Prompt and accurate diagnosis of ventricular arrhythmias with a novel index based on phase space reconstruction of ECG

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ABSTRACT

Aim: To develop a statistical index based on the phase space reconstruction (PSR) of the electrocardiogram (ECG) for the accurate and timely diagnosis of ventricular tachycardia (VT) and ventricular fibrillation (VF).

Methods: Thirty-two ECGs with sinus rhythm (SR) and 32 ECGs with VT/VF were analyzed using the PSR technique. In order to generate the phase portraits, the method of time delay embedding were employed with the insertion of delay "τ" in the original time-series $X(t)$ which produces a delayed version of the signal $X(t)$, the $Y(t) = X(t\text{-}\tau)$. Afterwards, PSR diagram was reconstructed by plotting Y(t) against X(t). Thereafter, the method of box counting was applied to analyse the behaviour of the PSR trajectories. Finally, measures of descriptive statistics as mean (μ), standard deviation (σ) and coefficient of variation ($CV = \sigma/\mu$), kurtosis (β) for the box counting of PSR diagrams are studied.

Results: During SR, CV was always <0.05, while with the onset of arrhythmia CV increased >0.05. Similar pattern was observed with β where <6 was considered as the cut-off point between SR and VT/VF. Therefore, the upper threshold was considered for the healthy subjects CV_{th}=0.05 and β_{th}<6. For optimisation of the accuracy, a new index (J) was proposed as a combination of β and CV.

$$J = w\frac{CV}{CV_{th}} + (1-w)\frac{\beta}{\beta_{th}}$$

The upper limit of index J was the value of 1 during SR. Furthermore CV, β and J crossed the cut-off point timely before the onset of arrhythmia (average time: 4 min 31 sec; SD: 2 min 30 sec); allowing sufficient time for taking preventive actions by physicians in clinical settings.

Conclusion: J improved ECG monitoring and interpretation, allowing the prompt and accurate diagnosis of ventricular arrhythmias.

Introduction

Sudden cardiac death (SCD), despite progress in epidemiology and interventions, remains a major clinical and public health problem and one of the leading causes of mortality in the western world [1]-[3]. SCD can present without warning or a recognized triggering mechanism. Consequently, methodologies for prediction of SCD acquire a unique and critical importance for management of this public health issue. Despite active research in the prediction of SCD, the annual incidence of SCD ranges between 50-100 per 100,000 in the general population [4].

SCD is often the result of ventricular tachyarrhythmias, such as ventricular tachycardia (VT) or fibrillation (VF). Approximately one third of these patients could survive with the timely use of a defibrillator [5], [6]. Furthermore, it is of vital importance to differentiate VT from a stable but fast sinus rhythm (SR). Despite the established criteria, correct diagnosis of VT remains a challenge [7]-[9].

Phase-space reconstruction (PSR) is a technique, widely used in the field of nonlinear dynamics, for detecting small desynchronization phenomena in a time-series data and was previously used in medicine by several investigators [10]-[14]. Briefly, in PSR technique a dynamic system's trajectory is reconstructed by plotting the original signal and its delayed version(s) along mutually orthogonal axes. This gives a closed contour for a periodic signal representing a limit cycle for the regular oscillations of the system under investigation. In healthy individuals, the consecutive ECG beats can be considered as almost periodic and therefore the PSR analysis would produce an almost closed contour (Fig 1). The PSR technique is sensitive for arrhythmia detection and identification of morphological changes in ECG.

The purpose of this study is to develop a statistical index based on the PSR of the electrocardiogram (ECG) for the accurate and timely diagnosis of ventricular arrhythmia.

Methods

Thirty-two ECGs from subjects with SR and 32 ECGs from subjects with VT/VF, available from the Physionet database, have been used in this study. Two expert cardiologists performed the selection of ECGs and the clinical annotation (identification of sinus rhythm, type of arrhythmia, abnormal ECG beats). For the analysis of ECG signals the boundaries of each heartbeat were detected reliably, with the use of automated time domain morphology and gradient (TDMG) algorithm.

For the PSR of the ECG, a window of 10 successive heartbeats was chosen. Since the PSR has better results if the signals are noise-free, all the ECG signals were filtered using a fourth-order Butterworth band-pass digital filter with the pass-band cut-off frequency of 1 Hz to 30 Hz, to eliminate the baseline wandering and high frequency measurement noise respectively. For the PSR, a 20ms delay was applied in the filtered and normalized ECGs. A total of 10 trajectories were obtained from a window of 10 ECG beats in two-dimensional (2-D) phase portraits, which was resized and then exported as a high-resolution grey-scale image of pixel size 1024×1024 (Fig 2).

Once the phase portrait is constructed, it is necessary to analyze the statistical behavior of the phase trajectories, as the number of trajectories and their spread. The wildly used technique of box counting was applied for that purpose. In this technique the entire phase portrait was represented as an image of $N \times N$ pixel, where N is an integer. The pixels through which at least one trajectory has passed were considered as black boxes (n_b) and the others were considered as white boxes (n_w).

The statistical analysis of these phase portraits were carried out using Matlab where the black and white pixels were assigned as “0” and “1” value, respectively. Subsequently the number of black pixels was counted as they indicated the measure of spread of the trajectories and the underlying desynchronisation phenomenon. The number of phase portrait windows was set to a value of 25, while each phase portrait contained the characteristics of 10 ECG beats. In this way the accuracy of the

histogram construction is ensured for the number of black boxes to calculate all the higher order statistical moments (Fig 3).

Statistical analyses of the phase portraits

Statistical measures like mean (μ), standard deviation (σ), skewness (γ), kurtosis (β) and coefficient of variation ($CV = \sigma/\mu$) values of the number of black boxes visited by the phase-space trajectories for each window of 25 ECG beats were estimated while their combinations were contributed in the development of the new index.

Results

In the 32 healthy subjects with SR, the analysis showed that μ and σ trends are almost uniform throughout the time. On the other hand, in the arrhythmic subjects both μ and σ showed sudden increase at the time of VT/VF onset. In order to identify the onset of arrhythmia accurately, $CV = \sigma/\mu$ trends were introduced. It has been observed that CV is always bounded within an upper limit of $CV<0.05$, having values between >0 and <0.05. On the other hand, the arrhythmic subjects showed an increase in CV, which correlates with the onset of arrhythmia. During the arrhythmia the CV remained stable above the value of >0.05. Therefore, the upper threshold was considered for the healthy subjects $CV_{th}=0.05$. Similar pattern was observed also with the kurtosis, in which despite the inter-person variability in each case, the kurtosis remained below an upper limit of $\beta_{th}<6$ which was considered as the cut-off point between subjects with SR and VT/VF. In order to optimize the accuracy of our diagnosis a new index (J) was proposed as a regularized and weighted combination of both the trends β and CV:

$$J = w\frac{CV}{CV_{th}} + (1-w)\frac{\beta}{\beta_{th}}$$

The upper normal limit of index J is the value of $J_{th} = 1$ while the crossing of upper bounds CV_{th} and β_{th} will be reflected in crossing of the threshold for the index of $J_{th}=1$ (Fig 4). In the above equation, the weight w keeps the balance in the impact of CV and β trends in index J. So in healthy subjects with equal weights on the two parts the w would be 0.5. While in the arrhythmic subjects, it is observed that the trends cross the

critical threshold of $J = 1$ at different time instants (Fig 5). For $w = 0$ the full emphasis is on the kurtosis and with gradual increase of w, the impact of CV increases slowly and consequently impact of kurtosis decreases. With w=1, the prediction index simply represents the CV trend.

The next step in our analysis was to examine if the new index may help the early identification of VA. In 29 subjects of the group with VA, CV presented an acute and constant increase above the value of 0.05 earlier than the actual arrhythmic event and remained significantly increased until the event. It means that the trajectory spread around the mean becomes more significant over the time indicating towards the build-up a desynchronization process leading to arrhythmia. In these subjects the time period, in which the increase in the CV value noted before the arrhythmic event, extend from a minimum period of 53 beats and a maximum period of 827 beats, with an average time of 356 beats with standard deviation of 192 beats (Fig 5). In only 3 subjects, the CV crossed the cut-off value of 0.05 a short time period (32,34,34/beats) before the onset of arrhythmia. Another interesting observation is that after the appearance of VPB the value of J index raised significantly. In detailed, VPBs occurred in 27 of subjects with VA and in all of them the J index increased earlier before the appearance of VA. No VPBs noted in the 3 subects in whom the J index raised in a short period before the VA.

Discussion

The goal of this study was to quantify the PSR analysis of ECG and introduce a novel statistical index for the diagnosis of ventricular arrhythmia. This hybrid index (J) is a combination of coefficient of variation (CV) and the kurtosis (β) for the phase space diagrams of 10 beats. We identified that a threshold of <0.05 for CV, of <6 for β, and finally of <1 for J *to* precisely differentiate ventricular arrhythmia from sinus rhythm. Furthermore CV, β and J crossed the above threshold in individuals with VA promptly before the onset of arrhythmia. The average time between the initial diagnostic increase of CV, β and J and the onset of arrhythmia was 4 min 31 sec (SD: 2 min 30 sec) or 356 beats (SD: ±192 beats) while the minimum and the maximum time was 14 sec and 8 min 40 sec respectively. Finally, VPBs were observed to play

a crucial role in the triggering of VA.

The phase-space analysis technique has been used successfully over the years as a method for the detection of coronary occlusion, the identification of ECG arrhythmias, analyses of QRS-complex time series, for distinguishing extrasystoles from normal heartbeats and for the understanding of heart rhythm dynamics [15]-[26]. However, in the above studies, the PSR method relies on visual examination of trajectories in PSR [27]. Visual assessment is bound to inter- and intra-observer variability that should be quantified if this method is to become practical. To our knowledge, this is the first study to quantify the PSR analysis and proposing a novel, easy to interpreter, index.

Ventricular arrhythmias represent a common problem for physicians in every day clinical practice. They may present with a variety of clinical symptoms such as palpitations, chest pounding or long-lasting tachycardia accompanied with dyspnea, chest discomfort, hypotension and syncope. Most concerns are directed towards the risk of SCD due to the unpredictable occurrence of sustained ventricular tachyarrhythmia, which have the electrocardiographic appearance of VT or VF. In contrast to VF, VTs are relatively organized tachyarrhythmia with discrete QRS complexes and must be differentiated from fast SR. Because of the hemodynamic consequences that accompany the onset of lethal VA, a preventive approach for treating VA is preferable. The ability to quickly identify and/or predict the impending onset of VA is highly desirable.

The proposed *J* index can -accurately and timely- diagnose the malignant arrhythmias and can be a beneficial clinical tool especially for physicians, general practitioners and medical staff with limited expertise in cardiology. Furthermore, it will be useful in telemonitoring of patients with heart disease, as it will allow the analysis of a great amount of recordings. In addition, due to the promptly diagnosis of VA, *J* index can serve as a flag to alert the clinicians for the up-coming arrhythmic event. In the accident and emergency department or in the critical care unit provision of sufficient time for taking therapeutic actions can be proved life saving. Finally, *J* index will be helpful in the investigation of triggering mechanism of ventricular arrhythmias [28]-

[30].

Limitations: This is a pilot study based on ECG recordings already published electronically. A large-scale prospective study is needed to confirm the power of the proposed arrhythmia index in the clinical management of patients.

Conclusion: In this study, we developed a novel statistical index *J* based on PSR of ECG for the accurate and promptly diagnosis of ventricular arrhythmia. The index *J* can be a beneficial clinical tool for physicians, general practitioners and medical staff with limited expertise in cardiology and also for critical care units where accurate and timely diagnosis is vital.

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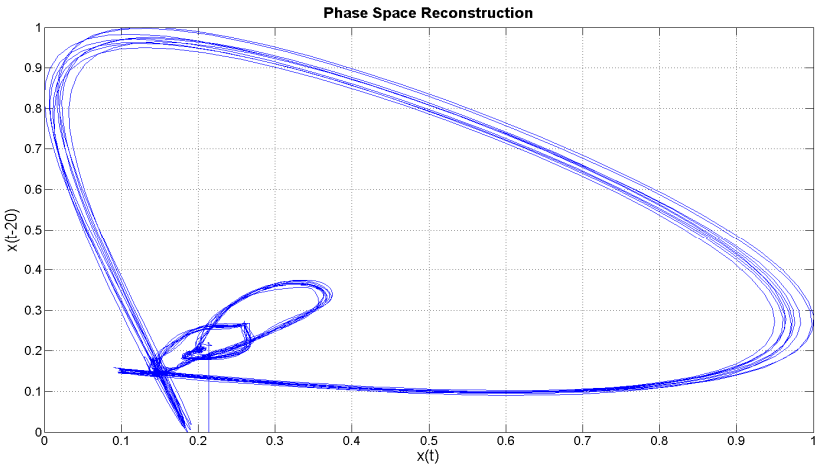

Figure 1. Space phase reconstruction of 10 heart beats from a sinus rhythm ECG.

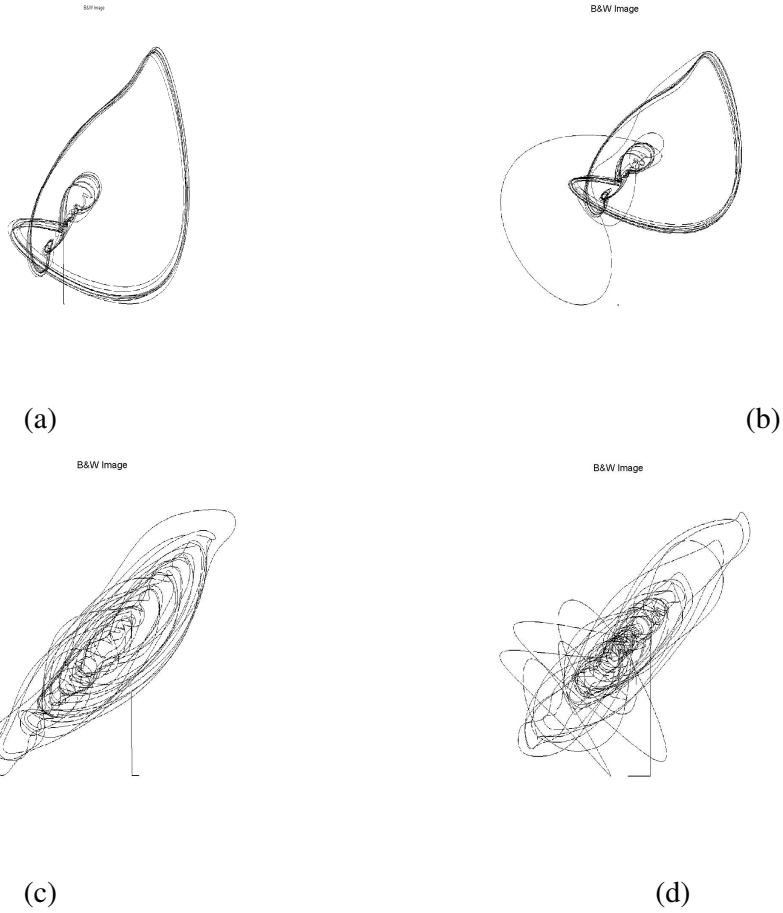

Figure 2. Black and white image of a window of ten beats for: (a) SR on ECG, (b) SR with VPB on ECG, (c) VT on ECG, (d) VF on ECG.

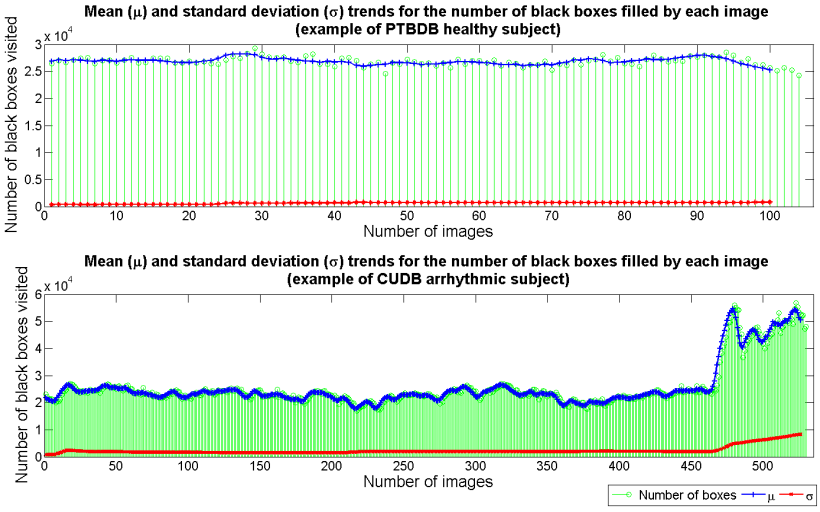

Figure 3. Box counting mean and standard deviation trends for patient with healthy and arrhythmic patient respectively.

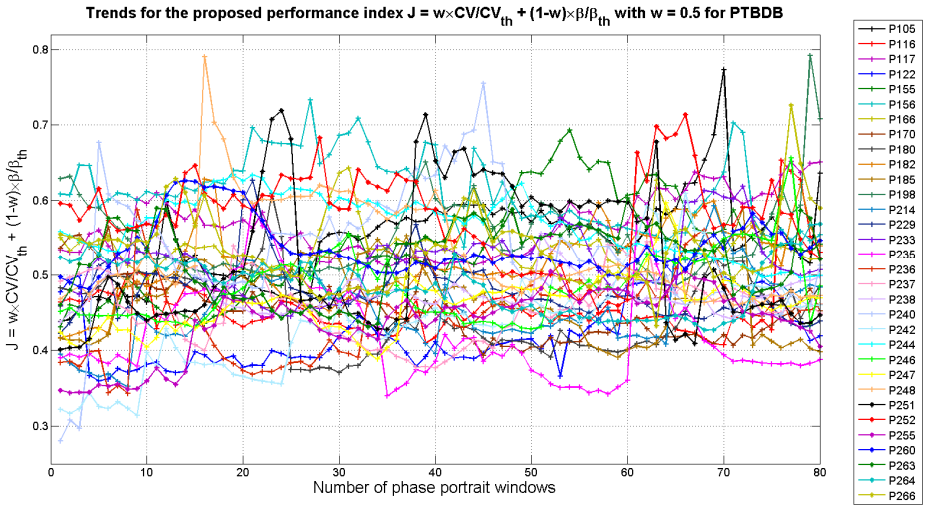

Figure 4. Trends of *J* index in subjects with SR.

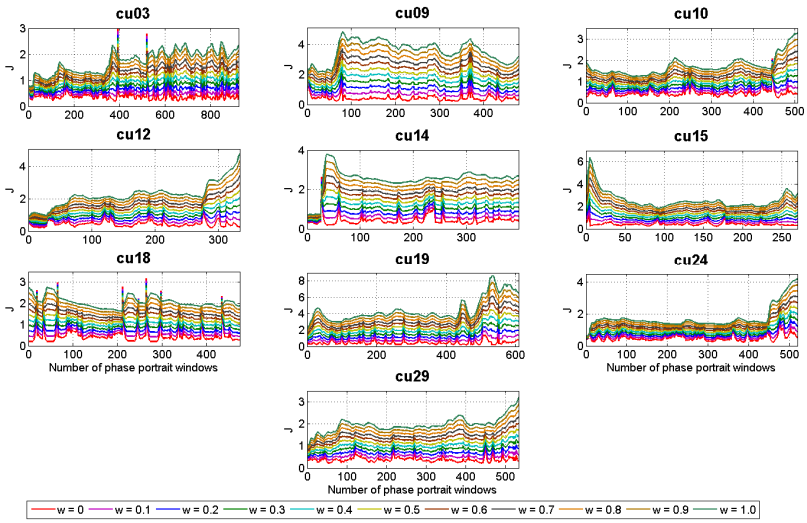

Figure 5. Trend of *J* index in subjects with VA.

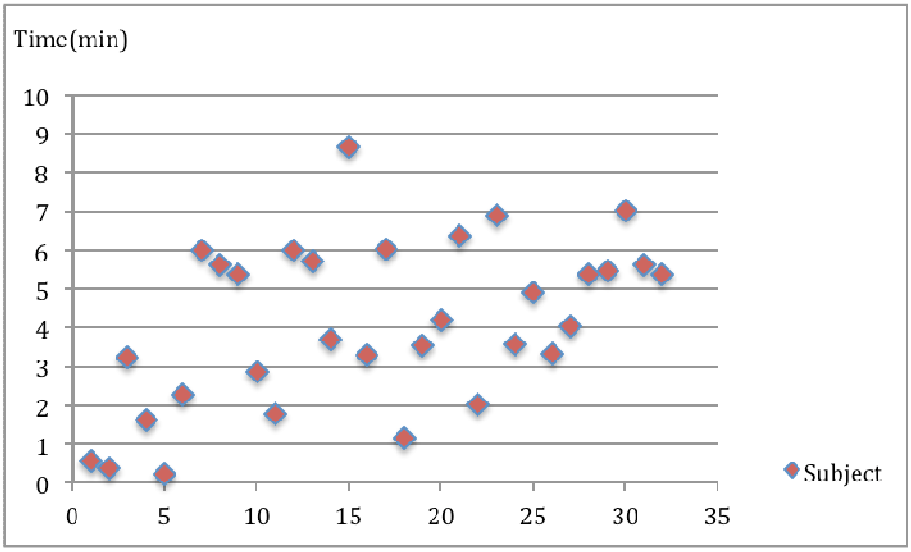

Figure 6. The time difference (in min) between the diagnosis of ventricular arrhythmia with the *J* index and ECG in the 32 subjects.