Incidence of Distinct Repetitive Atrial Activation Patterns as a Metric for Atrial Fibrillation Complexity

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Abstract

Highly complex and irregular atrial activation patterns during atrial fibrillation (AF) can occasionally be interrupted by repetitive atrial activation patterns (RAAPs). These patterns are thought to be generated by mechanisms that initiate or maintain AF episodes are therefore, might be more diverse in patients with more complex forms of AF. We quantified RAAP diversity by the half decay time of the ratio of the unprecedented RAAPs to the total number of RAAPs in a goat model with different durations of sustained AF [3 weeks (3wkAF, n=8) and 22 weeks (22wkAF, n=8)]. 32 recordings from left and right atria (LA/RA) of each goat were analyzed. 24 out of 32 curves could be modeled as exponential decay functions with adjusted R-squared>0.75 while others presented more irregular decaying patterns (3wkAF LA:2 RA:3, 22wkAF LA:1 RA:2). Half decay rates were significantly shorter in LAs of 3wkAF goats (δ_{3wkAF}=23.67s vs. δ_{22wkAF}= 32.86s, $p<0.05$, Mann-Whitney U-test). There was no significant difference in RA.

1. Introduction

In patients with paroxysmal atrial fibrillation (AF), rapid high-frequency sources that are responsible for AF maintenance are in pulmonary veins (PV) and electrical isolation of these regions usually terminates AF [1]. As the disease progresses, atrial myocardium outside PVs becomes a substrate for AF leading to more complex activation patterns [2] [3] [4]. In these patients, isolation of PV region is not effective anymore.

Repetitive atrial activation patterns (RAAPs) are frequently observed during analysis of atrial electrograms and have been associated with AF maintenance mechanisms [5] and structural remodeling associated with AF [6]. RAAPs were reported to be more prevalent and more stable in paroxysmal AF patients [7]. In persistent AF, however, the underlying complex substrate might lead to a more diverse set of short lasting RAAPs. In this study, we explored the changes in the RAAP diversity between goats with 3 and 22 weeks of AF (3wkAF and 22wkAF) and evaluated this diversity as a surrogate metric for AF complexity.

2. Materials and Methods

2.1. High-Density Contact Mapping of AF

High-density unipolar atrial electrograms were recorded for 60-seconds on left/right atria (LA/RA) of a goat model with different durations of sustained AF [3 weeks (3wkAF, n=8) and 22 weeks (22wkAF, n=8)] using a 249-electrode mapping array (2.4mm inter-electrode distance). Ventricular far field artefacts were detected and eliminated using single beat QRST-template cancellation.

2.2. Detection of RAAPs During AF

RAAPs were detected using a recurrence plot-based approach defined in [5][8]. Briefly, unipolar electrograms were transformed to activation phase signals: time intervals between successive activation times are linearly filled with phase values between $-\pi$ and π (Fig. 1A). Each time was point was represented by an activation phase snapshot- activation phase values on all electrodes for that time instant (Fig 1B). Time points with similar activation phase snapshots were recorded in a recurrence plot where RAAPs produced square blocks filled with diagonal lines (Fig 1C). Blocks that lasted at least for two consecutive cycles and showed high point density (minimum of 0.9 recurrences per AF cycle) were labelled as RAAPs.

To explore which RAAPs represented similar or distinct activation wavefronts, RAAPs were clustered using cross-recurrence rate (Fig. 1D). Cross-recurrence rate between to time intervals was defined as the point density within the rectangular block in the recurrence plot formed by respective time intervals. RAAPs that do not present above-threshold cross-recurrence rate (0.9 recurrences per

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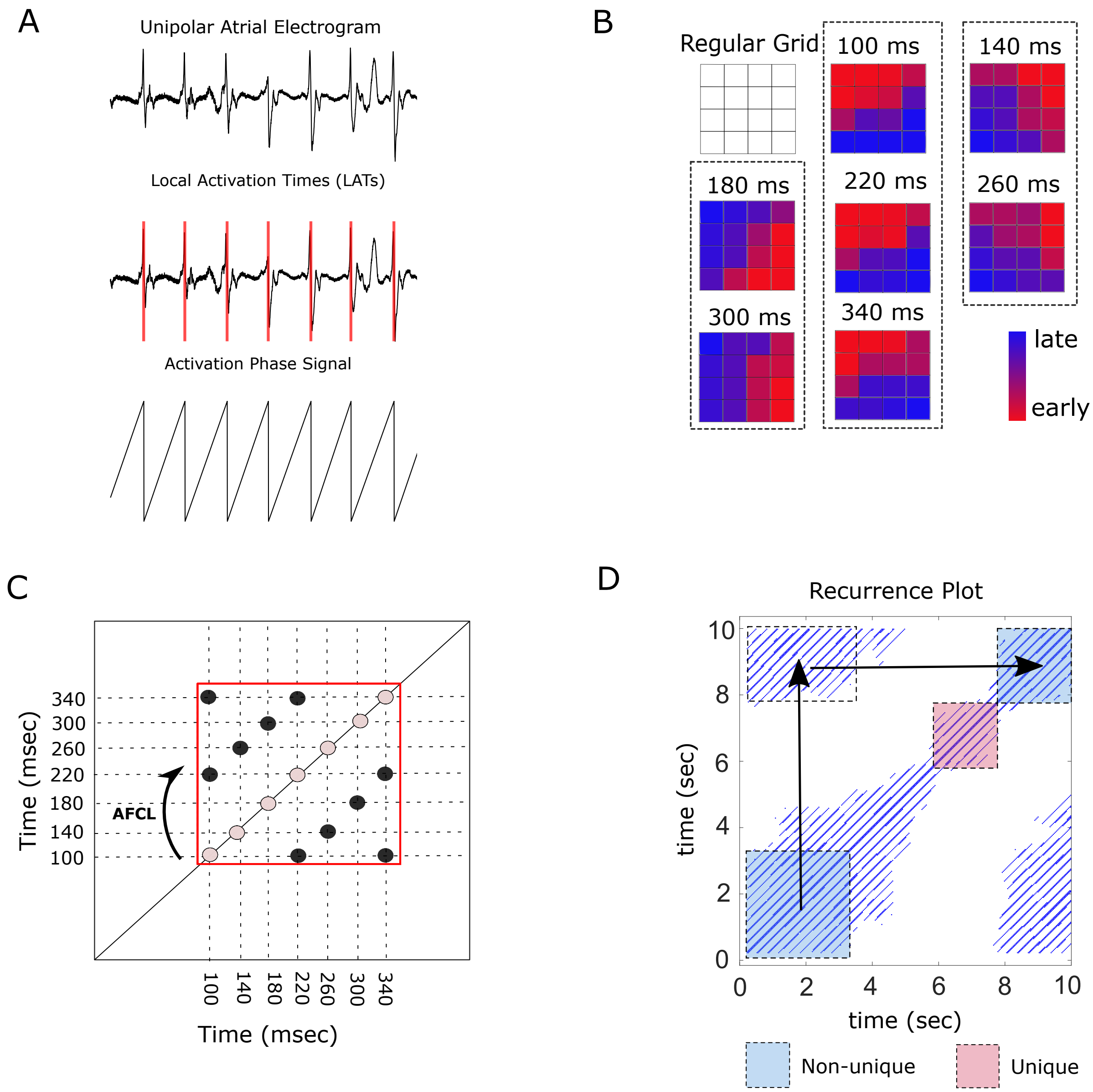

Figure 1. RAAP detection framework. (A) Generation of activation phase signals through activation phase interpolation (B) Activation phase snapshots representing the spatial activation information on each time instant, (C) Recurrence plot construction, (D) Detection and annotation of unprecedented RAAPs.

AF cycle) with any other RAAP were annotated as *unprecedented*. Unprecedented pattern ratio ($UPR(t)$) was defined as: number of unprecedented RAAPs divided by number of all RAAPs that were detected before time point t. UPR was computed in steps of 1 seconds for all recordings. Resulting curves were modeled as exponential decay functions: $c(t) = exp(-\lambda t)$. Half-decay time $c_{0.5}$ was defined as $\frac{ln2}{\lambda}$ and used to characterize each recording.

3. Results

32 recordings were analyzed (LA:16, RA:16). Average UPR curves for 60 seconds were calculated for LA and RA of 3wkAF and 22wkAF goats. UPR curves showed a decreasing trend in all conditions (Fig. 2A) while UPR values after 60 seconds showed no statistically significance difference between different groups (see Fig. 2B).

24 out of 32 UPR curves were successfully modeled as exponential decay functions with adjusted R-

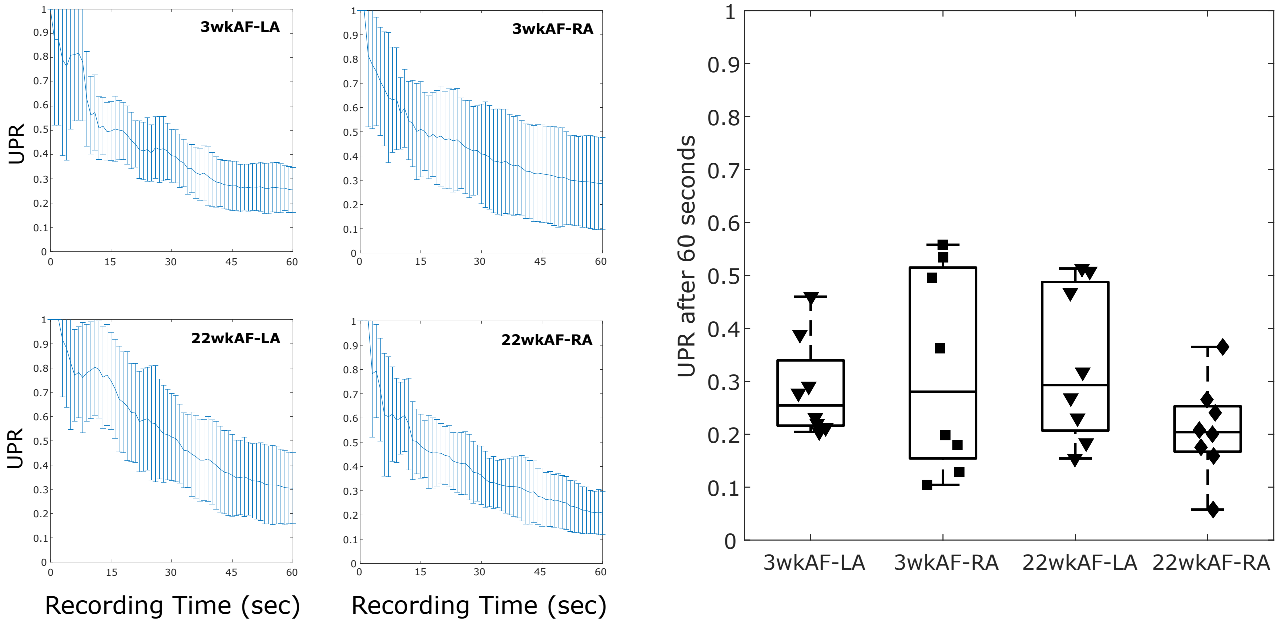

Figure 2. (Left) Unprecedented pattern ratio (UPR) curves for left and right atria (LA and RA) of different groups of goats- 3 weeks (3wkAF) and 22 weeks (22wkAF) of AF. (Right) UPR values after 60 seconds for each goat.

squared>0.75 with the original UPR curves. Remaining 8 recordings exhibited irregular decaying patterns and were excluded from the further analysis (3wkAF LA:2 RA:3, 22wkAF LA:1 RA:2). Half decay rates were significantly shorter in LAs of 3wkAF goats (λ_{3wkAF} =23.67s vs. λ_{22wkAF} = 32.86s, p<0.05, Mann-Whitney U-test). There was no significant difference in RA.

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4. Discussion

The decays of UPR curves were quick for all conditions such that, on average, 30% of the RAAPs were unique after 60 seconds. Such decrease in a relatively short time might be an evidence of the role of more deterministic mechanisms in governing electrical wave propagation during AF fibrillation.

The complexity of the activation patterns (number of waves) typically increases with AF duration [9]. In line with this, our results indicated significantly higher half decay times of UPR curves for 22wkAF goats. In other words, atria of goats with longer AF durations were able to harbor more diverse RAAPs than those with 3wkAF. This might be additional evidence in favor of the linkage between RAAPs and AF driving mechanisms or substrate. Such a relationship might form a basis for utilization of RAAP-derived metrics of AF complexity quantification. We are planning to compare our proposed candidate complexity metric with other conventional metrics such as number of waves and fractionation index in a future study.

Sequential mapping of activation patterns during AF is still an unresolved topic. To be able to map AF patterns sequentially, a certain degree of spatiotemporal stability is required. In a recent study by Mann et. al [10], such stability was shown in human endocardial recordings where 30 second-long recordings were sufficient to capture more than 90% of the activation patterns in a single region. Our results were also in line with spatiotemporal stability, but 30 seconds-long recordings could only capture half of the RAAPs in our dataset. This contradiction might be due to the pattern preselection performed in that study. Mann et al. limited themselves with single peripheral wavefronts while we have analyzed a larger and more challenging set of RAAPs with diverse pattern properties, e.g. wavefront directions, cycle lengths, patterns areas.

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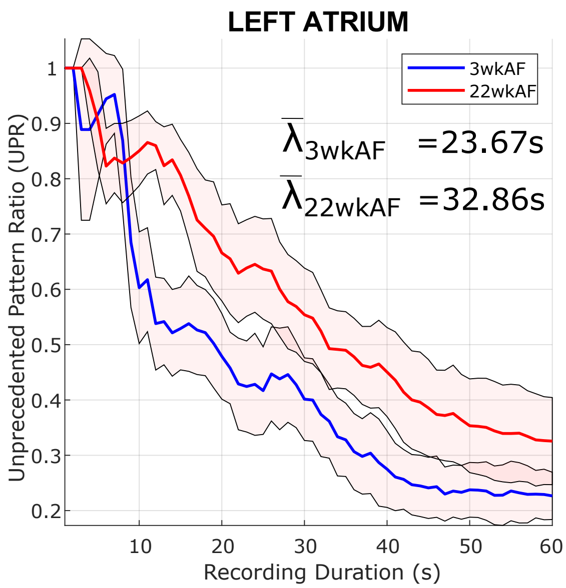

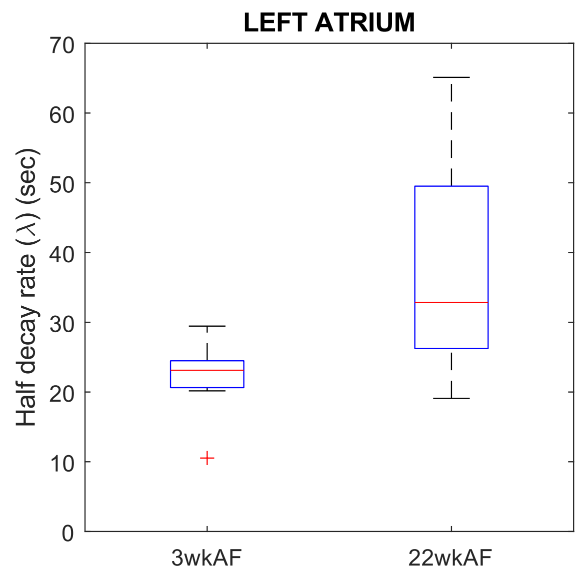

Figure 3. (Left) Unprecented Pattern Ratio (UPR) curves for left atria (LA) of different groups of goats- 3 weeks (3wkAF) and 22 weeks (22wkAF) of AF. (Right) Distributions of half-decay times among different groups for LA.

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