Non-Linear Dynamics of Atrial Rate During Atrial Fibrillation Assessed by Recurrence Plot Analysis

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Abstract

Aim of this study was to use Recurrence Plot Analysis to test the hypothesis of deterministic non-linear dynamics of Atrial Period (AP) during type I Atrial Fibrillation (AF) (Wells’ classification). We used three variables to quantify Recurrence Plots: Percent Recurrence (PR), Percent Determinism (PD) and Entropy of Recurrences (ER). We analyzed bipolar intra-atrial electrograms of electrically induced AF recorded in 3 different atrial sites in 15 informed subjects. The AP of each site was obtained by using a peak detection algorithm based on threshold crossing. We compared the real data results with those obtained from their stochastic surrogate series (phase randomization). PR, PD and ER values obtained for the surrogate data were significantly lower than those values from original data, confirming the hypothesis of a non-linear deterministic dynamics of the atrial depolarization period during AF.

1. Introduction

AF has often been studied as an irregular and random phenomenon, with no relationship between consecutive beats. Although the debate about whether or not AF is a random process is still open, experimental data obtained by high density mapping of cardiac electrical activity during AF showed that this disorder is likely associated to multiple meandering activation wavelets [1-3], which propagate throughout the surface of the atria in complex patterns. According to these findings, other studies attempted to detect a spatial correlation of atrial activation processes during AF [4] as well as any deterministic dynamics underlying AF [5,6]. On the other hand AF dynamics has been studied by applying non-linear methods together with the surrogate data analysis, revealing that AF does not seem to be generated by a linear stochastic process (null hypothesis).

The purpose of this paper was to detect specific recurrent structures characterizing the depolarization periods in different atrial sites during AF, by using the Recurrence Plot Analysis (RPA). Moreover, we used surrogate data analysis (phase randomization) to assess whether the observed recurrences have stochastic or deterministic features.

2. Methods and material

2.1. Data acquisition and experimental protocol

The electrophysiological study was performed in 15 informed subjects (13 men) aged 42-72 years (mean 57±5 years). The following electrode catheters were used: a 6F 5-mm spaced decapolar catheter whose distal electrodes were placed in the high right atrium near the sinus node; a 5-mm spaced decapolar electrode catheter placed in the coronary sinus, advanced via a right femoral approach.

AF was electrically induced and electrograms were simultaneously recorded in three different sites: at the sinus node (High Right Atrium, HRA); four cm beyond the coronary sinus os (Distal Coronary Sinus, DCS); at the coronary sinus os (CSO). AF was induced by atrial burst pacing in the high right atrium at a rate of 400-700/min. When AF persisted, low energy electrical cardioversion was performed by using a custom-built external defibrillator (Telelectronics 5410).

Intra-atrial electrograms were real-time sampled (National Instrument, AT-MIO-16E2, 1000 samples/sec, 16-bit resolution) and stored for further analysis. Each recording was then scored by an expert cardiologist to classify the rhythms according to Wells’ criteria: normal sinus rhythm and atrial fibrillation of types I, II, III and IV. We analyzed those segments showing type I AF. For each data segment, Atrial Period (AP) was automatically calculated as the interval between two consecutive detected electrograms. Electrogram detection was performed by using an algorithm based on the crossing of an adaptable threshold, with an exponential time decay to allow for variability in waveform amplitude [8].

Each AP series was expressed as a function of the depolarization occurrence time, and then evenly interpolated using third order polynomials (cubic splines) and re-sampled at 10 Hz. This procedure furnished a uniform representation for AP fluctuation of the three sites, also preserving time synchronization among data.

Cross-correlation and RP analysis were performed over 30 non-overlapping epochs lasting 10 seconds.
2.2. Cross-correlation analysis

The Cross Correlation Function (CCF) was used to detect any linear relationship between the rates of atrial depolarization in the 3 sites. We computed a normalized CCF for each AP pair. We estimated CCF for each epoch and we assessed the degree of linearity by adopting the maximum CCF value. So as to account for any delays among signals we calculated the CCF maximum over the points laying close to the zero lag.

2.3. Recurrence plot analysis

A Recurrence Plot is a graphical tool which can be used to observe whether recurrences characterize interactions between two or more signals [9] [10]. In a bidimensional case (signals x(t) and y(t)) RP is a representation of the normalized distance between the points [x(i),y(i)] and [x(j),y(j)], plotted in the time-to-time domain (i,j). If the two points are sufficiently close to each other, i.e. the distance is lower than a fixed threshold, a dot is plotted in (i,j). Among the norms proposed in literature to calculate the distance we used the Euclidean norm, i.e.:

\[ D(i,j) = \frac{\sqrt{(x(i)-x(j))^2 + (y(i)-y(j))^2}}{\text{var}(x) + \text{var}(y)} \]

We set the distance threshold as the 15% of the maximum distance value, computed as the 95th percentile. In order to quantify RP, we considered three particular descriptors: the percentage of plot occupied by recurrent points, namely Percent Recurrence (PR), the percentage of recurrent points forming diagonal lines, called Percent Determinism (PD), and the Entropy of Recurrence (ER) that is the Shannon entropy of the diagonal segment lengths distribution, measured in bits of information. Fig. 1 shows an RP, with the isolated recurrent points in light gray (PR) together with those organized in diagonal lines in dark gray (PD); ER quantifies the probabilities of each diagonal line length. In order to investigate the dynamics underlying AP during AF, we computed RP for each AP pair: HRA vs. DCS, HRA vs. CSO and DCS vs. CSO.

2.4. Surrogate data

In order to test the null hypothesis of a linear stochastic process underlying AF dynamics, we used surrogate data analysis [11]. A surrogate is an artificially generated random signal which can be obtained by the phase randomization of the original one. This procedure preserves the linear features of the original data (mean and power spectral density), while the underlying non-linear structure is lost. Surrogate data were obtained as follows: first, each AP series was Fourier transformed; then the original phase was substituted by a random series uniformly distributed between 0 and 2π; finally, the surrogate signal was obtained by taking the inverse Fourier transform. Ten surrogates were extracted for each original series. From the statistical comparison between real and surrogate RPA data, the null hypothesis can be rejected.

3. Results

Fig. 2 shows the AP of one subject during type I AF in each site (solid lines), together with their randomized counterparts (dashed lines). CCF results for one subject are shown in Fig. 3: the maximum CCF for each epoch is plotted against the corresponding epoch number. The values are always lower than 0.2, suggesting a non-linear relationship between the rates of atrial depolarization in the three different sites. RPA results for the same subject, averaged over all the epochs, are reported in tables I, II and III for HRA-CSO, HRA-DCS and CSO-DCS, respectively. PR, PD and ER decrease because of phase randomization. Student t-test was used for statistical analysis. The PD results of each epoch plotted vs. the epoch number are shown in Fig. 4, for the original (solid lines) and surrogate data (dashed lines).

Fig. 5 shows the corresponding RPs. Original RP data are clearly more complex than the randomized ones, i.e. more recurrent points organized in diagonal lines. Similar results were obtained for the other fourteen subjects.
between the RPA results of original and surrogate data highlights some deterministic features of AP during AF. These AP features likely reflect the complex patterns of multiple meandering wavelets which are claimed to sustain AF. In conclusion, our results revealed that AP during AF is governed by deterministic mechanisms, detectable by non-linear techniques. This finding admits the use of AP analysis to probe the spatio-temporal complex patterns of atrial walls activation.

4. Discussion and conclusion

In this paper we attempted to investigate this spatial and temporal organization of atrial activation by analyzing the interaction between the rates of atrial depolarization in 3 different atrial sites. To this purpose we performed both a linear and a non-linear analysis, based on CCF and RP, respectively. Since an RP is a representation of the distance between different time series in a time-to-time domain, it contains spatial and temporal information, resulting in a useful tool to analyze non-linear spatio-temporal interactions. CCF results don’t show any linear relationship between the APs in 3 different sites during AF. RPA seems, instead, to indicate a more complex interaction: the significant difference

<table>
<thead>
<tr>
<th>Table I: HRA-CSO</th>
<th>Original data</th>
<th>Surrogate data</th>
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<tbody>
<tr>
<td>PR 16.02±3.60</td>
<td>6.43±0.37</td>
<td>P &lt; 0.001</td>
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<tr>
<td>PD 17.61±7.82</td>
<td>2.88±0.98</td>
<td>P &lt; 0.001</td>
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<tr>
<td>ER 1.17±0.35</td>
<td>0.21±0.20</td>
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<th>Table II: HRA-DCS</th>
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<th>Surrogate data</th>
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<td>PR 23.44±6.64</td>
<td>6.47±0.32</td>
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<tr>
<td>PD 33.55±14.97</td>
<td>3.77±1.18</td>
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<td>ER 1.72±0.56</td>
<td>0.31±0.24</td>
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<th>Table III: CSO-DCS</th>
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<td>PR 16.34±2.59</td>
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<tr>
<td>PD 18.01±16.61</td>
<td>2.82±1.03</td>
<td>p &lt; 0.001</td>
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<tr>
<td>ER 1.12±0.38</td>
<td>0.20±0.19</td>
<td>p &lt; 0.001</td>
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Fig. 5: RPs of one epoch of the 3 AP pairs for the original (A, C, E) and surrogate (B, D, F) data: HRA-CSO (A,B), HRA-DCS (C,D), CSO-DCS (E,F).

References


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