
HeRO[®] ES

Version 3.1
System Manual



MPSC
The Power To Predict

COPYRIGHT © 2015 BY MEDICAL PREDICTIVE SCIENCE CORP.
ALL RIGHTS RESERVED. UNAUTHORIZED REPRODUCTION IS STRICTLY PROHIBITED.

Do not alter, translate, transfer, disclose, or use these materials or any part thereof in any form by any means except by prior written authorization from Medical Predictive Science Corporation.

Medical Predictive Science Corporation, Inc. makes no warranties, express or implied, regarding these materials, including but not limited to any warranties of merchantability or fitness for a particular purpose. Medical Predictive Science Corporation, Inc. makes these materials available solely on an "as-is" basis. Medical Predictive Science Corporation, Inc. accepts no responsibility for altered or edited versions of these materials.

Medical Predictive Science Corporation, Inc. reserves the right to revise and improve its products as it sees fit. This publication describes the state of the product at the time of this publication only, and may not represent or describe the product at all times in the future.

Electronic Access to HeRO System Manuals

HeRO User Manuals are available in electronic form. To access the electronic copies of the documents, you will need a device connected to the Internet and have installed Adobe Acrobat Reader. There is a link to obtain Adobe Acrobat Reader on the HeRO website.

You can access the HeRO website by clicking "Help" from a HeRO screen, or by typing http://www.heroscore.com/Technical_Support.htm from a web browser. If you need help accessing the electronic copies of the documents or to request a printed copy at any time contact the appropriate representative on page 2 of this manual.

Single printed copies are available at no additional cost and will be delivered within seven days of receiving the request.

Document Number: MPSC-INS-1625 (R1.10)



EMERGO EUROPE
Molenstraat 15
2513 BH, The Hague
The Netherlands



HeRO, The Power to Predict, and the MPSC logo are trademarks or registered trademarks of Medical Predictive Science Corporation, Inc.

Microsoft and Windows are registered trademarks of Microsoft Corporation.

Contact Information

Distributor List

Austria

Connect Medizintechnik GmbH
Gspanngasse 4
A-2130 Mistelbach,
Austria
Ph: +43 2572 32400
FAX: +43 2572 20404
Email: office@connect-medizintechnik.at
Web: www.connect-medizintechnik.at

The Netherlands

Medisize bv
Edisonstraat 1
2181 AB Hillegom
PH: +31 (0)252-576 888
Email: info@medisize.com
Web: www.medisize.com

United Kingdom

SLE Ltd
Twin Bridges Business Park
232 Selsdon Road
South Croydon CR2 6PL, UK
Ph: +44 (0) 208 6811414 ext 251
Fax: +44 (0) 208 6498570
Web: www.sle.co.uk

Kuwait

Al-Essa Medical & Scientific Equipment Co.
W.L.L.
#118 Sector C, Street 33,
Shuwaikh Ind. Area, Kuwait
PH: +965 2 483 4510
FAX: +965 2 484 0629
Email: alessa@alessakuwait.com
Web: www.alessakuwait.com

Saudi Arabia

Gulf Neocare
PO Box 365899
Riyadh, 11391
Saudi Arabia
PH: +996 1 464 8545
Web: www.gulfneocare.com

Manufacturer and for all other Countries

Medical Predictive Science Corporation
2246 Ivy Rd, Suite 17
Charlottesville VA 22903 USA
T: +1 434-220-0714
Fax: + 1 240-220-6098
E-mail: info@heroscore.com
www.heroscore.com

EC Authorized Representative

Emergo European Authorized Representation
Molenstraat 15
2513 BH, The Hague
The Netherlands
Telephone: +31.70.345.8570
Fax: +31.70.346.7299

TABLE OF CONTENTS

Electronic Access to HeRO System Manuals	1
Contact Information	2
Distributor List	2
Manufacturer and for all other Countries	2
EC Authorized Representative	2
Introduction	5
Indications for Use.....	6
Contraindications	6
Precautions	6
Using this Manual.....	6
Overview	7
Server (only for HeRO ES Enhanced)	8
Network Data Acquisition Interface (NDAI; only for HeRO ES Enhanced).....	8
Viewing Stations (only for HeRO ES Enhanced)	8
Using HeRO ES	10
Setting Up.....	10
Viewing the HeRO Score	11
The HeRO ES Solo Window	11
Activating the HeRO ES Solo Window.....	12
Continuous HeRO Monitoring	12
Window Position and Size.....	12
HeRO ES Patient Window.....	12
Pausing an Alarm	13
Discharge Button.....	13
Scrollbar	13
Help.....	13
Viewing the HeRO Score on the HeRO viewing station (only for HeRO ES Enhanced)	14
Plan View.....	14
Pod View.....	16
Patient View.....	17
Status and Error Messages	18
Alarms	20
Admitting and Discharging Patients	21
Automatic Admit and Discharge.....	21

TABLE OF CONTENTS

Clearing Data Manually.....	21
Interpreting Results.....	22
Troubleshooting.....	23
Customer Service.....	26
Appendix A: Theory of Operation.....	27
Algorithms for Calculating RRI Parameters.....	27
QRS Detection.....	27
Data Packaging.....	28
Data Conditioning Prior to Calculation of HRV.....	28
Mathematical Analysis.....	28
Histogram Based Parameters.....	28
Sample Asymmetry Analysis.....	28
Sample Entropy.....	29
Mathematical Modeling.....	30
Logistic Regression.....	30
Fold Increase Score.....	30
HeRO Score.....	30
References:.....	31
Appendix B: Glossary.....	32
Appendix C: Use of HeRO Score in the Assessment of Infection.....	35

Introduction

HeRO provides an automated, noninvasive method to detect transient decelerations and reduced baseline heart rate variability. **HeRO** continuously acquires, records, measures and analyzes variations in RR Intervals, and provides ongoing display of this information.

HeRO is used to:

- Continuously acquire heart rate data from an existing physiological monitor
- Identify and determine the length of time between individual heart beats (the R-R Interval)
- Calculate a set of measures from these R-R Intervals to characterize the heart rate pattern
- Compute an “index” based on the degree of decelerations and reduced baseline variability in these patterns,
- Calculate the **HeRO** Score, which expresses the index as a fold-increase risk of sepsis relative to the overall NICU population, and
- Provide this information to clinicians in a timely and intuitive fashion.

HeRO ES is a stand-alone implementation of **HeRO** that processes heart rate data on the Philips Integrated PC (iPC) and shows the **HeRO** Scores at the bedside, on the main display of the physiological monitor.

HeRO ES Enhanced, is an optional upgrade that merges the functionality of **HeRO Symphony** and **HeRO ES** enabling a server based implementation and central monitoring while still displaying **HeRO** information on the physiological monitor.

Indications for Use

HeRO is intended to acquire, store, analyze, and report on ECG data collected from infants. **HeRO** is intended to be used by trained operators under the direct supervision of a licensed health care practitioner in a hospital neonatal or pediatric ICU environment.

HeRO is intended to be used for the analysis of the variability in RR Intervals (heart rate) and to report measurements of the variability of heart rate data (HRV). The HRV measurements reported by **HeRO** are specialized in nature, and intended to identify periods of transient decelerations and/or reduced baseline variability in the heart rate.

HeRO is intended to provide specialized HRV measurements and may detect arrhythmias, that when combined with other risk factors, can be used as an aid in assessing the risk of sepsis in infants. The use of the HeRO monitoring improves survival in very low birth weight neonates.

HeRO ES acquires data from a user-supplied ECG monitor, and requires a monitor with an integrated PC.

Installation, training, maintenance and support are to be performed by Medical Predictive Science Corporation employees or contractors who have been certified by Medical Predictive Science Corporation as qualified to perform such duties.

Contraindications

Patients with erratic, accelerated, or mechanically controlled irregular heart rhythms are not suitable for HRV evaluation. When shown, the ECG waveform displayed on the computer screen is not to be used for analysis of cardiac function.

Precautions


As is customary with good medical practice, the interpretation of any medical data should be made in conjunction with all other available medical history and diagnostic information about a patient. A low **HeRO** Score should never be used to deny or reduce treatment on a patient that is exhibiting clinical signs of sepsis.

Using this Manual

This manual is written for physicians, clinicians, nurses, care extenders and hospital IT personnel who are familiar with basic Windows software operation.

Clickable menu items or button names are designated by a box around the name, i.e. **Help**.

Labels of non-interactive graphs, or screen displays are indicated by bold type, i.e. **Main Menu**.

The  symbol is used in this manual and in the online help system to highlight warnings that could potentially affect patient care if not followed.

Overview

HeRO ES is a software application that runs on the Philips Integrated PC (iPC) option of the Philips Intellivue MX series physiological monitor. The iPC is a Windows PC that shares the screen and enclosure with the main patient monitoring hardware. HeRO ES acquires Heart Rate data from the patient monitor (over a dedicated internal network connection), computes hourly HeRO scores for the patient being monitored, and displays the results on the shared screen.

HeRO has no applied parts.

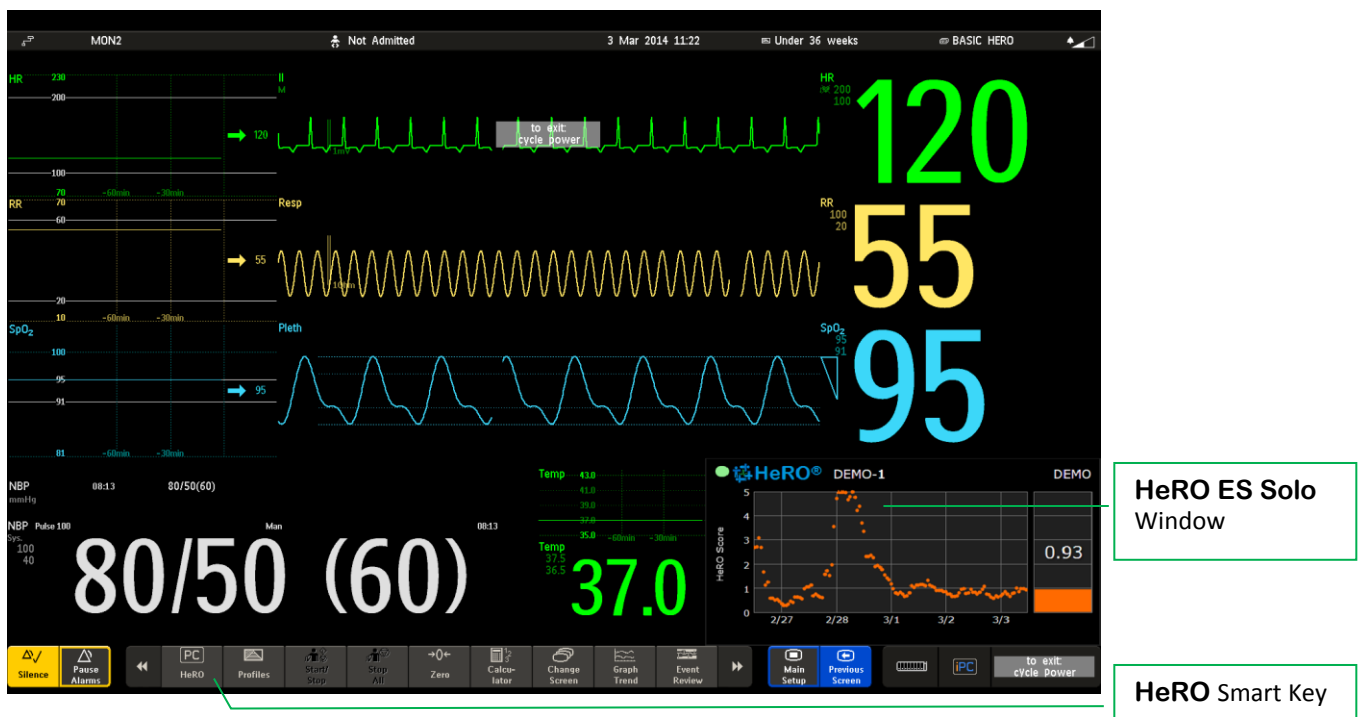


Figure 1: HeRO ES on the Philips Intellivue MX800 Physiological Monitor. In this example, the **HeRO ES** window is displayed along with the other vital signs using a dedicated screen layout that reserves space for the iPC display. Other screen layouts can be configured with or without the **HeRO ES** window. The patient monitor is typically configured to show the **HeRO** score on the default screen; users can change screens as needed in the course of patient care, then return to the **HeRO** screen as needed.

HeRO ES Enhanced, is an optional configuration that enables additional functionality by the incorporation of a **HeRO Server**. **HeRO ES Enhanced** consists of the iPC module installed in the physiological monitors, a Server, and one or more Viewing Stations. In this installation, the Server is configured to acquire data from the physiological monitor through the iPC.

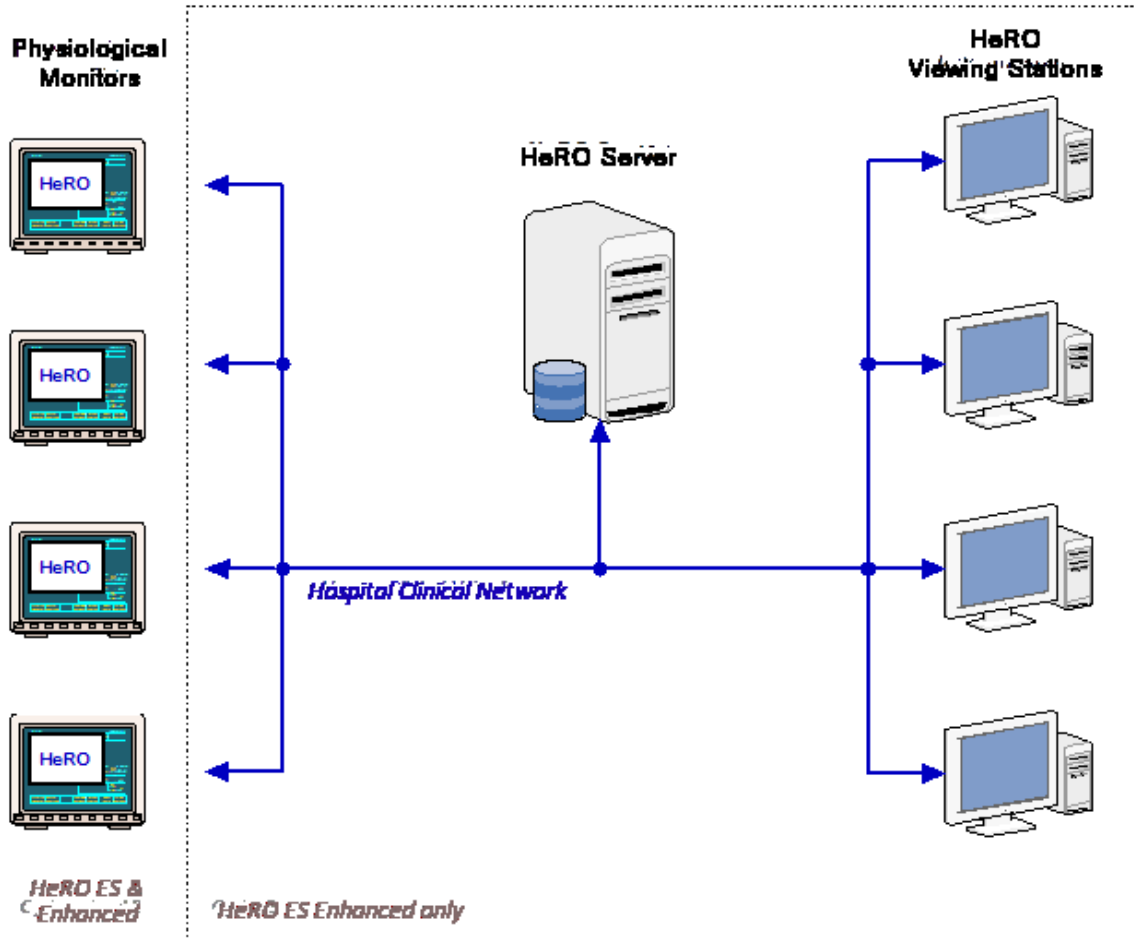


Figure 1: HeRO ES Enhanced Overview. The HeRO Server acquires the heart rate and patient demographics from the physiological monitor through the iPC.

Server (only for HeRO ES Enhanced)

The HeRO Server is a commercial server-class PC that is typically installed in a data closet or other similar location. It serves as the hub-of-the-wheel: it computes HeRO scores, stores the main HeRO database, coordinates patient transfers, and stores settings for the other components of the HeRO system.

Network Data Acquisition Interface (NDAI; only for HeRO ES Enhanced)

The Network Data Acquisition Interface (NDAI) is a software extension to HeRO ES that enables the Server to acquire heart rate data from the physiological monitor. This interface can also perform Patient Admit, Discharge, and Transfer (ADT) operations based on information retrieved from the physiological monitors.

Viewing Stations (only for HeRO ES Enhanced)

The Viewing Stations present the HeRO user interface to clinicians. In a typical installation, several dedicated viewing stations (small form factor computers with monitors) are deployed in

various points throughout the NICU. The system can also be configured to allow existing hospital PCs to access **HeRO** via web browser.

Using HeRO ES

Setting Up

The **HeRO ES** software shall be installed and configured by MPSC authorized technical personnel.

MPSC recommends that all Philips Integrated PCs (iPCs) that run **HeRO ES** be connected to a hospital intranet to facilitate license and software updates. In the case that the **HeRO ES Enhanced** option is installed, the iPC **must** be connected to the hospital intranet at all times. If required, additional network connections shall be the responsibility of hospital IT personnel.

If network problems arise, contact the hospital network administrator, or the local distributor listed on page 2 of this manual.

Viewing the HeRO Score

The HeRO ES Solo Window

The **HeRO** Score is shown on the **HeRO ES Solo Window**, which appears on the display of the Philips MX series monitor along with the other vital signs (see Figure 1).

The **HeRO ES Solo Window** displays the most recently computed **HeRO** Score as a numeric value, and also shows a graph that trends the values over the last five days.

HeRO ES computes a new **HeRO** score for the patient at the beginning of each hour (1:00, 2:00, etc). When a new patient is admitted to the monitor, it may take up to 3 hours for the first score to be shown.

HeRO ES will stop generating scores if the overall amount of data is insufficient or if there is not enough recent data to generate an accurate score. These gaps in the **HeRO** score trend can occur if the patient leaves the bed, or if the ECG signal is otherwise interrupted, for 30 minutes or more. When the ECG signal is restored, **HeRO ES** will resume generating scores as soon as enough new data is available. This may take up to an additional 3 hours.

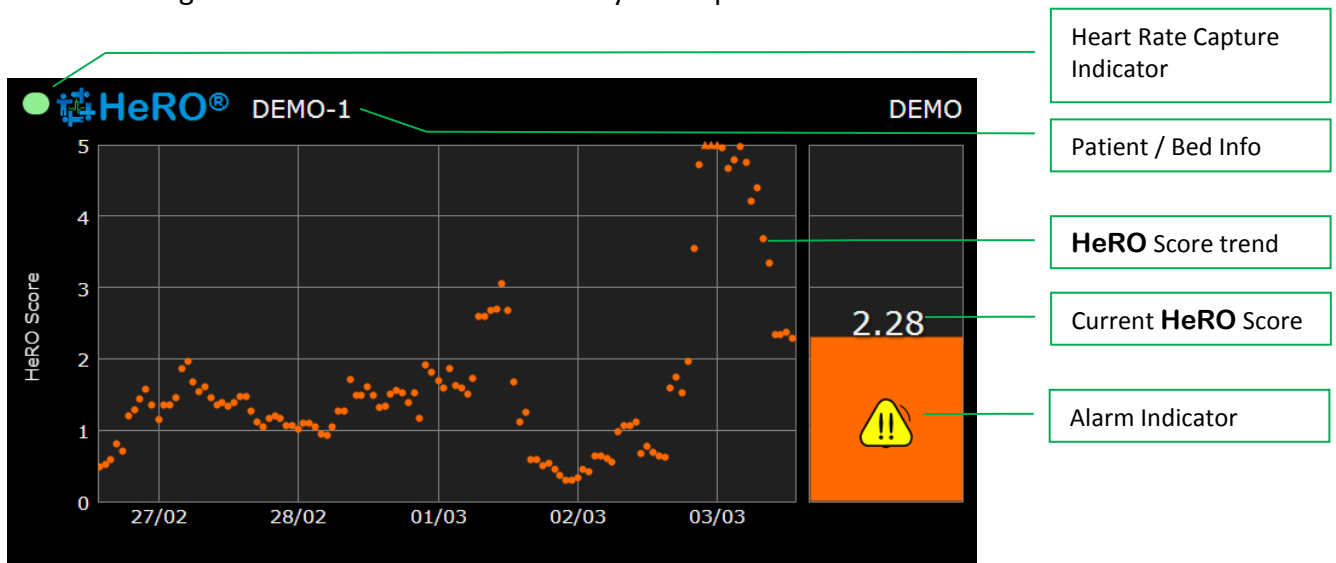


Figure 2. HeRO ES Solo Window. The main window displays the **HeRO** score as a numeric value and as a graphical 5 day trend, along with patient demographic information

Activating the HeRO ES Solo Window

Typically, the Philips Intellivue MX monitor and iPC are configured with a default screen layout that includes the **HeRO ES Solo Window**. If this is not the case, or if you have been using a different layout, you may need to manually activate the **HeRO ES Solo Window** by pressing the **HeRO** smart key on the Philips monitor (see Figure 1).

Continuous HeRO Monitoring

HeRO ES processes Heart Rate data and generates scores while the iPC is running, regardless of whether the **HeRO ES Window** is visible on the Intellivue screen. Therefore, it is perfectly acceptable to switch to other Intellivue screen layouts as needed without concern over disrupting **HeRO** monitoring. However, monitoring **is** interrupted while the iPC or the entire patient monitor is powered off.



HeRO monitoring is active only when the Philips iPC is running. The Intellivue MX patient monitor should be configured to automatically start the PC on power up. (To do this, enter Config mode, then select *Main Setup/Hardware/Internal PC/Auto Start PC/Enabled.*)

Window Position and Size

The typical **HeRO ES** configuration uses one or more dedicated Intellivue screen layouts that provide space for the **HeRO ES Window** to be shown alongside the other patient vital signs. In this configuration the window cannot be moved or re-sized.

HeRO ES Patient Window

The **HeRO ES Solo Window** is not interactive. In order to access interactive functions, you must activate the **HeRO ES Patient Window**, by switching to an iPC screen on the Intellivue that allows access to the Windows Taskbar, and clicking on the HeRO icon.

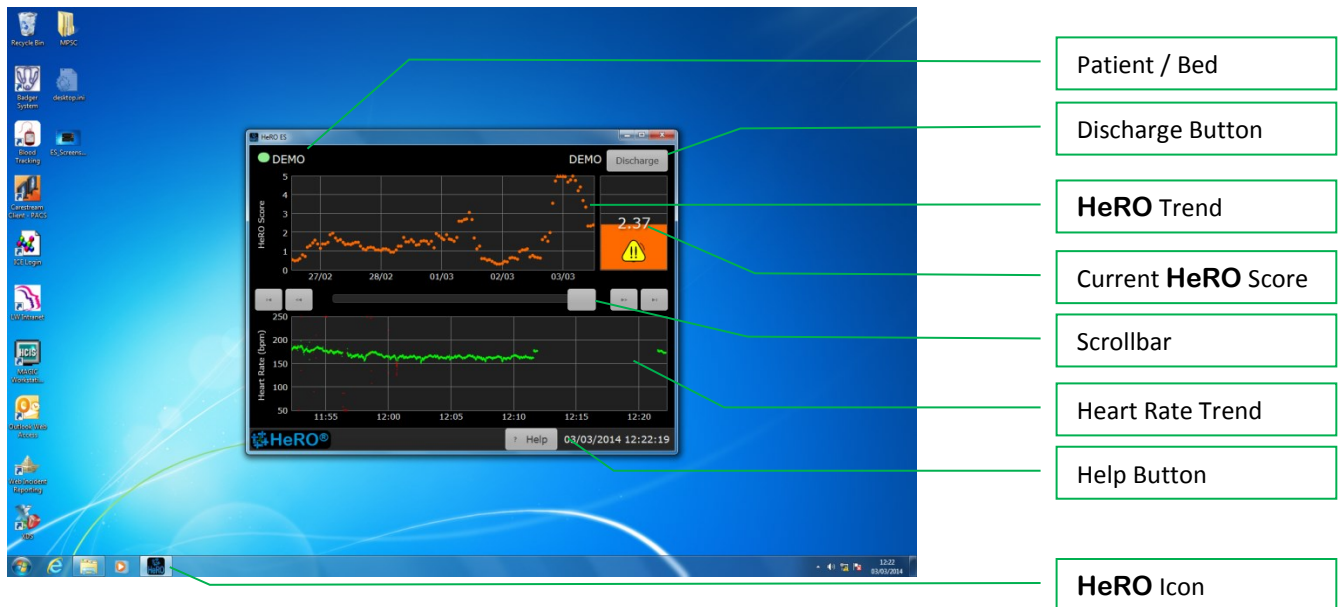


Figure 3. HeRO ES Patient Window. The main window displays the **HeRO** score as a numeric value and as a graphical 5 day trend, along with patient demographic information and a heart rate trend

Pausing an Alarm

HeRO ES includes a high score alarm to warn clinicians if a patient’s score rises above 2.0. When first activated, the alarm displays a flashing symbol. To pause the alarm (and stop the flashing), tap or click anywhere in the main area of the window, away from the edges. Refer to the section **Alarms** for more information.

Discharge Button

Deletes all data for the currently displayed patient. This feature is used to manually “reset” **HeRO ES** when the physiological monitor is connected to a new patient. Typically this is done automatically when the new patient is admitted to the Intellivue MX physiological monitor, but in some situations a manual clear function is useful. See the following section **Admitting and Discharging Patients** for details.

You will be asked to confirm the **Discharge** operation before any changes are made. Data collection will resume immediately and a new **HeRO Score** may take up to 3 hours to be generated.

In a **HeRO ES Enhanced** system, the **Discharge** button will only be available on the HeRO Viewing Stations, not the iPC.

Scrollbar

The scrollbar can be used to review Heart Rate and HeRO trend data. Click and drag the scrollbar button, or use the arrows to navigate.

Help

Displays the full user manual (this document).

Displays version information about **HeRO ES**.

Viewing the HeRO Score on the HeRO viewing station (only for HeRO ES Enhanced)

There are three display screens on the **HeRO** viewing station: the Plan View, the Pod View, and the Patient Detailed View. In all cases, a five day trend of the **HeRO** Score is plotted with the most recent score to the right.

Plan View

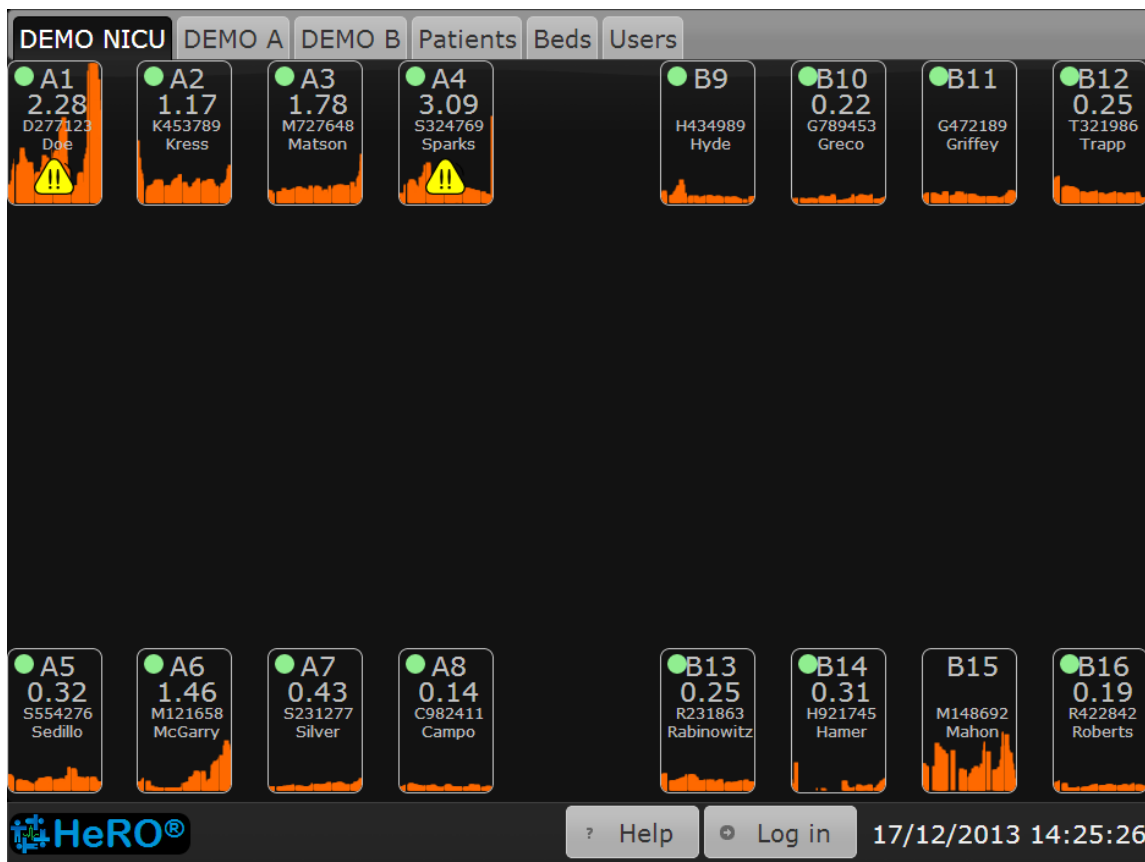


Figure 4. **Plan View** Screen. NOTE: The names and medical record numbers used in this and subsequent figures are fictitious, and do not represent real patients or users.

The **Plan View** (Figure 4) is a custom-designed view of the hospital unit. Each **Bed Icon** consists of the following elements:

- the bed number,
- a numeric display of the most recent **HeRO** Score,
- the patient medical record number and name (if a patient is assigned to the bed),
- a five-day trend of the **HeRO** Score, an alarm symbol, when appropriate, and
- a status indicator that is green when the system is receiving RR intervals or heart rate data for the bed, or gray otherwise.

In units that contain a large number of beds, the **HeRO** system can be configured with multiple **Plan View** screens, with each one covering a physical region within the unit.

The alarm is shown when the **HeRO** score is above 2.0. A flashing alarm can be paused by left clicking (or tapping, on touch screens) anywhere on the **Bed Icon**. Refer to the section **Alarms** for more information.

Clicking on a **Bed Icon** on the **Plan View** opens the **Patient View** screen for the patient assigned to that bed. Note that if an alarm is active, the first click on the **Bed Icon** will pause the alarm, and the second click will open the **Patient View**.

The system can be configured to obscure all identifying patient information on the **Plan View** and **Pod View**. In this case, the identifying information will become fully visible when a user logs in to the system by pressing the **Log in** button at the bottom right corner of the screen.

Click the **Help** button at the lower edge of the screen to display the help screen.

The **Bed Icon** may display informational or error messages to indicate problems or status changes. These messages, and their meanings, are summarized below. The messages differ based on the data acquisition method (DAD or NDAI) and, for NDAI installations, whether or not the interface is being used to provide patient admit/discharge/transfer information.

Pod View

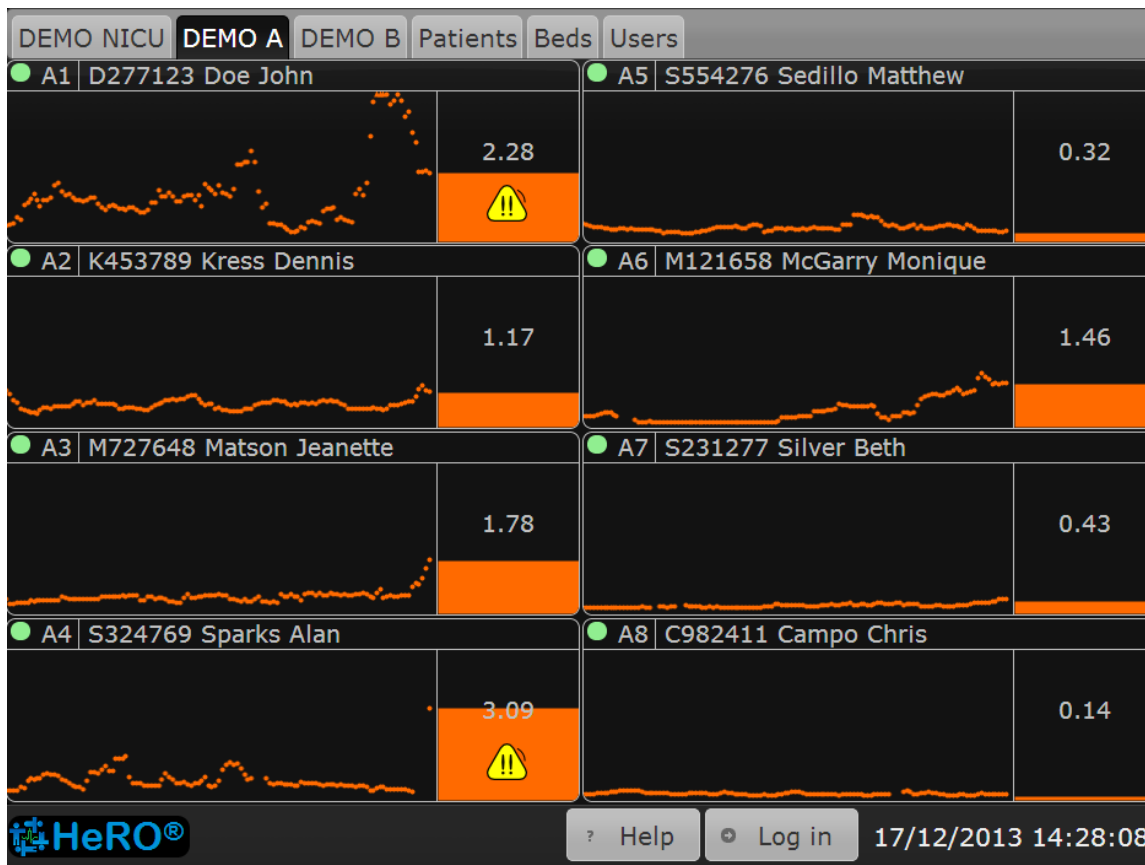


Figure 5. Pod View Screen

While the **Plan View** typically shows all beds in the unit, the **Pod View** provides a more detailed view of a small group of beds located in a particular section of the unit, with the icons arranged in a grid. A typical installation will be configured with multiple **Pod View** screens that collectively cover all of the beds in the unit. The elements composing each **Bed Icon** are similar to the **Plan View**:

- the bed number,
- the patient medical record number and name (if a patient is assigned to the bed),
- a five-day trend of the **HeRO** Score,
- a bar graph that shows the most recent **HeRO** Score,
- a numeric display of the most recent **HeRO** Score,
- an alarm symbol, when appropriate, and
- a status indicator that is green when the system is receiving RR intervals or heart rate data for the bed, or gray otherwise.

The alarm is shown when the **HeRO** score is above 2.0. A flashing alarm can be paused by left clicking (or tapping, on touch screens) anywhere on the **Bed Icon**. Refer to the section **Alarms** for more information.

As on the **Plan View**, clicking on a **Bed Icon** will show the **Patient View**. Note that if an alarm is active, the first click will pause the alarm, and the second click will open the **Patient View**.

The **Bed Icon** on the **Pod View** displays the same status and error messages as on the **Plan View**. Refer to the previous section for more information.

Patient View

The **Patient View** covers a single bed in the unit, providing a much more detailed look at the **HeRO Score** than either the **Plan View** or **Pod View**. The **Patient View** on the HeRO Viewing Station is the same as the HeRO ES Patient Window. Please refer to the instructions in the manual for HeRO ES Patient Window, with the following exception.

In a **HeRO ES Enhanced** system, the **Discharge** button will only be available on the HeRO Viewing Stations, not the iPC.

Status and Error Messages

The bottom section of the **Main Window** may display informational or error messages to indicate problems or status changes. These messages, and their meanings, are summarized below.

Message	Description
Comm Error	<p>There are two cases where this error will apply. With HeRO ES, the system is unable to communicate with the Intellivue MX patient monitor. With HeRO ES Enhanced, the message will also appear when the HeRO Server is unable to communicate with the iPC. In both cases, No Heart Rate information is being collected, and no HeRO Scores will be generated.</p> <p>This message may appear for up to 60 seconds when the patient monitor is first powered up. If the message does not disappear, there may be a hardware problem or a configuration error.</p>
No Heart Rate	<p>The system is communicating with the Intellivue patient monitor but is not receiving heart rate data. This typically indicates that the patient monitor is not able to calculate heart rate values due to an absent, weak, or noisy ECG waveform. Check the leads or change the lead pair selection to improve the quality of the ECG waveform.</p> <p>If this warning appears while the Intellivue is steadily displaying a numeric heart rate value, there may be a hardware problem or a configuration error.</p>
No MR Number	<p>The system is receiving data from the physiological monitor serving the bed, but no Medical Record Number is specified for the patient admitted to the monitor.</p>
No Name	<p>The system is receiving data from the physiological monitor serving the bed, but no Name is specified for the patient admitted to the monitor</p>
MR # Conflict	<p>The physiological mointors for the affected beds are reporting the same Medical Record Number for the admitted patient.</p>
System Comm Error	<p>The HeRO ES window application is not able to communicate with the services that acquire data and generate HeRO Scores. This message may appear for up to 60 seconds when the patient monitor is first powered up.</p>



	If the message does not disappear, there may be a hardware problem or a configuration error.
Error processing data	An error occurred while assigning heart rate data and HeRO Scores to a patient.
Updating patient data...	Heart Rate and/or HeRO Score data is being updated for the current patient.
Updating scores...	HeRO ES is recalculating scores for the current patient.
Invalid License	The HeRO ES software license installed on the iPC has an invalid signature or is otherwise corrupt.
License Expired	The HeRO ES software license for this patient monitor has expired. HeRO ES will continue to generate scores for the current patient but will not generate scores for any patients admitted in the future.
License Expires in n days	This warning message indicates that the software license will expire in the indicated amount of time.

For more detailed information about these messages, and suggestions for diagnosing and resolving problems, refer to the **Troubleshooting** section of this manual. If the situation is not resolved by following the suggested steps, contact Technical Support at the local representative listed on page 2 of this manual.

Alarms

The **HeRO** system includes a visual high score alarm that is designed to draw attention to patients with elevated risk. The alarms activate when a patient’s **HeRO** Score rises to, or beyond, a threshold value of 2.0.

The alarm state is indicated by one of the two Alarm Symbols shown below.

State	Appearance
Off	Symbol not shown
Active	 Symbol shown with exclamation points flashing
Paused	 Symbol shown with exclamation points solid

An active alarm may be paused by tapping (or clicking on) the flashing symbol or the surrounding area. The alarm will now display the Paused symbol, which will remain visible until the alarm resets.

When the patient’s score drops below the threshold, an Active or Paused alarm will reset to the Off state, and the alarm symbol will disappear. The alarm is automatically re-armed such that it will activate if the threshold value is exceeded in the future.

The alarm system in **HeRO** is implemented in software and does not require separate testing. If **HeRO** is operating, the alarm system is functional.

Admitting and Discharging Patients

When a new patient is transferred into the bed being monitored by **HeRO ES**, it is necessary to clear the stored **HeRO** scores and heart rate data from the previous patient. This ensures that the displayed numeric score and trend graph are based solely on heart rate data from the new patient.

Automatic Admit and Discharge

HeRO ES can detect the name and Medical Record Number (MRN) of the patient currently admitted to the Intellivue MX patient monitor. When **HeRO ES** detects a change in the demographic information, it will automatically clear the old patient data and create records for newly admitted patients.

To take advantage of this automatic admit/discharge functionality, simply use the Admit and Discharge functions of the Philips Intellivue system. When a patient moves into a bed, **Admit** the patient to the monitor, specifying a valid MRN (one which is unique to that patient). When the patient leaves the bed, use the **Discharge** function to clear the patient data from the Intellivue. Note that it is not necessary to Discharge a patient that is leaving the bed temporarily but will soon return (e.g. for surgery).

Clearing Data Manually

If your work flow does not make use of the Admit and Discharge functionality of the Philips Intellivue system (that is, you do not admit patients to monitors or you leave “dummy” patients admitted all of the time), you must manually clear the **HeRO ES** patient data when moving a new patient into the monitored bed.

To manually clear patient data, click **Discharge** in the **HeRO ES Patient Window**. Finally, click **Yes** to confirm the operation.



You **must** use one of the above methods of handling Admit and Discharge operations to ensure accuracy of the displayed scores.

Interpreting Results

HeRO results provide a quantitative assessment of characteristic RR variability patterns, which may precede the clinical indications of developing illness. Clinical research has shown that reduced baseline variability and transient decelerations of heart rate (bradycardia) are related to fetal and neonatal distress¹. The **HeRO Score** is reported as a fold increase in risk of sepsis relative to the general NICU population.

HeRO HRV data provides a new tool for clinical assessment so that standard diagnostic and therapeutic decisions are better founded. As is customary with good medical practice, the interpretation of any medical test should be made in conjunction with all other available medical history and diagnostic information about a patient.

Patients with High HeRO Scores (>2.0) are 6x more likely to develop sepsis in the next three days than patients with Low HeRO Scores (<1.0). The HeRO system includes an alarm function to draw attention to these patients. Refer to the section **Alarms**.

A randomized controlled trial of 3000 VLBW infants demonstrated that patients whose HeRO Scores were displayed to clinicians experienced 22% fewer deaths than patients whose HeRO Scores were not displayed to clinicians.

The computational methodology used to determine patient status is described in **Appendix A: Theory of Operation**. **Appendix C: Use of the HeRO Score in the Assessment of Infection** provides numerous examples of HeRO trends around the time of clinically significant events.

Troubleshooting

For Technical Support, please contact the local distributor as listed on Page 2 of this manual.

Problem: **HeRO ES Solo Window** is not visible

Description: **Solo Window** is not shown on the Intellivue MX screen.

Cause	Resolution
iPC window is not visible	Change the screen layout on the Intellivue MX patient monitor to one that includes an iPC desktop window.
HeRO ES client application is not running	Manually start the HeRO ES client application via Philips smart key, XDS LaunchPad, Windows desktop shortcut, or Windows start menu.
iPC is not running	Manually start the iPC via the Philips menu (<i>Main Setup/Internal PC/Switch PC On</i>). Ensure that the Intellivue MX monitor is configured to automatically start the iPC when the monitor is powered up. (Enter config mode, then select <i>Main Setup/Hardware/Internal PC/Auto Start PC/Enabled</i> .)
iPC/XDS configuration error	Reconfigure the XDS display settings to restore proper operation of the shared screen. Contact Philips Technical Support if necessary.
iPC hardware problem	Contact Philips Technical Support

Problem: *Comm Error* message appears during normal use (not monitor start up)

Description: **HeRO ES** is unable to communicate with the Intellivue MX patient monitor.

Cause	Resolution
Intellivue and/or iPC are starting up	Wait for HeRO ES to initialize communication with the Intellivue (up to 60 seconds)
Internal iPC network error	Reboot the iPC
Configuration error	Contact MPSC Technical Support.
Hardware problem	Contact MPSC Technical Support.

Problem: *No Heart Rate* message is displayed.

Description: The system is not receiving heart rate data from the Intellivue MX patient monitor.

Cause	Resolution
Patient monitor is not attached to a patient or is not monitoring ECG.	None necessary. This is normal behavior.
Patient monitor is not able to calculate heart rate.	Check ECG lead placement and lead pair selection.
HeRO services are not operating correctly.	Contact MPSC Technical Support.

Problem: *System Comm Error* message is displayed during normal use (not monitor start up)

Description: The **HeRO ES** window application is not able to communicate with the services that acquire data and generate HeRO Scores.

Cause	Resolution
iPC is starting up	Wait for HeRO ES to initialize (up to 60 seconds)
Internal iPC network error	Reboot the iPC
Configuration error	Contact MPSC Technical Support.

Problem: *Error Processing Data* message is displayed

Description: An error occurred while assigning heart rate data and HeRO Scores to a patient.

Cause	Resolution
Internal database error	Reboot the iPC. Verify that proper operation is restored.
Database corruption	Contact MPSC Technical Support.

Problem: *HeRO Failed to Start* message is displayed

Description: The HeRO data processing services did not start.

Cause	Resolution
Internal iPC network error	Reboot the iPC.
Configuration error	Contact MPSC Technical Support.

Problem: *Invalid License* message is displayed

Description: The software license installed on the iPC has an invalid signature or is otherwise corrupt.

Cause	Resolution
License file has been tampered with or was otherwise damaged.	Contact MPSC Technical Support

Problem: *License Expired* message is displayed

Description: The software license has expired.

Cause	Resolution
Expired license	Contact MPSC Sales or Technical Support

Customer Service

If network problems arise, contact the hospital network administrator or Technical Support).

Complaints may be reported via telephone or submitted in writing to the local distributor as listed on page 2 of this manual.

Appendix A: Theory of Operation

HeRO uses sophisticated mathematical modeling techniques to analyze Heart Rate data for characteristic patterns of variability. In order to accomplish this, raw data must be screened and converted into a statistically useful form. Then, significant relationships must be calculated to determine the relative degree of transient decelerations and reduced baseline variability present in the heart rate data.

Algorithms for Calculating RRI Parameters

QRS Detection

The QRS detector of the **HeRO** system has been tuned for “quality”, not “quantity”. As such, observers may find that many seemingly valid QRS complexes are not identified by the system. This is consistent with the intended use of the device, which is to identify periods of transient decelerations and reduced baseline variability in the heart rate. As such, it is not as important that every single RR Interval be identified as it is that identified intervals be valid.

After the QRS detection algorithm identifies candidate QRS complexes, the corresponding intervals are checked for validity. Intervals that are outside of a range of +/- 20% of the mean of the last fifteen intervals are discarded. Also discarded are intervals whose difference from the previous interval is not within five standard deviations of the mean of the previous 512 differences. These rules are justified by the presence on all ECG waveforms of certain artifactual signals caused by myoelectrical noise, clinician interference, or other spurious inputs. When the signal-to-noise ratio of the true electrocardiograph drops below a certain level (caused by poor lead placement, inadequate electrode contact, etc), these spurious inputs can be mistakenly recognized as a QRS complex. The criteria for RR interval validation discussed above ensure that the subsequent HRV analyses are only performed on valid interval data.

While the rules above will inevitably lead to the rejection of some valid QRS complexes, and therefore to a bias toward reporting lower variability than actually exists, the system is still able to perform its intended function of identifying *reduced* variability and transient decelerations.

The operator can gain insight into the operations of the QRS detection algorithm and validation rules by observing the trends on the **Patient View** screen. On the ECG graph, QRS complexes marked with a green triangle indicate the termination of a valid RR Interval. Those with red marks indicate an invalid interval. Those with no marks indicate QRS complexes that were not identified by the system, and usually occur during or immediately after a spurious ECG signal. The **Heart Rate** trend plots this information against time. Points plotted in green represent valid RR intervals, points in red represent invalid RR intervals, while epochs of time in which QRS complexes were not identified are represented by “gaps” in the **Heart Rate** trend. Note

that subsequent data processing is not performed on data collected during time epochs in which the “gaps” occur, nor data marked as invalid.

Data Packaging

Sets of 4096 consecutive RR intervals are recorded, and the start and stop times noted. Each set represents 20 minutes (at a heart rate of 200 beats/min) to 41 minutes (at a heart rate of 100 beats/min). Sets with artifactual intervals are defined as:

- Lasting more than 45 minutes (heart rate less than 100 beats per minute)
- 5 consecutive minutes without detecting a heartbeat with valid RR interval values (at which point the RR interval is reset).

The data from these sets are not included in the analysis.

Data Conditioning Prior to Calculation of HRV

The mean RR interval is calculated on the raw data. The RR intervals are filtered by subtracting a $(2M+1)$ point moving average window

$$RR(n) = \frac{1}{2M+1} \sum_{j=-M}^M RR(n-j)$$

where n is the index of the RR interval (1 to 4096) and $M=100$. The standard deviation of the filtered RR intervals is calculated. Then each RR interval is divided by the standard deviation. The result is a set of high-pass filtered, normalized RR intervals with mean ≈ 0 and standard deviation ≈ 1 .

Mathematical Analysis

Histogram Based Parameters

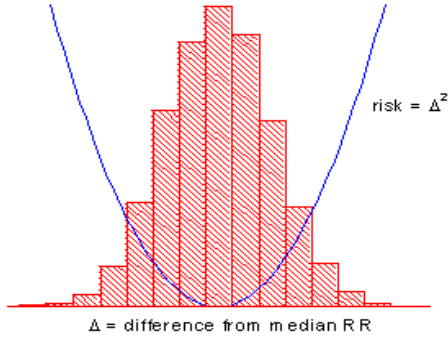
From each set of 4096 High-Pass filtered, normalized RR intervals, the 10th, 25th, 50th, 75th, and 90th percentiles and the first, second, third, and fourth moments are calculated.

Sample Asymmetry Analysis

One characteristic of transient decelerations is a marked asymmetry of the distribution of RR intervals accompanied by an occurrence of large deviations, especially to the right of the distribution median. This phenomenon is quantified through Sample Asymmetry analysis. The first step is to construct a quadratic function that will be used for weighting the deviation of each RR interval from a median, computed on a data block containing 4096 beats (approximately 25 minutes of data). The Figure presents a function $r(x_i) = (x_i - m)^2$, where x_i is the magnitude of an RR interval # i and m is the median of the data. The two branches of this parabola quantify deviations towards increase (right half) and decrease (left half) of an RR interval with respect to the median. Given a series of (4,096) RR intervals $x_1, x_2, \dots, x_{4096}$, we

compute $r_1(x_i)=r(x_i)$ if $x_i < m$, 0 otherwise; and $r_2(x_i)=r(x_i)$ if $x_i > m$, 0 otherwise for each RR reading x_i . Finally the R_1 (left asymmetry) and R_2 (right asymmetry) are computed as:

$$R_1 = \frac{1}{4096} \sum_{i=1}^{4096} r_1(x_i) \quad \text{and} \quad R_2 = \frac{1}{4096} \sum_{i=1}^{4096} r_2(x_i) \quad \text{respectively.}$$

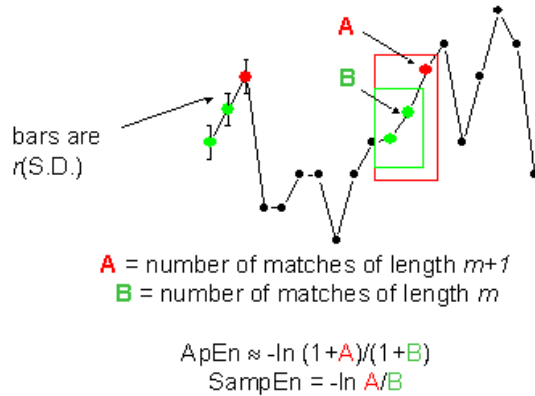


In other words, R_1 and R_2 are non-negative quantities that increase when the number and/or the magnitude of large deviations from the median increases. Intuitively, a distribution of RR intervals that is skewed to the right will result in $R_2 > R_1$.

Figure 6. Sample Asymmetry

Sample Entropy

Sample Entropy is a measure of regularity in time series that is suitable to HRV analysis². Sample Entropy (m,r,N) is the negative natural log of the conditional probability that two sequences similar within a tolerance r for m points remain similar at the next point, where N is the total number of points and self-matches are not included. A low value of SampEn is interpreted as showing increased regularity or order in the data. SampEn is very similar to approximate entropy (ApEn) but has reduced bias, especially for short data sets. Sample entropy (SampEn) is calculated with $m=3, r=0.2$ using filtered, normalized data³.



For regular, repeating data, A/B nears 1 and entropy nears 0.

Figure 7. Sample Entropy

Mathematical Modeling

Logistic Regression

Since no single measure will reliably detect all of the abnormal records, multivariable predictive mathematical models are employed. One such model is a **logistic regression**.

The mathematical model uses variables for HRV measures including standard deviation, sample entropy, and asymmetry function analysis.

These variables are inserted into a logistic equation of the form:

$$p = e^A / (1 + e^A)$$

where

$$A = \beta_0 + \beta_1 \bullet V_1 + \beta_2 \bullet V_2 + \dots \beta_n \bullet V_n$$

and where $V_{1\dots n}$ represent various measures of heart rate variability.

Fold Increase Score

The model output score is scaled by a constant to determine the Fold Increase Score. Computing this score is analogous to dividing a particular Logistic Regression score by the average Logistic Regression score seen in the overall NICU population. Thus, any score less than 1.0 is below average, while any score above 1.0 is above average. The Fold Increase Score is graphed on a scale from 0.0 to 5.0.

HeRO Score

The **HeRO** Score is generated by taking the maximum of two Fold Increase scores, each of which is ultimately derived from a Logistic Regression equation with unique coefficients. Each of the sets of coefficients has been developed to address a specific Heart Rate pattern. Combining the outputs of different sets of coefficients yields a more sensitive result than a single set of coefficients can.

Please see the section *Interpreting Results* for a discussion of the relevance of the HRV score.

References:

¹Griffin MP, Scollan DF, Moorman JR. The dynamic range of neonatal heart rate variability. *J. Cardiovascular Electrophysiology*. 1994; 5:112-124.

^{2,3} Richman JS, Moorman JR. Physiological time-series analysis using approximate entropy and sample entropy. *American Journal of Physiology*. 2000;278:H2039-2049.

Appendix B: Glossary

ANOVA: Analysis Of Variance

Area under Receiver Operating Characteristics: a plot of sensitivity vs. specificity at a variety of thresholds. A totally random test produces an ROC area of 0.5, while a perfect test produces an ROC area of 1.0

Artifact or artefact: Spurious signal not consistent with the expected results. May be produced by a defective machine, electrical interference, patient movement or loose electrodes.

Bradycardia: slow heart beat

Cubic spline: a commonly used interpolation technique

Cumulative Distribution Function (CDF): the cumulative sum of the histogram of a set of data

Demographics: Statistical characteristics of the population (in this case , significant demographics include birth weight, gestational age and post-conceptual age)

ECG (or EKG)= electrocardiogram: Record of the electrical activity of the heart, showing waves called P, Q, R, S, and T waves. The Q, R, S and T waves are related to contraction of the ventricles

Fiduciary point: the single point representing the R-wave in a QRS complex

Gestational age: Prenatal age of fetus from conception to birth

High-pass filtering: a signal processing technique that removes low-frequency and DC components of a signal

Histogram: graph of frequency distribution by means of rectangles whose widths represent class (R-R) intervals and whose areas are proportional to the corresponding frequencies

HR: Heart Rate

HRV: Heart Rate Variability

Kurtosis: The peakedness or flatness of the graph of a frequency distribution (especially with respect to the concentration of values near the mean as compared with the normal distribution)

Logistic regression: a regression model that fits binary outputs to the curve represented by $e^a/(1+e^a)$

Model Output: Results of mathematical equation computed hourly; based on demographic data and/or RRI parameters collected in the preceding 12 hours (ex. Demographic Risk Model, HRV Score)

Moment: the expected value of a positive integral power of a random variable

Moving average window: A filter that averages a signal over a “window” of time

Normalization: Process by which a statistical moment is altered by subtracting the mean and dividing by the standard deviation, so that the Mean = 0 and the SD = 1.

P50: 50th percentile data point

Post-conceptual age: Current age of neonate, from conception to present

Reduced Baseline Variability: epochs of heart rate data in which the trend has "gone flat" or has less variability in the baseline heart rate. This is invariably linked to a decrease in the second moment (standard deviation).

ROC: Receiver Operating Characteristic

R-R Interval or RRI: Interval between heartbeats

RRI Parameter: A statistic computed on an RRI set of 4096 interval (ex. “M1” = mean of RRI)

RRI Set: 4096 consecutive heartbeats (R-R intervals)

SD: Standard Deviation

SEM: Standard Error of the Mean

Signal processing: The process of breaking down an electrical signal into components that can be analyzed through a variety of algorithms

Skewness: Lack of symmetry in a frequency distribution. A symmetrical histogram has a skewness of 0, while a histogram with a tail of values larger than the median has a positive skewness.

Transient Deceleration: epochs of heart rate data in which the trend indicates a deceleration of the heart rate, for a period of roughly 30-100 heart beats (transient period), followed by an acceleration. These patterns are reflected by a decrease in Sample Entropy.

Appendix C: Use of HeRO Score in the Assessment of Infection

HeRO Clinical Instructions

The HeRO Score is to be used as another piece of adjunctive information in the assessment of sepsis.

The HeRO Score represents the fold-increase in risk that a particular patient will develop sepsis in the next 24 hours. For each patient monitored, the HeRO Score is generated each hour, based on the last 12 hours of heart rate data. Abnormal Heart Rate Characteristics (transient decelerations and reduced baseline variability) are detected and quantified by the HeRO algorithms to render the HeRO Score. The HeRO Score is considered:

- Low** if it is less than 1.0,
- Intermediate** if it is between 1.0 and 2.0,
- High** if it is above 2.0.

The HeRO Score is to be used alongside existing clinical observations such as increase in apneas and bradycardias, increase in oxygen or ventilation, feeding intolerance, hypotonia, lethargy, temperature instability, hypotension, grunting, vomiting, jaundice, shock, petechiae, purpura, or abdominal distention.

HeRO Score

	Not measured	Low	Inter-mediate	High
Not measured	1.0	<1	1-2	>2
0	0.7	0.5	1	2.5
1	2	1	2	4
≥2	3	3	3	4

Figure 1. Sepsis Risk Scorecard. From Griffin, 2007, Heart Rate Characteristics and Clinical Signs in Neonatal Sepsis.

Appendix C: Use of HeRO Score in the Assessment of Infection

An elevated HeRO Score is not a diagnosis of sepsis; it is an indication that sepsis is more likely. While an elevated HeRO Score should arouse suspicion of sepsis, diagnosis must be confirmed with other clinical signs, laboratory work, and/or culture results.

Conversely, a low HeRO Score does not rule out sepsis; it indicates that sepsis is less likely. A patient that has a low HeRO Score, yet is exhibiting signs and symptoms of sepsis, should be evaluated without regard to the low HeRO Score. A low HeRO Score should not be used to withhold treatment.

Figure 1 shows a table for bedside use in estimating the risk of impending sepsis in the NICU using a clinical score and HeRO monitoring. The clinical score assesses points for the following conditions used in diagnosing sepsis: apnea, increased ventilatory support, temperature instability, lethargy or hypotonia, feeding intolerance, I:T ratio, WBC, and hyperglycemia. When neither the clinical score nor the HeRO Score is measured, the fold-increase in risk of illness is 1.0. The clinical score alone differentiates infants across a spectrum of risk, as does the HeRO Score. Knowledge of both allows greater refinement in the estimation of risk. For example, an infant with a clinical score of 0 generally has lower risk of illness, but the concurrent finding of a high-risk HeRO Score identifies a subset with 2.5-fold increase in risk. For infants with 2 points or more, that is, with clinical findings of illness, knowledge of the HeRO Score adds little and even a low-risk HeRO Score does not cancel out the clinical presentation. This is in keeping with the idea that the HeRO Score is adjunctive to clinical information, and is not a standalone substitute for medical personnel.

Other than sepsis, there are many reasons for an elevated HeRO Score. It is believed that an elevated level of circulating cytokines early in sepsis causes the SA node of the heart to respond abnormally to the parasympathetic and sympathetic branches of the autonomic nervous system. Hence, any condition that is believed to result in cytokine release is also likely to cause elevated HeRO Scores. These conditions include urinary tract infection, necrotizing enterocolitis, intraventricular hemorrhage, and respiratory distress, among others. It is also well known that anesthetics and vasodilators affect the autonomic nervous systems. Hence, patients returning from surgery or after a routine eye exam will have elevated HeRO Scores.

The HeRO Score can also be driven artificially low. Steroids are well known to suppress immune system activity, and thus cytokines. Patients on steroids have been observed to be in a state of super-variability in heart rate, thus driving their HeRO Scores down.

In most cases of sepsis, the HeRO Score correlates with the clinical symptoms: e.g. apneas and bradycardias are increased, the patient is feeding intolerant, the temperature is unstable, and the HeRO Score is rising. In very rare cases, even in the presence of these other clinical abnormalities, the HeRO Score will remain low. However, the power of the HeRO System lies in the fact that in most cases of sepsis, the HeRO Score is an early manifestation of sepsis. In such a case, where the HeRO Score is high but the patient is clinically normal, the clinician is instructed to obtain lab work and treat based on the results. If the lab work returns normal, the clinician should continue to observe the patient. However, if the lab work is abnormal, the clinician should perform a sepsis work-up and initiate broad-spectrum antibiotic therapy. The culture results should be used to guide or discontinue future therapy.

Appendix C: Use of HeRO Score in the Assessment of Infection

Interpretation Examples

The following screenshots from the HeRO System represent one patient's stay in the NICU while monitored by the HeRO System (note that the HeRO Scores were generated but not displayed to clinicians). While the number of events experienced by this patient is unusual, the course of stay offers a remarkably broad set of clinical scenarios for interpretation.

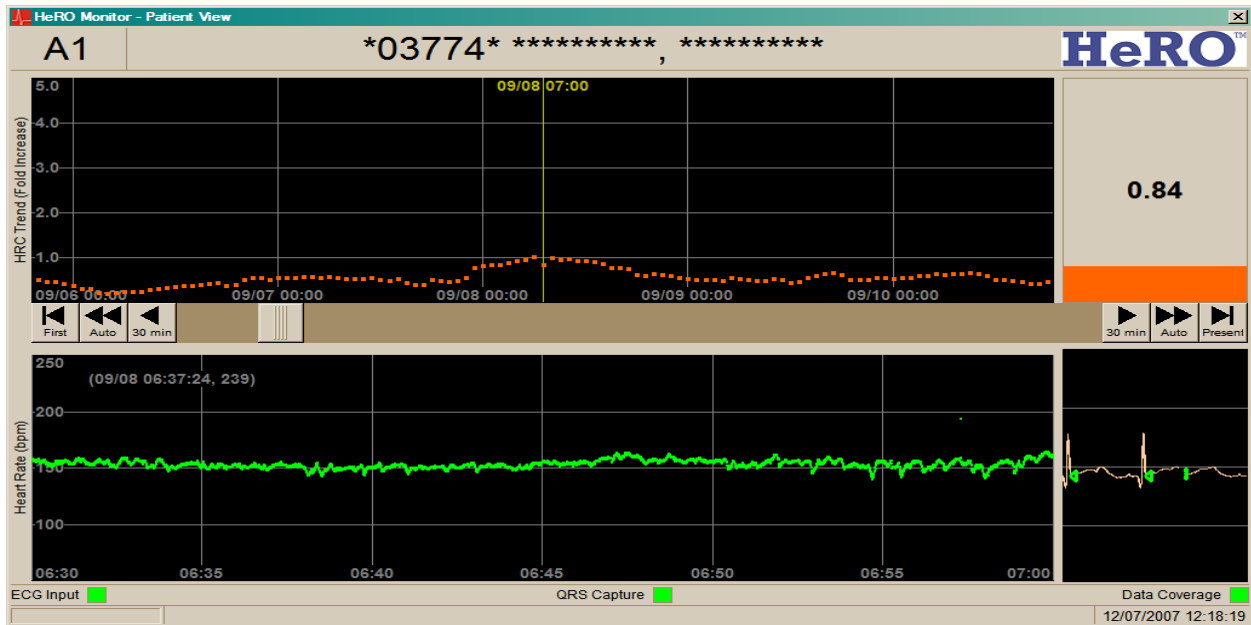


Figure 2

Patient presents as a Caucasian female, 770 grams at birth, 24 weeks gestational age. HeRO Scores were generated for this patient, but not displayed to clinicians. Clinical annotations are marked in blue. During the initial days in the NICU, the HeRO Score trends low. During the course of this example trend, the clinician is instructed to take no action based on the HeRO Score, although treatment should not be withheld if clinical signs of sepsis are present.

Appendix C: Use of HeRO Score in the Assessment of Infection

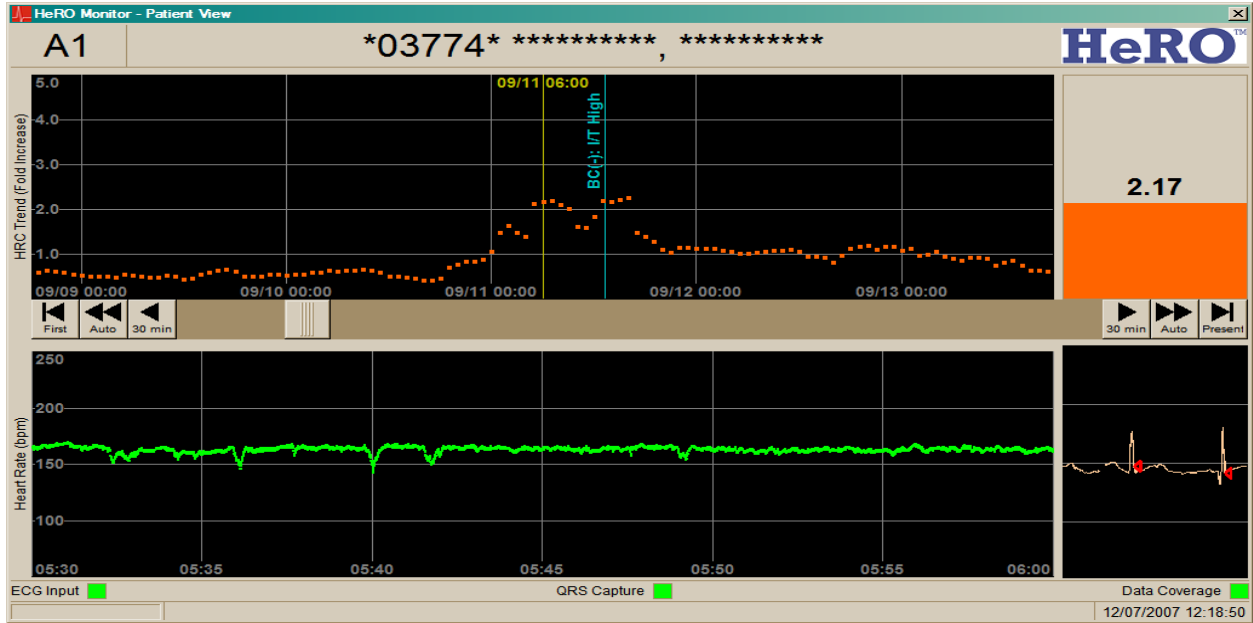


Figure 3

At approximately twelve days of age, the patient exhibits episodes of reduced heart rate variability punctuated by transient decelerations. This causes the HeRO Score to rise approximately 12 to 18 hours prior to an episode of clinical sepsis (i.e. sepsis observed clinically and treated with antibiotics without confirmation by blood culture). In this example, if the HeRO Score were present, the clinician is instructed to obtain the lab work when the HeRO Score first went above 2.0, eight hours prior to the culture time.

Appendix C: Use of HeRO Score in the Assessment of Infection

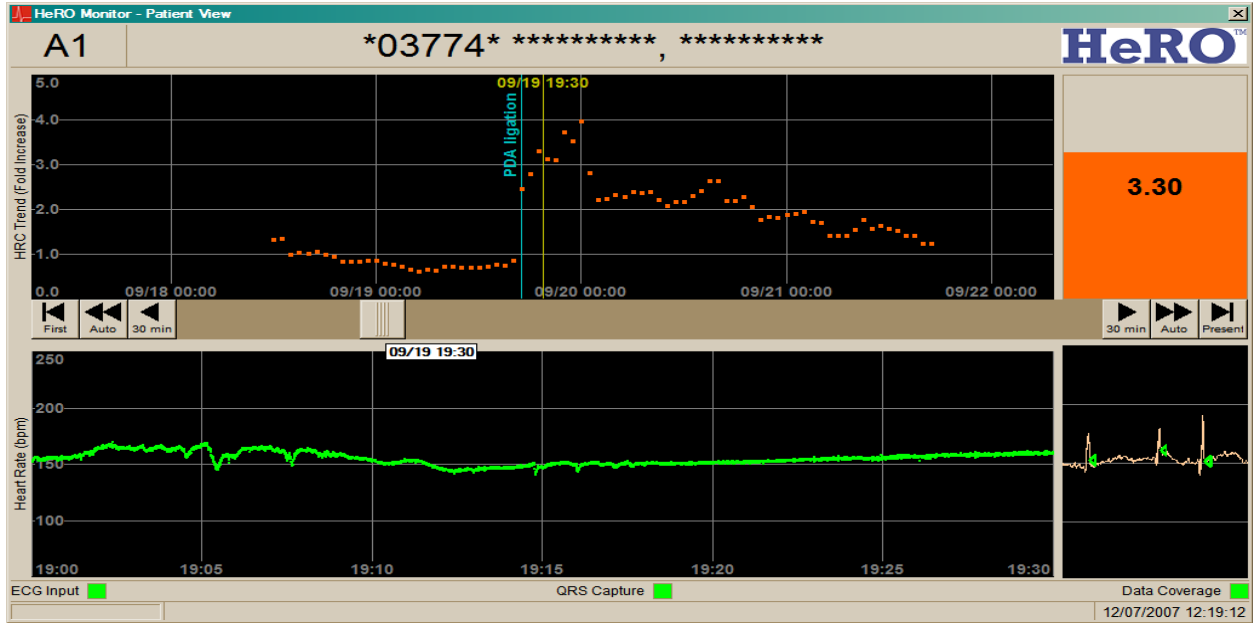


Figure 4

At approximately three weeks of age, the patient returns from surgery. Anesthesia results in a complete loss of variability in the heart rate, and a corresponding elevation in the HeRO Score. Over the next 48 hours, variability returns to the heart rate and the HeRO Score returns to normal. In this example, the clinician is instructed to ignore the elevated HeRO Score because it was caused by anesthesia.

Appendix C: Use of HeRO Score in the Assessment of Infection

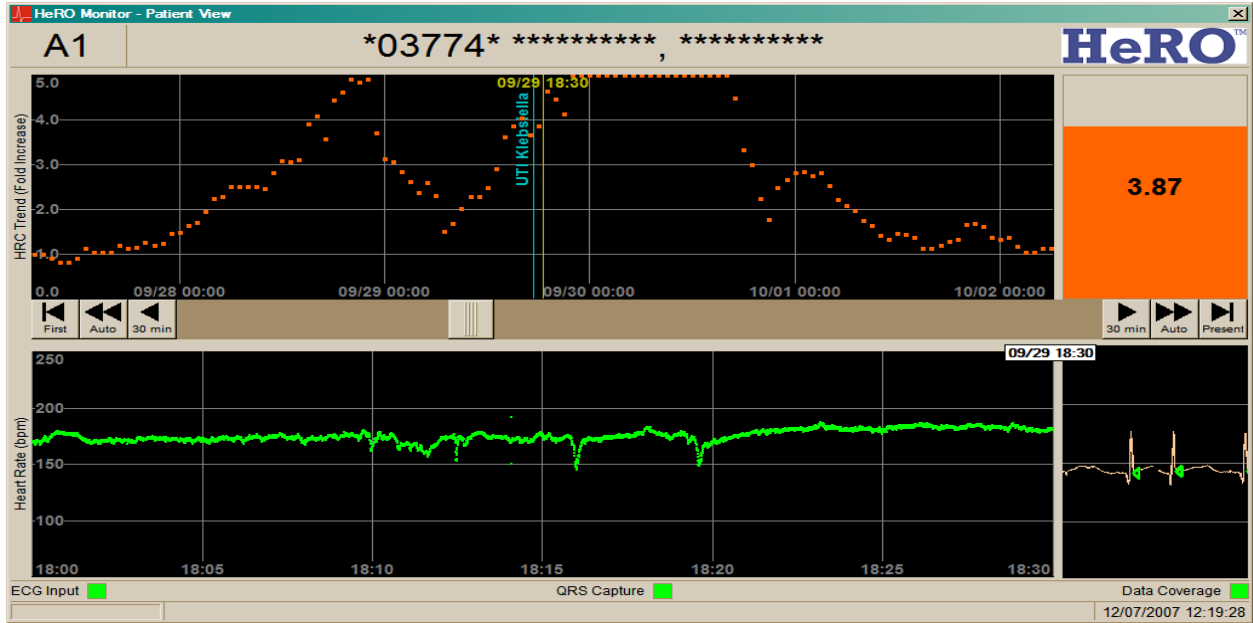


Figure 5

At approximately four weeks of age, the patient again exhibits a loss of variability punctuated by transient decelerations, resulting in a spike in the HeRO Score that begins approximately 36 hours prior to the diagnosis of Urinary Tract Infection with *Klebsiella* (the blue line indicates the time the culture sample was taken). In this example, the clinician is instructed to begin lab work at the first elevation of the HeRO Score above 2.0, approximately 36 hours prior to the urine culture.

Appendix C: Use of HeRO Score in the Assessment of Infection

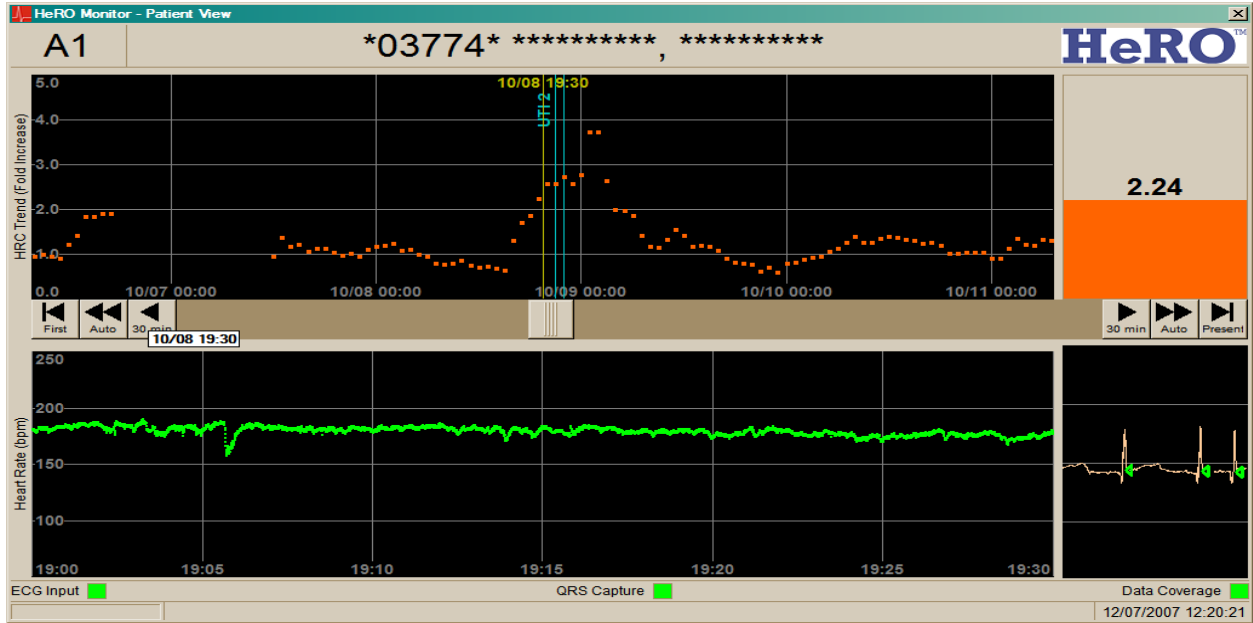


Figure 6

At approximately six weeks of age, the patient's HeRO Score again spikes, in this case 3 to 5 hours prior to diagnosis of another UTI. In this example, the clinician is instructed to begin lab work at the first elevation of the HeRO Score above 2.0, approximately two hours prior to the urine culture.

Appendix C: Use of HeRO Score in the Assessment of Infection

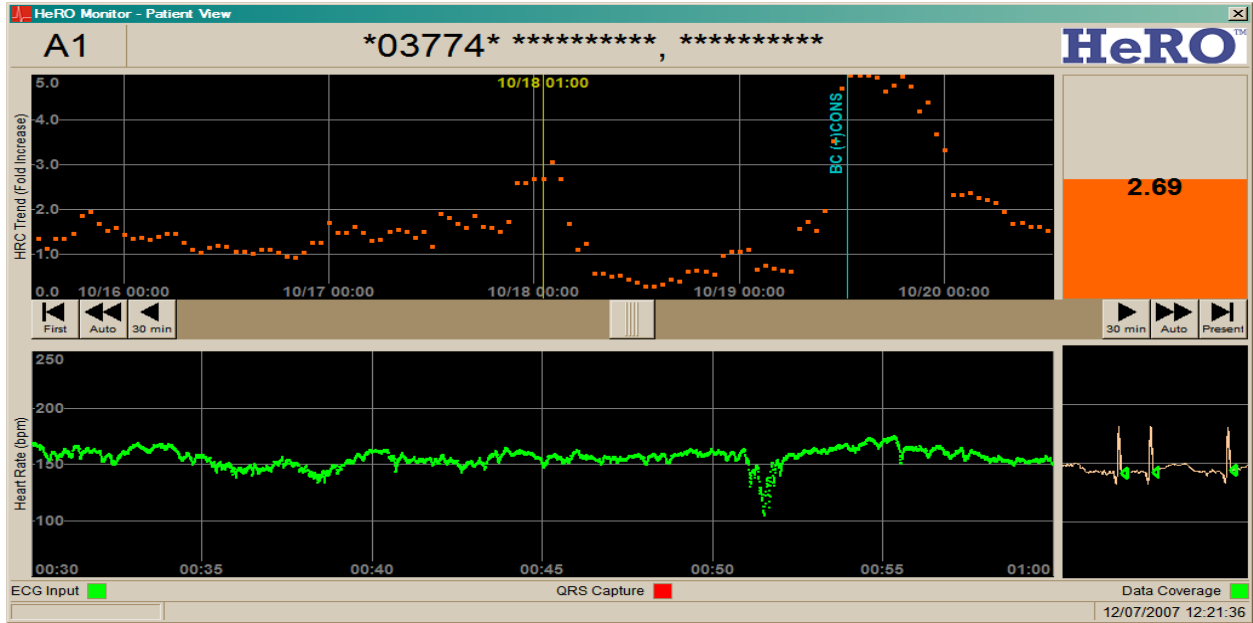


Figure 7

At approximately seven weeks of age, the patient's HeRO Score again spikes prior to diagnosis. In this case, the blood culture was positive for coagulase negative staphylococcus. In this example, the clinician is instructed to begin lab work at the first elevation of HeRO Score above 2.0, approximately 36 hours prior to the blood culture.

Appendix C: Use of HeRO Score in the Assessment of Infection

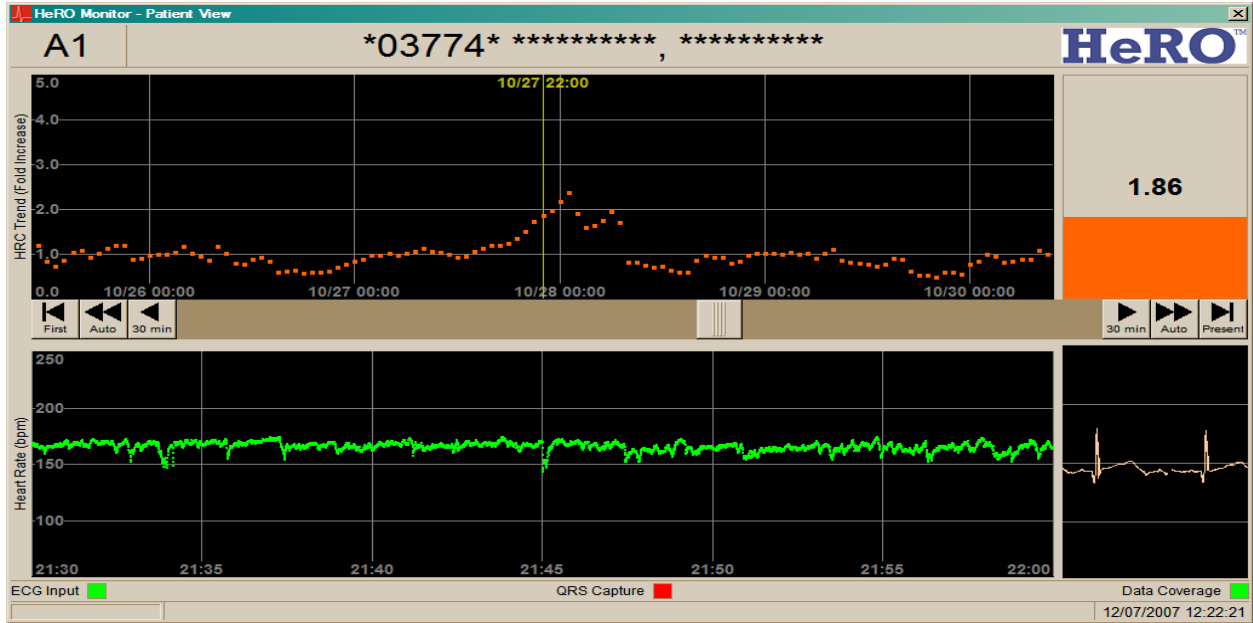


Figure 8

At approximately eight weeks of age, the patient exhibits a spike in HeRO Score that is not associated with any clinical event (i.e. a False Positive). In this example, the clinician is instructed to begin lab work at the first elevation of the HeRO Score above 2.0, which would have led to an unnecessary heel stick (presumably).

Appendix C: Use of HeRO Score in the Assessment of Infection

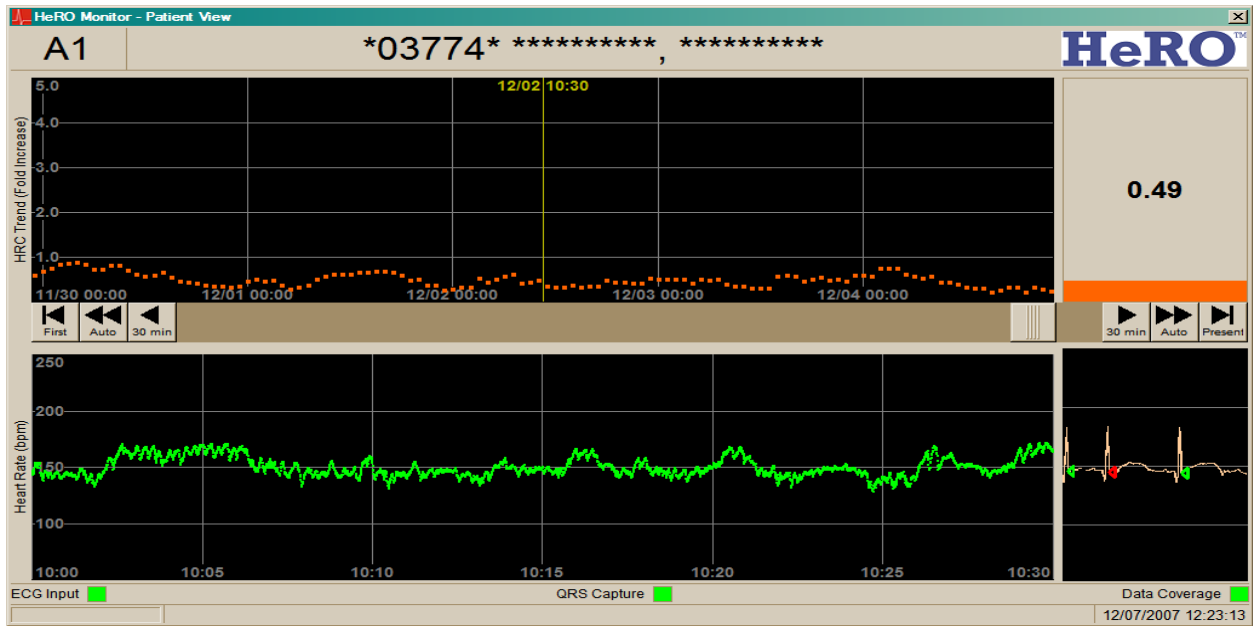


Figure 9

The remainder of the patient's stay in the NICU is marked by a low trend of HeRO Scores. The patient is discharged home after 94 days in the NICU. In this example, the clinician is instructed to take no action based on the HeRO Score.