HeRO®*symphony*

Version 3.1
System Manual

MPSC

The Power To Predict

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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.

This manual may be viewed from within the **HeRO** application by clicking Help on
any **HeRO** screen. It is also available on the Internet at
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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 an ECG signal or 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.

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 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

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

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

General Precautions
The following requirements apply to all **HeRO** system configurations.

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.

⚠ **Warning:** Other software applications should not be installed on the **HeRO** Server computer or on the dedicated Viewing Station computers.

⚠ **Warning:** The **HeRO** Server and dedicated Viewing Station computers are not rated for use in the patient environment.

AD2-DAD Precautions
The following precautions apply specifically to the **HeRO** AD2 Data Acquisition Device (AD2-DAD), which is used to acquire analog ECG waveforms from the Defib/Sync jack on the patient monitor. They do not apply to **HeRO** systems that use network based data acquisition (NDAI). (Refer to the *Overview* section for details about system configurations.)

The **HeRO** AD2-DAD is not suitable for use in the presence of flammable anesthetic mixture with air or with oxygen or with nitrous oxide.
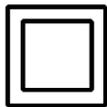
▢ The **HeRO** AD2-DAD is a Class II device and is intended to be used only with the following supplied power adapter:

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

⚠ **Warning:** This equipment is intended for use by healthcare professionals only. This equipment may cause radio interference or may disrupt the operation of nearby equipment. It may be necessary to take mitigation measures, such as re-orienting or relocating the equipment or shielding the location.

⚠ **Warning:** The **HeRO** AD2-DAD 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**: The **HeRO** AD2-DAD is classified as Medical Electronic Equipment. As such it requires special precautions regarding Electromagnetic Compatibility (EMC). Refer to the ***AD2-DAD Installation Requirements*** section for more information.

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 screen or button names are designated by a box around the name, i.e. Summary .

Labels of non-interactive graphs, screen displays, or pop-up windows 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 consists of Data Acquisition Devices (DADs), a Server, and one or more Viewing Stations. In some installations, the Server is configured to acquire data from the Physiological Monitoring Network, and the Data Acquisition Devices are not used. **HeRO** has no applied parts.
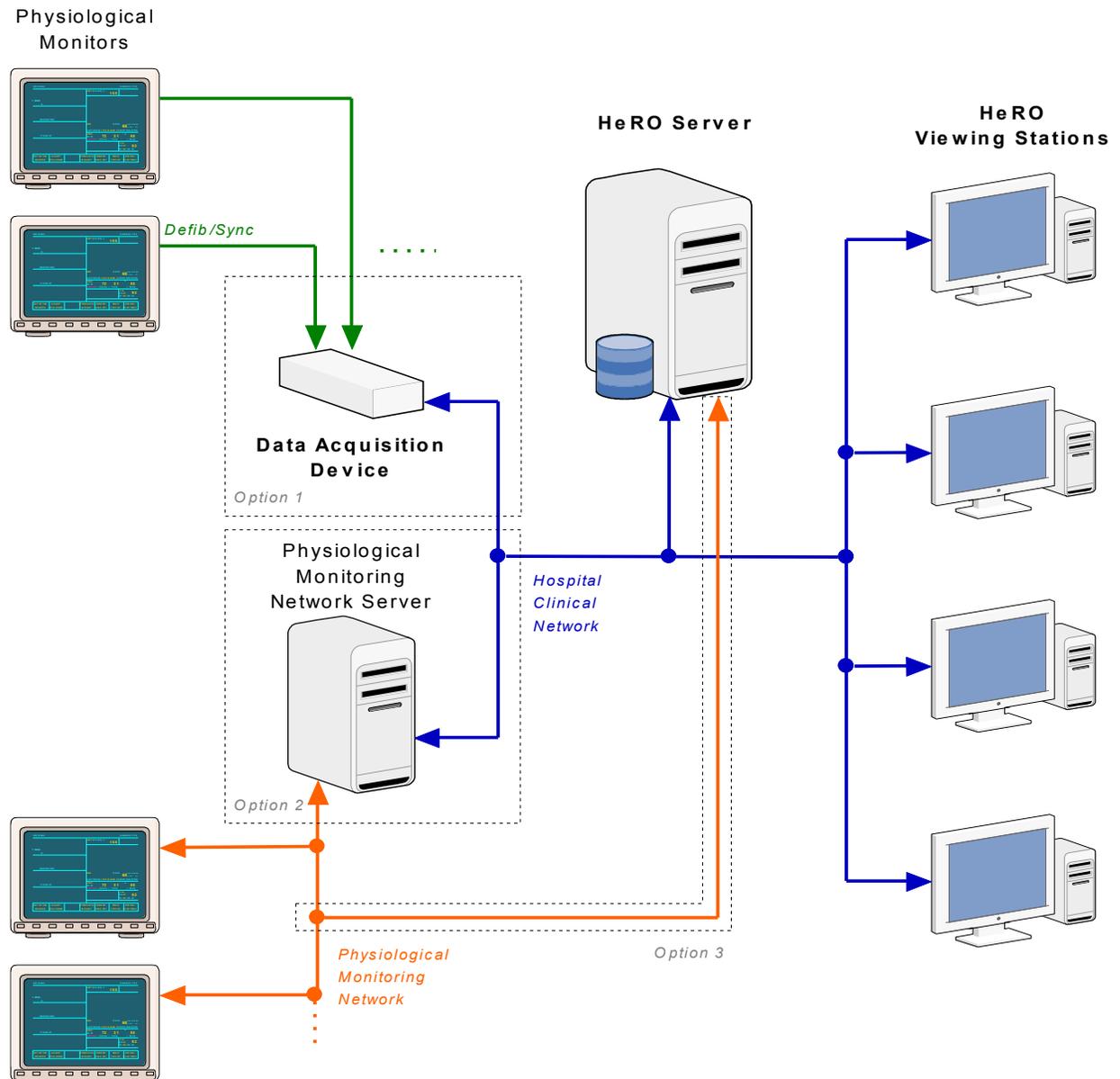
Figure 1: HeRO System Overview. In Configuration 1, **HeRO** Data Acquisition Devices collect heart rate data from the Defib/Sync jack on the physiological monitors. In Configuration 2, the **HeRO** Server queries a physiological monitoring network server for heart rate data over the hospital clinical network. In Configuration 3, the **HeRO** Server acquires the heart rate data directly from the physiological monitoring network.

Data Acquisition Device (DAD)

The Data Acquisition Device is used to gather ECG waveform data from an existing physiological monitor and perform mathematical algorithms to determine patterns of HRV. The AD2-DAD is a small, brick-sized device that is connected to an analog signal output on the physiological monitor and to the hospital Clinical Network. It is approved for installation in the patient environment or in a data closet.

Server

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)

The Network Data Acquisition Interface (NDAI) is a software extension to the **HeRO** product that enables the Server to acquire heart rate data from the Physiological Monitoring network. This interface replaces the DAD devices and the associated cabling. If so configured, the interface can also perform Patient Admit, Discharge, and Transfer (ADT) operations based on information retrieved from the physiological monitors. Depending on the type of monitors and configuration of the monitoring network, **HeRO** may sit directly on the physiological monitoring network (Figure 1, Configuration 3), or it may acquire heart rate data indirectly by communicating to an intermediate server that sites on the Physiological Monitoring Network server (Figure 1, Configuration 2).

Viewing Stations

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

Setting Up

In installations using Data Acquisition Devices, each ECG monitor is connected to a DAD using an analog signal cable connected to the Defib/Sync port on the physiological monitor. Appropriate cabling is provided and installed by authorized installers along with the **HeRO** system to ensure compatibility with the existing ECG monitors. Contact MPSC for support when upgrading or moving ECG monitors. Both the ECG monitors and **HeRO** DAD systems are stationary. Do not attempt to disconnect the cable without first contacting MPSC.

In sites using Networked Data Acquisition, no new connections are made to the physiological monitors. The interface is configured during installation of the **HeRO** system. Contact MPSC for support when upgrading or moving ECG monitors.

The **HeRO** system will identify QRS complexes from the currently selected ECG waveform channel (i.e. I, II, III) on the ECG monitor. Please consult the ECG monitor documentation for instructions on changing the active ECG channel. Hospital IT staff will install appropriate network connections for the **HeRO** system. MPSC recommends standard Category 5 (or higher), shielded twisted-pair (STP) Ethernet cabling to the standard network jacks on the DAD, Server, and Viewing Stations.
If network problems arise, contact the hospital network administrator, or MPSC Technical Support (toll free 1-800-394-1625).

Viewing the HeRO Score

The **HeRO** Score can be viewed from three different screens: the Plan View, the Pod View, and the Patient View. In all cases, a five day trend of the **HeRO** Score is plotted wherein the trend goes from left, 5 days ago, to right, current.

Plan View

Figure 2. 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 2) 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, 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.

Clicking on a **Bed Icon** within the **Plan View** opens the **Patient View** screen for the patient assigned to that bed.
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.

Message	Applies To	Description
Comm Error	DAD	The system is unable to communicate with the DAD device serving the bed.
No Wave	NDAI	The system is not receiving ECG waveform data from the networked monitor serving the bed.
No Heart Rate	NDAI	The system is not receiving Heart Rate data from the networked monitor serving the bed.
No MR #	NDAI with ADT	The system is receiving data from the physiological monitor serving the bed, but no Medical Record Number is specified for the patient admitted to that monitor.
No Name	NDAI with ADT	The system is receiving data from the physiological monitor serving the bed, but no Name is specified for the patient admitted to that monitor.
MR # Conflict	NDAI with ADT	The physiological monitors for the affected beds are reporting the same Medical Record Number for the admitted patient.

Updating Patient	NDAI with ADT	The network data acquisition interface is in the process of receiving updated patient information from the physiological monitor. This message should disappear after a few minutes, and does not indicate an error condition unless it fails to disappear.

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 (toll free 1-800-394-1625).

Pod View
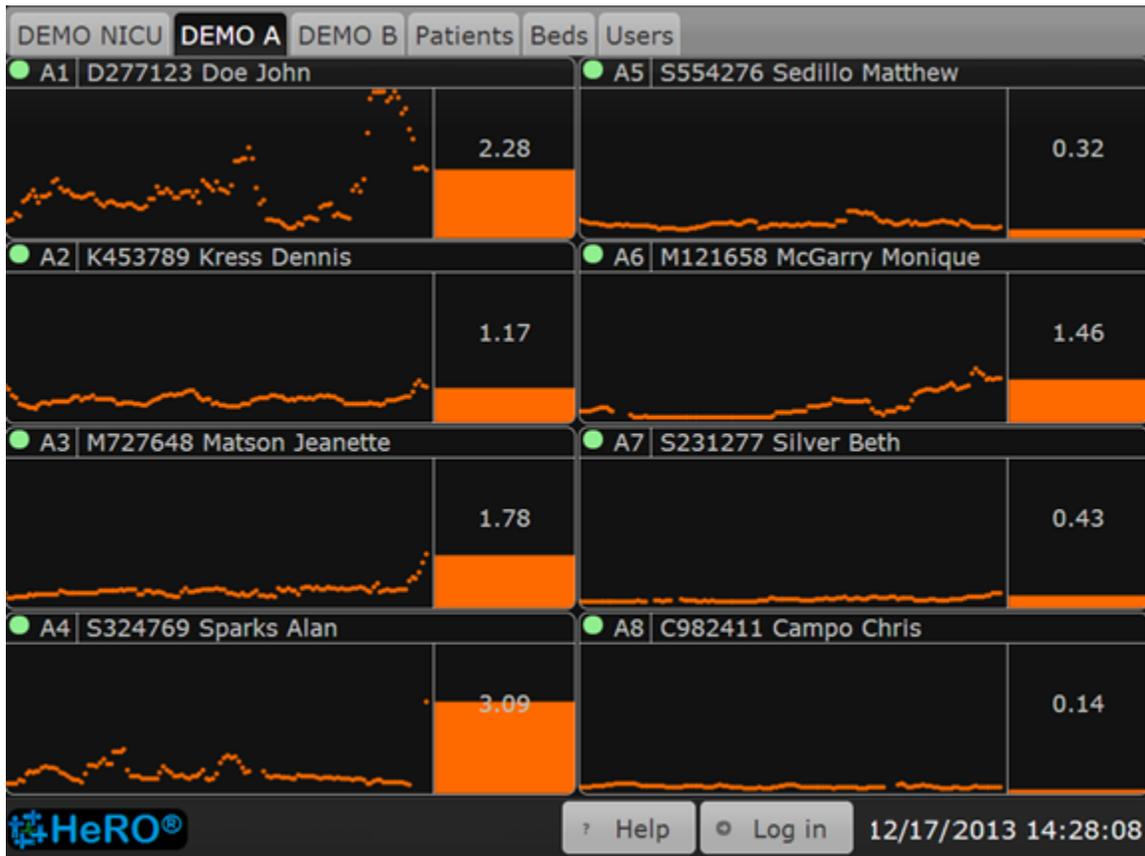
Figure 3. Pod View Screen

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, computed hourly
- a bar graph with a numeric indication of the most recent **HeRO** Score, and
- a status indicator that is green when the system is receiving RR intervals or heart rate data for the bed, or gray otherwise.

As on the Plan View, clicking on a Bed Icon will show 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
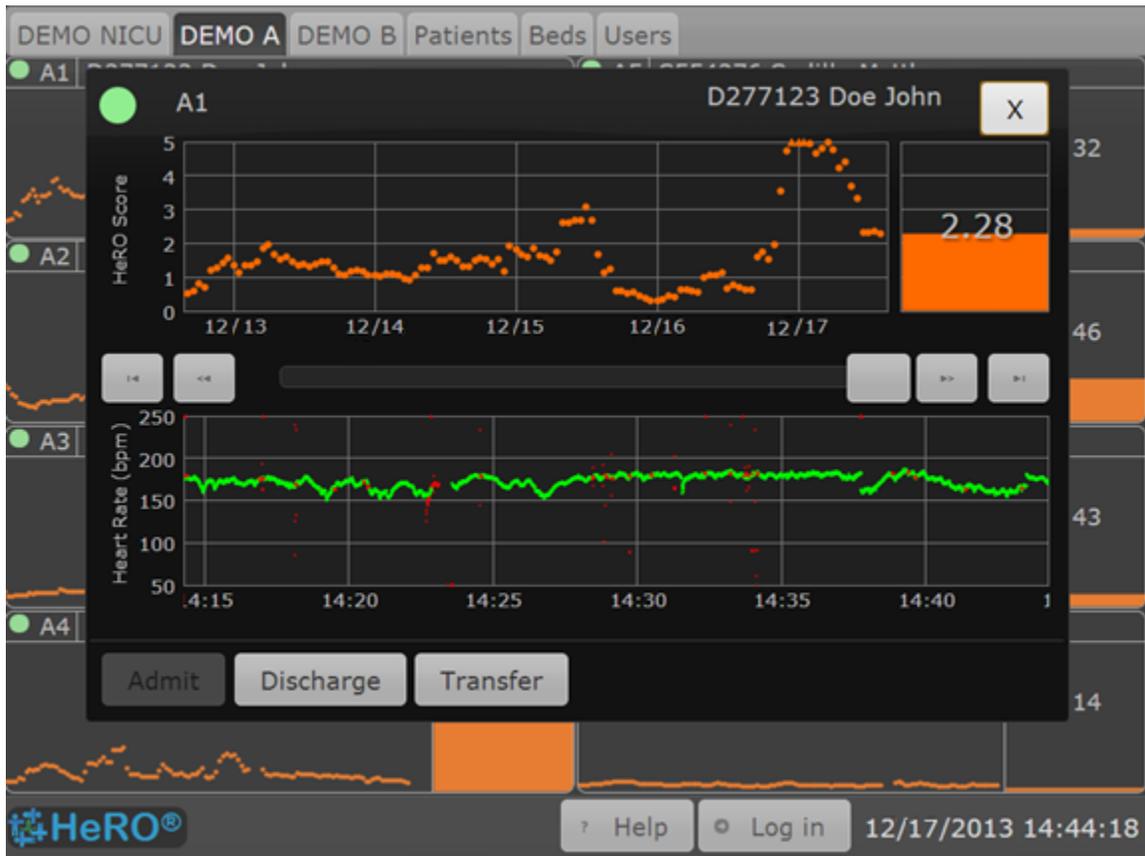
Figure 4. Patient View Screen

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 contains the following elements:

- 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 and numeric representation of the most recent HeRO Score,
- a 30-minute Heart Rate trend,
- a one-second ECG trace (not shown for all system configurations), 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 scroll bar and the four arrow buttons allow the user to navigate through the previous fifteen days of patient 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. At all times, the ECG trace (when displayed) continues to show current, real-time data.

> ⚠️ The ECG waveform 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.

The **Admit**, **Discharge** and **Transfer** buttons on the **Patient View** can be used to admit a patient to an empty bed, to discharge a patient from the current bed, or to transfer the patient from the current bed to another. Refer to the section **Tracking Patients: Admit, Discharge and Transfer** for further information. To close the **Patient View**, click the **X** button at the upper right corner.

Tracking Patients: Admission, Discharge, and Transfer

The **HeRO** system provides a simple, intuitive interface for tracking the current location of patients within the unit to ensure that all identified heart rate data is attributed to the correct patient. When a patient moves within the unit, **HeRO** can be updated by Admitting a patient to a bed, Discharging a patient from a bed, or Transferring a patient from one bed to another.

While a patient is admitted to a bed, the heart rate information received from that bed is assigned to that patient in real time. This information is then used to compute the **HeRO** Score and trend, which is also stored in the patient record. When a patient is discharged from one bed and admitted to another, or transferred directly from one bed to another, the associated demographic and heart rate data 'follows' the patient to that bed. In this way, the **HeRO** Score trend for a particular patient remains accurate as the patient is moved from bed to bed within the unit.

The operations described in this section can be performed with the `Admit`, `Discharge` and `Transfer` buttons that appear on the `Patient View`, the `Patients` screen, and the `Beds` screen.

For sites configured to retrieve ADT information from the Network Data Acquisition Interface, the **HeRO** system is not used to admit or transfer patients. For such installations, the following three sections *Admitting a Patient*, *Transferring a Patient*, and *Resolving Bed Assignment Conflicts* are informational only, as this functionality is disabled in **HeRO**. Refer to *ADT with Networked Data Acquisition*.

Entering Patient Demographics

Before a patient can be monitored by **HeRO**, you must enter some basic demographic information for the patient. On the Patients screen, click the New Patient button to show the New Patient dialog (see Figure 5). Enter a Last Name, First Name (optional), and MR Number for the new patient, then click Save. Both the Last Name and MR Number are required information for the patient. The new patient now appears on the Patients screen (see Figure 6) and can be admitted to a bed.

Figure 5. New Patient dialog.

Figure 6. Patients screen

Admitting a Patient

Once the demographic information has been entered, click the Admit button on the Patients screen to admit the patient to a bed. This will display the Admit Patient dialog (see Figure 7).
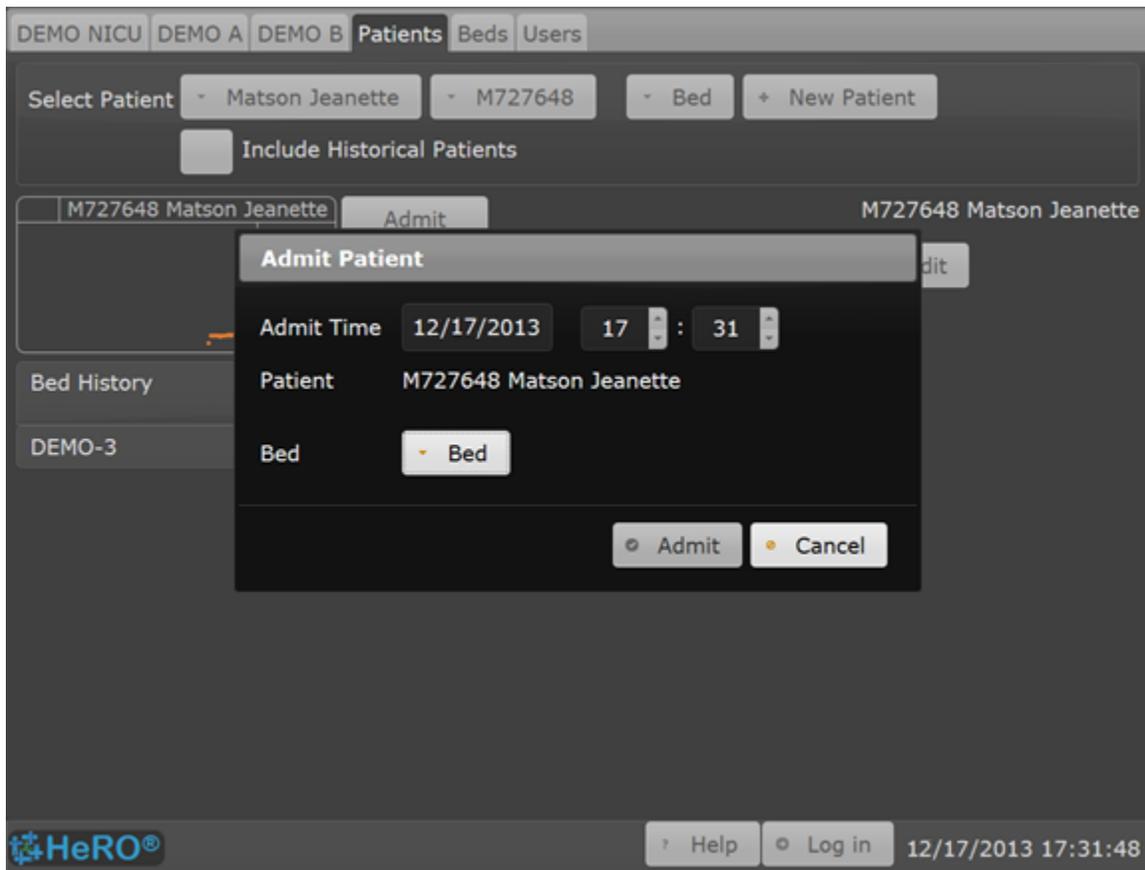
Figure 7. Admit Patient dialog

The **Admit Patient** dialog displays a **Bed** list that shows all of the beds to which the patient can be assigned. Click or tap on the list to display the choices, and then scroll to the desired bed and click to select it.

The **Admit Patient** dialog also contains date and time input controls for the **Admit Time**, which is the effective date and time of the admit operation. When the dialog is first displayed, the **Admit Time** is set to the present time. If you know that the patient was actually moved into the bed at a significantly earlier time, you should enter the correct time. This reduces the likelihood of accidentally assigning heart rate data to the wrong patient.

To complete the admit operation, click **Admit**. If you do not wish to perform the admit, click **Cancel**.

To quickly admit a patient that has already been entered into the system into a different bed, you can access the **Admit Patient** dialog from the **Patient View** for that bed, or from the **Beds** page. In this case, the **Bed** item shown on the dialog is fixed, and you will select the **Patient** to be admitted to the bed. The patient may be selected from either of two drop down lists which show the eligible patients in **Name** or **MR Number** order.

Discharging a Patient

Patients are discharged from beds using the **Discharge Patient** dialog, which can be opened by clicking the **Discharge** buttons on the **Patients** screen, the **Beds** screen, or the **Patient View**. You will be prompted to log in to the system before the dialog is shown.
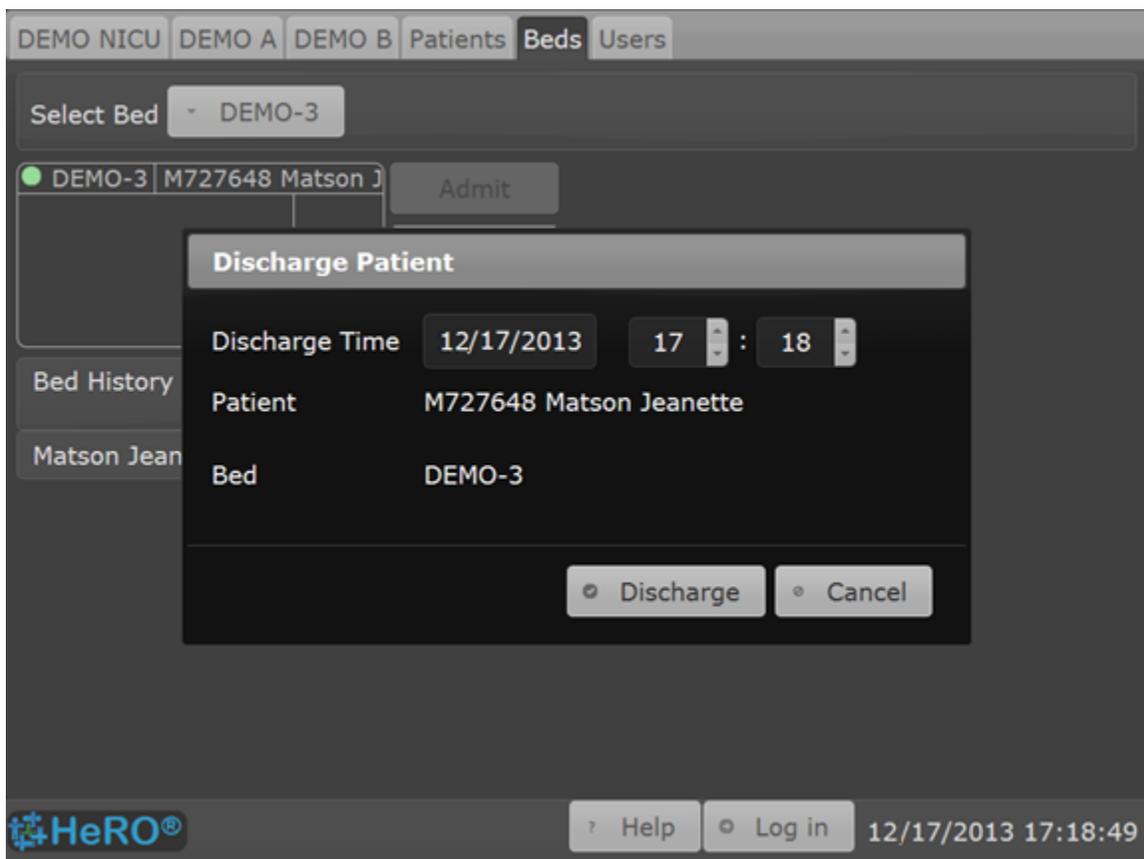
Figure 8. **Discharge Patient** dialog

The **Discharge Patient** dialog displays the bed name and patient information for the bed that is about to be discharged, along with date and time input fields for the **Discharge Time**. When the dialog is first displayed, **Discharge Time** is set to the current date and time. If you know that the patient was moved out of the bed at a significantly earlier time, you should update these fields before performing the discharge. This reduces the likelihood of accidentally assigning RR interval data to the wrong patient.

To complete the discharge operation, click **Discharge**. If you do not wish to perform the discharge, click **Cancel**.

Transferring a Patient

The Transfer Patient dialog is used when a patient is moved from one bed to another. This dialog can be shown by clicking the Transfer buttons on the Patients screen, the Beds screen, or the Patient View. You will be prompted to log in to the system before the dialog is shown.
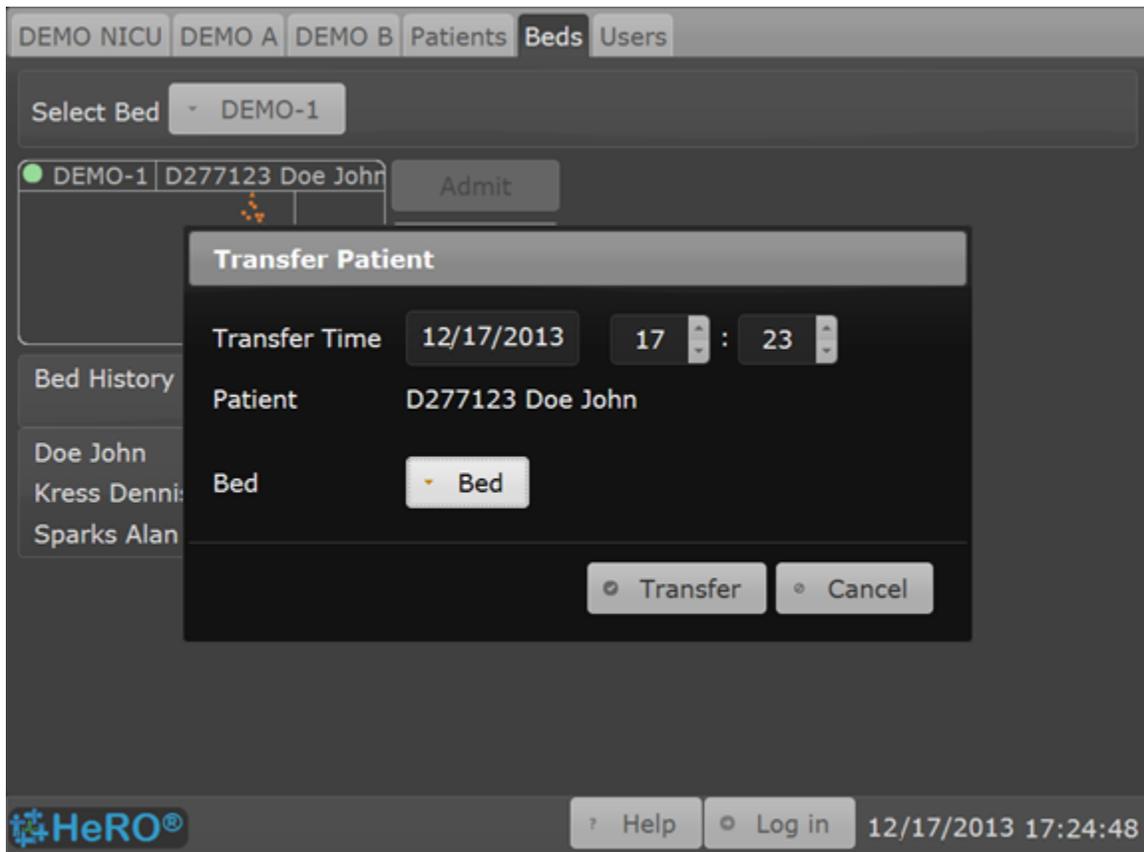
Figure 9. Transfer Patient dialog

The Transfer Patient dialog displays the name of the patient that is about to be transferred to a new bed. It also contains a drop down Bed list that is used to select the bed into which the patient will be transferred, along with date and time input fields for the **Transfer Time.**

The **Bed** list shows all beds that the patient can be transferred to at the specified **Transfer Time**. Beds that have other patients admitted at this time (or after it) are not shown in the list.

When the dialog is first displayed, the **Transfer Time** is set to the current date and time. If you know that the patient was actually moved at a significantly earlier time, you should update these fields before performing the transfer. This reduces the likelihood of accidentally assigning RR interval data to the wrong patient.

To complete the transfer operation, click **Transfer**. If you do not wish to perform the transfer, click **Cancel**.

Tip: To select an item from a long list of options, type in the first few letters of the item. This will reduce the number of choices displayed so you can more quickly make your selection.

Resolving Conflicts in the Bed Assignments

The **Beds** screen (see Figure 10) gives the user an overview of all of the admit, discharge and transfer operations for all of the beds covered by **HeRO**.
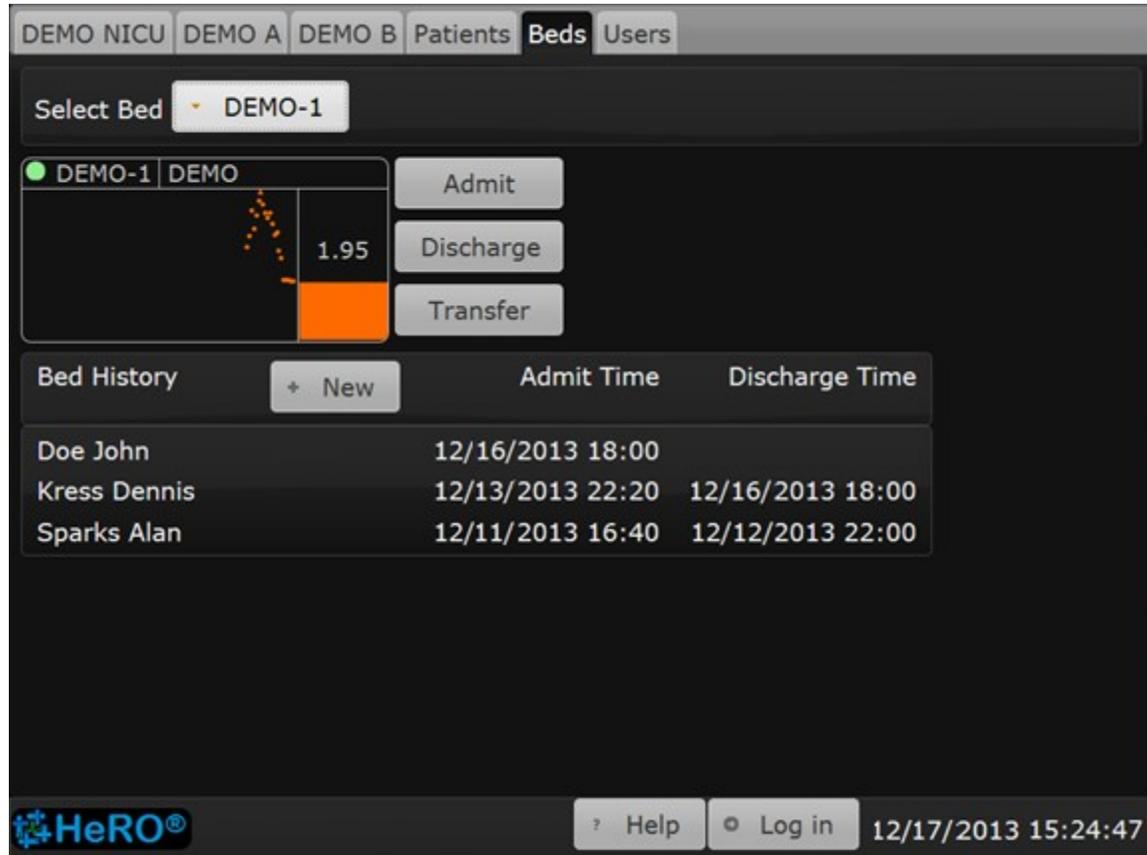
Figure 10. **Beds** Screen

The **Beds** screen contains a drop down Bed list that is used to select a bed for display. When a bed is selected, the screen displays a **Bed Icon** that shows a real-time trend of the **HeRO** score for the bed, and a list of bed history entries showing all of the patients that have been assigned to the selected bed over time.

To change a bed history entry, first **Log in** to **HeRO**. Use the **Bed** drop down list on the **Select Bed** bar to select the correct bed, and then click or tap the desired item where it appears in the Bed History list. This will display the **Bed History** dialog (see figure 11).
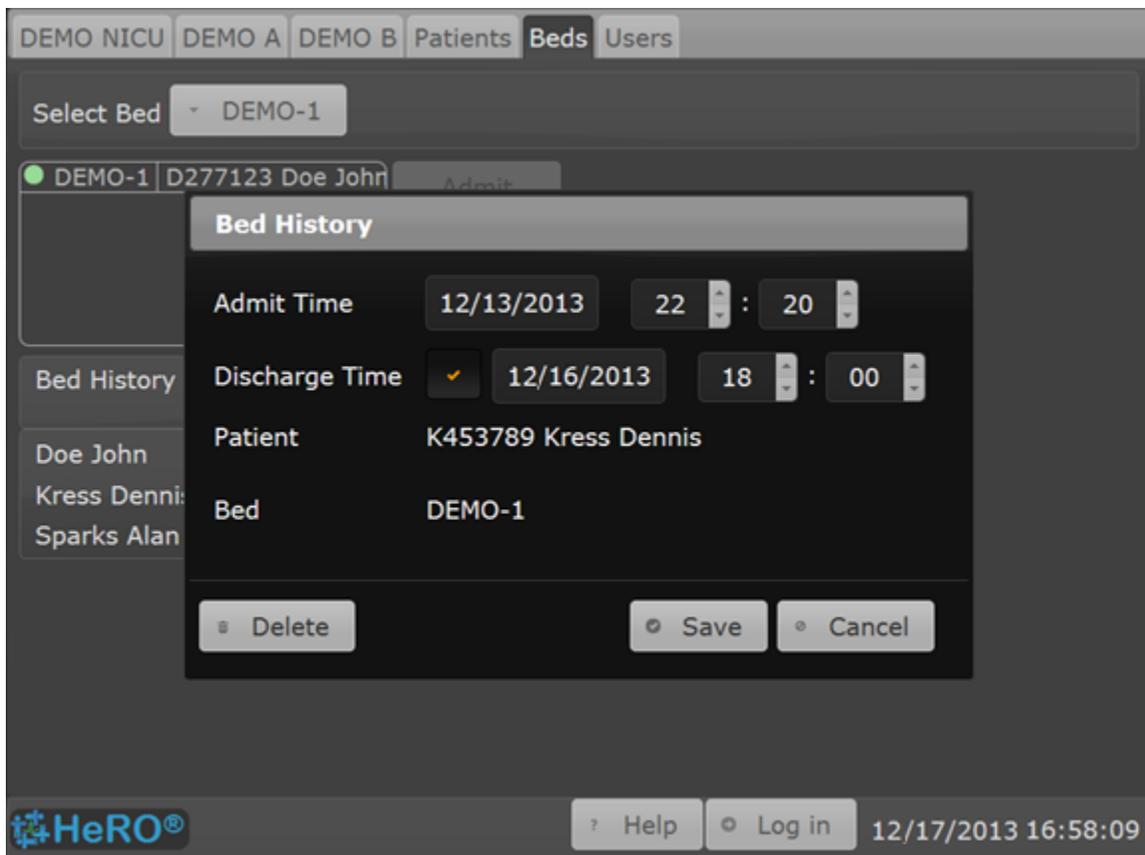
Figure 11. Bed History dialog.

The **Bed History** dialog is used to create new bed history entries or to change existing entries.

To create a new bed history entry, click the **New** button at the top of the **Bed History** list that is shown on the **Beds** screen. The **Bed History** dialog will open to show an empty bed history entry for the selected bed. You must select the Patient and enter an **Admit Time**. You may optionally enter a **Discharge Time** as well.

It is also possible to create new bed history entries from the **Bed History** shown on the **Patients** screen. Click or tap on the **New** button to open a **Bed History** dialog for the new entry. In this case, the patient is already assigned, and you will select the bed from the drop down list.

To edit an existing bed history entry from the list, simply click on the item. The **Bed History** dialog may then be used to make changes to the **Admit Time** and **Discharge Time** of an individual bed history entry to reflect the actual start and

end times of the bed assignment. Unchecking the **Discharge Time** box removes the discharge time from the bed history entry, which means that the patient is still in the bed.

To completely delete the bed history entry, click the **Delete** button. Deleting a bed history entry removes RR intervals from the patient record and re-computes the **HeRO** Scores, as though the patient had never been admitted to the bed.

Once all necessary changes have been made, press **Save**. To cancel the changes, press **Cancel**.

Editing Patient Information
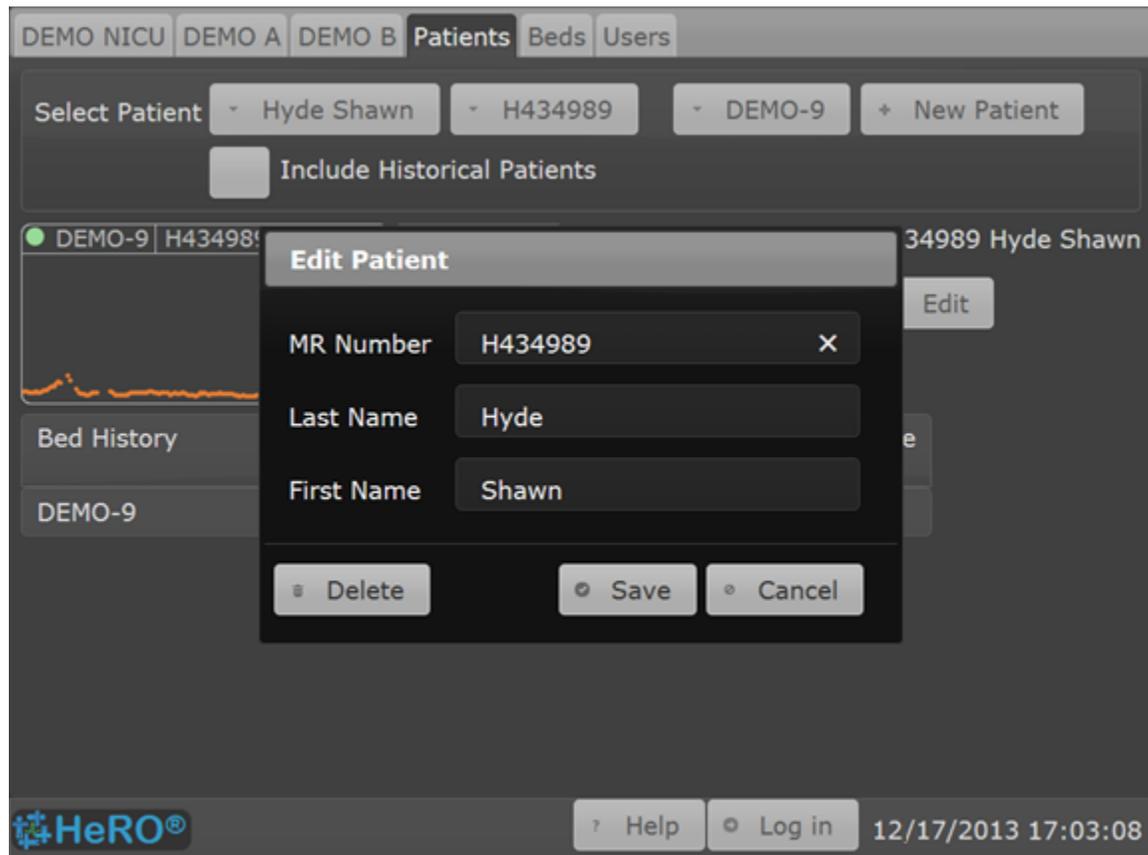
Figure 12. Editing a Patient

The Patients screen may be used to update the patient information that was entered when the patient was first admitted to a **HeRO** bed. It can also be used to delete duplicate patients or those that were entered by mistake.

The **HeRO** system automatically hides patients that have not been admitted to a **HeRO** bed for a long period of time. This prevents the drop-down lists from filling up with patients that are no longer being monitored. Checking the Include Historical Patients check box will display all patients in the lists.

To edit patient information, perform the following steps:

1. Log In to **HeRO**, by pressing the button at the bottom right, then entering your user name and password.

2. On the **Patients** screen, select a patient from the **Name** or **MR Number** drop-down lists. If necessary, check the **Include Historical Patients** box so that the desired patient appears in the lists.
3. Click the **Edit** button to open the **Edit Patient** dialog (see figure 12).
4. Make all desired changes.
5. Click the **Save** button.

To delete a patient from the system, perform the same steps as above, but click **Delete** instead of **Edit**. You will be asked to confirm the operation.

⚠ **Warning:** Deleting a patient removes all of the patient's information, bed history and **HeRO** score trends from the system.

ADT with Networked Data Acquisition

When the **HeRO** system is set up to use the Network Data Acquisition Interface (NDAI) to acquire heart rate data from the physiological monitoring network, it may also be configured to request patient admit information from the physiological monitors, so that it can perform automatic patient admit and transfer operations. In this mode of operation, patients are admitted, discharged and transferred at the central station that is associated with the physiological monitors, and the **HeRO** system performs the equivalent admit, discharge and transfer operations.

The Network Data Acquisition ADT interface uses the Medical Record Number as the "key" to identify a particular patient within the NICU. **Changes to the Medical Record Number drive patient admit and transfer operations.** The interface also synchronizes the patient name with information received from the monitors, but no ADT operations are performed as a result of name changes.

To use this system, it is necessary to enter accurate Medical Record Number and Patient Name information at the physiological monitoring system central station, or directly on the monitor, when admitting a patient to the NICU. When the patient moves to another bed, use the Patient Transfer function on the central station or the monitor to "move" the demographic information to the new location. (If a specific Transfer function is not available, you may simply "discharge" one monitor and then "admit" the patient to the new monitor by re-entering the demographic information. In this case, you must ensure that the Medical Record Number matches exactly.)

When using the NDAI ADT interface, do not admit patients with incomplete or "dummy" Medical Record Numbers to the monitors. This may cause the **HeRO**

ADT interface to create multiple patient records for the same patient, which will result in incomplete **HeRO** Score information for that patient. (If the Patient Name is unknown at the time of admission, it is acceptable to enter a "dummy" name such as "Smith, Boy". The name can be updated later as needed, and the changes will be reflected in **HeRO**.)

Due to the way in which the patient information is reported by some types of physiological monitors, when the information is changed at the central station, there may be a delay of a few minutes before the update is reflected in the **HeRO** system. During this time, the Plan and Pod Views will display an **UPDATING** message on the affected bed (or beds, in the case of a transfer from one bed to another).

When the NDAI ADT interface is enabled, the corresponding "manual" admit, discharge and transfer functions of the **HeRO** system (as described earlier) are disabled.

The remainder of this section presents detailed information about the operation of the Networked Data Acquisition ADT interface.

The **HeRO** NDAI ADT interface performs the following operations based on changes reported by the monitors. Related error conditions are displayed on the Plan and Pod Views:

- When a new MR Number is received from the physiological monitor, the **HeRO** ADT interface creates a new patient in the **HeRO** system and assigns the MR Number and Name to that patient. If no Patient Name is provided, the interface sets the **NO NAME** error condition to indicate that name information should be entered at the physiological monitor central station.
- When an empty MR Number is received in a bed that had previously contained a patient, the **HeRO** ADT interface double-checks the patient name information. If the name information is also empty, the **HeRO** patient is discharged from the bed.
  If the interface receives an empty MR Number but the monitor is still reporting the Patient Name of an admitted patient, the interface sets the **NO MR#** error condition to indicate the inconsistency. To resolve the error, either (a) remove the Patient Name (if the patient has indeed left the bed) or (b) supply the missing MR Number (if a patient is admitted to the monitor).
- When a MR Number "moves" from one monitor to another – that is, a patient is transferred at the physiological monitoring system central station – the **HeRO** patient is transferred into the new bed location.

- When the MR Number reported by a monitor matches that reported by another monitor in the NICU, the interface notes a conflict – it is not clear where the patient is located – and sets the **MR# CONFLICT** error condition. To resolve the error, discharge the patient from one of the beds.
- When the MR Number reported by a monitor stays the same, but the associated Patient Name changes, the name of the corresponding **HeRO** patient is updated to match the new name.

For detailed information about the error conditions described above, refer to the ***Troubleshooting*** section.

The **HeRO** ADT interface also performs some automatic operations to "clean up" in situations where the demographic information provided by the physiological monitors is missing or incomplete. These functions are configurable for each site.

- If a particular patient monitor fails to report its demographic information for several minutes (because the monitor is in a "discharged" state, disconnected from the network, or turned off), the interface will discharge transfer the associated **HeRO** patient from that bed. (If the monitor later begins reporting demographic information, the interface will automatically re-admit the patient to the bed.)

- If a particular patient has not been assigned to any NICU beds for a period of several days, the interface automatically archives the **HeRO** patient record. This means that it is not necessary to use the **HeRO** Archive function to "manually" archive patients from the system.

Users

Figure 13. Users screen

The Users screen (see Figure 13) shows a list of all of the authorized users of the **HeRO** system. In order to view the list and add or delete users, you must Log in and have been granted Admin privileges.

Adding a User

To add a user to **HeRO**:
1. Press the New User button on the Users screen. You will be immediately prompted to enter the **User Name**. The prefix of the user's email address is a good choice.
2. Enter the user's **Last Name** and **First Name**.
3. You may choose to enter an **Email Address** for the user. This is optional. **HeRO** does not make use of this information and does not send email messages.
4. Enter **Password** settings as dictated by your institution's security policies. You may use the Change Password button to assign a password, or check the User Can Change Password and User Must Change Password at Next Login to force the user to choose their own password when they first log in to the system.
5. Set the **User Type** to either Standard or Admin by clicking the appropriate button. Use Admin for administrative users who must manage other user accounts on the **HeRO** system.
6. When you are finished, click Save to save your changes.

Modifying User Information

To remove a user from **HeRO,** select the user from the User Name or Name lists on the **Select User** bar at the top of the screen, and then press the Delete button. You will be asked to confirm the deletion.

To edit user information, select the user from one of the drop down lists on the **Select User** bar, and then click Edit button. Make any necessary changes and then click the Save button. If you do not wish to update the user record, click the Cancel button.

The Change Password button is used to assign a new password or to change an existing password. The Reset Password button clears the assigned password without creating a new one. This can be used in combination with User Must Change Password at Next Login to force the user to choose their own password.

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[1-7]. 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 Indicator

The **Bed Icon** and **Patient View** contain a green indicator located in the upper left corner. This indicator is shown when the system is receiving heart rate data for the bed. If it does not appear for a particular bed, check the following.

- Check for other error messages that may indicate a communication error within the system.
- Check for loose or disconnected cables.
- Verify that the ECG monitor is turned on and is displaying an ECG waveform and a Heart Rate value. If the monitor is showing steady, reasonable values, contact Technical Support for assistance.
- Ensure that ECG leads are positioned and attached appropriately.
- Make sure the appropriate set of leads is selected on the ECG monitor. See the Operator Manual for the Physiological Monitor for instructions.
- Artifacts may arise from patient movement. Continue observing the system to see if the situation resolves once the patient is no longer moving.
- Compare the ECG signal displayed on the **Patient View** to the one on the ECG monitor. If these differ markedly, contact Technical Support for assistance. Note that some system configurations do not show ECG waveforms.

The **HeRO** system requires several hours of patient data to compute a score. After admitting a patient to a bed, even if the indicator is green, it may take up to three hours until the first score is generated.

Bed Icon Error Messages

Message: Comm Error
Description: The system is unable to communicate with the DAD device serving the bed.

Cause	Resolution
DAD device not receiving power.	Check connections at DAD unit and power supply brick.
DAD device not connected to network.	Check network connections. Contact hospital IT personnel to check for network outage.

DAD requires reboot.	Remove power connector, wait for full 10 seconds, restore power, and wait while DAD boots.
DAD device defective.	Contact MPSC Technical Support.

Message: No Wave
Description: The system is not receiving ECG waveform data from the networked monitor serving the bed.

Cause	Resolution
No patient admitted to monitor.	Admit patient to monitor.
Monitor is turned off.	Turn on monitor.
Trouble with physiological monitoring network.	Check operation of physiological monitor Central Station. Contact appropriate support personnel to resolve any issues.
HeRO NDAI interface is not operating correctly.	Contact MPSC Technical Support.

Message: No Heart Rate
Description: The system is not receiving heart rate data from the networked monitor serving the bed.

Cause	Resolution
No patient admitted to monitor.	Admit patient to monitor.
Monitor is turned off.	Turn on monitor.
Trouble with physiological monitoring network.	Check operation of physiological monitor Central Station. Contact appropriate support personnel to resolve any issues.
HeRO NDAI interface is not operating correctly.	Contact MPSC Technical Support.

Message: No MR #
Description: The system is receiving data from the physiological monitor serving the bed, but no valid Medical Record Number is specified for the patient admitted to that monitor.

Cause	Resolution

Patient is admitted to the monitor, but no valid MR Number was provided.	Edit the patient admit info shown on the physiological monitor Central Station to include a valid MR Number.

Message: No Name
Description: The system is receiving data from the physiological monitor serving the bed, but no Name is specified for the patient admitted to that monitor.

Cause	Resolution
Patient is admitted to the monitor, but no Name was provided.	Edit the patient admit info shown on the physiological monitor Central Station to include a valid Name. (If the name is unknown, it is acceptable to use a "dummy" name such as "Smith, Boy". The name can be updated later as needed.)

Message: MR Number Conflict
Description: The physiological monitors for the affected beds are reporting the same Medical Record Number for the admitted patient.

Cause	Resolution
Two or more monitors report the same MR Number for the admitted patient.	Discharge the patient from one of the monitors.

Message: Updating Patient
Description: The network data acquisition interface is in the process of receiving updated patient information from the physiological monitor. This message should disappear after a few minutes, and does not indicate an error condition unless it fails to disappear.

Cause	Resolution
The physiological monitor takes a few minutes to make updated admit information available on the network.	This is normal operation.

Admit/Discharge/Transfer Error Messages

Message: Failed to admit patient [...] to bed [...]
Description: This message is shown when an Admit operation fails to complete.

Cause	Resolution
The manual ADT system was not able to complete the process of assigning patient data to the new bed.	Wait a few moments and try to perform the Admit operation again. If it fails, contact MPSC Technical Support.

Message: Cannot admit patient [...] due to a conflict ([...] is assigned to bed [...] at [...]).
Description: This message is shown when an Admit operation cannot be performed because it would cause a conflict in the Bed History.

Cause	Resolution
The specified patient is admitted to a different bed at the requested **Admit Time**, or the specified bed has a different patient admitted at the requested **Admit Time**.	Pick a new **Admit Time**, or review the bed assignments to address the conflicts and try to perform the Admit operation again. If it fails, contact MPSC Technical Support.

Message: Failed to discharge patient [...] from bed [...]
Description: This message is shown when a Discharge operation fails to complete.

Cause	Resolution
The manual ADT system was not able to complete the process of updating the patient data to reflect the new discharge.	Wait a few moments and try to perform the Discharge operation again. If it fails, contact MPSC Technical Support.

Message: Failed to transfer patient [...] to bed [...]
Description: This message is shown when a Transfer operation fails to complete.

Cause	Resolution
The manual ADT system was not able to complete the process of updating the patient data to reflect the discharge from the old bed and the admit to the new one.	Wait a few moments and try to perform the Transfer operation again. If it fails, contact MPSC Technical Support.

Message: Cannot transfer patient [...] due to a conflict ([...] is assigned to bed [...] at [...]).

Description: This message is shown when a Transfer operation cannot be performed because it would cause a conflict in the Bed History.

Cause	Resolution
The specified patient is admitted to a different bed at the requested **Transfer Time**, or the specified bed has a different patient admitted at the requested **Transfer Time**.	Pick a new **Transfer Time**, or review the bed assignments to address the conflicts and try to perform the Transfer operation again. If it fails, contact MPSC Technical Support.

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	0° to 50° C (32° to 120° F)	-30° to 60° C (-23° to 140° F)
Relative Humidity	30% - 80% RH	10% - 95% RH
Altitude	0 to 5000 meters (16,000 ft)	0 to 12000 meters (39,000 ft)

Cleaning

The hardware components of the **HeRO** system (including, as applicable, the Server computer, Viewing Stations, AD2-DADs, and cables) may be dusted or wiped with a damp cloth as needed.

Maintenance

Apart from cleaning (see above), the hardware components of the **HeRO** system do not require regular maintenance. When necessary, MPSC technical personnel shall perform any necessary configuration changes or hardware replacements. MPSC recommends the installation of operating system patches and/or anti-virus updates on the Server computer as these become available. Dedicated viewing station computers shall be updated by MPSC support personnel.

Accessories

The following user installable accessories are available from MPSC:
- Cable to connect AD2-DAD devices directly to the ECG monitor Defib/Sync jack
- Cable to connect AD2-DAD device to CAT5 wall plate jack
- Cable to connect ECG monitor to CAT5 wall plate jack

Disposal

The hardware components of the **HeRO** system shall be returned to MPSC for disposal unless other arrangements are made. The components do not contain hazardous materials and may be treated like commercial computing equipment with regard to disposal or recycling.

AD2-DAD Technical Info and Installation Guidelines

Installation of the **HeRO** AD2 Data Acquistion Device shall be performed by MPSC technical personnel or authorized representatives. The following information is provided for reference. For assistance with installation or reconfiguration, contact MPSC Technical Support at 1-800-394-1625.

Site Location

The AD2-DAD may be installed in the following locations:
- a server room or data closet that is cabled to the NICU such that a separate cable run is provided for each bed. This is the preferred installation method.
- in the NICU. The AD2 is approved for use within the "patient vicinity" that extends within 1.5 meters of the patient. Individual cables are run from the AD2 locations to the ECG monitors and to the network drops (one per AD2).

The 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

The AD2-DAD requires the following connections and cable types:

Connection	Cable Type	Maximum Length	Notes
ECG signal input (from Defib/Sync jack on ECG monitor)	CAT5	100 meters	• Each AD2 can connect to up to 4 ECG monitors. • Connector adapters are required at AD2 (BNC connector) and at Defib/Sync jack (manufacturer specific connector)
	Coaxial	100 meters	• Each AD2 can connect to up to 4 ECG monitors. • A connector adapter is

			required at the Defib/Sync jack (manufacturer specific connector)
Network	CAT5 shielded	100 meters	The AD2-DAD is compatible with 10- and 100BaseT networks.
Power	2 wire power cord (provided)	2 meters	The AD2-DAD uses an external medical grade power supply rated for 110-240VAC input voltage. It is not approved for use with any other power supply. The 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 to the public low voltage power supply network that supplies buildings used for domestic purposes.

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

Description of Markings

The following markings are used on the AD2-DAD labeling:

Marking	Description
	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.
EC REP	Contact information for European Community Representative.

Modifications

The AD2-DAD is not user serviceable and must not be modified in any way. Defective units must be returned to MPSC for replacement. The **HeRO** System 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

The **HeRO** System is 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 the **HeRO** System from service.

Electrical Isolation

The AD2-DAD is electrically isolated via the provided medical grade power supply, specified below. It is not approved for use with any other type of power supply.

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

Electromagnetic Compatibility

Guidance and manufacturer's declaration – electromagnetic emissions		
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.		
Emissions test	**Compliance**	**Electromagnetic environment – guidance**
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	

<table>
<tr><td colspan="4" align="center">Guidance and manufacturer's declaration – electromagnetic immunity</td></tr>
<tr><td colspan="4">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.</td></tr>
<tr><td>IMMUNITY test</td><td>IEC 60601 test level</td><td>Compliance level</td><td>Electromagnetic environment – guidance</td></tr>
<tr><td>Electrostatic discharge (ESD)

IEC 61000-4-2</td><td>± 6 kV contact

± 8 kV air</td><td>± 6 kV contact

± 8 kV air</td><td>Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.</td></tr>
<tr><td>Electrical fast transient/burst

IEC 61000-4-4</td><td>± 2 kV for power supply lines

± 1 kV for input/output Lines</td><td>± 2 kV for power supply lines

± 1 kV for input/output Lines</td><td>Mains power quality should be that of a typical commercial or hospital environment.</td></tr>
<tr><td>Surge

IEC 61000-4-5</td><td>± 1 kV line(s) to line(s)

± 2 kV line(s) to earth</td><td>± 1 kV line(s) to line(s)

± 2 kV line(s) to earth</td><td>Mains power quality should be that of a typical commercial or hospital environment.</td></tr>
<tr><td>Voltage dips, short interruptions and voltage variations on power supply input lines

IEC 61000-4-11</td><td><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</td><td><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</td><td>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.</td></tr>
<tr><td>Power frequency (50/60 Hz) magnetic field

IEC 61000-4-8</td><td>3 A/m</td><td>3 A/m</td><td>Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.</td></tr>
<tr><td colspan="4">NOTE U_T is the a.c. mains voltage prior to application of the test level.</td></tr>
</table>

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
Conducted RF IEC 61000-4-6	3 Vrms 150 kHz to 80 MHz	3 V	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.
Radiated RF IEC 61000-4-3	3 V/m 80 MHz to 2,5 GHz	3 V/m	**Recommended separation distance** $$d = 1.2\sqrt{P}$$ $$d = 1.2\sqrt{P}$$ 80 MHz to 800MHz $$d = 2.3\sqrt{P}$$ 800 MHz to 2.5GHz where *P* is the maximum output pow er rating of the transmitter in w atts (W) according to the transmitter manufacturer and *d* is the recommended separation distance in metres (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey,[a] should be less than the compliance level in each frequency range.[b] Interference may occur in the vicinity of equipment marked w ith the follow ing symbol:

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.

[a] 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 w ith 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 w hich 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.

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

<table>
<tr><td colspan="4">Recommended separation distances between
portable and mobile RF communications equipment and the HeRO System</td></tr>
<tr><td colspan="4">The HeRO System is intended for use in an electromagnetic environment in w hich radiated RF disturbances are controlled. The customer or the user of the HeRO System can help prevent electromagnetic interference by maintaining a minimum distance betw een portable and mobile RF communications equipment (transmitters) and the HeRO System as recommended below , according to the maximum output pow er of the communications equipment.</td></tr>
<tr><td rowspan="2">Rated maximum output pow er of transmitter

W</td><td colspan="3">Separation distance according to frequency of transmitter

m</td></tr>
<tr><td>150 kHz to 80 MHz
$d = 1.2\sqrt{P}$</td><td>80 MHz to 800 MHz
$d = 1.2\sqrt{P}$</td><td>800 MHz to 2,5 GHz
$d = 2.3\sqrt{P}$</td></tr>
<tr><td>0.01</td><td>0.12</td><td>0.12</td><td>0.23</td></tr>
<tr><td>0.1</td><td>0.38</td><td>0.38</td><td>0.73</td></tr>
<tr><td>1</td><td>1.2</td><td>1.2</td><td>2.3</td></tr>
<tr><td>10</td><td>3.8</td><td>3.8</td><td>7.3</td></tr>
<tr><td>100</td><td>12</td><td>12</td><td>23</td></tr>
<tr><td colspan="4">For transmitters rated at a maximum output pow er not listed above, the recommended separation distance d in metres (m) can be estimated using the equation applicable to the frequency of the transmitter, w here P is the maximum output pow er rating of the transmitter in w atts (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.</td></tr>
</table>

Customer Service

If network problems arise, contact the hospital network administrator or MPSC Technical Support (toll free 1-800-394-1625).

Complaints may be reported via telephone or submitted in writing to the following address:

MPSC, 1233 Cedars Court Suite 201, Charlottesville, VA 22903

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 $x_1, x_2, \ldots x_{4096}$, 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:

$$R_1 = \frac{1}{4096}\sum_{i=1}^{4096} r_1(x_i)$$ and $$R_2 = \frac{1}{4096}\sum_{i=1}^{4096} r_2(x_i)$$ respectively.
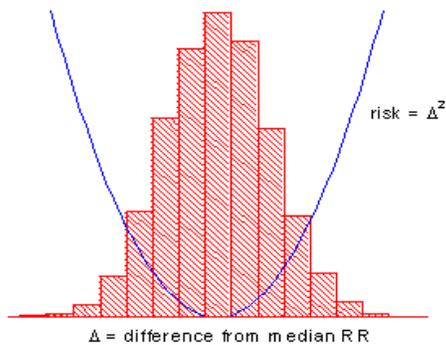
In other words, R1 and R2 are non-negative quantities that increase when the number and/or the magnitude of large deviations from the median increases. Intuitively, a distribution of RR intervals that is skewed to the right will result in R2 > R1.

Figure 13. Sample Asymmetry

Sample Entropy
Sample Entropy is a measure of regularity in time series that is suitable to HRV analysis[8]. 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[8].

A = number of matches of length $m+1$
B = number of matches of length m
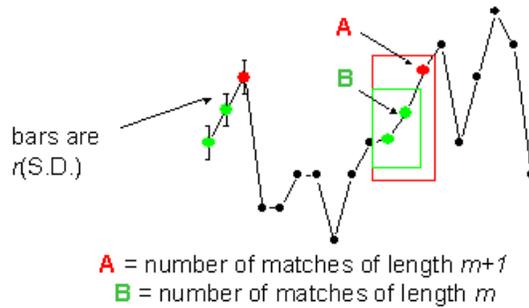
$$ApEn \approx -\ln (1+A)/(1+B)$$
$$SampEn = -\ln A/B$$

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

Figure 14. 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

$$A = \beta_0 + \beta_1 \bullet V_1 + \beta_2 \bullet V_2 + ... \beta n \bullet Vn$$

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 then a single set of coefficients can.

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

References:

[1]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.

[2]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.

[3]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

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.

[4]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.

[5]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.

[6]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).

[7]Griffin MP, Lake DE, Bissonette EA, Harrell FE, O'Shea TM, Moorman JR. Heart rate characteristics: novel physiomarkers 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.

[8]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.

Appendix B: Glossary

ANOVA: Analysis Of Variance

AD2 (AD2-DAD): A type of Data Acquisition Device that acquires ECG waveform data via analog connection to the Defib/Sync jack on the patient monitor.

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

Data Acquisition Device (DAD): A device that acquires ECG waveform data for the system. The AD2-DAD is the only type of DAD that is currently supported by the system.

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

Historical Patient: a patient that has not been admitted to a **HeRO** bed for a long period of time (typically 30 days). By default, these patients are not shown.

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

Networked Data Acquisition Interface (NDAI): This is a system configuration in which the heart rate data is acquired from the patient monitoring network.

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-conceptional 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.