Heart Rate Turbulence

Physician’s Guide

2020044-105 Revision A

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Contents

Introduction

Manual Overview

Revision History

Each page of the document has the document part number and revision letter at the bottom of the page. The revision letter identifies the document's update level.

Revision History, PN 2020044-105		
Revision	Date	Comment
A	1 November 2005	Initial release of this manual, corresponds with version 1.0 of the Heart Rate Turbulence Software.

Purpose

This manual contains descriptions of Heart Rate Turbulence (HRT) and the measurement of HRT to help the clinician understand how the HRT measurement software works and how to most effectively use HRT applications. This manual contains an overview of HRT, examples of measurements made by GE systems, and the theory behind measuring HRT.

Intended Audience

This manual is intended for qualified health care professionals using the heart rate turbulence option in hospitals, doctor's offices, or other clinical environments.

Intended Use

The Heart Rate Turbulence (HRT) analysis program is intended for use in a hospital, doctor's office, or clinic environment under the direct supervision of a licensed health care practitioner. The intended use of the HRT analysis program is to analyze ECG signals, provide measurements of HRT in patients undergoing cardiovascular disease testing for interpretation by qualified by health care practitioners for the purposes of risk stratification and prediction of sudden cardiac death. The HRT analysis program only provides measurements, not interpretations. The HRT program is to be used in conjunction with the patient's clinical history, symptoms, and other diagnostic tests for final clinical judgment.

CAUTION
INTERPRETATION — Interpretation of the HRT analysis must be confirmed by a qualified physician or cardiologist, and should be used only as an adjunct to clinical history, symptoms, and the results of other non-invasive and or invasive tests.

Overview

Heart Rate Turbulence (HRT) is the physiological, bi-phasic response of the sinus node to premature ventricular contractions. It consists of a short initial acceleration followed by a deceleration of the heart rate. HRT can be quantified by two numerical parameters, namely the Turbulence Onset (TO) and the Turbulence Slope (TS). The underlying mechanisms of HRT have not been fully identified.

HRT is most probably an autonomous baroreflex. The premature ventricular contraction causes a brief disturbance of the arterial blood pressure (low amplitude of the premature beat, high amplitude of the ensuing normal beat). When the autonomic control system is intact, this fleeting change is registered immediately with an instantaneous response in the form of HRT. If the autonomic control system is impaired, this reaction is either weakened or entirely missing.

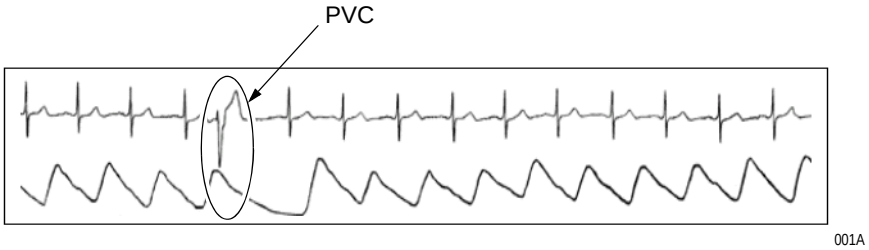
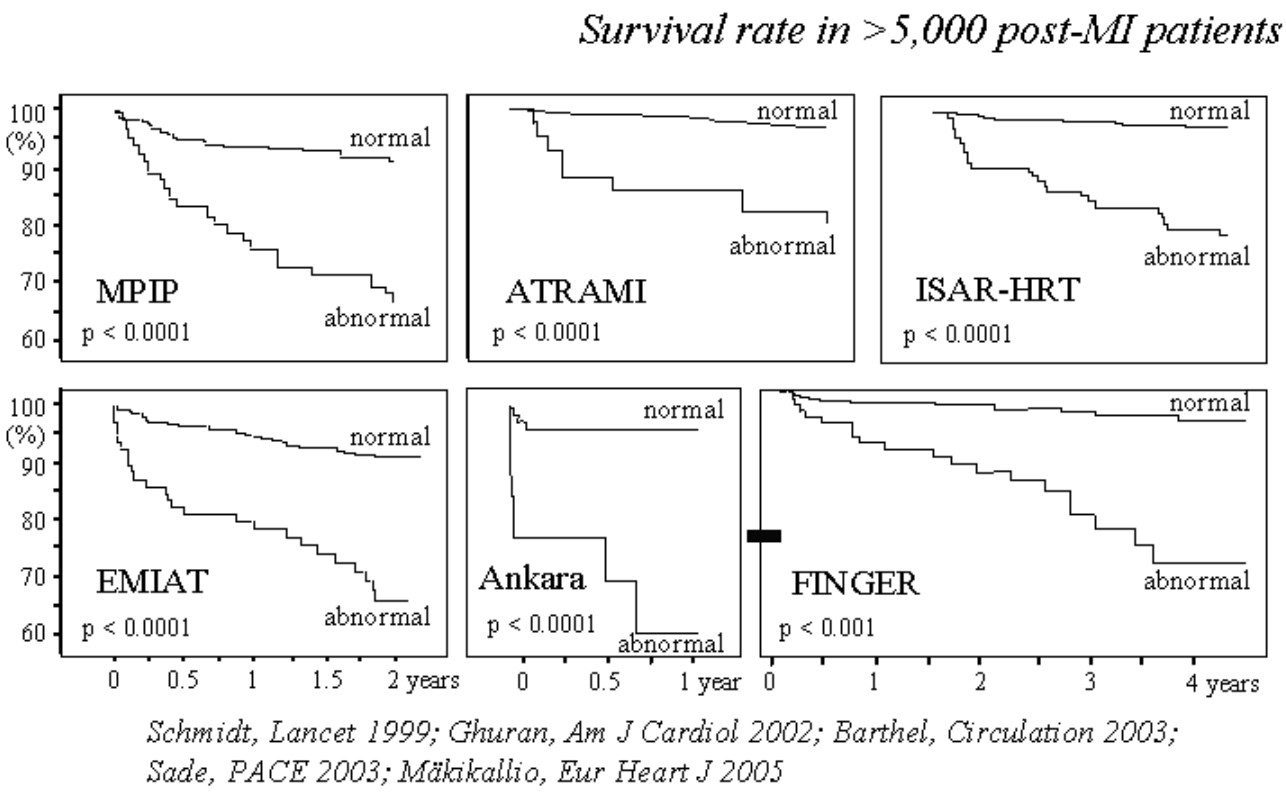


Figure 1

Figure 1 shows premature ventricular contraction (PVC) and its impact on the arterial blood pressure. The blood pressure has impact to the baroreceptors. HRT is most probably an autonomous baroreflex.

HRT analysis is suitable for assessing the risk following myocardial infarction. After analyzing the data of more than 5,000 post-infarction patients, it was established that HRT is — independent of other risk predictors — the most powerful ECG-related risk predictor.



Schmidt, Lancet 1999; Ghuran, Am J Cardiol 2002; Barthel, Circulation 2003; Sade, PACE 2003; Mäkikallio, Eur Heart J 2005

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The predictive value of HRT is comparable with that of the ejection fraction of the left ventricle.

The HRT-Algorithm

Quantification of HRT

Turbulence Onset (TO) is the percentage difference between the heart rate immediately following PVC and the heart rate immediately preceding PVC. It is calculated using the equation

$TO = 100 * ((RR_1 + RR_2) - (RR_{-2} + RR_{-1})) / (RR_{-2} + RR_{-1})$

with RR_{-2} and RR_{-1} being the first two normal intervals preceding the PVC and RR1 and RR2 the first two normal intervals following the PVC. Initially, TO is determined for each individual PVC, followed by the determination of the average value of all individual measurements. Positive values for TO indicate deceleration of the sinus rhythm, and negative values indicate acceleration of the sinus rhythm.

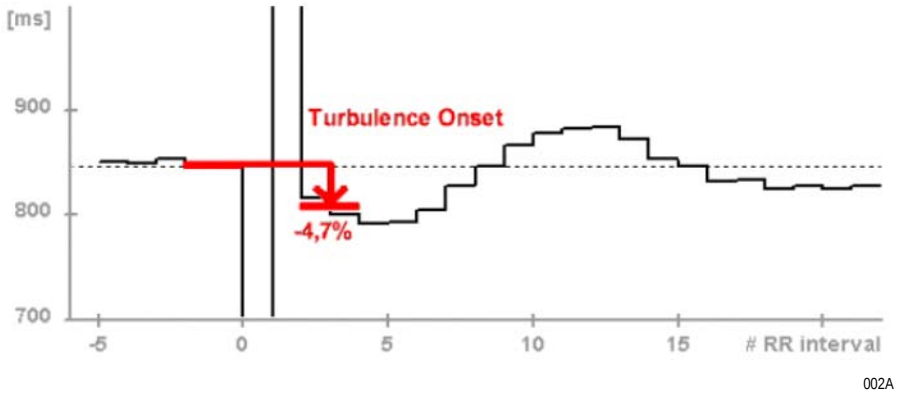


Figure 2

Figure 2 shows Turbulence Onset (TO) the percentage difference between the average value of the first two normal intervals following the PVC and the last two normal intervals preceding the PVC. Initially, TO is determined for each individual PVC, followed by the determination of the average value of all individual measurements.

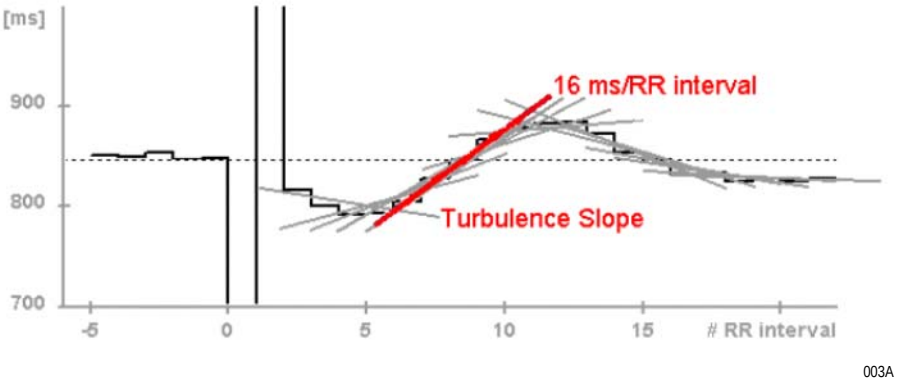


Figure 3

Figure 3 shows the TS, the steepest slope of a linear regression line through five consecutive measurement points in the averaged tachogram. The TS calculations are based on the averaged tachogram and expressed in milliseconds per RR interval.

Filters

The algorithm for HRT quantification can only deliver usable results if the triggering event was a true PVC (and not an artifact, T-wave or

something similar). Also, the sinus rhythm immediately preceding and following the PVC is free from arrhythmia, artifacts and false classifications. In order to fulfill these requirements, filters are used to reject HRT calculation. Rejection is provoked by RR intervals with the following characteristics:

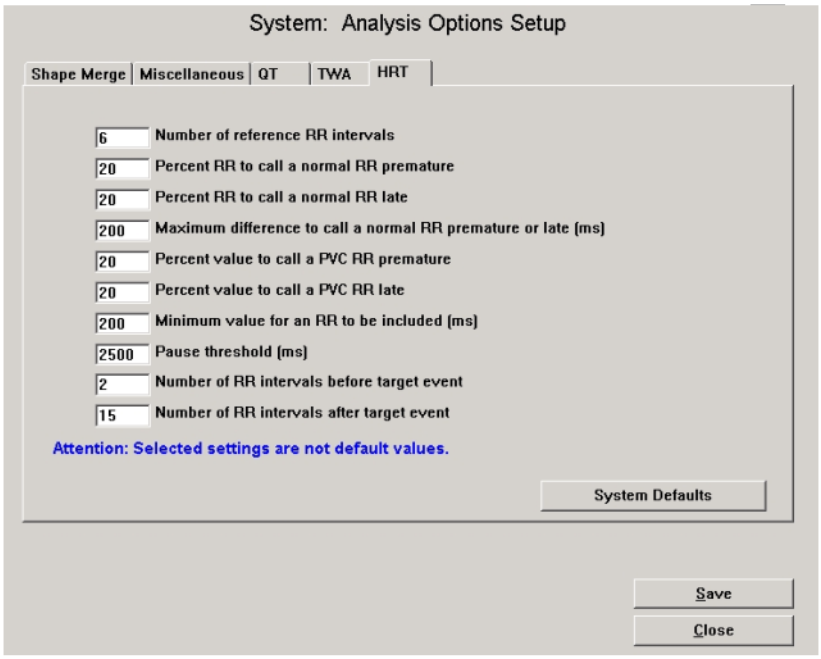
- < 200 milliseconds
- > 2500 milliseconds
- > 200 milliseconds difference to the preceding sinus interval
- > 20% difference to the reference interval (mean of the 5 last sinus intervals)

In addition, the HRT calculations are limited to PVCs:

- with a minimum prematurity of 20%
- with a post-extrasystole interval which is at least 20% longer than the normal interval
- having 2 normal RR intervals before
- having 15 normal RR intervals after

Analysis Option Definitions

The analysis options for HRT can be configured on the MARS system in *System >> System Setup >> Analysis Options >> HRT*.



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Turbulence Onset

This is the percentage difference between the averaged value of first two normal intervals following the PVC and the last two normal intervals preceding the PVC.

Turbulence Slope

This is the steepest slope of the linear regression through five consecutive measurements in the averaged tachogram.

Turbulence Correlation

This is the steepest correlation coefficient of the linear regression through five consecutive measurements in the averaged tachogram.

Reference Interval

The reference interval is the mean of the 5 normal to normal RR intervals prior to the trigger. The reference interval serves as a measure of the actual heart rate. Some RR interval filters used in the HRT algorithm refer to the reference interval, e.g. the 80% PVC coupling interval filter.

Single Premature PVC with Compensatory Pause

A PVC that is enclosed by normal beats AND with a coupling interval (the RR interval between the last normal and the PVC) that is less than 80% of the reference interval AND with a post-extrasystolic pause (the RR interval following the PVC) that is greater than 120% of the reference interval

This is the criteria for PVCs that are selected in the HRT algorithm.

Percent RR to Call a Normal RR Premature

For the calculation of the HRT tachogram, target sequences containing highly varying normal-to-normal intervals are eliminated. This value controls the amount of prematurity (expressed in percentage units) to exclude a target sequence. For example (with this limit set to 20%) a potential target sequence will be eliminated if it will include two consecutive normal-to-normal intervals (RR1 and RR2) such that RR2 < 0.8*RR1.

Percent RR to Call a Normal RR Late

This parameter is the same as previous one but used to control how late a normal RR interval will be. For example (with this limit set to 20%) a potential target sequence will be eliminated if it will include two consecutive normal-to-normal intervals (RR1 and RR2) such that RR2 > 1.2*RR1.

Max Difference to Call a Normal RR Premature or Late

The concept is the same of previous two variables, i.e. to control target sequences containing highly varying normal-to-normal intervals. This variable controls the absolute difference between two consecutive RR intervals. For example (with this limit set to 200 msec) a potential target sequence will be eliminated if it will include two consecutive normal-to-

normal intervals (RR_1 and RR_2) such that $RR_2 > RR_1+200$ or if $RR_2 < RR_1-200$.

Percent Value to Call a PVC RR Premature and Percent Value to Call a PVC RR Late

PVC related intervals are defined as the RR intervals directly adjacent to a ventricular premature beat, i.e. the coupling interval and compensatory pause. For the calculation of the HRT tachogram, target sequences are eliminated when the coupling interval or post-extrasystolic pause are shorter than a percent value of the reference interval. The two percent thresholds are controlled by the premature and late variables. For example (with both variables set to 20%), a target sequence will be eliminated if the coupling interval is > 80% of the reference interval or if the post-extrasystolic pause is < 120% of the reference interval.

Minimum Value for an RR to be Included

A target sequence will be eliminated if one of the RR intervals in the tachogram will be shorter than this limit.

Pause

A target sequence will be eliminated if one of the RR intervals in the tachogram will be longer than this limit.

RR Before

This variable determines how many RR intervals before the target events are included in the analysis. The code that draws the HRT tachogram considers this variable when determining the number of RR intervals to draw.

RR After

This variable determines how many RR intervals after the target events are included in the analysis. The code that draws the HRT tachogram considers this variable when determining the number of RR intervals to draw.

Assessment of the Heart Rate Turbulence Analysis Results

Identification of high-risk patients after acute myocardial infarction is essential for successful prophylactic therapy. The absence of the Heart Rate Turbulence after ventricular premature beats is a very potent postinfarction risk stratifier that is independent of other known risk factors and which is stronger than other presently available ECG-based risk predictors [1].

Absence of HRT is defined by the TO, the TS, and the combination of both TO and TS, namely:

Scenario 1 — TO > 0%, or

Scenario 2 — TS < 2.5 milliseconds/RR interval, or

Scenario 3 — TO > 0% and TS < 2.5 milliseconds/RR interval

The highest predictive power is shown in scenario 3.

With the population of the Multicentre Post-Infarction Program, and the population of the European Myocardial Amiodarone Trial, risk ratios of 3.2 were achieved [1]. In another population even a risk ratio of 5.9 was achieved [2]. The risk, or hazard ratio is calculated from Kaplan-Meyer survival curves, and is approximately the ratio of the percentages of those people who died with fulfilling the criteria for scenario 3 above and the percentage of those people who died without fulfilling the criteria for scenario 3 above.

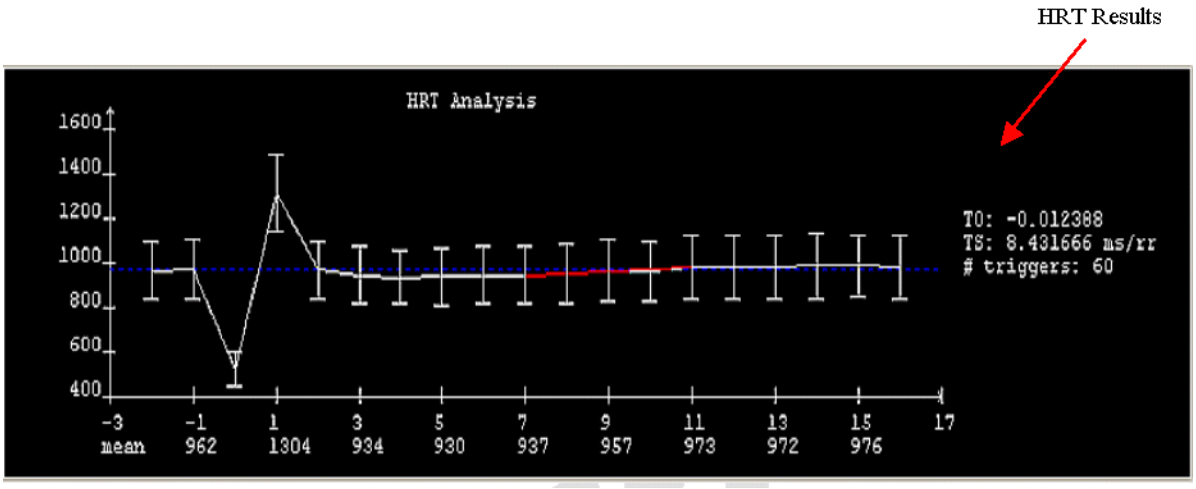

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Figure 4

Figure 4 shows the HRT analysis results of a low risk patient (TO < 0%, TS > 2.5 milliseconds/RR interval). The number of episodes with detected isolated PVCs (triggers) was 60. The averaged tachogram represents all detected episodes with a PVC that met the filter/inclusion criteria.

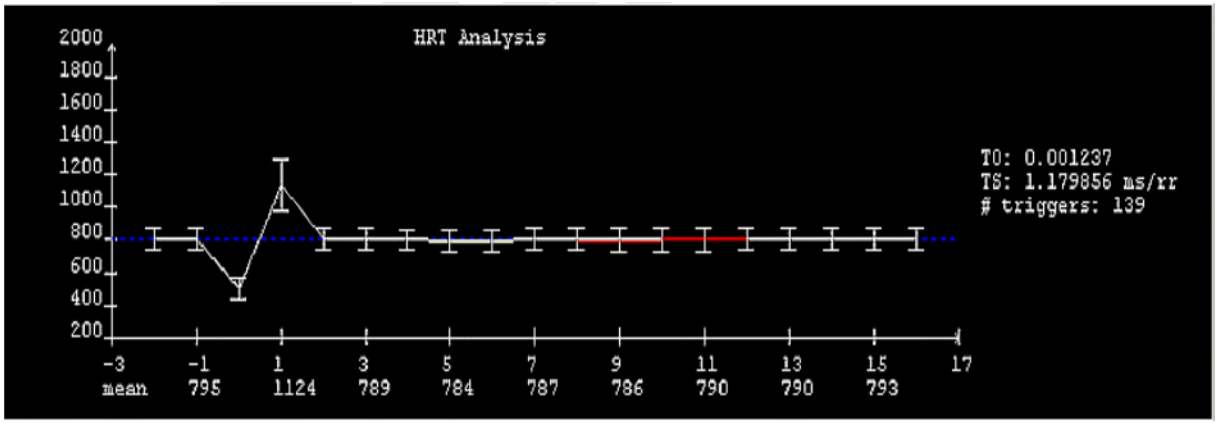

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Figure 5

Figure 5 shows the HRT analysis results of a high risk patient (TO > 0%, TS 2.5 milliseconds/RR interval). The number of episodes with detected isolated PVCs (triggers) was 139. The averaged tachogram represents all detected episodes with a PVC that met the filter/inclusion criteria.

Prerequisite for good HRT analysis results are true PVCs. Artifacts for example, when they are misinterpreted as PVCs, can change the representative average tachogram, causing the resulting TO and TS to become erroneous. Because of this, the HRT option has filters (see "Filters" on page 4) implemented to exclude tachograms with false positive PVCs. The filter settings are configurable by the user. Normally these filter settings are sufficient but it can be useful to change them in order to get better results for a single patient.

The HRT option provides graphical displays to give the user the possibility to assess the correctness of the averaged tachograms (see figures 4 and 5). Those possibilities are

- all used tachograms one upon the other (superimposed, see figure 6). Outliers are visible in this diagram.
- possibility to display every single tachogram, with the ability to delete it (see figure 7), removing it from the averaged tachogram. This is shown with the corresponding ECG episode.
- possibility to display every excluded tachogram (see figure 8).

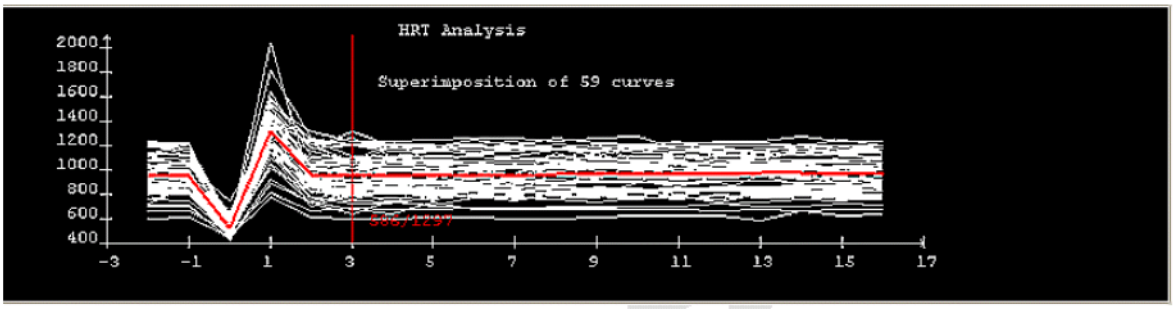

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Figure 6

Figure 6 shows all used tachograms one upon the other (superimposed).

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Figure 7

Figure 7 shows a single tachogram (above) together with the corresponding ECG episode (below). The user has the possibility to delete the tachogram, if it is not correctly labeled as a true PVC. After the deletion, it will not be part of the averaged tachogram, and it will not be included in the TO and TS measurements.

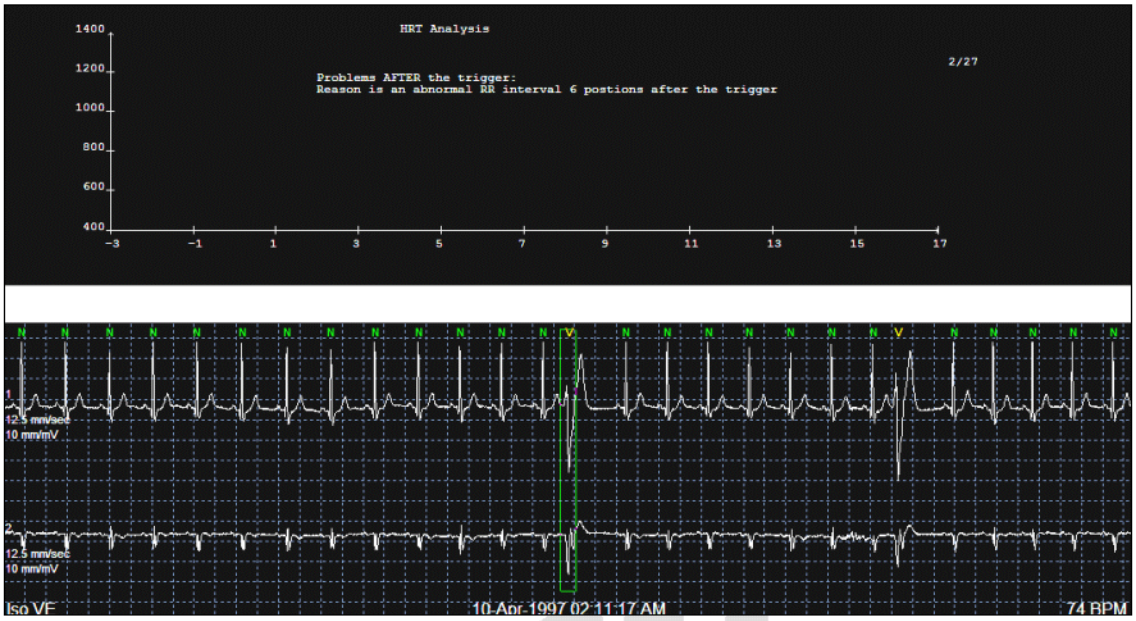

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Figure 8

Figure 8 shows an excluded single PVC (above) together with the corresponding ECG episode (below). The reason for its exclusion is the 2nd PVC, which is inside 15 RR intervals (see "Filters" on page 4).

Reports

Three different HRT report components are available for the HRT tool on the MARS Holter Analysis Workstation. These are configured in the *System* >> *System Setup* >> *Report Configuration* interface:

- HRT - Averaged Tachogram,
- HRT - Superimposed Tachogram, and
- HRT - Option Settings

These components may be included in any of the pre-defined report setups and/or be included in a user-defined report setup.

If the environment variable *HRT_RESEARCH_OUTPUT* is set to any value, a file containing the beat position and beat class for all triggers is written to a file. The file name is the slot file name without the .nat extension.

Limits of Heart Rate Turbulence Analysis

HRT is not always measurable. HRT obviously cannot be measured in patients who do not have PVCs. Also, it cannot be measured in patients with pacemaker rhythm or episodes of atrial fibrillation for the duration of the Holter recording.

Related Reading

Schmidt G. et al. Heart-rate turbulence after ventricular premature beats as a predictor of mortality after acute myocardial infarction. *Lancet* **353:**9162 1390–1396 (1999).

Barthel P. et al. Risk stratification after acute myocardial infarction by heart rate turbulence. *Circulation* **108** 1221–1226 (2003).

Ghuran, A. et al. Heart rate turbulence-based predictors of fatal and nonfatal cardiac arrest (The autonomic tone and reflexes after myocardial infarction substudy). *American Journal of Cardiology*; Vol. **89:**2 184–190 (2002).

Watanabe M.A. et al. Effects of ventricular premature stimulus coupling interval on blood pressure and heart rate turbulence. *Circulation*, **106** 325-330 (2002).

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