Study of Electrogram Organization and Synchronization in Paroxysmal and Persistent/Permanent Atrial Fibrillation

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***Abstract*—. In this study, we measure and compare organization and synchronization of electrograms (EGM) obtained from patients with different types of diagnosed atrial fibrillation (AF). The studied database is composed of 70 patients admitted for ablation procedure and previously classified as *paroxysmal* or *persistent/permanent* AF. From those patients we analyzed bipolar EGM recordings during AF which were acquired using a circular catheter placed in the pulmonary veins. Results, which are given next as median (IQR), suggest that shorter (145.9 (27) ms vs. 161.3 (33.6) ms, $p < 0.01$) and less stable AF cycle length (32.1 (36) ms vs. 7.2 (32.7) ms, $p < 0.01$) is associated with *persistent/permanent* AF. Moreover, a significant reduction of the synchronization (0.35 (0.44) vs. 0.47 (0.51), $p = 0.03$) and linear relation (0.27 (0.40) vs. 0.36 (0.47), $p = 0.01$) between EGMs from antipodal electrodes of the same catheter has been found in *persistent/permanent* AF patients.**

I. Introduction

One of the most common arrhythmias in clinical practice is atrial fibrillation (AF) whose prevalence is increasing with population aging, especially in developed countries, and mainly affects to the elderly. [1].

The mechanisms underlying the generation and perpetuation of AF are still incompletely understood [2]. One of the first mechanisms in describing the onset and perpetuation of AF was the wavelet hypothesis by Moe *et al.* [3], later confirmed by Allessie and co-workers [4]. Haïssaguerre *et al.* [5] additionally found that pulmonary veins play a relevant role on initiation and perpetuation of AF.

AF is usually classified in clinical routine in three different types [1]: 1) Paroxysmal AF, which spontaneously self- terminates within the first 24h, 2) Persistent AF, which does not self-terminate before 7 days and needs cardioversion, and 3) Permanent AF which is the advanced state of the arrhythmia, difficult to reverse to sinus rhythm using pharmacological treatment and a new AF episode can start after cardioversion.

The main hypothesis of this study is that paroxysmal AF is a more organized and synchronized arrhythmia than persistent and permanent AF. Therefore, in this study we aim to characterize EGM organization and synchronization in different types of AF. Thus could be used to determine areas of less organization and synchronization that may help in ablation treatments

This study was supported by a personal grant to A.A. ref: BES-2011-046644, by project TEC2010-21703-C03-02 from Ministerio de Economía y Competitividad, CICYT and FEDER. Also by DGA (Spain) and European Social Fund (EU) through Grupo Consolidado BSICoS and by CIBER de Bioingeniería, Biomateriales y Nanomedicina through Instituto de Salud Carlos III.

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II. Materials

The clinical data of this study was composed of 70 patients admitted for ablation procedure at Hospital Universitario Gregorio Marañón (Madrid, Spain). Prior the intervention, patients were clinically classified as *paroxysmal* AF (38 patients) and *persistent/permanent* AF (32 patients). Bipolar EGM signal acquisition was done using a 20-pole circular *Lasso*® catheter (*Biosense Webster Inc., Diamond Bar, CA, USA*) placed in the pulmonary veins with 977 Hz sampling frequency. Each patient requires different electrophysiological study yielding a total of 157 recordings (80 *paroxysmal* AF and 77 *persistent/permanent* AF) with different recording lengths (81 ± 49 s).

III. Methods

A. Signal pre-processing

Classic signal pre-processing based on [6] was applied on each bipolar EGM signal, i.e., 40 to 250 Hz band-pass filtering with fourth order Butterworth filter, then output rectification and finally a 20 Hz low-pass filtering with fourth order Butterworth filter. All studied indices presented in next sections were computed from this pre-processed EGM signal using a 10 second-length sliding window in steps of 1 second.

B. Single electrode indices

Dominant frequency (DF) was extracted as the frequency f_D within the range 1.5 to 25 Hz with maximal power spectral density (PSD), estimated using the Welch's method with a 2 second-length Hamming window and 50% overlapping. Additionally, we obtained from the estimated PSD the regularity index (I_R) [7] and organization index (I_O) [8].

Time activations were extracted using a wavelet-based algorithm [9]. From activation detections, activation cycle length (ACL) median value ACL_{med} and interquartile range ACL_{IQR} were obtained.

C. Paired electrode indices

For quantifying synchronization between a pair of electrodes, magnitude squared spectral coherence was computed and the average coherence Γ_{DFx} within an interval of $\pm$ 0.75 Hz around the maximum frequency in the cross PSD was extracted.

978-1-4799-3969-5/14/$31.00

Linear relation between electrodes was measured using the cross-covariance function. The maximum value of the cross-covariance function C_{max} and the time delay where this maximum occurs δ_C were extracted as indicators of the degree of linear relation and time delay between pairs of electrodes, respectively.

The median time delay between a pair of electrodes δ_{act} was extracted from the activation times series pairing activations within an absolute distance of 90 ms. Additionally, the interquartile range of those paired activation delays $IQR_{\delta_{act}}$ is extracted as delay stability measurement.

D. Signal and statistical analysis

In order to minimize the effects of noise and bad contact of the electrodes with the cardiac tissue that may compromise the measurements, we analyze the proposed indices from the 10 second-length excerpt of each recording maximizing the RMS value of I_O across the catheter electrodes.

Paired indices were computed from adjacent and antipodal electrodes. Time delay measurements (i.e. δ_C, δ_{act} and $IQR_{\delta_{act}}$) were only studied between those pair of electrodes with $\Gamma_{DFx} \geq 0.35$. For each studied index, the median value across the catheter electrodes was computed and their median and IQR values for each study group were presented.

Wilcoxon paired test was used for finding statistical differences between indices computed on *paroxysmal* and *persistent/permanent* AF recordings. To consider differences as statistically significant, a p-value ≤ 0.05 was required.

IV. Results

Organization and synchronization indices are presented in Table I. It shows that *persistent/permanent* AF has higher fibrillation rates than *paroxysmal* AF patients, either measured from estimated PSD or as the reciprocal of the ACL (both $p < 0.01$). Furthermore, The ACL stability, indicated by its interquartile range ACL_{IQR}, is lower for *persistent/permanent* AF patients ($p < 0.01$) as well as the organization measured through I_O ($p = 0.03$).

Indices measured from adjacent pairs of electrodes do not show differences between groups. In contrast, there is a significant reduction (p = 0.01) of the linear relation between antipodal electrodes for *persistent/permanent* AF patients as well as of the synchronization measured with the coherence value (p = 0.03). In addition, the delay between antipodal electrode pairs is bigger (p = 0.05) for *persistent/permanent* AF patients being in concordance with the reduction of the coherence (synchronization) and cross-covariance (linear relation) values.

V. Discussion and conclusion

This work was aimed to study the organization and synchronization of EGMs for different types of AF. We hypothesize that paroxysmal AF patients have a higher spatial organization and synchronization than persistent or permanent AF.

Results confirm the proposed hypothesis. On the one hand, higher and more unstable fibrillation rates are related with *persistent/permanent* AF. This fibrillation rate increase coincides with that reported in the bibliography [7]. On the other hand, spectral organization is lower for *persistent/permanent* AF patients. Moreover, there is decrease of the linear relation and synchronization as well as an increase of the time delay between antipodal electrodes, however no difference has been found in indices measured between adjacent electrodes. This indicates higher spatial decoupling and longer (or slower) pathways of EGMs in *persistent/permanent* AF patients.

TABLE I
MEDIAN (IQR) VALUES OF THE CATHETER MEDIAN ORGANIZATION AND SYNCHRONIZATION INDICES BY AF GROUP. * INDICATES P ≤ 0.05 AND ** INDICATES P ≤ 0.01 IN DIFFERENCES BETWEEN AF GROUPS.

	Measure	*Paroxysmal* AF	*Persisten/Permanent* AF
Single	f_D (Hz)	5.47 (1.37)**	6.05 (1.46)
	I_R	0.34 (0.13)	0.33 (0.12)
	I_O	0.53 (0.17)*	0.49 (0.14)
	ACL_{med} (ms)	161.3 (33.6)**	145.9 (27)
	ACL_{IQR} (ms)	7.2 (32.7)**	32.1 (36)
Adjacent	Γ_{DFx}	0.7 (0.23)	0.67 (0.4)
	C_{max}	0.57 (0.31)	0.59 (0.37)
	δ_C (ms)	6.1 (5.8)	4.1 (3.1)
	δ_{act} (ms)	5.6 (5.2)	4.1 (3.8)
	$IQR_{\delta_{act}}$ (ms)	14.8 (13.2)	12 (12.7)
Antipodal	Γ_{DFx}	0.47 (0.51)*	0.35 (0.44)
	C_{max}	0.36 (0.47)*	0.27 (0.40)
	δ_C (ms)	10.2 (15.9)	13.3 (18.6)
	δ_{act} (ms)	8.2 (13.3)*	10.7 (16.1)
	$IQR_{\delta_{act}}$ (ms)	16 (15.9)	19.2 (22.9)

Results show that the lack of organization and synchronization of EGMs is related with atrial remodeling, hence with more complex AF. Further research will try to relate these indices with the anatomical location of the catheter and/or outcomes of the ablation procedure.

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