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Flashback M1 Compensatory Reserve Monitor (Handheld)

with Flashback's Patented CRI Technology

Instructions for Use

Flashback TECHNOLOGIES

Flashback Technologies, Inc. | 1 Little West 12th Street, Suite 505
New York, NY, 10014 USA | flashbacktechnologies.com

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Caution: Federal (USA) law restricts sale by or on order of a physician.

Overview

Flashback Technologies' M1 Compensatory Reserve Monitor (Handheld) calculates and displays the percentage of the saturation of peripheral oxygen (SpO_2), heart rate (HR) in beats per minute, and Flashback Technologies' Compensatory Reserve Index (CRI™). The model M1 is made up of the M1 device and a Nonin 8000AA Sensor (1-meter cable). The Flashback M1 is intended for use in hospitals and ground ambulances, it is not intended for use in homes.

READ AND UNDERSTAND THE ENTIRE INSTRUCTIONS FOR USE BEFORE USING THE M1.

These instructions for use are intended for qualified medical providers.

Indications for Use

The M1 is indicated for continuous noninvasive monitoring of functional oxygen saturation of arterial hemoglobin (SpO_2), pulse rate (measured by an SpO_2 sensor), and the Compensatory Reserve Index (CRI), which trends changes in intravascular volume relative to the individual patient's response to hypovolemia.

For patients with a finger thickness of 0.3" to 1" in hospital and pre-hospital settings.

CRI trends with changes in intravascular volume relative to the individual patient's response to hypovolemia, and should only be used by qualified medical providers as an adjunct to rather than as a replacement for traditional hemodynamic measures. CRI is indicated for adults (19-36 years old) in the supine position under non-motion conditions and without cardiovascular disease. CRI has not been studied in trauma patients.

Contraindications

- Warning: MR-unsafe!

  - Do not expose the device to a magnetic resonance (MR) environment.
  - The device may present a risk of projectile injury due to the presence of ferromagnetic materials that can be attracted by the MR magnet core.
  - Thermal injury and burns may occur due to the metal components of the device that can heat during MR scanning.
  - The device may generate artifacts in the MR image.
  - The device may not function properly due to the strong magnetic and radiofrequency fields generated by the MR scanner.
  - Do not use the M1 in an MR environment or in an explosive atmosphere, or on infant or neonatal patients.
- The device is not defibrillation proof per IEC 60601-1.

Warnings

- The M1 is only indicated for use with the Nonin Model 8000AA adult articulated sensor (1-meter cable).
- Inspect the sensor application site at least every 10 minutes to ensure correct sensor alignment, skin integrity, and that the sensor temperature does not exceed 42˚C. Patient sensitivity to the sensor may vary due to medical status or skin condition.
- Avoid excessive pressure to the sensor application site as this may cause damage to the skin beneath the sensor.
- **ADJUNCT WARNING:** This device is intended only as an adjunct in patient assessment. It must be used in conjunction with other methods of assessing clinical signs and symptoms.
- General operation of the Model M1 may be affected by the use of a high-frequency electrosurgical unit (ESU).
- The use of accessories other than those specified in these instructions may result in increased electromagnetic emission and/or decreased immunity of this device.
- Keep the device away from young children. Small items such as the battery door, and battery are choking hazards.

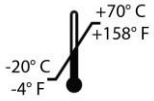
Cautions

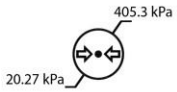
- The Model M1 has no audible alarms. Do not use the M1 as an unattended SpO_2 monitor.
- To prevent degraded SpO_2 performance and/or patient injury, verify sensor and pulse oximeter compatibility before use. Only the Nonin Model 8000AA adult articulated sensor with 1-meter cable should be used with the M1.
- Do not use a damaged sensor. If the sensor is damaged in any way, discontinue use immediately and replace the sensor.
- Do not use if any component of the device is visibly damaged. Do not use if the battery door is broken or fails to close tightly, as this may allow ingress or ESD damage to the device.
- The battery compartment should be inspected periodically for dust and fluid ingress, and any contaminants removed with a dry cloth.
- The battery compartment door should be closed when operating the device to ensure battery terminals are not exposed during usage.
- The Model M1 can only be powered by battery when used in patient care. The USB connection is only for use by authorized Flashback technicians. Use by end users will void the warranty.
- This equipment complies with IEC 60601-1-2:2014 for electromagnetic compatibility. This standard is designed to provide reasonable protection against harmful interference in a typical medical installation. However, because of the proliferation of radio-frequency transmitting equipment and other sources of electrical noise in healthcare and other environments, it is possible that high levels of such interference due to close proximity or strength of a source might disrupt the performance of this device. Medical electrical equipment needs special precautions regarding EMC, and all equipment must be installed and put into service according to the EMC information specified in this manual.
- Portable and mobile RF communications equipment may affect medical electrical equipment.
- A functional tester cannot be used to assess the accuracy of a pulse oximeter monitor or probe.
- Factors that may degrade M1 device performance or affect the accuracy of the measurements provided include the following:

    - Do not apply the sensor on the same arm as a blood pressure cuff, arterial catheter or infusion line(s) (IVs)
    - Finger is outside recommended size range or patient weight range
    - Cardiogreen and other intravascular dyes
    - Poor pulse quality
    - Artificial nails or fingernail polish
    - Excessive ambient light
    - Venous pulsations
    - Improperly applied device
    - Excessive motion
    - Carboxyhemoglobin
    - Dysfunctional hemoglobin
    - Moisture in the sensor or device
    - Improperly applied sensor
    - Methemoglobin
    - High-frequency electrosurgical interference
    - Residue (e.g., dried blood, dirt, grease, oil) in the light path
    - Incorrect sensor type
    - Cardiovascular dyes
    - Anemia or low hemoglobin concentrations
    - Sensor not at heart level
- The Model M1 may not work when circulation is reduced. Warm or rub the finger, or re- position the device.
- The Model M1 display will display dashes when there is no valid sensor data for an extended period. No readings or poor readings will prevent data updates.
- In some circumstances, the Model M1 may interpret motion as good pulse quality. Minimize patient motion as much as possible.
- Clean the Model M1 before applying it to a patient.
- The Model M1 is non-sterile. Do not sterilize, autoclave, or immerse the Model M1 in liquid.
- Do not pour or spray any liquids into the device.
- Do not use caustic or abrasive cleaning agents, or any cleaning products containing ammonium chloride or isopropyl alcohol.
- This Model M1 is a precision electronic instrument and must be repaired by qualified technical professionals. Field repair of the device is not possible. Do not attempt to open the case or repair the electronics. Opening the case will damage the device and void the warranty.
- Batteries may leak or explode if used or disposed of improperly. Remove the battery from the M1 if the device will be stored for more than 30 days.
- A power supply is not included with this ME Equipment and therefore should not be used as an ME System.
- Follow local, state, or national governing ordinances and recycling instructions regarding disposal or recycling of the device and device components.
- Care should be taken to avoid device contact with the patient, other than the Nonin Model 8000AA fingertip sensor.
- The operator should briefly touch the device (less than one second) to ensure that it is not overheating, before handling the device. If the external temperature of the device is greater than 48˚C, the device should immediately be turned off and the sensor removed from the patient. The

device should not be used again until the source of the excessive heat is mitigated (battery compartment short or otherwise).

Guide to Symbols

Symbol	Definition of Symbol
	Follow Instructions for Use
	Caution!
	Nonin 8000AA Sensor Type BF Applied Part (patient isolation from electrical shock)
	UL Mark for Canada and the United States with respect to electric shock, fire, and mechanical hazards only in accordance with IEC 60601-1, AAMI ANSI 60601-1 and CAN/CSA-C22.2 No. 60601.1.
SN	Serial Number
	Battery Orientation
	Lot Number
	Storage/shipping temperature range (wait 8 hours before using if device has been in this range)
	Storage/shipping humidity range (wait 8 hours before using if device has been in this range)

Symbol	Definition of Symbol
	Storage/shipping atmospheric temperature range
	Medical prescription required
IP33	Protected from water falling as a spray at any angle up to 60° from the vertical and ingress of solid foreign objects greater than or equal to 2.5 mm in diameter per IEC 60529.
	Do not expose the device to a magnetic resonance (MR) environment

Conventions Used in this Document

Additional information, tips, and hints are listed with a blue, circular, " i " icon.

Notices are listed with a yellow, triangular, exclamation point icon.

Getting Started with the M1

Insert Battery

Insert a 1.5V AA battery into the battery compartment located on the back of the unit. The battery compartment can be opened by pulling outward from the indentation on back of the device. The battery should be replaced with the negative side (-) pressed upon the battery contact containing a spring (see Figure 1). Close the battery compartment door to secure the battery. A fresh alkaline battery should power the device for at least 8 hours of continuous use.

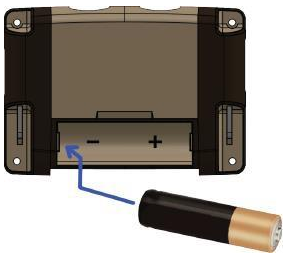


Figure 1 - Insert Battery

Use only an IEC LR06 1.5V AA battery. Usage of a similar sized battery containing a different voltage could damage the device.

Attaching the Nonin Sensor

Attach the Nonin sensor to the device by inserting the black end of the sensor into the DB9 connection on the left side of the M1 with the Nonin logo facing up (see Figure 2).

Figure 2 - Attaching the Nonin Sensor

Using the Nonin Articulated Clip Sensor

1. Insert a finger (preferably the index, middle, or ring finger) into the Adult Articulated Finger Clip Sensor (Figure 1) until the end of the finger reaches the finger stop. Keep the fingernail facing the sensor top (as shown in Figure 1). Ensure that long fingernails do not interfere with proper finger position.

2. For the best results when using the sensor for data collection, secure the sensor cable independently from the sensor with medical tape, preferably around the base of the finger. Make sure that the tape securing the cable does not restrict the blood flow (see Figure 3).

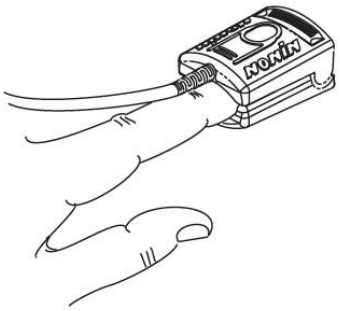


Figure 3 - Insert finger into sensor

The thumb is not recommended for use with the Adult Articulated Finger Clip Sensor.

Note: Proper sensor placement is critical for good performance. If the sensor is not positioned properly, light may bypass the tissue and result in inaccuracies.

Powering Up the M1

On the top of the device, hold down the power button for approximately 1 second and release. The power button is located on the top right of the device and is labeled with a "power" symbol (see Figure 4).

The readings for SpO_2 and HR will appear before CRI and are usually available within 2 to 4 seconds of sensor placement. The CRI reading is usually available within 5 to 20 seconds of sensor placement.

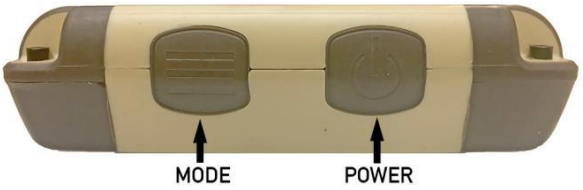


Figure 4 - Power on the M1

Guide to Software Symbols and Parameters

Parameters

HR	Heart Rate
SpO_2	Functional oxygen saturation of arterial hemoglobin (%SpO_2)
CRI	Compensatory Reserve Index

HR, SpO_2, and CRI values are displayed below their labels defined above.

No signal information will be available on the M1 until the sensor is connected to the unit and the sensor is applied to a fingertip. Dashes are displayed when no signal is available.

Graphical Interface Symbols

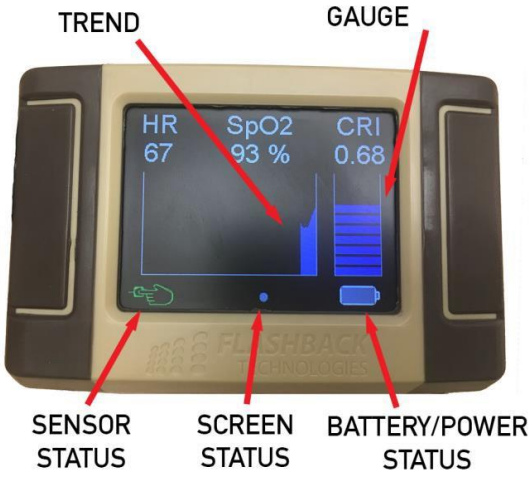


Figure 5 - M1 graphical user interface and symbols

Gauge

The “Gauge” to the right of the screen displays the current CRI reading in a bar chart and increments in 10ths.

Trend

The “Trend” graph to the left of the screen displays up to 20 minutes of the most recent CRI trend values. The trend value is updated every 5 seconds with the average CRI over the last minute. The trend moves from left to right and therefore, the most recent average is on the right (see Figure 6).

	If the sensor is not connected or there is no signal, the trend will continue to move, leaving empty space in the graph, in order to indicate time has passed since data has been collected.

Figure 6 - CRI trend

Sensor Status

The Sensor Status indicator displays the status of the:

- Sensor connection to the device
- Sensor connection to the finger
- Finger signal quality

There are four Sensor Status states:

	Sensor not connected to the device or is not detected by device
	Sensor connected/detected; no finger signal
	Sensor connected/detected; poor finger signal
	Sensor connected/detected; finger signal is satisfactory

The sensor may be disconnected and connected at any time from either the device or the finger. Please allow up to 5 seconds for a new connection to take place.

Screen Status

The screen indicator consists of 3 moving dots. The moving dots indicate that the screen is not frozen.

In the event of a screen freeze, all data displayed is invalid.

Battery Status

There are two Battery Status indicator states:

	The battery has greater than 20 minutes of use remaining.
	Replace the battery. Less than 20 minutes of device use may remain.

The battery status indicator is only valid when an alkaline battery is used.

Adjusting the Screen Brightness

The screen starts up in “Normal” brightness mode. There are three levels of brightness.

- Normal
- Bright
- Brightest

The screen brightness may be changed by pressing and releasing the “Mode” button. The “Mode” button is located on the top of the device on the left side. Each press will cycle the brightness mode. Using the lowest acceptable brightness level will prolong battery life.

Powering off the M1

The device can be powered off by pressing and holding the power button for approximately 5 seconds, or until the device shuts down.

Battery Replacement

The M1 uses one 1.5 volt AA battery. The battery compartment can be opened by pulling outward from the indentation on back of the device (see Figure 7). The old battery may be removed by turning the device with the opening facing down and tapping the device lightly on your hand to shake the battery free. The new battery should be replaced with the negative side pressed upon the battery contact containing a spring. Close the battery compartment door to secure the battery. A fresh alkaline battery should power the device for at least 8 hours of continuous use.

Figure 7 - Replacing the AA battery

Software Version

The current version of the software can be viewed by pressing and holding down the "Mode" button. The "Information Screen" will be displayed until the "Mode" button is released. The version is displayed as "#.#.#_#.#.#."

Cleaning the Reusable Sensor

Cautions:

- Clean the sensor before applying it to a new patient.
- Unplug the sensor from the M1 before cleaning.
- Do not sterilize, autoclave, or immerse the sensors in liquid of any kind. Do not pour or spray any liquids into the sensor. Do not sterilize with EtO.
- Do not use caustic or abrasive cleaning agents on the sensors. Do not use cleaning agents containing ammonium chloride or isopropyl alcohol.

Cleaning Method:

1. To clean the sensor, wipe all patient contact surfaces with a soft cloth dampened with a mild detergent or a 10% bleach/90% water solution (household bleach [containing less than 10% sodium hypochlorite]).
2. Allow the sensor to dry thoroughly before reusing.

Note: Do not open the sensor's case more than 90°, or the case may be damaged. The figure at right shows the appropriate opening of the case for cleaning (see Figure 8).

Note: To minimize cable deterioration when cleaning the cable, gently wipe away from the plug end towards the sensor end.

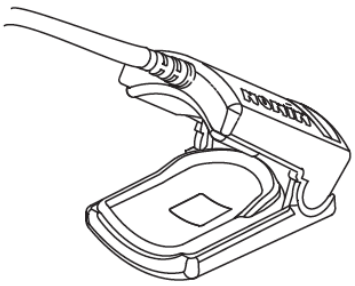


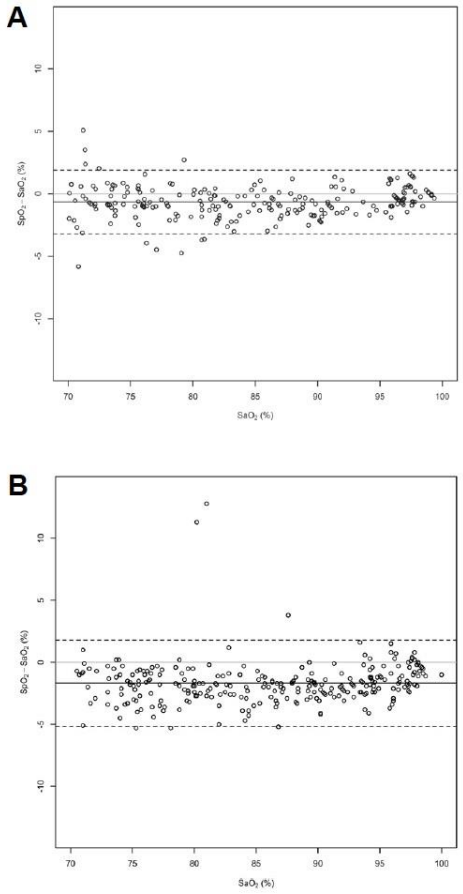
Figure 8 - Cleaning the reusable sensor

Cleaning the M1

If the body of the M1 needs to be cleaned, gently wipe the surfaces with a soft cloth dampened with a mild detergent or a 10% bleach/90% water solution (household bleach [containing less than 10% sodium hypochlorite]).

- Do not sterilize, autoclave, or immerse the M1 in liquid of any kind. Do not pour or spray any liquids onto the M1. Do not sterilize with EtO.
- Do not use caustic or abrasive cleaning agents on the M1. Do not use cleaning agents containing ammonium chloride or isopropyl alcohol.

Nonin 8000AA Articulated Sensor Specifications



Specifications

SpO_2 Accuracy (Adults/Peds)[1, 2]:

Range	Oxygen Saturation (A_{rms}*) (figure A)	Motion Oxygen Saturation (A_{rms}*) (figure B)
70 – 100%	±2	±3
70 – 80%	±2	±3
80 – 90%	±2	±3
90 – 100%	±2	±2

SpO_2 Low Perfusion Accuracy: 70% to 100% ±2 digits (A_{rms}*)[1]
Pulse Rate Accuracy: 18 to 300 BPM ±3 digits (A_{rms}*)[1]
Pulse Rate Low Perfusion Accuracy: 40 to 240 BPM ±3 digits (A_{rms}*)[1]
Temperature: [3, 4]

Operating:	0 °C to 40 °C (32 °F to 104 °F)
Storage/Transportation:	-40 °C to 70 °C (-40 °F to 158 °F)

Humidity: [3, 4]

Operating:	10% to 95% non-condensing
Storage/Transportation:	10% to 95% non-condensing

* ±1 A_{rms} encompasses 68% of the population.
[1] Additional accuracy and performance information can be found in the sensor accuracy document on the operator's manual CD.
[2] Accuracy specifications based on Nonin's PureSAT® SpO_2 technology and PureLight® sensor technology.
[3] For combined oximeter/sensor specifications, refer to the applicable oximetry system's operator's manual.
[4] Range as tested with Nonin's PureSAT SpO_2 technology.

Measurement Wavelengths and Output Power**

Red:	660 nanometers @ 3 mW nominal
Infrared:	910 nanometers @ 3 mW nominal

** This information is especially useful for clinicians.

Compliance

This product complies with ISO 10993.
Not made from natural rubber latex.

Nonin OEM III Specifications

The M1 utilizes the internal Nonin OEM III module to generate SpO_2 measurements.

Nonin® OEM III Specifications

1.	**Displayed Oxygen Saturation Range (SpO_2)**		0 to 100%	
2.	**Displayed Pulse Rate Range**		18 to 321 beats per minute (BPM)	
3.	**Measurement Wavelengths and Output Power****			
		Red:	660 nanometers @ 0.8 mW maximum average	
		Infrared (using NONIN PureLight® Sensor):	910 nanometers @ 1.2 mW maximum average	
4.	**SpO_2 Accuracy (A_{rms}*)**		70-100%	
			Adults/Pediatrics	**Neonates**
	No Motion			
	REUSABLE:	Finger Clip:	± 2 digits	± 3 digits
		Flex:	± 3 digits	± 3 digits
		Soft Sensor:	± 2 digits	N/A
		8000R:	± 3 digits	N/A
		8000Q:	± 4 digits	N/A
	DISPOSABLE:	6000 Series:	± 2 digits	± 3 digits
		7000 Series	± 3 digits	± 4 digits
	Motion			
	REUSABLE:	Finger Clip:	± 2 digits	± 3 digits
		Flex:	± 3 digits	± 4 digits
		Soft Sensor:	± 3 digits	± 4 digits
	Low Perfusion	All Sensors:	± 2 digits	± 3 digits
5.	**Pulse Rate Accuracy**			
			Adults/Pediatrics	**Neonates**
	No Motion (18-300 BPM)			
	RESUABLE:	Finger Clip:	± 3 digits	± 3 digits
		Flex:	± 3 digits	± 3 digits
		Soft Sensor:	± 3 digits	± 3 digits
		8000R:	± 3 digits	± 3 digits
		8000Q:	± 3 digits	± 3 digits
	DISPOSABLE:	6000 Series:	± 3 digits	± 3 digits
		7000 Series:	± 3 digits	± 3 digits
	Motion (40-240 BPM)			
	REUSABLE:	Finger Clip:	± 5 digits	± 5 digits
		Flex:	± 5 digits	± 5 digits
		Soft Sensor:	± 5 digits	± 5 digits
	Low Perfusion (40-240 BPM)	All Sensors:	± 3 digits	± 3 digits

Flashback Technical Support

Technical Support is available by phone or email. Most issues will be addressed within 24 hours of receipt of a support request. The contact information for technical support is:

(949) 674-3559
support@flashbacktechnologies.com

When emailing technical support, please include the following information:

- Software Version
- Preferred Method for Response (phone or email)
- If phone is preferred, best time to call with time zone and phone number
- As much detail about the problem as you can recall. Listing numbered steps leading up to the issue can be very helpful.

Troubleshooting

Problem	Solution
M1 does not power on; or device shuts down	Press firmly on power button and hold for at least 3 seconds; or until screen turns on OR Replace battery with a new one. Ensure you are using one alkaline 1.5 volt AA battery.
CRI is not displayed	Ensure snug connection between M1 and sensor OR Ensure Sensor Status state (bottom left corner of M1 display) shows a completely green outline; and does not display a question mark ("?") or red outline.
Device screen flickers on and then off when powering on device.	Press firmly and hold power button down until screen displays.
M1 does not power off	Press firmly on power button and hold for at least 5 seconds; or until screen turns off.

Calibration

The model M1 does NOT require calibration.

Electromagnetic Compatibility

The M1 is suitable for the electromagnetic environment of typical prehospital or hospital settings.

During the immunity testing described below the M1 continued to sense, calculate and display the percentage of the saturation of peripheral oxygen (SpO_2) within ±2% of simulator set point, heart rate (HR) in beats per minute within ± 3 beats of simulator set point, and Flashback Technologies' Compensatory Reserve Index (CRI) within ±0.10 of pretest range for the simulator set point.

WARNINGS:

- Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the M1 System, including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result.
- The M1 should not be used adjacent to or stacked with other equipment. If adjacent or stacked use is necessary, the M1 should be observed to verify normal operation. If operation is not normal, the M1 or the other equipment should be moved.
- Use of accessories, transducers and cables other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

Emissions

Electromagnetic Emissions		
The M1 is intended for use in the electromagnetic environment specified below. The customer or the user of the M1 should assure that it is used in such an environment.		
Emission Tests	**Compliance**	**Electromagnetic Environment – Guidance**
RF emissions CISPR 11	Group 1	The M1 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.
RF emissions CISPR 11	Class B	The M1 is suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.

Immunity

Electromagnetic Immunity		
The M1 is intended for use in the electromagnetic environment specified below. The customer or the user of the M1 should assure that it is used in such an environment.		
Immunity Tests	**Compliance Level**	**Electromagnetic Environment – Guidance**
Electrostatic discharge (ESD) IEC 61000-4-2	± 8kV contact ± 15kV air	The relative humidity should be at least 5 %
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	30A/m	Power frequency magnetic fields from common appliances in the home are not expected to affect the device. Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment. Keep the M1 away from sources of high levels of power line magnetic fields (in excess of 30 A/m) to reduce the likelihood of interference.
NOTE: UT is the A/C. mains voltage prior to application of the test level.		

Electromagnetic Immunity			
The M1 is intended for use in the electromagnetic environment specified below. The customer or the user of the M1 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 Vrms 6 V rms in ISM and amateur radio bands	The M1 is suitable for the electromagnetic environment of typical homes, commercial or hospital settings.
Radiated RF IEC 61000-4-3	20 V/m 80 MHz to 2.7 GHz	20 V/m	

The device has also been tested for immunity to proximity fields from RF wireless communications equipment with the following parameters:

Frequency (Hz)	Modulation	Level V/m
385	Pulse, 18 Hz, 50% DC	27
450	FM, 1 kHz Sine, ±5 Hz Deviation	28
710, 745, 780	Pulse, 217 Hz, 50% DC	9
810, 870, 930	Pulse, 18 Hz, 50% DC	28
1720, 1845, 1970	Pulse, 18 Hz, 50% DC	28
2450		28
5240, 5500, 5785		9

M1 Compliance

The M1 is not compliant with ISO 10993. Therefore, care should be taken to prevent the device from making contact with the patient's tissue (note: This does not apply to the sensor which is ISO 10993 Compliant). Metal loops are integrated in the case to attach the device to a litter, rail, or other object.

Opening the case of the M1 will void its warranty and the device will stop functioning. The user cannot patch or modify the device. The device will maintain its compliancy throughout its service life.

Nonin 8000AA Warranty

1 year from the date of delivery.
The device's expected service life is 1 year.

M1 Warranty

1 year from date of delivery.
The device's expected service life is 5 years.
The device's expected shelf life is 2 years (remove battery when storing).

M1 Data Sheet

Dimensions	**Length**	**Width**	**Height**
	3.5”	2.5”	1”
	88mm	64mm	25mm
Weight	**Ounces**	**Grams**	
	4oz	113.4g	
Display	Daylight readable TFT-color, 2.4”		

The Compensatory Reserve Index (CRI)

Healthy human organ systems are dynamically coupled and physiologically stable. Compensatory mechanisms (e.g. preload, baroreflexes, respiration, etc.), which serve to maintain physiological stability in the setting of acute blood loss, vary in effectiveness among individuals: Some patients reach Cardiovascular (CV) collapse after relatively little blood loss (<1 liter); Some can tolerate 30%+ blood loss before CV collapse. However, as blood loss continues compensatory mechanisms eventually breakdown.

Due to these compensatory mechanisms, traditional vital signs (HR, BP, RR, SpO_2) do not deteriorate until the patient is already near collapse and at risk for poor tissue perfusion, progressive acidosis and sudden, unexpected hemodynamic decompensation.

The Compensatory Reserve Index (CRI) provides a single number between normovolemia (1) and CV collapse (0) for monitoring central volume changes in patients. CRI is formalized for Effective Volume Loss (EVL) as:

$$\text{CRI} = 1 - \frac{EVL_{current}}{EVL_{collapse}} Eq(1)$$

Specifically, **CRI represents the proportion of remaining volume loss the individual can tolerate before collapse** (see Figure 9).

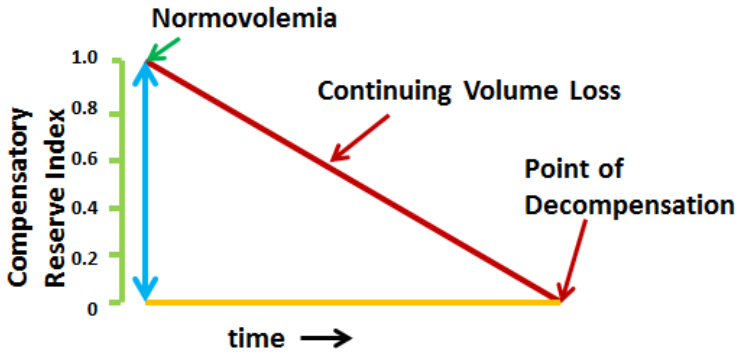


Figure 9 - The Compensatory Reserve Index

As we can see from the equation above, in order to directly compute CRI, we would need to know both the current volume of blood lost by the patient, and the total volume loss that patient could ultimately tolerate before experiencing CV collapse. We can do this retrospectively for controlled experiments, where $EVL_{current}$ and $EVL_{collapse}$ can be reliably estimated, for example in controlled blood draws or simulated hemorrhage experiments using Lower Body Negative Pressure (LBNP).

Estimating CRI from Pulsatile Waveforms

Pulsatile physiological waveforms (BP, PPG, etc.) encode significant information about the state of the cardiopulmonary system. Flashback's data analytics technology is capable of generating accurate models from noisy high dimensional datasets like the LBNP reference database. This dataset allows us to calculate reference CRI values for each subject from known LBNP (mmHg), and our analytics system uses these and accompanying sensor data to create a mapping from waveforms to CRI estimates (see Figure 10Figure 10).

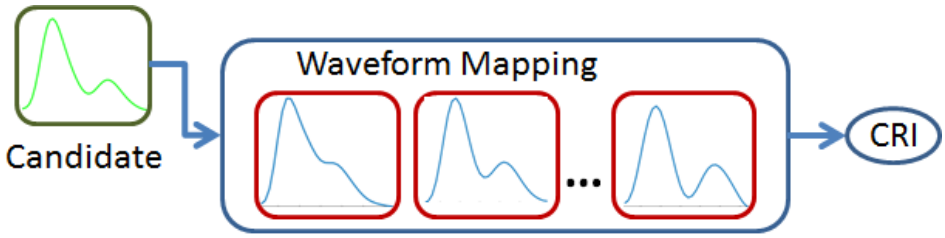


Figure 10 - Estimating CRI

In this case, CRI is based on the IR PPG signal from the Nonin OEM III/8000AA.

Performance of CRI

CRI is a new physiological monitoring parameter which trends with intravascular volume and can be used by clinicians, in concert with other hemodynamic measures, to assess volume status.

CRI uses a standard photoplethysmogram (PPG) waveform, which makes it noninvasive, compact and easy to use. It can be applied at any point during volume changes and does not require reference measurements. The monitor will display initial CRI estimates after a few seconds and then updates continuously.

In a 20% blood draw study, Flashback's CRI monitors were demonstrated to be more responsive to volume loss than standard vital signs. See Figure 11, used with permission, (Convertino, Howard, et al. 2015).

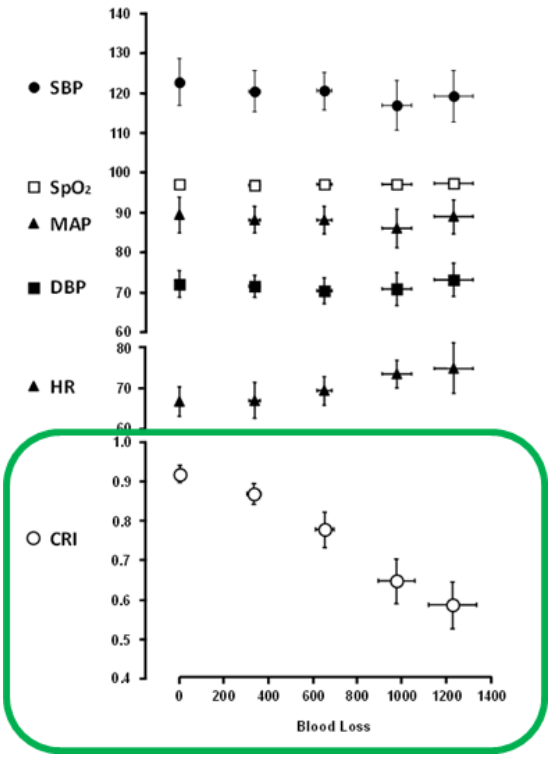


Figure 11 - Performance of CRI

In the same study, CRI was able to capture the varying risk resulting from patients with different tolerances to total volume loss, by accurately calculating lower values at lower absolute loss volumes for patients with lower tolerance (S. Moulton, et al. 2017).

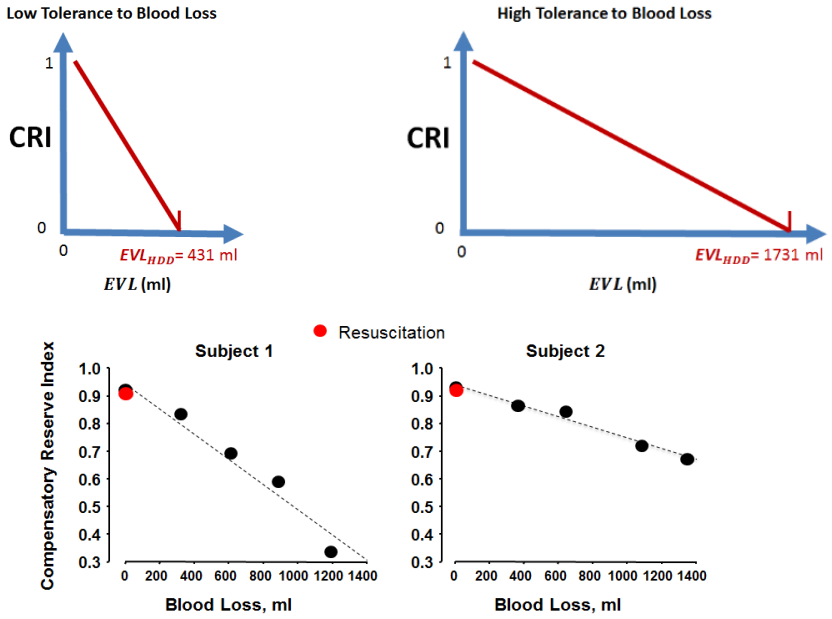


Figure 12 - CRI in patients with different tolerances to total volume loss

Summary of Clinical Study

Background Information Regarding Use of CRI

Compensatory Reserve

Acute hemorrhage initiates a complex cascade of physiologic responses that are triggered and mediated by cellular signals, resulting in a wide array of cardiopulmonary changes throughout the body. Some of these changes can be measured using standard vital signs (e.g., heart rate [HR], systolic and diastolic blood pressures, electrocardiography, respiratory rate, and pulse oximetry). Researchers and clinicians who have studied and observed how these parameters change in the setting of acute blood loss have long assumed that hypotension and other signs and symptoms of hemorrhagic shock mark the beginning of circulatory compromise, rather than the beginning of decompensation. This fundamental assumption has been based on the observation that humans are able to compensate for large volumes of blood loss with little change in standard vital signs (S. Moulton, et al. 2013). **The unique capacity of cardiovascular mechanisms to compensate for the intravascular volume loss an individual can tolerate before experiencing the symptoms of cardiovascular instability and decompensation can be described as the Compensatory Reserve.**

Development of the Compensatory Reserve Index (CRI)

The Compensatory Reserve Index (CRI) was initially developed using data obtained from a well validated laboratory method of simulating acute blood loss, the Lower Body Negative Pressure (LBNP) model (Convertino, Grudic, et al. 2013). A large reference database composed of sensor data collected for each

subject provided the basis for building models to estimate *CRI, the proportion of remaining volume loss the individual can tolerate before collapse (Equation 1)*. A robust CRI estimate requires analysis of the continuous pulsatile waveform signal and comparison to a reference database. The estimated CRI is determined by the most similar signal in the database.

Clinical Validation of CRI

To characterize the relationship of CRI to significant blood loss and to support regulatory clearance, Flashback Technologies conducted a prospective validation study that enrolled 42 healthy volunteers (19 to 36) undergoing stepwise removal and replacement of approximately 20% of total blood volume while in the supine position at rest (non-motion). The methodology and preliminary results from the first 20 subjects have been reported by (Convertino, Howard, et al. 2015) and the full dataset by (S. Moulton, et al. 2017).

Results from the dataset of 42 volunteers demonstrate:

- Trending Intravascular Volume Changes: 32 of the 42 subjects completed the full protocol. For these subjects, the correlation between CRI and blood volume loss is greater than 0.9 ($p<0.05$).
    - Correlation between average CRI values (at constant intravascular volume) and intravascular volume loss is greater than 0.94 (95% confidence 0.92 to 0.96).
    - Correlation between one-minute average CRI and intravascular volume loss is greater than 0.9 (95% confidence 0.87 to 0.93).
- In this population 'normal' CRI values (obtained from all 42 subjects) before intravascular volume loss were significantly above 0.7 (see box and whisker plots in Figure 13, and Figure 14).
    - Before intravascular volume loss 95% of CRI values were above 0.75 and 98% of CRI values were above 0.7.
    - Before intravascular volume loss the mean CRI value was 0.9 (95% confidence 0.89 to 0.91) with a standard deviation of 0.077 (95% confidence 0.053 to 0.078).
- At 20 % intravascular blood loss volume, CRI values (obtained from the 32 subjects that completed the full protocol) were significantly lower than those before blood loss (see box and whisker plots in Figure 13 and Figure 14).
    - At 20% intravascular blood loss volume the mean CRI value was 0.6 (95% confidence 0.57 to 0.63) with a standard deviation of 0.17 (95% confidence 0.16 to 0.17).
- When comparing one-minute average CRI values before blood loss to those at 20% intravascular blood loss volume (for the 32 subjects that completed the full protocol), the average drop was 0.35 (95% confidence 0.29 to 0.4) with a standard deviation of 0.15 (95% confidence 0.11 to 0.2).
- CRI values when subjects were experiencing symptoms associated with hemodynamic decompensation were significantly lower than when subjects had no symptoms (see box and whisker plots in Figure 13 and Figure 14).
    - Seventeen percent of the subjects (7/42) experienced 'Hemodynamic Decompensation' during conduct of the study.
        - As evidenced by a drop in systolic BP from 119 mmHg to <80 mmHg and a significant drop in Mean Arterial Pressure (average decrease in MAP was 43 mmHg; average MAP prior to intravascular volume loss = 93 mmHg, range 91-95; average MAP at the point of hemodynamic decompensation was 50 mmHg, range 44-58).
    - During symptoms the mean CRI value was 0.15 (95% confidence 0.12 to 0.17) with a standard deviation of 0.08 (95% confidence 0.05 to 0.09).
    - During symptoms more than 97% of CRI values were below 0.3, while when no symptoms were present 98% of CRI values were above 0.3.

- CRI values after blood replacement return to values consistent with those before blood loss (see box and whisker plots in Figure 13 and Figure 14).
    - After blood replacement, the mean CRI value was 0.89 (95% confidence 0.89 to 0.9) with a standard deviation of 0.076 (95% confidence 0.071 to 0.077).
- Linear mixed model analysis with CRI as the outcome and intravascular volume changes as the predictor support the conclusion that M1s give consistent CRI estimates, even when they are turned on and off.
    - There is no significant effect associated with using CRI estimates from different M1 devices (95% confidence).
    - Turning an M1 device on and off has no significant effect on CRI estimates (95% confidence).
- Linear mixed model analysis with CRI as the outcome and intravascular volume changes as the predictor support the conclusion that CRI trends with changes in intravascular volume.
    - CRI trends with changes in intravascular volume (95% confidence).

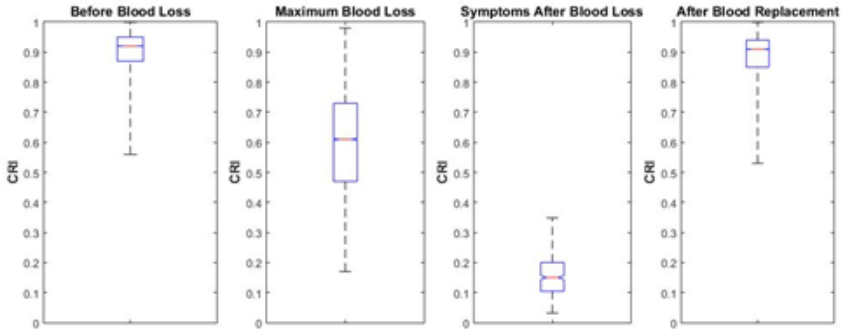


Figure 13 - Box and Whisker plots of instantaneous CRI values, before blood loss, at maximum blood loss

Figure 13 – Box and Whisker plots of instantaneous CRI values, before blood loss, at maximum blood loss (at end of blood withdrawal for subjects completing ~20% blood volume withdrawal), during symptoms (at end of blood withdrawal for subjects experiencing symptoms and not completing ~20% blood loss), and after blood replacement. For each panel above, the number of subjects was 42, 32, 7, and 32, respectively.

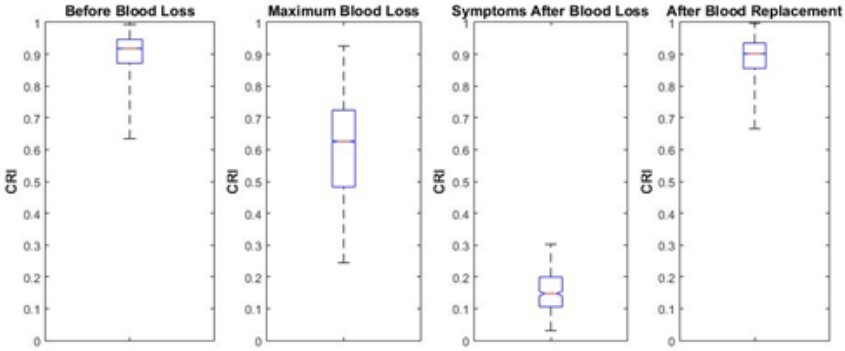


Figure 14 - Box and Whisker plots of one minute average CRI values, before blood loss, at maximum blood loss

Figure 14 – Box and Whisker plots of one-minute average CRI values, before blood loss, at maximum blood loss (at end of blood withdrawal for subjects completing ~20% blood volume withdrawal), during symptoms (at end of blood withdrawal for subjects experiencing symptoms and not completing ~20% blood loss), and after blood replacement. For each panel above, the number of subjects was 42, 32, 7, and 32, respectively.

Conclusions

The results of this study met the pre-specified pass/fail criteria and thus provide supporting evidence that CRI trends with intravascular volume changes as compared to direct measurement of blood volume decrease and increase. It should be noted that this clinical validation of CRI was performed using healthy volunteers aged 19-36 years under supine, non-motion conditions.

Clinical Use Considerations

Clinical users of the M1 should understand the basic principles regarding the derivation of the CRI value as well as the strengths and limitations of research conducted to date. As noted above, in normal volunteers under laboratory conditions, CRI was found to correlate closely with changes in intravascular blood volume (up to ~ 20% of blood volume loss). **Nonetheless, this device is intended as an adjunct in patient assessment. It must be used in conjunction with other methods of assessing clinical signs and symptoms.**

CRI estimates are based on reference data collected in ideal conditions. Progressive declines to low CRI values indicate measurements based on subjects in clinical studies exhibiting symptoms of increasing hemodynamic instability, most notably precipitous hypotension and clinical symptoms associated with shock. However, since many known and unknown factors (artifacts, advanced age, cardiovascular disease, medications, acute trauma, etc.) may affect these measurements, changes in CRI should always be interpreted cautiously as a **potential** indicator of changes in patient status due to volume change. It is recommended that users carefully consider the clinical conditions and evaluate conventional vital signs when interpreting changes in CRI.

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