolar electrogram at a particular site is determined by the direction of activation and remains relatively constant during each activation. In AF, we hypothesized that similar activations from beat to beat, as would be expected to occur near the arrhythmia source, can be quantified by examining the repeatability of electrogram morphologies from beat to beat. In this study, we report a modified recurrence plot analysis to observe the nonlinear dynamics of AF electrogram morphologies that may offer new insights into the dynamics of AF and may provide a new clinical technique to mapping AF.

Methods

Patient population

Electrograms from patients who were in AF at the time of their ablation procedure were collected before ablation. Patients had no prior ablation or surgical interventions in their atria. All patients provided written informed consent. The study was approved by the Institutional Review Board of Northwestern University.

Mapping and electrogram recordings

Bipolar electrograms were sequentially obtained from multiple sites in the right and left atria (RA and LA) and stored on the Prucka CardioLab EP system (GE Healthcare, Waukesha, WI) at a sample rate of 977 Hz. The majority of the signals were collected with a NaviStar catheter (Biosense Webster, Inc, Diamond Bar, CA), but diagnostic catheters were used for coronary sinus recordings and were also used for multisite recordings in some patients. At least 15 seconds of electrograms were recorded at each site. Recording sites were documented using an electroanatomic mapping system (NavX, St Jude Medical, Inc, Saint Paul, MN; or Carto XP, Biosense Webster). Electrograms were obtained from distributed RA (appendage, lateral wall, superior and inferior vena cava junctions, posterior wall, and septum) and LA (septum, roof, posterior wall, appendage, and the ostia of the 4 PVs) locations.

In addition, we analyzed 36 electrograms recorded from multiple sites in the RA in 7 patients with typical atrial flutter to compare recurrence analysis during AF with a nonfibrillatory arrhythmia where stable activation patterns were expected.

Electrogram morphology recurrence analysis

MATLAB (MathWorks, Inc, Natick, MA) was used for all aspects of the signal processing performed in this study. Electrogram morphology recurrence plots of each AF electrogram recording were created by first performing activation detections of the electrogram signal using an iterative technique developed and validated by our laboratory.[16] The same algorithm was used for the detection of complex activations and in the setting of continuously fractionated sites. Other details are in the Online Supplement.

Recurrence analysis was then performed on the original signal after 40-Hz high-pass filtering. The morphology recurrence plot is a modification of a recurrence plot analysis first described by Eckmann et al.[17] To create the morphology recurrence plot, a 100-ms window for each detected activation was cross-correlated with every other activation in the recording. The maximum normalized cross-correlation value was determined for each combination of activations. The result was a set of N × N maximum cross-correlation values, where N is the number of activations. The process is illustrated in a 6-activation example in Figure 1A. The N × N cross-correlation values can then be plotted in a 2-dimensional color map, as shown in Figure 1B. In this plot, the x-axis and y-axis represent the first and the second activation template, respectively, that are cross-correlated. The points in dark red represent the combination with highest

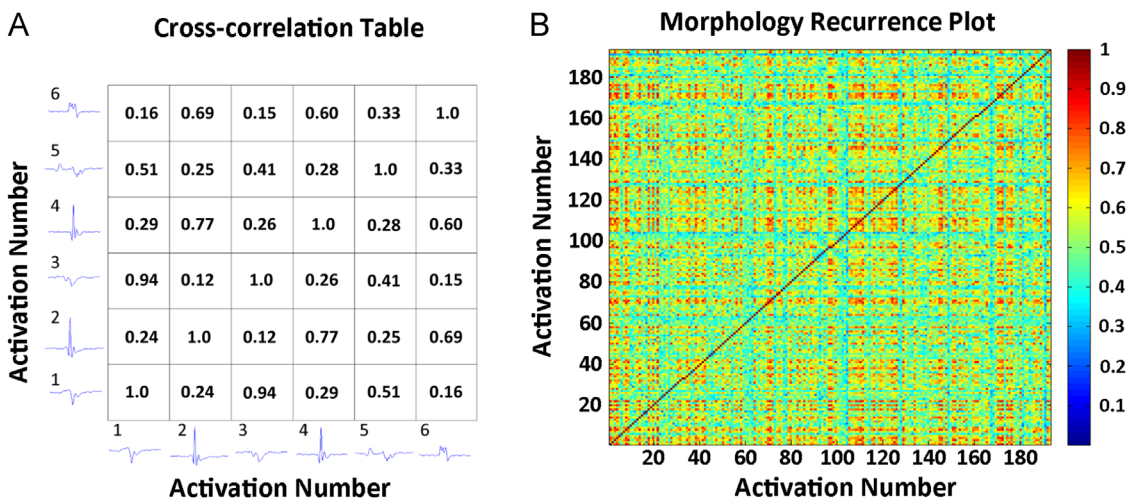

Figure 1 **A:** Illustration of a cross-correlation matrix for the first 6 activations of an atrial fibrillation electrogram. **B:** Illustration of a color-coded cross-correlation matrix of all activations. Red areas indicate high cross-correlation values and thus morphology recurrence. Nonred areas indicate pairs of activations with less similar morphologies.