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# HeRO<sup>®</sup> *solo* & HeRO<sup>®</sup> *duet*

Version 3.1  
System Manual

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**MPSC**  
The Power To Predict

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## **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](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-1626** (R1.07)

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### 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 relative to the overall NICU population, and
- Provide this information to clinicians in a timely and intuitive fashion.

**HeRO solo** and **HeRO duet** are self-contained implementations of **HeRO** and are built upon the same technology platform. The monitors share a hardware platform, with the difference being in the number of patients monitored. Each processes ECG data from one (*solo*) or two (*duet*) patient monitors and shows **HeRO Scores** for the monitored bed(s).

In this document, **HeRO solo** or **HeRO duet** refer to the **HeRO Display** and, as applicable, the **HeRO Data Acquisition Device (AD2)**.

### ***Indications for Use***

**HeRO**<sup>®</sup> 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 only specialized HRV measurements and is not intended to produce any interpretation of those measurements or any kind of diagnosis.

The specialized HRV measurements produced by **HeRO** have not been approved by the FDA for any specific clinical diagnosis.

**HeRO** acquires data from a user-supplied ECG monitor, and requires a user-supplied local area network.

### ***Installation Training and Maintenance***

Initial training 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. Assembly, relocation, and ongoing maintenance are the responsibility of the user.

### ***Contraindications***

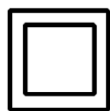
**HeRO** is not intended for use with patients more than 180 days old or weighing over 5000g. Patients with erratic, accelerated, or mechanically controlled irregular heart rhythms are not suitable for HRV evaluation. When shown, the ECG waveform displayed on the computer screen is not to be used for 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.

**HeRO solo** and **HeRO duet** are not suitable for use in the presence of flammable anesthetic in mixture with air, oxygen, or nitrous oxide.



The **HeRO Data Acquisition Device (AD2)** is a Class II device and intended to be used only with the following supplied power adapter:

GlobTek, Inc. Model GTM21089-1305-T2 5.0V, 2.6A Medical Power Supply.

The **HeRO Display** is a Class I device and intended to be used only with the following power adapters:

SINPRO, Inc. Model MPU50-105 12.0V, 3.75A Medical Power Supply, EDAC Model EM10681V 19V, 3.78A Medical AC Adaptor, or MPSC supplied equivalent.



**Warning:** To avoid the risk of electric shock, this equipment must only be connected to a supply mains with protective earth.



**Warning:** The power supply must only be plugged into the **HeRO Display**, through the power port on the bottom. Attaching this power supply to the **HeRO Data Acquisition Device (AD2)** may cause damage to the **HeRO Data Acquisition Device (AD2)**.



**Warning:** This equipment is intended for use by healthcare professionals only.



**Warning:** The **HeRO Data Acquisition Device (AD2)** requires a minimum ECG waveform amplitude (at the ECG monitor Defib/Sync port) of +/- 1 volt (i.e. 2 volts peak to peak) for correct operation. Operation with lower amplitude input signals may cause inaccurate results.



**Warning:** **HeRO solo** and **HeRO duet** are classified as Medical Electronic Equipment. As such, they require special precautions regarding Electromagnetic Compatibility (EMC). Refer to the **HeRO Technical Information and Installation Guidelines** section for more information.









**Warning:** Other software applications should not be installed on the **HeRO Display**.



***Environmental Requirements***

The following environmental requirements apply to the hardware components of the HeRO system (i.e. the Server computer, dedicated Viewing Stations, and AD2-DAD devices with their associated cabling, if present).


Parameter	Operating Range	Storage / Transport Range
Temperature	32°F  95°F	-4°F  140°F
Relative Humidity	10%  90%	10%  90%
Altitude	0 ft  9840 ft	0 ft  9840 ft

***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.

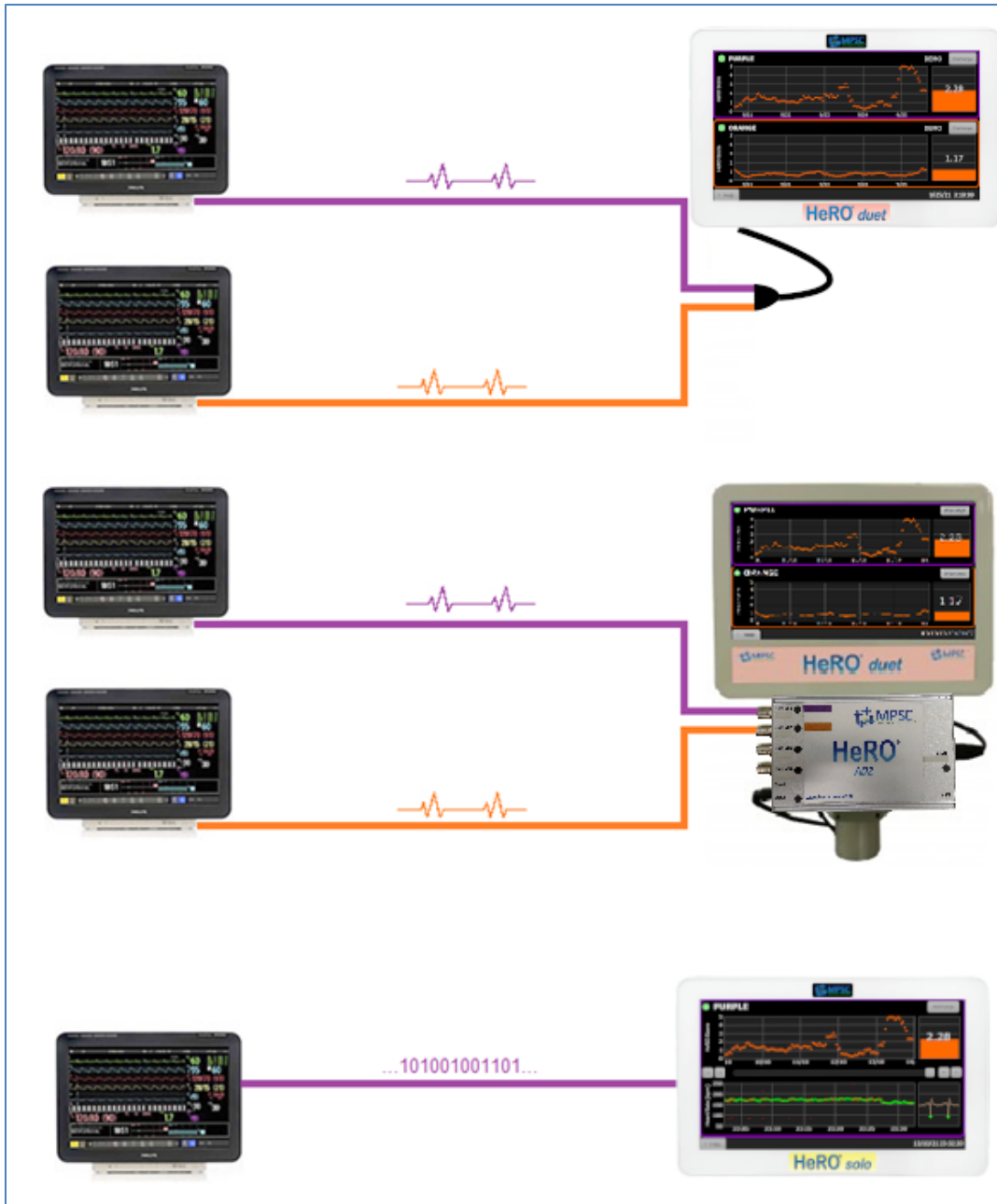
Clickable menu items or button names are designated by a box around the name, i.e. **Help**.

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

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 solo** and **HeRO duet** are standalone monitoring systems that acquire heart rate data from an existing physiological monitor or monitors. **HeRO Scores** for the patient(s) being monitored are computed hourly and displayed on the **HeRO Display**.



**Figure 1: HeRO solo and duet Overview.** Above, **HeRO duet** configured to acquire the analog ECG waveform from the Defib/Sync jacks on two monitors using line-in acquisition or the optional **HeRO Data Acquisition Device (AD2)**. Below, a **HeRO solo** configured to acquire RS-232 heart rate data directly into the **HeRO Display**.

## ***Data Acquisition***

HeRO solo and duet support three modes of data acquisition depending on the configuration purchased:

- 1) Using cables provided with the device, the analog signal output from the physiological monitor can be connected to the provided ECG input adaptor. This adaptor connects between one or two cables and to the pink colored input on the bottom of the **HeRO Display**.
- 2) The **HeRO Data Acquisition Device (AD2)** is used to gather ECG waveform data from an existing physiological monitor and perform mathematical algorithms to determine patterns of HRV. The **HeRO Data Acquisition Device (AD2)** is a small, brick-sized device that is connected to an analog signal output on the physiological monitor and to the **HeRO Display**.
- 3) The **HeRO Display** can be connected directly to the RS-232 port on certain physiological monitors. When connected via RS-232, **HeRO** will use the ECG-derived heart rate.

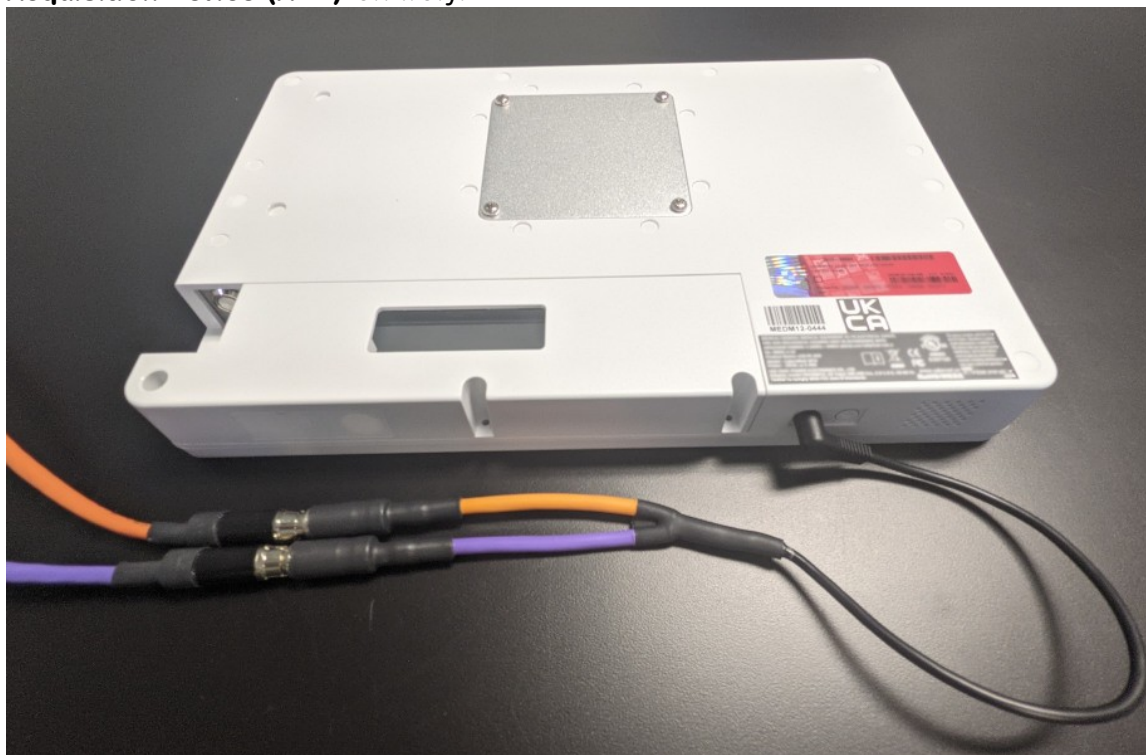
Both the **HeRO Display** and the **HeRO Data Acquisition Device (AD2)** are approved for installation in the patient environment.

## Using HeRO *solo* and HeRO *duet*

### ***Setting Up***

HeRO *solo* and HeRO *duet* are configured by MPSC prior to shipment. Instructions for assembly are included in the packing box and can be completed by hospital personnel. Relocation and ongoing maintenance are the responsibility of the user facility.

Below is an example of a **HeRO *duet*** with cables for two patient monitors, one with a purple cable and the second with an orange cable, that are connected to the **HeRO *duet*** as shown in Figure 2. **HeRO *solo*** hardware appears identical, omitting the orange patient cable. RS-232 configurations, meanwhile, omit the **HeRO Data Acquisition Device (AD2)** entirely.





**Figure 2a.** HeRO *duet* cabling when using the duet ECG input adaptor. The purple patient cable is connected into the purple lead, and the orange cable into the orange lead. The ECG input adaptor plugs into the pink colored port on the bottom of the HeRO Display.



**Figure 2b.** HeRO *duet* cabling when using the HeRO Data Acquisition Device (AD2). The purple patient cable is inserted into the Channel 0 port, and the orange cable into the Channel 1 port. An Ethernet cable connects the HeRO Data Acquisition Device (AD2) to the HeRO display. HeRO *solo* cabling is identical except for the omission of the second, orange patient cable. Not shown, RS-232 installations omit the HeRO Data Acquisition Device (AD2) entirely.

### ***Powering down***

Please turn off the HeRO *solo* or HeRO *duet* before unplugging any of the power cords connected to the unit. Some units have a circular power button  on the bottom of the unit that is illuminated green when powered on. Other units have a circular power button  on the back of the HeRO Display. For both units, press the button for approximately 1 second and wait for the unit to shut down.

## ***Viewing the HeRO Score***

Each **HeRO solo** displays the **HeRO Score** and trend for one patient.

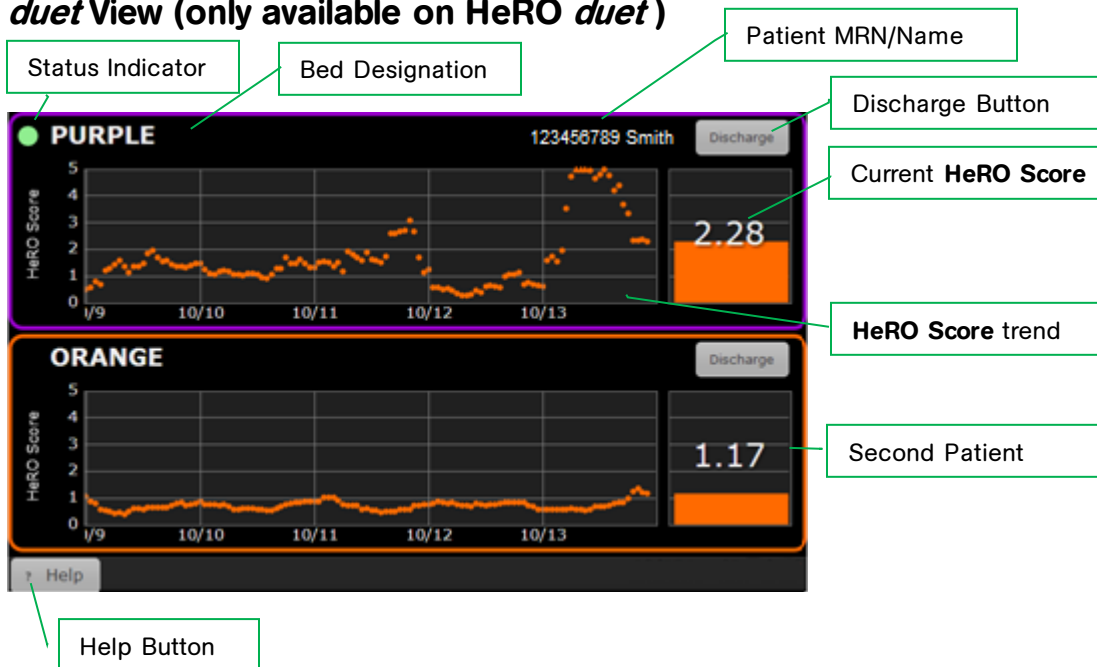
Each **HeRO duet** displays the **HeRO Score** and trend for up to two patients (as shown in in Figure 3).

The **HeRO Display** shows the most recently computed **HeRO Score** for each patient as a numeric value, and also shows a graph that trends the values over the last five days.

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

**HeRO** will stop generating scores for an individual patient if there is an insufficient amount of heart rate data or if there is not enough recent heart rate data to generate an accurate score. These gaps in the **HeRO Score** trend can occur if the patient leaves the bed, if the heart rate signal is otherwise interrupted for 30 minutes or more, or for patients with low heart rates due to cooling. When valid heart rate signal is restored, **HeRO** will resume generating scores as soon as enough new data is available. This may take up to an additional 3 hours.

**duet View (only available on HeRO duet)**



**Figure 3. duet View** Screen. **HeRO Scores** are shown for two beds labeled “Purple” and “Orange”.

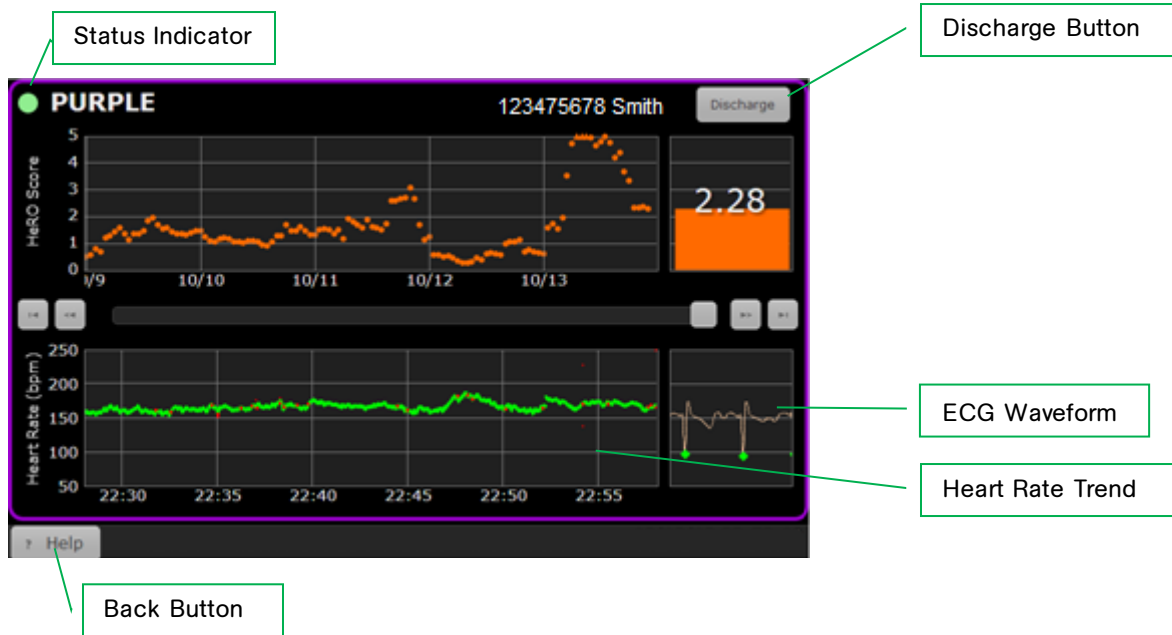
The **duet View** provides the most recent **HeRO Score** and 5-day trend for two patients. The elements composing each **Bed Icon** are:

- the bed designation (Purple or Orange for ECG input systems, the Bed Label of the monitor for RS-232 systems),
- The Name and MRN of the patient (RS-232 systems only)
- a five-day trend of the **HeRO Score**,
- a bar graph that shows the current **HeRO Score**,
- a numeric display of the current **HeRO Score**, and
- a status indicator that is green when the system is receiving heart rate data for the bed, and dark otherwise.

Tapping on a **Bed Icon** will bring up the **Patient View**.

Tap the **Help** button to display the online help (this manual). When the help screen is displayed, the button label will change to **Back**. Tap the button again to return to the **duet View**.

**Patient View (HeRO solo and HeRO duet)**



**Figure 4. Patient View** Screen

The **Patient View** covers a single bed, providing a more detailed look at the **HeRO** information. The **Patient View** contains the following elements:

- the bed identifier (Purple or Orange for **HeRO Data Acquisition Device (AD2)** systems, the Bed Label of the monitor for RS-232 systems),
- The Name and MRN of the patient (RS-232 systems only)
- a five-day trend of the **HeRO Score**,
- a bar graph that shows the **HeRO Score**,
- a numeric display of the **HeRO Score**,
- a 30-minute Heart Rate trend,
- a real-time ECG Waveform (disabled when using RS-232); see warning below
- a status indicator that is green when the system is receiving heart rate data for the bed.

The scroll bar and the four arrow buttons allow the user to navigate through several days worth of data. The 30-minute heart rate trend, the bar graph, and the numeric representation will display data from the currently selected time epoch. When historical data is being viewed, a yellow cursor in the **HeRO Score** trend indicates the location of the current time epoch.





The ECG waveform, when displayed by **HeRO**, should not be used as a diagnostic ECG. In addition, due to latency in the waveform display, this ECG trace should not be used as a trigger for defibrillation.

When viewing the Patient View on **HeRO duet**, tap the **Back** button to return to the **duet View**.

### **Discharge Button**

Deletes all data for the currently displayed patient and clears the **HeRO Scores** from the **duet View** and the **Patient View**. Use this when connecting a new patient to the physiological monitor (this process will occur *automatically* when the serial RS-232 interface is used and HeRO detects a new Medical Record Number from the monitor).

You will be asked to confirm the **Discharge** operation before any changes are made. Data collection will resume immediately, but it may take up to 3 hours before the first **HeRO Score** is generated.

## **Activating HeRO *solo* and HeRO *duet***

**HeRO *solo*** is delivered configured to collect data from one physiological monitor. In order to begin generating **HeRO Scores**, the purple cable must be connected to the patient's physiological monitor.

**HeRO *duet*** is delivered configured to collect data from two physiological monitors. In order to begin generating **HeRO Scores**, the purple and orange cables must be connected to the patients' physiological monitors.

In both cases, please note the following:

- The typical time to generate the first **HeRO Score** for a new patient is 3 hours, and that **HeRO** utilizes up to the last 12 hours of heart rate data for each score generation. Thus, **HeRO** should remain dedicated to a patient bed for as long as possible.
- A **Discharge** operation must be completed any time the **HeRO *solo*** or **HeRO *duet*** is moved from one physiological monitor to another, or when a new patient is connected to the monitor.

## **Continuous HeRO Monitoring**

**HeRO** processes heart rate data and generates scores while the **HeRO Display** is running. However, monitoring is interrupted while the **HeRO Display** or the **HeRO Data Acquisition Device (AD2)**, if present, is powered off.



**HeRO monitoring is active only when HeRO Display and HeRO Data Acquisition Device (AD2), if present, are running.**

## Status and Error Messages

The top section of each bed in the **duet View** and the **Patient View** may display informational or error messages to indicate problems or status changes. These messages, and their meanings, are summarized below.

Message	Description
Comm Error	The <b>HeRO Display</b> is not able to communicate with the services that acquire data and generate <b>HeRO Scores</b> . This message may appear for up to 60 seconds when the patient monitor is first powered up. If the message persists, there may be a hardware problem or a configuration error. Check power to the <b>HeRO Data Acquisition Device (AD2)</b> and reseal all communication cables to the <b>HeRO Display</b> .
<b>HeRO</b> is starting	The <b>HeRO</b> data processing services are starting. <b>HeRO</b> monitoring should begin within 5 minutes.
<b>HeRO</b> failed to start	<b>HeRO</b> data processing services could not be started. This may indicate a hardware problem or a configuration error.
Are you sure that you want to discharge bed (Purple/Orange)?	This message is displayed when the <b>Discharge</b> on the <b>Patient View</b> is clicked. No patient data has been changed at this point. You may choose to continue or cancel the operation.
Discharging bed (Purple/Orange)	A <b>Discharge</b> operation has been confirmed and is under way. The message will be cleared when the operation completes, and only indicates an error condition if the message does not disappear within 60 seconds.
Failed to discharge bed (Purple/Orange)	A <b>Discharge</b> operation has failed. Scores from the previous patient may still be displayed. Restart the <b>HeRO Display</b> unit and perform the operation again if necessary.
License is not valid	The software license is not valid.
License Expires	The software license has expired.

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 MPSC Technical Support.

## **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 distress<sup>1-7</sup>. The **HeRO Score** is reported as a fold increase 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.

Warning: A low **HeRO** score should never be used to deny or reduce treatment on a patient that is exhibiting clinical signs of sepsis.

The computational methodology used to determine patient status is described in **Appendix A: Theory of Operation**.

## Troubleshooting

### ***Bed Icon Error Messages***

**Message:** COM ERROR

**Problem:** **HeRO Main Window** is not visible

**Description:** **Main Window** is not shown on the **HeRO** Display.

<b>Cause</b>	<b>Resolution</b>
<b>HeRO</b> application screen does not appear, and unit displays the Windows desktop. Client application is not running	Manually start the <b>HeRO</b> application by double-tapping Windows desktop shortcut, or by selecting it in the Windows start menu.
<b>HeRO Display</b> will not start.	Restart <b>HeRO Display</b> by unplugging and replugging the monitor.  Ensure that both the power cord for the <b>HeRO Display</b> and the <b>Data Acquisition Device (AD2)</b> are both plugged in to an energized power outlet.

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

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

<b>Cause</b>	<b>Resolution</b>
<b>HeRO</b> is starting up	Wait for <b>HeRO Display</b> to initialize (up to 5 minutes).
Configuration error	Contact MPSC Technical Support.

**Problem:** *HeRO Failed to Start* message is displayed

**Description:** The **HeRO** data processing services did not start.

<b>Cause</b>	<b>Resolution</b>
Internal PC error	Reboot <b>HeRO Display</b> by unplugging and replugging the power cable.
Configuration error	Contact MPSC Technical Support.

**Problem:** *License is not valid* message is displayed

**Description:** The software license has an invalid signature or is otherwise corrupt.

<b>Cause</b>	<b>Resolution</b>
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.

<b>Cause</b>	<b>Resolution</b>
Expired license	Contact MPSC Sales or Technical Support

## HeRO Technical Information and Installation Guidelines

The **HeRO Display** and **Data Acquisition Device (AD2)** are parts of the **HeRO solo** and **duet**. The following information is provided for reference. For assistance with installation or reconfiguration, contact Technical Support.

### **Site Location**

**HeRO solo** and **HeRO duet** are installed in the NICU. **HeRO** is approved for use within the “patient vicinity” that extends within 1.5 meters of the patient. The **HeRO Data Acquisition Device (AD2)** is an optional part of **HeRO**. Individual cables are run from the physiological monitors to the **HeRO solo** or **duet**.

The **HeRO Data Acquisition Device (AD2)** is not approved for installation in close proximity to, or stacked with, other equipment that is sensitive to Radio Frequency (RF) or Electromagnetic Interference (EMI) emissions, or that generates significant RF or EMI emissions.

### **Cabling**

**HeRO** requires the following connections and cable types:

Connection	Cable Type	Maximum Length	Notes
ECG signal input (from Defib/Sync or RS-232 jack on physiological monitor)	Proprietary	5 meters	<ul style="list-style-type: none"> <li>The cable end at the Defib/Sync or RS-232 jack is a manufacturer specific connector.</li> <li><b>HeRO</b> is intended to connect to one (<b>solo</b>) and up to 2 (<b>duet</b>) ECG monitors.</li> </ul>
<b>Data Acquisition Device (AD2) to HeRO Display</b>	CAT5	0.5 meters	
<b>Data Acquisition Device (AD2) Power</b>	2 wire power cord (provided)	6 meters	<p>The Data Acquisition Device (AD2) uses an external medical grade power supply rated for 110-240VAC input voltage. It is not approved for use with any other power supply.</p> <p>The Data Acquisition Device (AD2) is a CISPR11 Class A device and is not approved for use in buildings used for domestic purposes, or in other locations that directly connect</p>

## TECHNICAL INFORMATION

Connection	Cable Type	Maximum Length	Notes
			to the public low voltage power supply network that supplies buildings used for domestic purposes.
<b>HeRO Display</b>	3 wire power cord (provided)	6 meters	The <b>HeRO Display</b> uses an external medical grade power supply rated for 110-240VAC input voltage. It is not approved for use with any other power supply.

Connections using unapproved cable types or lengths may result in increased RF or EMI emissions or decreased immunity to these types of emissions.

### ***Cleaning***

The hardware components of **HeRO solo** or **duet** may be cleaned as needed per the instructions below.

#### **HeRO Display, Data Acquisition Device (AD2), and cables**

- Disconnect this equipment from any AC outlet before cleaning. The equipment can be wiped or dusted with a damp cloth. Do not use liquid or spray detergents for cleaning.








#### **HeRO roll stand, desk stand, and wall mount**

- The mounting assembly may be cleaned with most mild, non-abrasive solutions commonly used in the hospital environment (e.g. diluted bleach, ammonia, or alcohol solutions).
- The surface finish will be permanently damaged by strong chemicals and solvents such as acetone and trichloroethylene. Do not use steel wool or other abrasive material to clean the mounting assembly. Damage caused by the use of unapproved substances or processes will not be covered by warranty. We recommended that you test any cleaning solution on a small area of the mounting assembly that is not visible to verify compatibility.
- Never submerge the roll stand or allow liquids to enter the mounting assemblies. Wipe any cleaning agents off the mounting assembly immediately using a water-dampened cloth. Dry all mounting assemblies thoroughly after cleaning.



**Description of Markings**

The following markings are used on the **Data Acquisition Device (AD2)** labeling:

Marking	Description
	Manufacturer
	Class II equipment
	Consult Operating Instructions before use
	Medical Safety Certification
	Certification of conformity to European Community directives
	Do not dispose of equipment in trash. Return to manufacturer to be repaired or recycled.
	Contact information for European Community Representative.

The following markings are used on the **HeRO Display** labeling:

Marking	Description
	Manufacturer
	Medical Safety Certification
	Certification of conformity to European Community directives
	Do not dispose of equipment in trash. Return to manufacturer to be repaired or recycled.
	FCC-Approved Equipment Authorization.

***Modifications***

**HeRO solo** and **duet** are not user serviceable and must not be modified in any way. Defective units must be returned to MPSC for replacement.

**HeRO** is designed for continuous operation—the user should not turn off the device, or take any other steps, in order to reduce environmental impact.

***Environmental Impact***

**HeRO solo** and **duet** are designed to minimize impact on the environment. Due to the continuous nature of **HeRO** monitoring, it is not recommended that the system or its components be powered down at any point to conserve electricity. Follow the instructions on disposal above when removing **HeRO** from service.

***Electrical Isolation***

The **HeRO Data Acquisition Device (AD2)** is electrically isolated via the provided medical grade power supply. It is not approved for use with any other type of power supply.

The **HeRO Display** is electrically isolated via the provided medical grade power supply. It is not approved for use with any other type of power supply.


***Electromagnetic Compatibility***

<b>Guidance and manufacturer’s declaration – electromagnetic emissions</b>		
The HeRO System is intended for use in the electromagnetic environment specified below . The customer or the user of the HeRO System should assure that it is used in such an environment.		
<b>Emissions test</b>	<b>Compliance</b>	<b>Electromagnetic environment – guidance</b>
RF emissions CISPR 11	Group 1	The HeRO System uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
CISPR 11	Class A	The HeRO System is suitable for use in all establishments other than domestic and those directly connected to the public low - voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Class A/D	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	PASS	

<b>Guidance and manufacturer's declaration – electromagnetic immunity</b>			
The HeRO System is intended for use in the electromagnetic environment specified below. The customer or the user of the HeRO System should assure that it is used in such an environment.			
IMMUNITY test	IEC 60601 test level	Compliance level	Electromagnetic environment – guidance
Electrostatic discharge (ESD)  IEC 61000-4-2	± 6 kV contact  ± 8 kV air	± 6 kV contact  ± 8 kV air	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.
Electrical fast transient/burst  IEC 61000-4-4	± 2 kV for power supply lines  ± 1 kV for input/output Lines	± 2 kV for power supply lines  ± 1 kV for input/output Lines	Mains power quality should be that of a typical commercial or hospital environment.
Surge  IEC 61000-4-5	± 1 kV line(s) to line(s)  ± 2 kV line(s) to earth	± 1 kV line(s) to line(s)  ± 2 kV line(s) to earth	Mains power quality should be that of a typical commercial or hospital environment.
Voltage dips, short interruptions and voltage variations on power supply input lines  IEC 61000-4-11	<5 % $U_t$ (>95 % dip in $U_t$ ) for 0,5 cycle  40 % $U_t$ (60 % dip in $U_t$ ) for 5 cycles  70 % $U_t$ (30 % dip in $U_t$ ) for 25 cycles  <5 % $U_t$ (>95 % dip in $U_t$ ) for 5 s	<5 % $U_t$ (>95 % dip in $U_t$ ) for 0,5 cycle  40 % $U_t$ (60 % dip in $U_t$ ) for 5 cycles  70 % $U_t$ (30 % dip in $U_t$ ) for 25 cycles  <5 % $U_t$ (>95 % dip in $U_t$ ) for 5 s	Mains power quality should be that of a typical commercial or hospital environment. typical commercial or hospital environment. If the user of the HeRO System requires continued operation during power mains interruptions, it is recommended that the HeRO System be powered from an uninterruptible power supply or a battery.
Power frequency (50/60 Hz) magnetic field  IEC 61000-4-8	3 A/m	3 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
NOTE $U_t$ is the a.c. mains voltage prior to application of the test level.			

**Guidance and manufacturer’s declaration – electromagnetic immunity**

The HeRO System is intended for use in the electromagnetic environment specified below . The customer or the user of the HeRO System should assure that it is used in such an environment.

IMMUNITY test	IEC 60601 test level	Compliance level	Electromagnetic environment – guidance
<p>Conducted RF IEC 61000-4-6</p> <p>Radiated RF IEC 61000-4-3</p>	<p>3 Vrms 150 kHz to 80 MHz</p> <p>3 V/m 80 MHz to 2,5 GHz</p>	<p>3 V</p> <p>3 V/m</p>	<p>Portable and mobile RF communications equipment should be used no closer to any part of the HeRO System, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter.</p> <p><b>Recommended separation distance</b></p> $d = 1.2\sqrt{P}$ $d = 1.2\sqrt{P}$ <p>80 MHz to 800MHz</p> $d = 2.3\sqrt{P}$ <p>800 MHz to 2.5GHz</p> <p>where <math>P</math> is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and <math>d</math> is the recommended separation distance in metres (m).</p> <p>Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey,<sup>a</sup> should be less than the compliance level in each frequency range.<sup>b</sup></p> <p>Interference may occur in the vicinity of equipment marked with the following symbol:</p> 

NOTE 1 At 80 MHz and 800 MHz, the higher frequency range applies.

NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

<sup>a</sup> Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the HeRO System is used exceeds the applicable RF compliance level above, the HeRO System should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the HeRO System.

<sup>b</sup> Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3 V/m.

**Recommended separation distances between portable and mobile RF communications equipment and the HeRO System**

The HeRO System is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the HeRO System can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the HeRO System as recommended below, according to the maximum output power of the communications equipment.

Rated maximum output power of transmitter  W	Separation distance according to frequency of transmitter  m		
	150 kHz to 80 MHz $d = 1.2\sqrt{P}$	80 MHz to 800 MHz $d = 1.2\sqrt{P}$	800 MHz to 2,5 GHz $d = 2.3\sqrt{P}$
0.01	0.12	0.12	0.23
0.1	0.38	0.38	0.73
1	1.2	1.2	2.3
10	3.8	3.8	7.3
100	12	12	23

For transmitters rated at a maximum output power not listed above, the recommended separation distance  $d$  in metres (m) can be estimated using the equation applicable to the frequency of the transmitter, where  $P$  is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.

NOTE 1 At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.

NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

### **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  $\approx 0$  and standard deviation  $\approx 1$ .

### Mathematical Analysis

#### Histogram Based Parameters

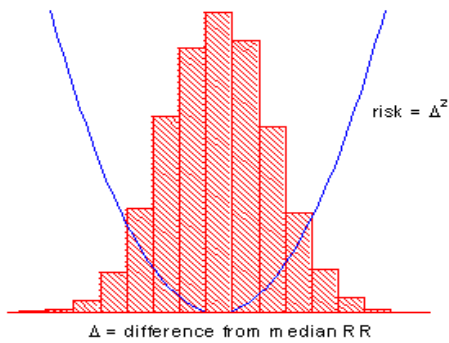
From each set of 4096 High-Pass filtered, normalized RR intervals, the 10<sup>th</sup>, 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>, and 90<sup>th</sup> percentiles and the first, second, third, and fourth moments are calculated.

#### 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:

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



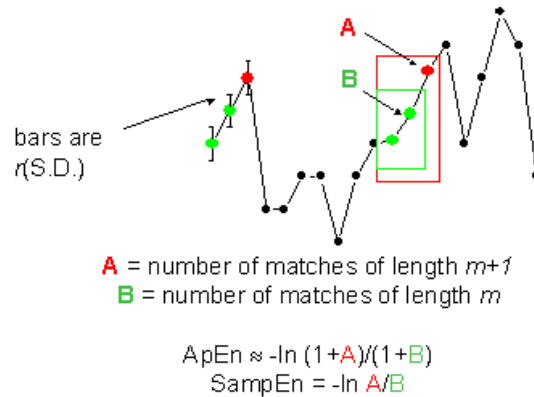
In other words,  $R_1$  and  $R_2$  are non-negative quantities that increase when the number and/or the magnitude of large deviations from the median increases. Intuitively, a distribution of RR intervals that is skewed to the right will result in  $R_2 > R_1$ .

**Figure A1. Sample Asymmetry**

**Sample Entropy**

Sample Entropy is a measure of regularity in time series that is suitable to HRV analysis<sup>8</sup>. 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 data<sup>8</sup>.





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

**Figure A2. 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  $V_{1...n}$  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 **HeRO Score**.

### **References:**

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

The authors systematically examined heart rate variability while patients transitioned from healthy to ill. They found decreased variability during illness, with increased variability during recovery, which were captured in time-domain, frequency-domain, and neural network measures. However, the authors were unable to rule out the possible influence of dopamine on the results.

<sup>2</sup>Moorman JR, Delos JB, Flower AA, Cao H, Kovatchev BP, Richman JS, Lake DE. Cardiovascular oscillations at the bedside: early diagnosis of neonatal sepsis using heart rate characteristics. *Physiological Measures*, 2011.

The authors applied statistical analysis to time series of heart rate in order to improve the timing of the diagnosis of sepsis in premature infants. They found standard deviation, sample asymmetry and sample entropy to be strong predictors, and were able to diagnose and treat infection prior to clinical illness. The authors noted no weaknesses nor limitations.

<sup>3</sup>Addison K, Griffin MP, Moorman JR, Lake DE, O'Shea TM. Heart rate characteristics and neurodevelopmental outcome in very low birth weight infants. *J Perinatol*. 29:750-6, 2009.

The authors compared the cumulative Heart Rate Characteristics scores of patients during the NICU stays with Bayley-II score assessed at 18 months. They found that patients with higher HRC were at increased risk of Cerebral Palsy and delayed early cognitive development. The authors noted that the sample was small and represented a pool at higher than normal risk of neurodevelopmental impairment. Also, the analysis was retrospective in nature, and the dataset did not contain known confounders. Finally, the

## APPENDIX A: THEORY OF OPERATION

assessors of neurological development were aware of patients' medical history, which could have created bias, and the assessments have limited sensitivity for CP and delayed cognitive development.

<sup>4</sup>Stone ML, Tatum PM, Weitkamp JH, Mukherjee AB, Attridge J, McGahren ED, Rodgers BM, Lake DE, Moorman JR, Fairchild KD. Abnormal heart rate characteristics before clinical diagnosis of necrotizing enterocolitis. *J Perinatol.* (2013) May 30.

The authors hypothesized that diagnosis of NEC would be preceded by abnormal heart rate characteristics, similar to sepsis. They found that patients that developed surgical NEC had higher HRC index 1 to 3 days prior to diagnosis than those with medical NEC. They also found that the HRC index rose 6 hours prior to diagnosis in medical NEC, and 16 hours prior to diagnosis in surgical NEC. The authors noted that the number of patients examined in this analysis was small, and it was done in the context of a larger RCT that did not have a mandated intervention based on the HRC index.

<sup>5</sup>Vergales BD, Zanelli SA, Matsumoto JA, Goodkin HP, Lake DE, Moorman JR, Fairchild KD. Depressed Heart Rate Variability is Associated with Abnormal EEG, MRI, and Death in Neonates with Hypoxic Ischemic Encephalopathy. *Am J Perinatol.* (2013) Dec 17.

The authors hypothesized that lower heart rate variability would be associated with abnormal EEG and MRI's in the brains of patients with HIE. They found lower HRV to be significantly associated with both death and abnormal EEG/MRI. The authors noted that they were unable to determine a relationship between abnormal HRC and long term outcomes.

<sup>6</sup>Moorman JR, Carlo WA, Kattwinkel J, Schelonka RL, Porcelli PJ, Navarrete CT, Bancalari E, Aschner JL, Walker MW, Perez JA, Palmer C, Wagner DP, Stukenborg GJ, Lake DE, O'Shea TM. Mortality benefit of heart rate characteristics monitoring in very low birth weight infants: a randomized trial. *J Pediatr* 2011.

In a randomized controlled trial of 3003 very low birth weight infants, the mortality rate was 8.1% among patients where HeRO was used as an additional piece of data, compared with 10.2% among controls ( $p=0.04$ ). The authors noted that the study lacked a definition of significantly rising score as well as a mandated intervention. A 2.3 day improvement in the primary study endpoint, days alive and not on ventilatory support, was not statistically significant ( $p=0.08$ ).

<sup>7</sup>Griffin MP, Lake DE, Bissonette EA, Harrell FE, O'Shea TM, Moorman JR. Heart rate characteristics: novel physiologic markers to predict neonatal infection and death. *Pediatrics* 116:1070-4, 2005.

The researchers evaluated 1022 patients in two NICUs to determine the relationship between HRC index and death, urinary tract infection, and sepsis. They found that patients with high HRC indices were 5-6x more likely to experience one of the adverse events in the next 24 hours compared to patients with low HRC indices. Further, they found that patients with both high HRC and abnormal lab tests were 6-7x more likely to experience an adverse event than those patients with neither. However, they also determined that the positive predictive value for death, UTI, or confirmed sepsis in the next 7 days was 15%, and that illnesses other than UTI and sepsis could cause elevated HRC, including respiratory decompensation, chronic lung disease, NEC, and intraventricular hemorrhage.

<sup>8</sup>Richman JS, Moorman JR. Physiological time-series analysis using approximate entropy and sample entropy. *American Journal of Physiology.* 2000;278:H2039-2049.

The authors developed a novel complexity measure, Sample Entropy, and compared it with Approximate Entropy. They found that the new measure agreed with theory better than Approximate Entropy, and posited that Sample Entropy would be useful in analyzing the dynamics of heart rate.

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## **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:** 50<sup>th</sup> 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.