

Heart Rate Turbulence Modulation with Coupling Interval and Heart Rate

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Abstract

Heart Rate Turbulence (HRT) is a powerful risk stratification criterion in patients with cardiac disorders. Several physiological factors affect HRT, mainly, heart rate (HR), and coupling interval (CI). However, classical HRT assessment uses an average of the available individual tachograms that can blur relevant physiological relationships and it does not take into account their impact on HRT. We hypothesized that quantifying the impact of CI and HR on individual tachograms, by using robust signal processing techniques, will allow to compute local HRT measurements, yielding a more complete and meaningful HRT characterization. We studied 11 patients who were referred for electrophysiological studies. Sequences of single ventricular extrastimuli were delivered with controlled HR and adjusted CI. Turbulence Slope and Turbulence Onset were computed in denoised individual tachograms, and their effect was studied. Results showed that HRT decreased when increasing the HR and the CI. Our denoising approach allowed, for the first time, to clearly quantify these results in individual patients and even in isolated tachograms. The effect of HR and CI on the HRT that can be taken into account by denoising isolated tachograms, yielding a more accurate physiological description of HRT.

1. Introduction

Heart Rate Turbulence (HRT) is the physiological response to a spontaneous ventricular premature complex (VPC). In normal subjects, it consists of an initial acceleration and its subsequent deceleration of the sinus heart rate. It has been shown to be a powerful risk stratification predictor in patients with high-risk of cardiac disease [1, 2]. Assessment of the HRT is often made by using the so-called VPC-tachogram, which is constructed by averaging the RR-intervals sequences surrounding isolated tachograms. The aim of this averaging procedure is to re-

duce the noise that masks the HRT pattern.

The HRT is mostly assessed by means of two parameters, namely, the Turbulence Onset (TO) and the Turbulence Slope (TS). The former representing the amount of sinus acceleration following a VPC, and the latter representing the rate of sinus deceleration after the sinus acceleration [2]. HRT probably reflects the baroreflex activity triggered by an inefficient hemodynamic ventricular contraction, and hence, the VPC prematurity should modulate the HRT. The influence of other several factors has been well documented [2], specifically, the heart rate (HR) modulates the strength of the HRT response, with reduced HRT at higher HR.

The usual procedure to assess the HRT implies averaging all the available isolated VPC tachograms to construct the VPC-tachogram, in which TS and TO are computed. However, this procedure can mask the influence of different physiological factors, since it assumes that all HRT responses to isolated tachograms as equivalents, when they may have different physiological conditions, leading to different HRT patterns, and therefore different TS and TO values. In [3], the impact of the VPC prematurity on the HRT was studied in a population. A method to take into account the impact of HR was developed in [4], but demanding a large number of valid individual tachograms.

The aim of this work was to quantify the modulation of the HRT by two physiological factors, namely, the HR and the CI. We studied 11 patients referred for electrophysiological (EP) studies. Sequences of single ventricular extrastimuli were delivered with different CI and drug-controlled HR. These physiological factors were compared with TS and TO parameters obtained from isolated tachograms, by using a previously tachogram denoising method based on support vector machine (SVM) regression [5].

The structure of the paper is as follows. In Section 2, the denoising processing method, as well as the dataset and the method to assess the relationship between HRT and physiological variables, are presented. In Section 3, the

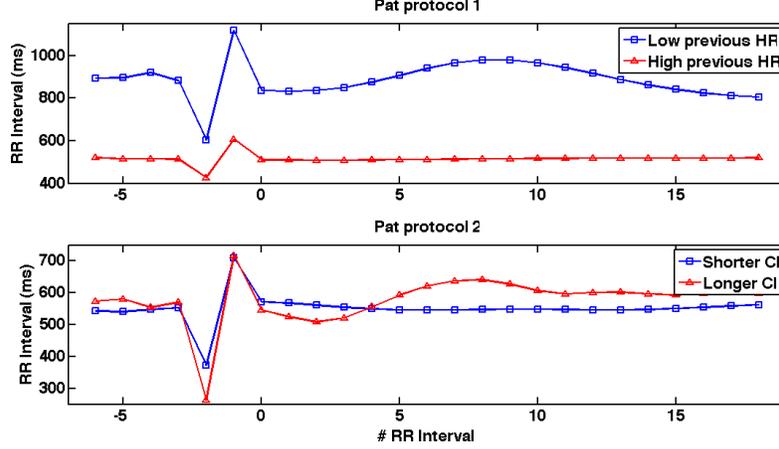


Figure 1. Top panel: two local tachograms, from a patient in Protocol–I, denoised with the SVM processing at two different conditions, namely low previous HR (no-isoproterenol) and with high previous HR (isoproterenol). Bottom panel: two local tachograms, from a patient in Protocol–II, denoised with SVM processing at two different CI values.

results are reported. Finally, in Section 4, conclusions are summarized.

2. Methods and data

2.1. SVM filtering method

The HRT signal comprises around 15-20 beats, so it is an extremely short signal duration for conventional denoising or filtering techniques. The RR intervals in the local tachogram under study are denoted by $\{x_n, n = 1, \dots, 20\}$, and it is composed by two contributions, one given by the actual HRT response to be estimated, $\{s_n, n = 1, \dots, 20\}$, and the other (to be filtered out) given by noise contributions from different sources, $\{e_n, n = 1, \dots, 20\}$. The HRT signal model is then

$$x_n = s_n + e_n, \quad n = 1, \dots, 20 \quad (1)$$

The filtering method used in this paper is based on a SVM modeling approach, previously developed in [5]. The SVM regressor can be seen as a nonparametric procedure, in the sense that it does not rely on any specified form of the HRT. Also, considered the ε -Huber cost [6], which represents a cost function that can adapt to the noise distribution. Due to the short length of the signal, non-parametric bootstrap resampling is used for free parameter tuning. The SVM nonlinear regression model is given by

$$x_n = s_n + e_n = \langle \mathbf{w}, \phi(n) \rangle + b + e_n \quad (2)$$

where $\phi(n)$ is a nonlinear application of n to a possibly high-dimensional (say P -dimensional) feature space \mathfrak{F} , where a linear approximation is built by the dot product with vector $\mathbf{w} \in \mathfrak{F}$. The time series model for a sample

at time instant m is:

$$\hat{s}_m = \sum_{n=1}^{20} (\alpha_n - \alpha_n^*) \langle \phi(n), \phi(m) \rangle + b \quad (3)$$

which is a weighted function of the nonlinearly observed times in the feature space, and where $\alpha_n^{(*)}$ are the Lagrange multipliers solving the optimization problem (see details in [5]). Only a reduced subset of the Lagrange multipliers is nonzero, which are called the *support vectors*, and the HRT solution is built in terms of them.

In this work we used a *Gaussian Mercer's* kernel, given by

$$K_G(t, u) = \exp\left(-\frac{(t-u)^2}{2\sigma^2}\right) \quad (4)$$

where σ is the width of the Gaussian kernel, and it must be properly chosen. For a fixed value of σ , it is fulfilled that $K_G(t, u) = \langle \phi(t), \phi(u) \rangle$ in some unknown feature space. Thus, the final solution of SVM for HRT denoising can be expressed simply as

$$\hat{s}_m = \sum_{n=1}^{20} (\alpha_n - \alpha_n^*) K_G(n, m) + b \quad (5)$$

which is just a linear combination of shifted Gaussian kernels of a given width. Errors due to finite observations lengths are compensated by mirrorizing the extrema [7].

2.2. Ventricular extrastimuli protocol

We included 11 patients referred for EP studies in the Hospital Universitario Virgen de la Arrixaca (Murcia, Spain). The study was approved by the local Ethics Committee and all participants granted a signed informed

consent. The investigational protocol was performed during sinus rhythm at the end of the EP study after ablation procedures. Sequences of 10 single ventricular extrastimuli were delivered every 20 seconds from the apex of the right ventricle. The study was subdivided in two protocols, one to analyze the influence of HR on HRT (Protocol–I, with 5 patients), and the other to study the combined influence of HR and coupling interval on HRT (Protocol–II, with 6 patients). The HR was modified in Protocol–I by using isoproterenol, so that 10 VPC were delivered with and without isoproterenol. In Protocol–II there were two stages. Phase–I, 10 VPC were delivered without isoproterenol and with extrastimuli prematurity starting at 80% of the preceding sinus RR-Interval, and decreasing it by 70 ms each extrastimuli. Phase –II, 10 VPC were delivered with isoproterenol (high HR) and with the same extrastimuli prematurity control.

In Protocol–I, we studied the impact of the HR on the HRT pattern, as quantified by TS and TO in each filtered isolated tachogram. Previous HR was computed as the average of the 3 sinus RR-Interval preceding the VPC. The impact was evaluated for each patient individually. Figure 1 (top panel) shows two filtered local tachograms from a patient in Protocol–I, with basal HR (no-isoproterenol) and with high HR (with isoproterenol).

In Protocol–II, we studied the combined influence of the HR and the prematurity of the VPC (coupling interval) on the HRT, quantified by TS in each filtered local tachogram, for each patient individually. Figure 1 (bottom panel) shows two filtered local tachograms from a patient in Protocol–II, with two different CI values. In order to quantify the impact of these factors the TS parameter was sorted according to the normalized coupling interval (NCI) [3], computed as:

$$NCI = \frac{\text{Coupling Interval}}{\text{Preceding Sinus Interval}} \quad (6)$$

and the slope of the linear regression was used to assess the attenuation in the HRT due to the coupling interval.

3. Results

Table 1 shows the results obtained in Protocol–I. The values of TS and TO parameters (mean±standard deviation) are reported, with (high previous HR) and without (low previous HR) isoproterenol. Every patient (except patient 2) showed a decreasing in the TS parameter and an increasing in the TO parameter. These results agreed with the hypothesis that higher previous HR lead to attenuated HRT [2]. In some cases, the attenuation due to the HR led to values previously documented as pathological in the literature [2]. Figure 2 shows a box-plot representing the TS and TO parameters versus the previous HR in patient 5.

Pat	Previous HR(ms)	TS	TO
pat 1	$HR_l = 986.35$	26.75 ± 17.55	-4.62 ± 4.88
	$HR_h = 676.91$	14.64 ± 8.48	-0.83 ± 4.37
pat 2	$HR_l = 792.24$	4.76 ± 2.00	-1.85 ± 3.40
	$HR_h = 639.33$	4.98 ± 3.40	-0.60 ± 3.00
pat 3	$HR_l = 700.56$	6.18 ± 4.29	-1.00 ± 2.57
	$HR_h = 641.16$	5.91 ± 2.30	-0.86 ± 2.02
pat 4	$HR_l = 1088.02$	24.06 ± 11.74	-6.29 ± 2.78
	$HR_h = 870.06$	18.65 ± 9.54	-5.23 ± 3.31
pat 5	$HR_l = 786.30$	13.76 ± 7.37	-3.84 ± 2.11
	$HR_h = 514.69$	2.03 ± 1.87	-0.73 ± 1.00

Table 1. Protocol–I. TS and TO parameters computed on each filtered local tachogram (mean±standard deviation). Previous HR was computed as the mean of the 3 sinus RR-interval preceding the VPC, for both no-isoproterenol (low HR, HR_l) and isoproterenol (high HR, HR_h) conditions.

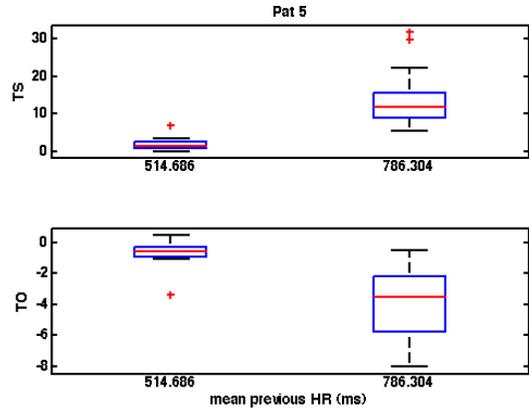


Figure 2. TS and TO parameters versus the previous HR. HRT parameters were computed on each filtered local tachogram for patient 5 in the Protocol–I.

Table 2 shows the results in Protocol–II. The slopes of the regression lines between TS parameters and NCI , correlation coefficient r , and TS (mean±standard deviation) were calculated for each patient and both phase–I (low previous HR) and phase–II (high previous HR). Both phases showed a decreased HRT with increasing NCI (except for one phase in one patient). The slopes decreased with increased HR. Hence, when HRT is attenuated by the HR factor, the impact of the CI is reduced. Figure 3 shows an example of a patient in Protocol–II for both phases.

4. Conclusions

We assessed the relationship between the HRT and the local physiological variables responsible for the modulation of the HRT, namely the HR and the coupling interval, using SVM denoised isolated tachograms.

To analyse the impact of HR and coupling interval in HRT modulation, a study with 11 patients referred to EP

Pat	Previous HR(ms)	<i>TS</i> vs <i>NCI</i>		<i>TS</i> (m±std)
		Slope	<i>r</i>	
pat 1	$HR_{ph1} = 946.42$	-0.143	0.50	6.67 ± 4.82
	$HR_{ph2} = 697.56$	-0.039	0.536	1.33 ± 0.91
pat 2	$HR_{ph1} = 577.12$	-0.324	0.512	16.70 ± 10.68
	$HR_{ph2} = 457.69$	0.076	0.2	6.65 ± 6.88
pat 3	$HR_{ph1} = 730.47$	-0.00	0	2.77 ± 1.25
	$HR_{ph2} = 606.80$	-0.064	0.55	1.96 ± 1.51
pat 4	$HR_{ph1} = 454.90$	-0.037	0.40	5.48 ± 1.54
	$HR_{ph2} = 350.19$	-0.050	0.34	4.28 ± 1.89
pat 5	$HR_{ph1} = 711.51$	-0.340	0.60	17.29 ± 8.23
	$HR_{ph2} = 609.62$	-0.069	0.2	11.20 ± 5.49
pat 6	$HR_{ph1} = 961.09$	-0.047	0.23	15.22 ± 3.13
	$HR_{ph2} = 720.41$	-0.116	0.56	14.25 ± 6.12

Table 2. Slopes of regression lines between *TS* and *NCI* for patients in Protocol-II for both phase-I HR_{ph1} , and phase-II HR_{ph2} . Pearson's correlation coefficient is also reported, as well as *TS* values (mean±standard deviation)

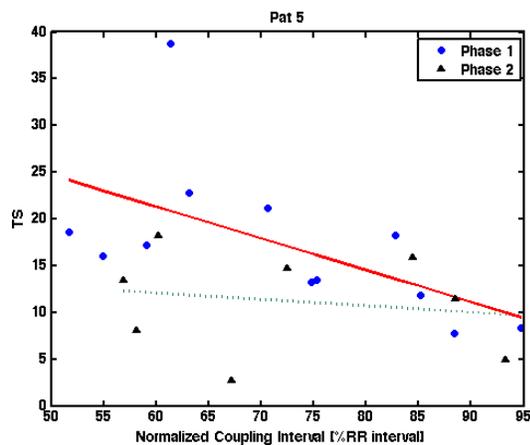


Figure 3. Relationship between the *TS* parameter and the *NCI* for phase-I and phase-II and their regression lines, solid-line phase-I, and dotted-line phase-II.

studies was made. Filtering local tachograms using SVM approach allowed, for the first time, to study the relationship between HRT and its main physiological modulating factors, on individual patients. The findings of this work are in agreement with previous ones in populational studies[3, 4]. Both, populational and individual analysis, are aligned with the baroreflex source hypothesis of the HRT. Hence, the more premature the VPC, and the higher the HR, the stronger the HRT. Filtering isolated tachograms allowed to take into account the impact of the HR and the CI when assessing the HRT, which could improve the prognostic value of the HRT.

Further studies will investigate how to incorporate the information of the physiological conditions in which a VPC occurs, e.g. by some standardization of the HRT to the HR and CI.

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