Spatiotemporal organization during ablation of persistent atrial fibrillation

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BACKGROUND Targeting complex fractionated atrial electrograms improves the outcome of ablation of persistent atrial fibrillation (AF); however, the mechanism(s) responsible for the generation of complex fractionated atrial electrogram signals and efficacy of ablation is not clear.

OBJECTIVE The aim of this study was to gain mechanistic insight into ablation of persistent AF by evaluating the spatiotemporal patterns of atrial organization during ablation.

METHODS Intracardiac recordings from 18 ablation procedures were analyzed. Signals recorded by right atrial/coronary sinus catheters were processed. We quantified atrial organization using recurrence maps and recurrence percentage (Rec%) methodology and generated temporally dense time series of cycle lengths and Rec%.

RESULTS A total of 162 intra-atrial recordings were categorized into type I (sudden jump in Rec%), type II (gradual increase), and type III (no increase). Type I was the most common form and was seen in 57% ± 4% of the recordings. A typical pattern was the initial appearance of local organization, which then expanded to adjacent channels in discrete jumps until eventually an organized atrial flutter emerged. This pattern is consistent with the atrial organization signature expected from ablation of a single spiral wave with fibrillatory conduction to the rest of atria.

CONCLUSION Temporally dense spatiotemporal assessment of atrial organization during the ablation of persistent AF is feasible and provides complementary information to cycle length measurements. Atrial organization starts locally and expands spatially in discrete jumps. The regularization of AF to atrial flutter exhibits characteristics of *phase transition* in complex systems.

KEYWORDS Atrial fibrillation; Ablation; Signal processing; Recurrence maps; Complex fractionated atrial electrograms

ABBREVIATIONS AF = atrial fibrillation; **AFL** = atrial flutter; **CFAE** = complex fractionated atrial electrogram; **CL** = cycle length; **CS** = coronary sinus; **LA** = left atrium/atrial; **PVI** = pulmonary vein isolation; **RA** = right atrium/atrial; **Rec%** = recurrence percentage

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Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is associated with increased morbidity and mortality.[1] Both pharmacological and catheter-based interventions are used for rhythm control in patients with AF. Pulmonary vein isolation (PVI) has proved to be successful in control of paroxysmal AF.[2] However, as a stand-alone procedure, PVI is less successful in patients with persistent AF. Hence, a multitude of approaches have been developed for the ablation of persistent AF.[3]

The catheter ablation of persistent AF is based on the placement of lesions in the left atrium (LA) and occasionally in the right atrium (RA) in addition to PVI lesions. These additional lesions are either anatomical (eg, roof line or mitral isthmus line) or electrogram based. Complex fractionated atrial electrograms (CFAEs) are defined as fractionated Q5 short cycle length (CL) and low-amplitude atrial signals, which are a common target of ablation of persistent AF.[4]

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A meta-analysis of the published clinical trials found that CFAE-targeted ablation improved the outcome of ablation in persistent, but not paroxysmal, AF.[5] Nevertheless, the benefit of CFAE-targeted ablation procedures is modest, and long-term freedom from AF remains elusive in many patients with persistent AF. Newer techniques based on direct visualizations of rotors responsible for persistence of AF are under active development and herald an era of mechanistic approaches to ablation.[6,7]

Despite these advances, there is still debate about the exact mechanism(s) responsible for persistence of AF: a single spiral wave (mother rotor) with fibrillatory conduction to the rest of atria or multiple meandering rotors.[8–10] Even less is known regarding the mechanism of ablation and how the resulting lesions disrupt fibrillation. Lessons learned from CFAE-targeted ablation procedures can enhance our knowledge and guide the planning of ablation.

In this article, our main goal is to study how ablation organizes atrial activity by assessing the spatiotemporal pattern of atrial organization during ablation procedures. We posit that this pattern depends on the underlying mechanism of AF.

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In a computational modeling study of single spiral wave AF, Ashihara et al[11] postulated that ablation works by stopping slow conduction through CFAE areas and allows spiral waves to anchor to the ablated region with local regularization of atrial activity. Further ablation eliminates shortcuts through these sites and expands areas of regular activity. The expected organizational signature is the initial *local* regularization (anchoring), followed by stepwise growth of the organized areas. In another in silico analysis, Spector et al[12] studied the ablation of multiwavelet AF. They identified the requirement for a successful ablation procedure as placement of linear lesions from the edge of excitable tissue that expands the atrial boundary. Meandering waves collide with the expanded boundary and terminate. In this model, *global* atrial organization occurs in quantum steps associated with the elimination of each wavelet.

In order to distinguish between these 2 possibilities, we need a tool to quantify atrial organization. Multiple algorithms and methods have been proposed in this regard. In the frequency domain, the *regularity index* is defined as the ratio of the power under the dominant frequency peak to the total signal power.[13] It is easy to calculate, but lacks sufficient sensitivity to detect subtle changes in atrial organization. Time-domain methods are more sensitive, but also more complex to calculate. The *similarity index* reflects distance between pairs of local activation waves (atrial complexes) and has been used to map the spatial distribution of atrial organization in AF.[14,15] More recently, the related methodology of *recurrence maps* and recurrence percentages (Rec%), which is also based on pairwise comparison of atrial complexes, is shown to be particularly useful in the quantification of regularity during AF and forms the basis of this article.[16,17]

Methods

Patient population and ablation procedure

The procedural and data collection methods were previously described.[18] The study protocol was approved by the Emory University Institutional Review Board. The data were collected retrospectively from catheter ablation procedures for persistent AF performed at the Emory University Hospital, Atlanta, GA.

After a written informed consent was obtained, patients were brought to the electrophysiology laboratory in the fasting state and sedated. If a patient had been on a class IC or III antiarrhythmic medication before ablation, it was continued throughout the periprocedural period. All patients had persistent AF at the time of ablation. A duodecapolar catheter (Livewire, St Jude Medical, Inc, St Paul, MN) was placed in the RA and advanced into the coronary sinus (CS). An ablation catheter (Blazer II, Boston Scientific Corporation, Marlborough, MA) and, in the case of patients undergoing initial ablation, a basket mapping catheter (Constellation, Boston Scientific) were positioned in the LA and pulmonary veins. PVI was performed in patients undergoing their first ablation for persistent AF. CFAE-targeted ablation was performed beginning in the LA. CFAEs were defined as low-amplitude continuous or short CL (<120 ms) atrial signals.[19] RA lesions were delivered if there was reversal of the left-to-right frequency gradient during ablation. Only patients who transitioned to an organized atrial activity during ablation were selected for this study.

Signal processing

Electrophysiological studies were performed using the CardioLab System (GE Medical, XXXX, XX). All signals were filtered at 30–500 Hz, digitized with a resolution of 12 bits, and sampled at 977 Hz. After the procedure, 10 bipolar intracardiac channels recorded from the duodecapolar catheter in the RA/CS were downloaded for off-line analysis. Signal processing, statistical analysis, and visualization were performed using the Julia programming language.[20]

The beginning of the recorded signals coincided with the placement of the first ablation lesion, and the end point was the time of either the last ablation, infusion of ibutilide, or cardioversion. Each channel was partitioned into 16.77-second segments. The first signal-processing step was the detection of spikes in each segment using a *continuous wavelet transform*–based peak detection algorithm.[21] Peaks or spikes detected in this way corresponded to local atrial activation (Figure 1A). The CL was calculated as the median of interspike intervals.

Segments were split into 100-ms normalized windows centered at the spikes (Figure 1B). For each pair of spikes in a given segment, the corresponding windows were compared by overlaying them (Figure 1C) and finding the phase shift that maximized the cross-correlation between the windows. The goodness of the match was quantified as the correlation coefficient between the 2 windows. A value of 0 signified lack of any similarity between the atrial signals in the 2 windows, and a value of 1 signified identical signal complexes. The resulting correlation coefficients were listed in an $N \times N$ table, where N is the number of spikes in the segment (Figure 1D).

Recurrence maps are color-coded representations of these correlation coefficient tables (Figure 1E). The main power of recurrence maps is in the detection of subtle regularity and similarity among atrial complexes. For example, in Figure 2A the presence of a checkerboard pattern shows bursts of regular atrial activity in the midst of irregular AF.

To compare different recurrence maps, the information contained in each map is reduced into a Rec%. For each column, we calculate the percentage of the correlation values above 0.8 (the cutoff value is adopted from Ng et al[17]). The *Rec%* for the whole map is defined as the maximum value among all the columns, ranging from 0% to 100%. A value near 100% signifies regular atrial activity (Figure 2D) in contrast to irregular AF (Figure 2B). Intuitively, Rec% is equal to the fraction of atrial complexes that are similar to the predominate morphology. For the example in Figure 1, all the values in column 2 are above 0.8. Therefore, Rec% for this column and thus for the whole map is 100%.