A Novel Measure of Atrial Fibrillation Organization based on Symbolic Analysis

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Abstract

Measures of electrical activity organization in atrial electrogram (AEG) are used to guide the ablation treatment in subjects with atrial fibrillation (AF). We proposed an improved morphological index for measuring the degree of organization in AEGs. As for other indexes, the metric provides an estimate of the probability of founding couples of similar waves and it increases with a higher AF organization. However, it also considers the order of arrival of the wavefronts on a set of bipolar electrodes (BE). Doing so, the index is inherently influenced by the direction of propagation of the wavefronts.

To quantify organization, the AEGs were encoded with sequences of words of six symbols: three describing the order of arrival of the wavefronts on the BEs, while the others depending on the shape of each wave. The organization degree (OD) of each AEG was finally obtained as a function of the entropy of the sequence of words.

The method was tested on 10 subjects before and after infusion of isoproterenol (ISO). During sinus rhythm, the effects of ISO did not significantly altered the organization of the atria (on average OD= 0.75 *before and* 0.74 *after). Instead, in atrial fibrillation, ISO significantly reduced the level of organization (OD=* 0.35 *before vs* 0.32 *after,* $p < 0.05$*, paired t-test). The results were coherent with the pharmacological effects expected from the drug.*

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia encountered in clinical practise; it involves the electrical conduction system of the atrial chambers and produces a loss of volume of ejected blood, with a marked reduction of the quality of life of the patient. It is also strongly associated to an increased risk of stroke and embolic events, due to remodeling [1]. AF is characterized by a disorganized electrical activity on the atrial surface; this complex activity is due to different factors such as reentry circuits, ectopic foci, remodeling of the atrial tissue and a poor control of the autonomous nervous system [1, 2].

Since the underlying phenomenon is not completely understood, different clinical treatments are commonly used to reduce the effects of AF. Ablation therapy is a surgical treatment which tries to isolate the patches in the atria that could be the cause of the initiation or maintenance of AF. Usually, the isolation of the pulmonary veins is sufficient to stop AF. In other cases, to detect the portions of atrial surface that are candidate for ablation, measures of regularity of the electrical activity are usually performed [1]. Several measures were proposed in the last few decades, however, new approaches have been taken into account in order to improve the success rate of the ablation treatment.

Mainardi *et al.* [2] proposed two metrics to quantify the organization degree employing the surface ECG. They first built the series of local atrial periods (FF series) and then, they computed: i) the level of predictability of an autoregressive model fitted on the FF series; ii) the conditional entropy of the FF series. Both methods were able to distinguish different organization levels. An extension to multivariate analysis has been also present to measure the coupling among atrial sites [3].

Faes *et al.* [4] proposed a metric based on the morphological analysis of the waves in the AEG. The basic concept of morphological analysis is simple: the larger the number of electrical waves with different shapes measured in a certain site, the lesser the organization. The approach provides an estimate of the probability of finding a couple of similar waves in AEG during AF: They counted how many couples of waves were ”similar” (defined by a specific metric) with respect to the total number of couples of waves. In a second work, Faes and Ravelli [5] employed the same reasoning using a couple of AEG signals in order to link the regularity measured in a certain site with the one in another site.

In the present work we defined as “disordered” the status of a point crossed by wavefronts that come from different directions. Unfortunately, given the small number of electrodes typically available during ablation, it was not possible to estimate the direction of propagation and therefor, we designed a specific encoding to indirectly take direction into consideration. The work tries to exploit a further source of information present in multipolar AEGs, which includes the order of arrival of the wavefront on the BEs.

2. Methods

2.1. Dataset

The database contained 10 subjects with 4 different sets of AEGs each; every set of measurements was named accordingly to the experimental protocol phase (PP). A previously cited study employed this dataset to evaluate the effect of the pro-arrhythmic role of the autonomous nervous system, by means of infusion of ISO, on the electrical activity organization [2]. The protocol was divided into 4 phases:

1. Measurements in SR (mSR)
2. Measurements in SR after infusion of ISO (mSRISO)
3. Measurements in AF (mAF)
4. Measurements in AF after infusion of ISO (mAFISO)

Each sets contained the 12 standard leads for the surface ECG and 5 AEGs recordings collected using a coronary sinus (CS) catheter (the electrodes were spaced about two mm from each other and were linearly disposed along the catheter).

2.2. Motivation and algorithm

To understand the main idea behind the introduction of the new index, let us consider a dipole traveling along a straight line with constant velocity, in a homogeneous media. The electrical activity captured by two couples of electrodes very close to each other is practically identical, but only shifted in time (if the distance within the electrodes is significantly smaller than the distance from the dipole). With AEGs the situation is far more complex (inhomogeneities, curved surfaces, the wave sweeping directly the electrodes) but, when only one wave is present, the delay in the detection of the activity in two nearby BE is dictated by the propagation velocity. Also, during an ordered activation patter like in sinus rhythm, the same shape is obtained at the same BE over time and the relative timings of activation in nearby electrodes is maintained.

During atrial fibrillation, with a decreased atrial organization, the number of concurrent waves increases. When the same BE collects over time different wavefront shapes, it hints that they came from different directions. Also the different relative timing between BEs and its changes over time are a hallmark of a decreased organization. Thus the times of arrival, when linked to a wave shape, even if indirectly, offers a sort of "geometrical" information on the electrical activity of the atria.

Taking into account these considerations, our algorithm was composed of 4 consecutive steps; after the preprocessing (sec. 2.2.1), we localized the position of the waves on the AEG (sec. 2.2.2) and a clustering procedure was used to create groups of waves with approximatively the same shape (sec. 2.2.3). Finally, after coding what we called each "event" in the AEG, an estimate of the degree of the organization was computed as a function of the entropy of the symbolic sequence (sec. 2.2.4).

2.2.1. Preprocessing

A passband filter was applied to AEG to reduce the baseline wandering and the high frequency noise (0.5-250 Hz). However, the most relevant interference added to the AEG is the ventricular activity (VA); unfortunately, this disturb is overlapped to the atrial activity both in time and in frequency and so, it is not possible to use classical numerical filtering. During AF, cancellation of VA is commonly performed by template matching and substraction (TMS) [6]. We did so in this work.

2.2.2. Activation time (AT) detection

In order to estimate the position of the localized atrial activity (LAA), a set of numerical filters was applied to the AEG as in [4]. An adaptive threshold was used to detect peaks and a blank period was selected (50 ms) to avoid double detections of the same wave.

LAAs displaying a cross-correlation larger than 0.9 were used to build a template and they were aligned on it (± 4 ms); the process was repeated until convergence was reached. The alignment increased the quality of the clustering procedure described in the next section.

2.2.3. Clustering procedure

For each AT we defined a window of 90 ms centered on it and we built an input matrix containing the waves coming from all the leads. (Thus the size of the imput matrix was $90 \times N$ being N the number of detected waves). Principal component analysis (PCA) was applied to reduce the dimensionality of the input matrix. We selected a number of principal components (PC) that covered at least the 90% of the total power.

We used K-means, an unsupervised learning method [7], for automatically detecting clusters, due to the fact that this kind of machine learning technique is usually robust and able to generalize quite well. Also, it is not necessary to select a threshold on distances between clusters.

Since the initialization of the centroids was random, we reinforced the procedure repeating the training 10 times and taking into account only the solution that maximized the variance between centroids. The number of clusters

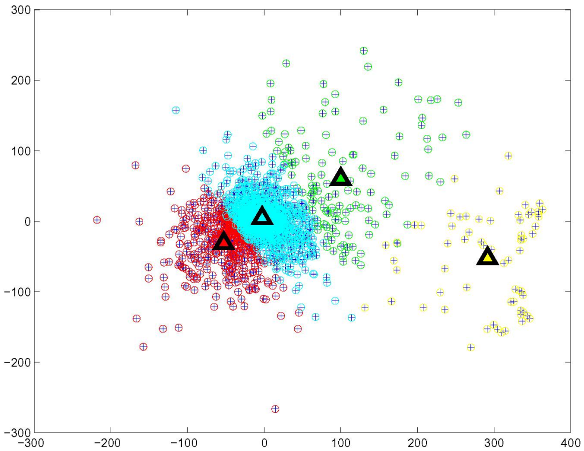

Figure 1. LAA waves during AF described by the first two PCs of the input matrix. Triangles mark the centroids as found by K-means.

was set to 4 to minimize the convergency time of the SE (see section 2.2.4) while still having a sufficient number of possible different shapes. Figure 1 shows the result of the clustering procedure for a subject in AF. It is interesting to notice that the shapes of the waves are grouped in well defined clusters using only the first two PCs.

2.2.4. Organization degree estimation

The detection of a wavefront in an electrode triggered what we called an "event". The following wavefronts in different electrodes were included in the event only if they occurred within 50 ms from the first activation (see figure 2). Otherwise they started a new event. Hence, an event could contain from one to three waves (and only one wave for each BE).

Every event was coded by words of 6 elements; the first three denoted the order of arrival of the wavefront on the BE using the number of the electrode, while the others coded the shape of the cluster. In the case of no activations, in one or two BE, they were encoded using a special value (zero). The words were composed as (t_1,t_2,t_3,l_1,l_2,l_3) where t_y was the number of the activated electrode and it was linked with the corresponding shape, l_x represented the cluster of the electrode x. For example (2, 1, 0, 3, 4, 0) means that an event on two BEs has been found and the first activated electrode has been the second with a cluster equals to 4. The second activated electrode has been the first with a cluster equals to 3.

The organization degree OD was calculated employing the Shannon Entropy (SE) of a series of words by

$$\mathrm{OD} = \frac{H_0 - H}{H_0} \quad (1)$$

where H_0 is the maximum SE, in which every words came from an uniform distribution and H is the SE of the series of words. OD was bounded between 0 and 1. Even if we built the encoding on a 6-dimensional space, the total number of possible words is equal to 492. When series were not long enough to provide a sufficient convergency of the entropy's estimate, we calculated the value of H_0 by Montecarlo simulations for each case.

3. Results

We applied the method on 7 subjects because 3 were discharged for the low quality of the recordings. For every set of recordings, three spatially closely BEs were analyzed: [CS1, CS2, CS3], [CS2, CS3, CS4], [CS3, CS4, CS5]. For each of them, the OD was calculated and the median value was taken into account to describe the organization of a subject during that specific protocol phase. The organization values obtained in the different phases were compared by means of a paired t-test. The computations were performed using MATLAB (The MathWorks, Inc.). For a comparison, the organization degree was also computed by using only words composed of three symbols (instead of six). When the times of arrival only were considered, we termed the index $\mathrm{OD}_{\mathrm{AT}}$, and OD_{S} when only the shapes were taken into account.

The results are summarized into table 1. In all series, the mean value of the OD of mSR was not significantly different to the mSRISO's one.

4. Conclusion

The method proposed in this work proved capable to distinguish different atrial activity organizations. It supported the idea that considering both the shapes and the times of arrival of the wavefronts permits a more complete description of atrial organization.

We compared the mean values of ODs in the different phases of a clinical protocol which included infusion of isoproterenol during SR and AF. During SR, the mean values of $\mathrm{OD}_{\mathrm{SR}}$ and $\mathrm{OD}_{\mathrm{SRISO}}$ were not significantly different. This is reasonable because, while the adrenergic drug increases the heart rate, the wavefronts still come from the same physical direction. In AF, the mean values were instead significantly different, which is justified by the in-

Table 1. Organization degrees in AF; the results are in the format mean(interquartile range); * $p < 0.05$

	mAF	mAFISO	
OD	0.35(0.32-0.36)	0.32(0.27-0.35)	*
$\mathrm{OD}_{\mathrm{AT}}$	0.11(0.05-0.11)	0.12(0.07-0.15)	
OD_{S}	0.32(0.28-0.35)	0.29(0.24-0.34)	

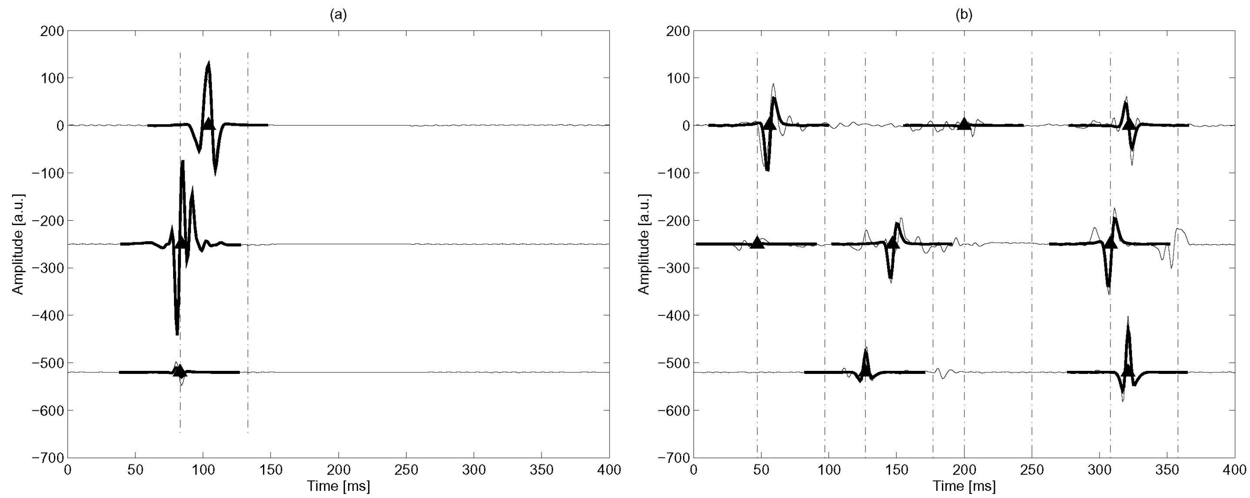

Figure 2. Events detected in SR (a) and AF (b). The position of LAA waves is marked with a triangle, while the thick black line is the mean template of the cluster. Each event is bracketed by a 50 ms window (sketched lines).

creased complexity of the fibrillatory status induced by the drug, as already detected by other studies [2].

It would have been also possible to build an organization index only using the times of arrival: if the same pattern persists in time the organization degree is higher. However we preferred to consider both the information provided by the shapes of the waves and their times of arrival for a more thorough description of the biological phenomena. The results back up our initial choice. In fact, for a comparison, we also estimated the organization degree by using only the information contained in the shapes of the wavefronts (OD_S) or in the times of arrival (OD_{AT}). Both of them were not capable of reliably detect the change in organization provided by the drug.

The method requires the selection of the number of BEs used to construct the codewords. In here, it was set to three. This was a compromise between a more fine symbolic description of the fibrillatory status, and the necessity to keep the number of possible words limited (as it has a clear effect on the convergence and reliability of SE estimates). However, the dependence of OD on the number of words should be quantitatively addressed in the future. Furthermore, future research should tackle the effects on the symbolic series of preprocessing, ATs detection, length of the series and clustering. In particular, related to the latter, PCA and K-means produced a reduction of the dimensionality of the problem (as in [8]), which was necessary to render reliable the entropy's estimate. However, using a small number of clusters (4), information might get lost as slightly different dipoles could have been forced to stay in the same cluster.

References

[1] The Task Force for the Management of Atrial Fibrillation of the ESC. Guidelines for the management of atrial fibrillation. European Heart Journal 2010;31:2369–2429.

[2] Mainardi LT, Corino VD, Lombardi L, Tondo C, Mantica M, Lombardi F, Cerutti S. Assessment of the dynamics of atrial signals and local atrial period series during atrial fibrillation: effects of isoproterenol administration. Biomed Eng OnLine 2004;3(37).

[3] Mainardi LT, Corino VD, Lombardi L, Tondo C, Mantica M, Lombardi F, Cerutti S. Linear and nonlinear coupling between atrial signals. three methods for the analysis of the relationships among atrial electrical activities in different sites. IEEE Eng Med Biol Mag 2006;25(6):63–70.

[4] Faes L, Nollo G, Antolini R, Gaita F, Ravelli F. A method for quantifying atrial fibrillation organization based on wave-morphology similarity. IEEE Trans Biomed Eng 2002; 49(12):1504–1513.

[5] Faes L, Ravelli F. A morphology-based approach to the evaluation of atrial fibrillation organization. IEEE Eng Med Biol Mag 2007;59–67.

[6] Rieta JJ, Hornero F. Comparative study of methods for ventricular activity cancellation in atrial electrograms of atrial fibrillation. Physiol Meas 2007;28:925–936.

[7] Seber GAF. Multivariate Observations. Hoboken, NJ: John Wiley & Sons, Inc., 1984.

[8] Faes L, Nollo G, Kirchner M, Olivetti E, Gaita F, Riccardi R, Antolini R. Principal component analysis and cluster analysis formeasuring the local organisation of human atrial fibrillation. Med Biol Eng Comput 2001;39:656663.

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