Changes in Cardiac Indices from Implanted Defibrillator-Stored Electrograms Due to Acquisition and Preprocessing Conditions

J Requena-Carrión[1], JL Rojo-Álvarez[1], E Everss[1], F Alonso-Atienza[1], JJ Sánchez-Muñoz[2], M Ortiz[3], A García-Alberola[2]

[1]Universidad Carlos III de Madrid, Leganés, Spain
[2]Hospital Universitario Virgen de la Arrixaca, Murcia, Spain
[3]Hospital Universitario Gregorio Marañón, Madrid, Spain

Abstract

A wide number of cardiac indices have been proposed to describe electrocardiograms (ECG) during Ventricular Fibrillation (VF), and they can be useful when analyzing electrograms (EGM) stored in Implantable Cardioverter Defibrillator (ICD) during spontaneous VF. However, the dependence of their measurement on acquisition and preprocessing conditions has not been so far statistically quantified. We propose a systematic procedure based on nonparametric bootstrap resampling methods to obtain standard errors and confidence intervals for a test. This test detects changes in the statistical distribution of cardiac indices from ICD-stored EGM during VF, due to discrepancies in acquisition and preprocessing conditions. As an application example, significant changes in the distributions of selected spectral indices due to lead configuration were found by comparing measurements obtained from simultaneously recorded unipolar and bipolar EGM during VF. Our nonparametric bootstrap approach can be readily applied to the measurement of cardiac indices, allowing us to study their changes under a diversity of conditions in a systematic way.

1. Introduction

Mechanisms of Ventricular Fibrillation (VF) have been investigated by analyzing electrocardiogram (ECG) signals. Various cardiac indices have been previously proposed for ECG [1,2,3], and it is expected that they will be extended to electrograms (EGM) stored at Implantable Cardioverter Defibrillators (ICD). There are several reasons why ICD- stored EGM constitute a valuable source of information: firstly, a high number of EGM recorded during spontaneous VF are available; secondly, the follow-up and intra-patient reproducibility can be analyzed for long time periods; and finally, ICD lead configuration can provide us with further insight on the underlying mechanisms of VF.

Nevertheless, EGM are usually recorded under a wide variety of acquisition and preprocessing conditions, such as electrode configuration or device manufacturer. Therefore, it should be first addressed whether measurements of cardiac indices obtained from EGM under different conditions agree, i.e., whether these measurements are significantly affected by changes in recording conditions. It is, thus, desirable to design a general procedure that allows us to investigate the effect that acquisition and preprocessing conditions might have on measurements of cardiac indices from ICD- stored EGM, by means of which the applicability of each cardiac index can be studied.

In this paper, we propose a general procedure based on nonparametric bootstrap resampling methods to investigate the effect of both acquisition and preprocessing conditions on the measurement of cardiac indices. Bootstrap methods constitute a family of computer-intensive statistical techniques that provide us with accurate estimates in situations in which standard methods cannot be applied [4]. The nonparametric approach will allow us to design a systematic procedure common to every cardiac index. In this procedure, expected values and standard errors for the measurement of every index will be estimated and changes in their probability density function (pdf) due to discrepancies in acquisition and preprocessing conditions will be detected in a test. As an application example, the effect of lead configuration on the measurements of several spectral cardiac indices will be studied by contrasting the pdf of measurements from unipolar EGM against the pdf of measurements from bipolar EGM during VF.

The paper is organized as follows. In Section 2, selected cardiac indices will be proposed, and the procedure based on nonparametric bootstrap resampling methods will be presented. In Section 3, ICD-stored EGM data base will be described and the effect of lead configuration on measurements of cardiac indices will be studied. Finally, in Section 4 benefits from such an approach will be discussed.

2. Methods

2.1. Selected spectral cardiac indices

In this paper, we focus on some relevant cardiac indices, based on the Power Spectrum Density (psd) normalized by the total power, $P_n(f)$. They are the following [1, 2, 3]:

- *Fundamental frequency and harmonics* (f_0,f_2,f_3): assuming that a VF episode, z, is a near-periodic process, $E(z(t)) = E(z(t-t_0))$, where E denotes statistical averaging and t_0 is the fundamental signal period, f_0 is the inverse of t_0. Here we considered two harmonics: $f_2 = 2 \times f_0, f_3 = 3 \times f_0$
- *Dominant frequency* (f_{dom}): frequency where the maximum of $P_n(f)$ occurs.
- *Normalized psd at harmonics* ($P_n(f_0)$,$P_n(f_2)$,$P_n(f_3)$).
- *Bandwidth at* f_0 *and* f_{dom} ($bw(f_0)$,$bw(f_{dom})$): the limits of the bandwidth are defined by a drop to 0.75 of the central frequency.
- *Organization index* (oi): ratio of the power under the harmonic to the total power. Frequency width at harmonics is defined by a drop to 0.10 of $P_n(f_{harmonic})$.
- *Median frequency* (f_m): gravity center of the psd.
- *Leakage* ($leak$): cross-correlation between the ECG segment and a sinusoidal waveform whose frequency is f_0.

It is worth noting that most of these cardiac indices assume within their definition a specific shape for the spectrum, namely a psd containing harmonically spaced peaks whose amplitude is scaled by a broad envelope. This shape reflects both the rhythmic activity of the heart and the particular arrhythmic mechanism.

2.2. Model of cardiac index measurement

Let N_p be the number of EGM stored in a data base and $\{V_i[n]; n = 0, \ldots, Q_i - 1; i = 1, \ldots, N_p\}$ be the i^{th} EGM, consisting of Q_i samples of voltage sensed by an ICD lead system, as a result of the movement of electrical charges along the myocardial walls $\{\boldsymbol{Z}_i(t)\}$. For each EGM we are usually interested in measuring a given cardiac index s, obtaining measurement s_i for EGM $V_i[n]$.

Denoting EGM acquisition conditions (such as lead configuration) by C_A, the following relation can be stated between $V_i[n]$ and the underlying process $\boldsymbol{Z}_i(t)$:

$$V_i = A(\boldsymbol{Z}_i(t), C_A) \tag{1}$$

where A is the unknown operator that maps $\boldsymbol{Z}_i(t)$ into $V_i[n]$ under acquisition conditions C_A. Furthermore, if we denote signal processing conditions (such as parameters in computing algorithms) by C_P, s_i can be computed from $V_i[n]$ through the operator P as follows:

$$s_i = P(V_i[n], C_P) \tag{2}$$

As a consequence of the dependence of the measurement of cardiac index s on the whole set of conditions $C = \{C_A, C_P\}$, $S = \{s_1, \ldots, s_{N_p}\}$ can be seen as a random sample from an unknown distribution $f_s(s|C)$.

2.3. Statistical procedure

Bootstrap methods [4] were introduced to calculate confidence intervals for parameter estimation in scenarios in which standard methods cannot be applied. Since then, they have been extended to many signal processing applications [5]. Our purpose here is to design a general procedure based on nonparametric bootstrap resampling methods to investigate the effect of changing conditions set C on the measurement of a given cardiac index.

This procedure is described as follows. Let C^r denote a set of specified reference conditions and C^a denote a set of alternative conditions, differing from C^r in the current value of at least one condition. For cardiac index s, we will be interested, on the one hand, in estimating distributions $f_\vartheta(\vartheta|C^r)$ and $f_\vartheta(\vartheta|C^a)$ of some statistic $\vartheta(s)$; and, on the other, in contrasting $f_s(s|C^r)$ against $f_s(s|C^a)$, to asses the effect of changing conditions from C^r to C^a on the measurement of s.

Defining sample S^r (S^a) as the collection of measurements of s obtained from EGM recorded under C^r (C^a) conditions, we first draw out B resamples ($B = 1000$) S^{r*} (S^{a*}) following bootstrap rules. Then, from each resample we calculate estimation $\hat{\vartheta}^*$, and we build up its histogram, which estimates $f_\vartheta(\vartheta|C^r)$ ($f_\vartheta(\vartheta|C^a)$). Fig. 1 shows the histograms for the mean and standard deviation (SD) of f_{dom} from two samples whose acquisition conditions differed in the lead configuration.

Furthermore, measurements of s from EGM obtained under C^r will be said to be statistically indistinguishable in strict sense from measurements from EGM obtained under C^a if:

$$f_s(s|C^r) = f_s(s|C^a) \tag{3}$$

We propose a simplified test to compare both distributions by contrasting their means and SD. In this test, null and alternative hypothesis are stated as follows:

- H_0: changing conditions from C^r to C^a does not affect significantly either the mean or the SD of s;
- H_A: changing conditions from C^r to C^a does affect significantly either the mean or the SD of s.

Therefore, if we denote the mean (SD) for conditions C^r and C^a respectively by $\mu(s^r)$ ($\sigma(s^r)$) and $\mu(s^a)$ ($\sigma(s^a)$), and define two new random variables as their differences:

$$\Delta\mu(s^r, s^a) = \mu(s^r) - \mu(s^a) \tag{4}$$

$$\Delta\sigma(s^r, s^a) = \sigma(s^r) - \sigma(s^a) \tag{5}$$

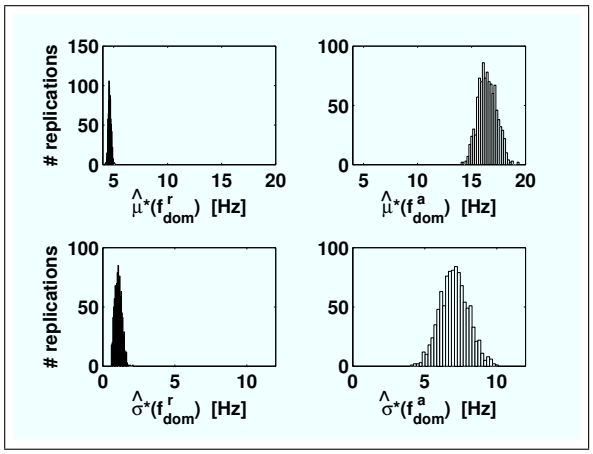

Figure 1. Distribution of $\hat{\mu^*}(f^r_{dom})$, $\hat{\mu^*}(f^a_{dom})$, $\hat{\sigma^*}(f^r_{dom})$ and $\hat{\sigma^*}(f^a_{dom})$, from which expected values and standard errors under C^r and C^a are estimated.

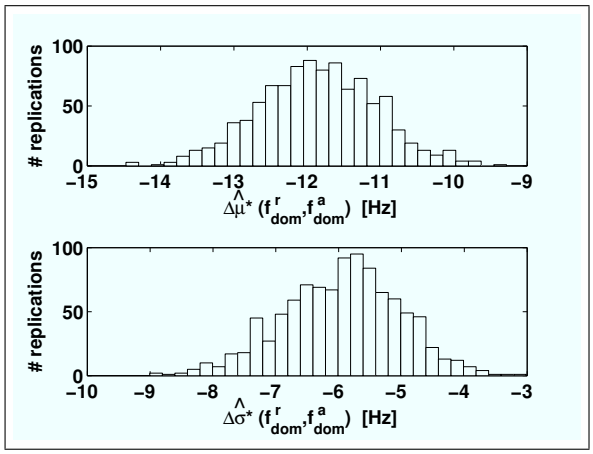

Figure 2. Distribution of $\Delta\hat{\mu^*}(f^r_{dom}, f^a_{dom})$ and $\Delta\hat{\sigma^*}(f^r_{dom}, f^a_{dom})$, from which confidence intervals are estimated to contrast in the test measurements of f_{dom} under C^r against C^a.

the test can be formulated as:

$$\begin{cases} H_0: & \Delta\mu(s^r, s^a) = 0 \text{ and } \Delta\sigma(s^r, s^a) = 0 \\ H_A: & \text{either } \Delta\mu(s^r, s^a) \neq 0 \text{ or } \Delta\sigma(s^r, s^a) \neq 0 \end{cases} \tag{6}$$

Since obtaining confidence intervals and hypothesis testing are dual problems, we first obtain the histograms for $\Delta\hat{\mu^*}(s^r, s^a)$ and $\Delta\hat{\sigma^*}(s^r, s^a)$ by means of bootstrap methods. These histograms are shown for f_{dom} in Fig. 2, when studying the effect of lead configuration. Next, based on a percentile approach, we extract confidence intervals at level α. Finally, if $\Delta\hat{\mu^*}(s^r, s^a) = 0$ and $\Delta\hat{\sigma^*}(s^r, s^a) = 0$ are within their confidence intervals, H_0 is not rejected; otherwise, H_0 is rejected and s is said not to be robust against changes from C^r to C^a.

3. Results

3.1. Data base description

A total of 4878 ICD- stored episodes were collected from 426 patients from Hospital Universitario Virgen de la Arrixaca (Murcia, Spain) and Hospital Universitario Gregorio Marañón (Madrid, Spain). Episodes were labeled according to the type of arrhythmia observed based on an expert's criteria, and 1079 episodes of VF were identified. In order to decrease the dependence on the intra-patient variability, only one episode from each patient was selected, reducing the number of episodes to 353.

3.2. Experiments

Acquisition conditions were identified for each EGM. In this experiment, we studied the effect of lead configuration on selected cardiac indices. Unipolar leads were proposed to belong to C^r, while bipolar leads were proposed to belong to C^a. Aiming to decrease the dependence on the model of ICD, we focused solely in episodes recorded by Guidant® devices and, in order to reduce biological variability, episodes that were not recorded simultaneously by both configurations were ruled out. Thus, two groups consisting of $N_p = 71$ EGM were formed: the first group comprised EGM sensed by unipolar leads and the second one comprised EGM sensed by bipolar leads.

Selected spectral cardiac indices were measured during the first 3 seconds of VF from each EGM, obtaining a sample of measurements for each index under C^r and C^a conditions. Histograms for $\hat{\mu^*}(s^r)$, $\hat{\mu^*}(s^a)$, $\hat{\sigma^*}(s^r)$ and $\hat{\sigma^*}(s^a)$ were obtained for $\alpha = 0.05$. This step is exemplified in Fig. 1 for f_{dom}. In this case, it is worth noting the large effect that lead configuration has on the distribution of both statistics, since $\hat{\mu^*}(f^r_{dom})$ are expected to be systematically lower than $\hat{\mu^*}(f^a_{dom})$. Similar conclusions can be extracted for $\hat{\sigma^*}(f^r_{dom})$ and $\hat{\sigma^*}(f^a_{dom})$. Furthermore, the unimodality of histograms would suggest that each group of EGM is homogeneous.

Histograms for $\Delta\hat{\mu^*}(s^r, s^a)$ and $\Delta\hat{\sigma^*}(s^r, s^a)$ were then estimated for $\alpha = 0.05$, and the hypothesis stated in (6) were tested. This histograms are exemplified in Fig. 2 for f_{dom}. As expected, both statistics are distributed over negative values and there is weak overlapping over zero, which suggests discrepancies statistically significant at low α levels. Table 1 summarizes the results of the experiments, showing the estimated means and standard errors for every spectral cardiac index, and the outcome of the hypothesis test. Notably, H_0 is rejected for every index, which indicates that they are not robust against changes in lead configuration. These discrepancies can be explained

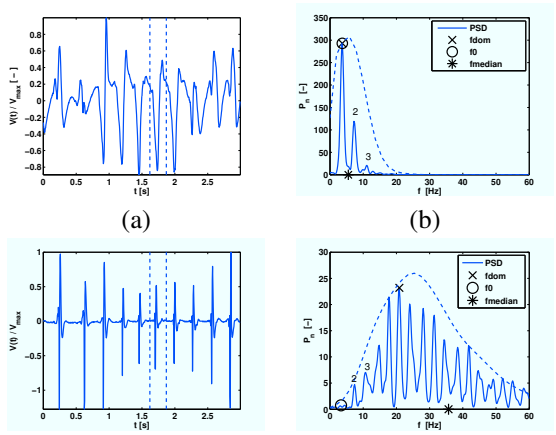

Figure 3. Panels (a) and (c) show respectively typical unipolar and bipolar recordings, and (b) and (d) show their estimated psd, along with relevant spectral characteristics. Dashed contours in (b) and (d) represent the envelope, obtained by frequency transforming EGM segments indicated by dashed lines in (a) and (c).

by looking at the shapes of the psd of unipolar and bipolar recordings. As shown in Fig. 3, compared to unipolar leads, the derivative effect of bipolar leads suppresses power at low frequencies while enhancing it at high frequencies, leading to a shift in the peak of the spectrum and f_m toward higher frequencies. For this reason, power concentrates at low frequencies in unipolar recordings, and f_{dom} usually coincides with f_0, while it concentrates at high frequencies in bipolar recordings, where f_{dom} moves to higher order harmonics. Furthermore, power at successively higher harmonics decreases faster in unipolar EGM compared to bipolar EGM, which agrees with the fact that the envelope of the spectrum is narrower in the former than the later case.

4. Discussion and conclusions

In this paper we propose a general procedure based on bootstrap methods to asses the effect of both acquisition and preprocessing conditions on measurements of cardiac indices obtained from EGM. On the one hand, histograms for relevant statistics of measurements are obtained; from them, valuable information, such as expected values and modality can be investigated. On the other hand, measurements obtained under different conditions are contrasted by applying a hypothesis test to look for statistical significant discrepancies. This procedure is exemplified by comparing two populations of EGM recorded, respectively, by unipolar and bipolar leads, showing that measurements of all selected spectral cardiac indices are sensitive to the choice of lead configuration. This work shows

	Unipolar (r)	Bipolar (a)
N_p	71	71
f_{dom} [Hz]	4.6±1.1	16.5*±7.1*
$bw(f_{dom})$ [Hz]	1.0±0.1	1.3*±1.0*
$P_n(f_{dom})$ [-]%	11.5±3.2	2.0*±1.0*
f_0 [Hz]	4.5±0.8	4.6±0.7*
$bw(f_0)$ [Hz]	1.5±1.3	9.8*±25.1*
$P_n(f_0)$ [-]%	10.8±4.0	0.2*±0.3*
$P_n(f_2)$ [-]%	2.0±2.0	1.0*±0.8*
$P_n(f_3)$ [-]%	0.5±0.4	1.5*±0.9*
$oi_{10} \times 10$ [-]	1.5±0.2	0.6*±0.4*
fm [Hz]	6.2±2.3	30.9*±6.6*
$leak$ [-]	0.9±0.1	0.8*±0.1

Table 1. Effect of lead configuration (leads vs.bipolar leads) on the measurement of selected spectral cardiac indices. Statistical significant discrepancies at a level of $\alpha = 0.05$ are designated by (*).

that statistical approaches to the study of cardiac indices are crucial for the investigation of its nature.

Acknowledgements

This work has been partially supported by research grant from Guidant Spain, and from Research Project GR/SAL/0471/2004 from Comunidad de Madrid. Jesús Requena Carrión is supported by grant 01-836-04 from Consejería de Educación de la Comunidad de Madrid.

References

[1] Reed M, Clegg G, Robertson C. Analysing the ventricular fibrillation waveform. Resuscitation 2003;57:11–20.

[2] Eftestøl T, Sunde K, Aase SO, Husøy JH, Steen PA. Predicting outcome of defibrillation by spectral characterization and nonparametric classification of ventricular fibrillation in patients with out-of-hospital cardiac arrest. Circulation 2000; 102:1523–9.

[3] Jekova I. Estimation of electrocardiogram peak frequency and periodicity during ventricular fibrillation. In Computers in Cardiology. 2003; 225–8.

[4] Efron B, Tibshirani R. An Introduction to the Bootstrap. Chapman&Hall, 1998.

[5] Zoubir AM, Boashash B. The bootstrap and its application in signal processing. IEEE Sign Proc Mag 1998;15:56–76.

Address for correspondence:

José Luis Rojo Álvarez
4.3.B.2, Avd. de la Universidad 30, Universidad Carlos III de Madrid,
28911, Leganés, Madrid (Spain)
E-mail to: jlrojo@tsc.uc3m.es