Verification of implantable cardioverter defibrillator (ICD) interventions by nonlinear analysis of heart rate variability – preliminary results

Andrzej Przybylski\textsuperscript{a,}*\textsuperscript{,} Rafał Baranowski\textsuperscript{a}, Jan Jacek Żebrowski\textsuperscript{b}, Hanna Szweda\textsuperscript{a}

\textsuperscript{a}Institute of Cardiology, Warsaw, Poland
\textsuperscript{b}Faculty of Physics, Warsaw University of Technology, Poland

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Abstract  Aims Conventional ICD algorithms yield approximately 10–30% of spurious interventions. Our aim was to check whether nonlinear dynamics methods might be useful in the verification of ICD interventions.

Methods and results We extracted 190 consecutive RR files (approximately 2000–9000 RR intervals long) from the ICDs of 70 patients (36 with coronary artery disease, 8 with hypertrophic cardiomyopathy, 19 with dilated cardiomyopathy and 7 with other diseases). The 3D phase space trajectories in delay coordinates, window pattern entropy, and algorithmic complexity of the RR intervals were examined within a 50 beat sliding window. Data were not filtered for arrhythmia and artefacts. Of the 83 recordings with appropriate interventions 79 were correctly recognised in a blind test. Two interventions were not identified in patients with fast atrial fibrillation and two in cases of complex and frequent forms of arrhythmia. There were nine spurious interventions. In all except one case (atrial fibrillation with a fast ventricular response) the analysis by nonlinear methods showed that the intervention was not necessary. All of the 98 control recordings were correctly identified in the blind test.

Conclusions The results show that nonlinear dynamics methods may be used to supplement the existing ICD detection algorithms to enhance the detection success rate.

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* Corresponding author. Spartanska 1 02-637 Warsaw, Poland. Tel.: +48 22 8441358; fax: +48 22 8449510.
E-mail address: przybyl@eko.net.pl (A. Przybylski).

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Introduction

The implantation of the cardioverter defibrillator (ICD) is an accepted method for the treatment of patients with malignant ventricular arrhythmias \[1\]. Despite technological progress, inappropriate ICD interventions are still a very important side-effect of this kind of therapy. About 10–30% of therapies delivered by ICDs have been estimated as inappropriate \[2–6\]. These are usually caused by supraventricular tachyarrhythmias, T-wave oversensing, noise or non-sustained ventricular arrhythmias \[4–6\]. The percentage of inappropriate interventions depends on the number of discriminating algorithms used. With only the high rate criterion active, this percentage is as high as 30% but the number of inappropriate treatments is somewhat lower when additional rhythm discriminators are used. Boriani et al. showed that a specificity of 90.9% and a sensitivity of 96% can be achieved with multiple discriminators \[7\].

The most important detection criterion is the length of consecutive RR intervals. Arrhythmia is detected if a certain number of RR intervals or if \(x\) out of consecutive \(y\) RR intervals are shorter than a pre-programmed value \[2,7\]. In single chamber devices, additional detection criteria like onset, stability and morphology enhance the specificity \[7\]. Dual chamber ICDs are able to compare atrial and ventricular rhythm and classify the arrhythmia using special, built-in algorithms. These detection algorithms are, however, not available in the ventricular fibrillation [VF] zone \[8,9\].

The analysis of heart rate variability (both standard and nonlinear measures) from the data stored in ICD memory has previously been used \[10–12\]. Lombardi et al. presented the changes in autonomic nervous tone before ventricular tachycardia (VT) onset \[10\]. The usefulness of nonlinear dynamics parameters of heart rate variability (HRV) to predict VT onset has been also reported \[13,14\].

The aim of our work was to use not only the length of RR intervals but also heart rate variability to verify the classification of heart rhythm by the ICD. This paper presents our preliminary results. Since we only had access to the RR intervals recorded by the ICD without verification of the full ECG, it was impossible to use standard HRV time or frequency domain analysis methods, which require arrhythmia filtration. We used methods of nonlinear dynamics that were proposed and used by our group in the studies of 24-h recordings of HRV \[15,16\] including recordings obtained during atrial fibrillation. These methods use a short sliding window (40–400 RR intervals long). Thus, they may also be used for short recordings.

Methods

Study population

One hundred ninety recordings obtained from 70 patients (36 with coronary artery disease, 8 with hypertrophic cardiomyopathy, 19 with dilated cardiomyopathy and 7 with other diseases) were analysed. The characteristics of the patients are presented in Table 1. All but three patients had single chamber devices. Only data from patients with devices compatible with the PDM 2000 (Biotronik) and STDWIN (Medtronic) softwares were analysed in the study. Both programmes allow transfer of the data from the ICD via a programmer to an external computer for further analysis. Patients, who had a predominantly paced rhythm, were excluded from the study. The VF zone was active in all patients with the lower threshold varying from 277 to 300 ms from patient to patient. The VT zone was switched on in all patients. Antitachycardia pacing (ATP) was a first therapy in the VT zone. The ventricular pacing base rate was 40–60 bpm.

Data analysis

The RR intervals stored in the ICD memory prior to intervention or assessed during control visits were analysed. The RR recordings were exported from the ICD using the PDM 2000 (Biotronik) and STDWIN (Medtronic) softwares. The recordings were from 2049 to 9176 RR intervals long (mean 7312 ± 3039).

Ninety-two RR files documented ICD interventions and 98 files were collected as control data sets during the patients’ follow-up visits. Episodes of ICD intervention were analysed and qualified by one cardiologist (A.P.) on the basis of the contents of the ICD Holter memory, primarily using intracardiac electrograms prior to arrhythmia detection and ICD intervention. Arrhythmia-related clinical symptoms were an additional differentiating factor. Judging from the stored intracardiac electrograms and clinical data, there were 83 appropriate ICD interventions and 9 were found to be spurious. They were caused by T-wave oversensing (four recordings) and by fast atrial fibrillation (five recordings). In all cases no technical problems with data transfer and analysis occurred.
Two methods were used for the nonlinear RR series analysis — window pattern entropy and algorithmic complexity [15,16]. Both are based on 3D phase trajectories in delay coordinates. In our earlier work [15,16], these complexity measures were introduced to study 24-h recordings of heart rate variability. Note that, as these measures are calculated in a short sliding window (50–400 intervals), there is no mathematical reason why they may not be applied to the above-described small data sets. Of course, in attempting to obtain a diagnostic tool for assessing the risk of cardiac arrest (CA), the question may be raised whether such a short data set contains enough information to assess such risk. In the context of the current paper, however, the risk of CA is known as these patients have ICDs. We are interested in finding the onset of VT or VF — phenomena which emerge usually on a short time scale.

Window pattern entropy is a statistical measure of signal variability and is calculated as a modified Shannon information entropy in a sliding window of a fixed length (50 RR intervals throughout this paper) [15,16]. For the standard calculation of the Shannon statistic, the probability density of obtaining a given RR interval length in the sliding window is used. The main modification of the standard Shannon approach consists of the use of a product of three such probability density distributions — each calculated for the sliding window shifted by \( \tau \) evolutions [16]. Due to this modification, pattern entropy is peculiar in that it increases when the time series is more ordered — contrary to the well-known properties of Shannon entropy. Another important consequence is that pattern entropy becomes much more sensitive to small changes in heart rate between the three windows. Use of this property will be further illustrated in the Results section. Pattern entropy is given in arbitrary units and, for convenience, all values of pattern entropy were multiplied by 10\(^4\).

In the second method, each point in the 3D delay coordinate space was represented by words of three symbols (seven different symbols were used) [15]. Thus, in the 3D space each 50 cycle sliding window was represented by a string 150 symbols long. What is most important in the context of this paper is that the symbols represented the relation of a given RR interval to the average heart rate within the window at its current position. To quantify the complexity of this string the Lempel—Ziv algorithmic complexity was applied [15,16]. In essence this algorithm, well known in computer science and used for data compression, divides the string into unique symbol sequences of varying lengths. The number of these sequences is a measure of the complexity of the heart rate variability within a window. The relation between pattern entropy and algorithmic complexity of HRV as well as of these measures to catecholamine levels is discussed elsewhere [15].

All RR interval recordings taken from defibrillators were analysed by two persons (R.B. and J.Z.) blinded to the clinical data and to the presence or absence of any ICD intervention. We analysed the RR intervals, window pattern entropy and

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient characteristics</th>
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<tr>
<td>Number of patients</td>
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<tr>
<td>Age (years)</td>
<td>19–79 (mean 54.9 ± 15.9)</td>
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<td>Male gender</td>
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<td>Aetiology</td>
<td>Coronary artery disease: 36 (51.4%); Dilated cardiomyopathy: 19 (27.1%); Hypertrophic cardiomyopathy: 8 (11.4%); Others: 7 (10%)</td>
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<td>Left ventricular ejection fraction (%)</td>
<td>15–65 (mean 35.8 ± 14.6)</td>
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<td>History of atrial tachyarrhythmias</td>
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<table>
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<tr>
<th>Devices</th>
<th>Count</th>
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<tr>
<td>Phylax XM</td>
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<tr>
<td>GEM II DR</td>
<td>1</td>
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<td>GEM III DR</td>
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algorithmic complexity as functions of the time in the period preceding the onset of the ICD intervention. Special attention was paid to the end part of each recording. RR data were taken from the control recordings (i.e. those without an intervention) or from recordings terminated just after an appropriate or an inappropriate intervention. In our preliminary study performed on a smaller data set (unpublished data), we found that, just before an appropriate intervention, a very sudden and simultaneous decrease of pattern entropy and algorithmic complexity is clearly visible. In the present study, in all 190 recordings the time evolution of these complexity measures was checked visually whether the slope of both pattern entropy and algorithmic complexity had rapidly decreased. The recording was labelled as appropriate or not based only on a visual inspection of the graphs of entropy and algorithmic complexity and no automatic mathematical decision algorithm was implemented, however a simple algorithm can easily be devised in the future. Note that both complexity measures fluctuate all the time but just before an intervention is needed the slope of the graphs as functions of the time undergoes a sharp, easily seen change. The observers in the blind test did not know a priori the number of recordings with interventions.

Results

When three parameters were analysed simultaneously for all files — RR intervals, window pattern entropy and algorithmic complexity — an outstanding feature of a proper intervention was observed. The sequence of short RR intervals detected by the ICD as the trigger for the intervention was accompanied by a sudden decrease of both the algorithmic complexity and of the window pattern entropy: Fig. 1 depicts an example for a patient with sinus rhythm and Fig. 2 an example for atrial fibrillation. The absence of a significant rapid reduction of algorithmic complexity and of window pattern entropy (left upper parts of Figs. 1 and 2) in the presence of short RR intervals was found to be an indicator of a false intervention. Control recordings were recognised in the same way.

The simultaneous sharp decrease of both window pattern entropy and of algorithmic complexity in the case of a proper intervention may be easily understood. Algorithmic complexity decreases because — as VT/VF sets in — the end of the sliding window encompasses adjacent RR intervals which are all below the average in the window (see the right panel of Fig. 1). This generates a substring of identical symbols and results in a lowered algorithmic complexity. Window pattern entropy for the same window position is decreased also because the onset of VT/VF generates peaks in the probability density which are far outside (Fig. 3 — right panel) the probability density distribution prior to the VT/VF onset (Fig. 3 — left panel). When this happens the product of the probability densities calculated in the three sliding windows will be lowered resulting in a decrease of the window pattern entropy. For an inappropriate intervention such as seen in the left panel of Fig. 1, the circumstances leading to a decrease of the pattern entropy do not arise. Moreover, an inspection of the tachogram in the right panel of Fig. 2 shows that in atrial fibrillation the same principle leading to a decrease of both complexity measures applies.

Seventy-nine out of 83 of the appropriate interventions were identified correctly. Two appropriate interventions were not identified in patients with fast atrial fibrillation and two in cases with frequent and complex forms of arrhythmia. Of the nine spurious interventions, in all except one case (atrial fibrillation with a fast ventricular response) the analysis by nonlinear methods recognised that the interventions were not necessary. The overall sensitivity of this model of detection was 94% and the specificity was 88%. All of the 98 control recordings were correctly identified in the blind test.

Discussion

The detection and correct classification of arrhythmias is one of the major challenges for both physicians and engineers involved in ICD therapy development [2]. Dual chamber devices which compare the atrial and ventricular rhythm using special algorithms (i.e. PRLogic®, Medtronic; SMART®, Biotronik; PARAD/PARAD®, Elamedical; Rate Branch®, St. Jude; Atrial View®, Guidant) should have better specificity for atrial arrhythmias than single chamber devices [8,9]. However, the study by Kuhlkamp did not show superiority of dual chamber devices [17]. A recent study showed that the specificity and sensitivity for a dual chamber detection algorithm was 89% and 99%, respectively (in the VT zone) [18]. Note that all available differentiating criteria are active only in the VT zone while all of the cases of spurious interventions reported in our paper were detected in the VF zone [2,8]. Moreover, single chamber devices are still the most frequently used ICDs in many countries (for economical but also for clinical reasons) [8].
The results of the DAVID trial did not show any clinical benefit of dual chamber ICDs in patients with a low left ventricular ejection fraction but without classical indication for pacing [19].

A very interesting study by Nanthakumar et al. [3] showed “less than ideal performance of stability interval” in differentiation between AF and VT, although the onset criterion was found to be sufficient enough to discriminate between sinus tachycardia and VT. In this context, our methods seem to be very interesting because the recognition of inappropriate shocks caused by atrial fibrillation with a fast ventricular response (detected in the VF zone) was highly accurate. We stress again that in the VF zone additional rhythm discriminators have not been implemented in currently available ICDs and rhythm differentiation in the VF zone has not been studied. Note that, here, we used only methods taken from the analysis of 24-h recordings and applied them directly to the data extracted from the ICD.

In this preliminary study we wanted only to verify if there is any possible advantage to support traditional algorithms by nonlinear dynamics methods. These methods, however, require modification. We must accept that four episodes of

Figure 1  Nonlinear dynamics assessment of ICD interventions: recognised as an inappropriate (T wave sensing — the left panel and the upper ECG trace) and as a correct (the right panel and lower ECG trace) intervention in patients with sinus rhythm. Scales adjusted for better visualisation of heart rhythm variability. WPE — window pattern entropy, AC — algorithmic complexity.
appropriate interventions were not recognised. In this context, another kind of analysis, based on symbolic word distributions [20] (not discussed here), seems to be very promising. This is a very important issue since 100% sensitivity in the VF zone must be attained. The important advantage of our methods is that they do not require arrhythmia and artefact filtration and can be used also in patients with atrial fibrillation.

The heterogeneity of our group showed that our methods are useful in spite of the underlying disease, concomitant pharmacological treatment, age and other factors.

The method presented here reacts to a rapid change in HRV. Although it does not anticipate VT/VF, it reflects the occurrence of short RR intervals in a way different from the standard algorithms of ICD. We do not expect to replace these algorithms with ours in spite of the 94% sensitivity and 88% specificity obtained in this study. We rather aim to find supportive solutions that — alongside the standard algorithms — can enhance the detection

Figure 2  Nonlinear dynamics assessment of ICD interventions: recognised as an inappropriate (the left panel, upper ECG trace) and as a correct (the right panel and the lower ECG trace) intervention in patients with atrial fibrillation. Scales adjusted for better visualisation of heart rhythm variability. WPE — window pattern entropy, AC — algorithmic complexity.
of lethal arrhythmias by ICD. It is also of special note that the parameters of the proposed supportive algorithms will probably require individual trimming taking into account clinical and electrocardiographic data.

**Limitations of the study**

As all preliminary studies this work has limitations, namely, the relatively moderate size of the group of patients, a different and varying number of recordings from a single patient and also a different and varying number of stored RR intervals within the group.

**Conclusions**

Preliminary results show that the nonlinear methods presented here may be used to supplement the existing ICD detection algorithms to enhance the detection success rate.

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**References**


