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Continued Development of a Multiplex Precision Medicine System for Early Warning of Progression Toward Hemodynamic Deterioration After Trauma (V3.0)

Human Trauma Effectiveness Study (n=480)

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Project Principal Investigator: Norman A. Paradis MD

Sponsor: United States Department of Defense

Site: University of Massachusetts Baystate Medical Center

Introduction

This study is **Phase 3** of a three-year DOD CDMRP funded project for development of a multi-technology poly-anatomic noninvasive system for early detection of occult hemorrhage that may be progressing toward hemodynamic instability.

Background

Early detection of ongoing hemorrhage (OH) before onset of shock is a universally acknowledged great unmet need, and particularly important after trauma. [1,2] Delays in the detection of OH are associated with a "failure to rescue" and a dramatic deterioration in prognosis once the onset of clinically frank shock has occurred. An early alert to the presence of OH with an acceptable rate of false-positives and false-negatives would save countless lives. Additionally, such technology would save critical time, money and effort by allowing medical resources to be applied more accurately – the essence of precision medicine. An automated system would monitor currently stable patients continuously, leaving clinicians free to care for patients in need of attention.

It is widely appreciated that the classic medical vital signs perform poorly until late in the progression to shock after traumatic injury. [3,4] Currently available techniques, including intermittent vital sign monitoring, laboratory analysis, and single measurement devices have inferior performance before clinically obvious physiologic distress. [3,5] The overall goal of this project is to develop a multi-technology noninvasive system for early detection of ongoing hemorrhage. The underlying hypothesis is that deep-learning developed algorithms obtaining diagnostic signals from multiple sources will outperform single technology solutions.

Hemorrhagic shock remains a leading cause of death on the battlefield as well in civilian communities. Early detection of ongoing hemorrhage before progression to frank shock would allow early intervention.

While the promise of innovative noninvasive testing has received wide attention, development of effective bedside technologies has thus far been limited and their performance disappointing. In 2014, ***Kim et al*** stated that "The results from this

meta- analysis found that inaccuracy and imprecision of continuous noninvasive arterial pressure monitoring devices are larger than what was defined as acceptable" and noninvasive blood pressure measurement is among the most fully developed of these technologies. [6] The failure of noninvasive technologies in the detection or diagnosis of complex disease states has been complete. We believe that this failure reflects the limitations of uniplex systems (a single sensor in a single location) and patient to patient variation in physiologic response. Uniplex systems sacrifice the entire diagnostic signal in anatomic-temporal patterns, which likely has significant discriminant power.

To date, technological innovation in early detection of ongoing hemorrhage has been of two broad categories: 1) a search to discover a single new measurement of tissue or organ status [7] or 2) application of more sophisticated mathematical techniques based on machine learning and signal processing. [8] The results of these approaches have been disappointing as evidenced by: 1) failure to subject the techniques to prospective clinical validation of effectiveness, 2) failure to submit the devices for regulatory clearance, 3) actual commercial failure.

As of this time, there are no effective noninvasive technologies for early alarm in occult ongoing hemorrhage or prediction of impending hemodynamic deterioration.

The dramatic advances in sensing technology and miniaturization have reached a stage at which it is now possible to: 1) put electromagnetic, optical and impedance technologies into small adhesive "dots" on the skin, 2) stream data from multiple anatomic locations, and 3) algorithmically transform these data such that the system alarms when it recognizes patterns suggestive of ongoing hemorrhage. We have been developing such a system, one that combines state-of-the-art noninvasive sensing technologies and advanced multivariable statistical algorithms. This system will be developed from its inception to be inexpensive and easily applied, even in austere settings.

Progress to Date: In years I and II the project made excellent progress in development of this technology. Using pre-existing data sets, we developed preliminary multivariate algorithms. We then developed a low-volume occult hemorrhage porcine model and utilized it for evaluation of a broad ensemble of noninvasive technologies and further development of the diagnostic/predictive algorithm.

We have successfully developed a sophisticated multivariate ML algorithm that provides superior performance at detecting/predicting bleed/no-bleed in occult hemorrhage and LBNP. The average ROC-AUC values are in the range of 97% 20-25 min. into our porcine low-volume occult hemorrhage model. This accuracy is far superior to all prior studies and better than our expectations at the start of the project with respect to what we anticipated being able to achieve at this stage of the project. We have successfully identified the principal drivers of this high accuracy: the largest contribution comes from the features generated from the raw impedance tomography signals, which in-and-of-themselves are able to provide an AUC value of higher than 80% on a consistent basis.

As originally hypothesized, we have demonstrated that multiplexing is superior to uniplexing: in particular, NIRS and other technologies continue to amplify the already-high baseline accuracy provided by impedance tomography by an additional 5-15% AUC increase. We have analyzed the additional predictive signal provided by different technologies and different anatomical locations and have identified the hierarchy of their relative performance. This will allow us to begin the process of "pruning" our platform so we can identify the minimal configuration necessary for excellent clinical performance. We have demonstrated that our approach significantly outperforms the existing bioimpedance cardiography (Cheetah) based approaches. We have shown that other than Impedance/TFC, no additional value is provided by Cheetah. We have finished preprocessing and univariate analyses using the LBNP data and started the multivariate ML algorithm enhancements now.

First Generation Prototype (Mark I)

We will carry forward the full ensemble of the earlier studies into our first study of trauma patients. Core specifications of the Mark I prototype include: 1) efficient

incorporation of all listed technologies in a cleanable enclosure, 2) power to subsystems protected by a medical grade uninterruptible power supply, 3) all components electrically grounded. Specifically, the Mark I clinical prototype system that will be used in the proposed study will include:

Sensing Technologies:

- Electrical impedance spectroscopy (EIS)
- Electrical impedance tomography (EIT)
- Near-infrared spectroscopy (NIRS)
- ECG – pulled from a dedicated clinical monitor to the Mark I
- Plethysmography – pulled from a dedicated clinical monitor to the Mark I
- O2 Saturation – pulled from a dedicated clinical monitor to the Mark I

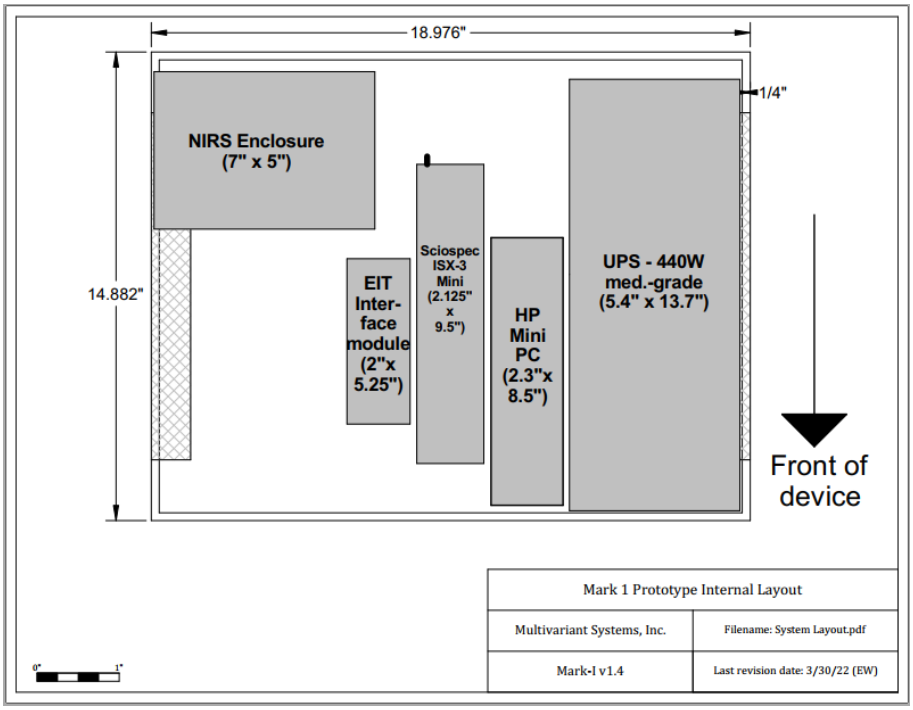
(Please note – detailed description of the impedance and infrared modules are in Appendix I)** I

Wearables – EIT/EIS/NIRS

EIT – 3 locations. First array: Thorax (on every subject);
Second array: will *alternate* between upper abdomen and
thigh for *every other* subject. 16 electrodes per location
EIS – 3 locations, 4 electrodes per location
NIRS – 3 locations, 1 probe per location: upper chest in region of thoracic EIT area, and either upper thigh or upper arm.

Mark I Additional Parameters

- **Cabling:** shortest possible to preserve data quality, all cables to patient zip-tied together to reduce clutter, RS232 from clinical monitor to Mark-1
- **Form factor:** Mark I enclosure and integrated monitor, dedicated clinical monitor, keyboard and mouse on a single cart



- **Connections:** Clinical monitor for ECG and plethysmography (RS 232), 120 VAC power cord, sensor cabling to patient, remote connection via wifi for transfer of data (local USB connection also available)
- **Interface:** Monitor, On/Off switch, keyboard, mouse, Windows operating system for operation of subsystem software
- **Storage:** Adequate for 12 hours of all technologies (local storage)
- **Power:** 120 VAC, Battery back-up

We engaged System Insights, LLC in January 2021 to design and fabricate the hardware and controls for the Mark I prototype. System Insights is an engineering consulting company based in Norwich, VT specializing in custom electrical and mechanical systems. This prototype integrates EIS, EIT, NIRS, and ECG/Plethysmography subsystems for data collection and subsequent machine learning efforts. Subsystems and all components are housed in an enclosure to withstand the medical environment. The EIS subsystem consists of a Sciospec OEM system (ISX-3 mini) for receiving electrode signals and compiling data. The EIT subsystem consists of a Sentec Pioneer set for receiving electrode signals and processing data. The NIRS system is a custom device developed by Dartmouth College. ECG and Plethysmography data will be collected from an onsite GE clinical monitor.

Initial efforts by System Insights involved defining requirements for the system and working with the project team to integrate each subsystem. Initial design discussions resulted in some internal design specification documents for review to ensure the systems would meet the study demands. System construction of the first prototype occurred from March through July 2021. In addition to the sub-systems discussed previously, the system includes a medical-grade uninterrupted power supply to allow time for data collection to be safely stopped in the event of a power disruption and a central computer to operate subsystem-specific software packages. The central computer will also store data for wireless transmission to the offsite server or through a USB port. The system can be operated remotely or locally for ease of data transfer and remote troubleshooting. Of particular importance is that an operation manual has been developed for training purposes.

(Please note – a copy of the training and utilization manual is included in Appendix II)** I

In summary: we have developed a promising multi-technology poly-anatomic approach to development of noninvasive sensing in the setting of occult hemorrhage. The year one and year two studies used a rack system composed of commercial impedance and optical components. After evaluating the performance of individual components, we have been able to "prune" the court technologies to: impedance tomography, impedance spectroscopy, NIRS, plethysmography and ECG. The impedance and optical technologies have been incorporated into a first-generation prototype.

Phase III Trauma Validation and Re-Training Trial

Approach/Methods

Summary: We will enroll 480 trauma patients in a "no significant risk" prospective clinical trial to: 1) evaluate the performance of our Mark I prototype, 2) validate the performance of the Phase II algorithm and 3) re-train the algorithm to Phase III iteration.

This is not a therapeutic study. All technologies are non-invasive.

The main outcome variables are non-invasive measurements that will be used for machine learning, not real-time patient management. The data generated will be used later for discovery and validation in traditional and innovative machine learning.

Inclusion criteria:

1. Age $\geq$ 18
2. Patients suffering blunt and/or penetrating trauma
3. Awake and alert with GCS $\geq$14 as indicated by the treating provider/care team
4. Triage systolic blood pressure greater than 90 and heart rate less than 120

Exclusion criteria:

1. Need for ongoing fluid or pressor support (standard local fluid resuscitation only)
2. Signs of clinically significant ongoing external hemorrhage with active bleeding documented on radiology/ultrasound during initial evaluation (approximately 15 minutes post ED arrival)
3. Respiratory distress with O2 saturation <96%
4. Pre-existing systemic illness, likely to alter systemic cardiovascular response to hemorrhage (overt clinical heart failure). Including congestive heart failure, and a paced cardiac rhythm.
5. Pregnant
6. Prisoner status
7. Anatomical abnormality or injury that would prevent placement of the electro-optical electrodes

Screening and Enrollment: The study team will approach ED patients initially evaluated by the Trauma team/ED care team in the Trauma room and currently being observed in a general ED bed who had met inclusion criteria. Those patients will participate in the informed consent process with study personnel following departmental and hospital SOP.

As a minimal risk study, there will be no change in the routine care of these patients.

Definition of hemodynamic deterioration - any of:

- A significant period (greater than 5 min.) of systolic blood pressure less than 90 associated with a heart rate greater than 110.
- 20% increase in HR from baseline
- 15% decrease in MAP from baseline
- Clinician defined need for greater than established initial fluid resuscitation (blood products intended to maintain blood pressure)
- A blood lactate result greater than 4 without nontraumatic causes of lactic acidosis

Study Design: Prospective Case Cohort

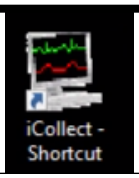
- Screening for enrollment will be undertaken in the Emergency Department (ED).
- Patients will be assigned a de-identified Research **Subject Number**
- Please note that at the discretion of the clinical study team, less than the complete ensemble of noninvasive sensing technologies may be utilized in specific cases based on patient comfort and clinical circumstances.

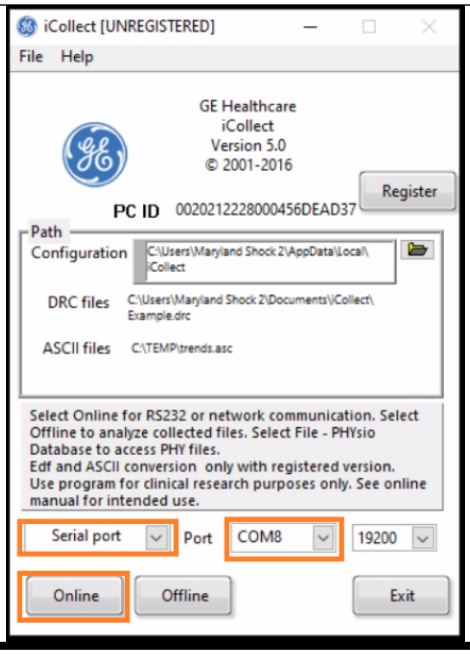
Placement of Sensing Technologies

- After confirmation of inclusion criteria, the absence of exclusion criteria, and informed consent is documented, trained research personnel will apply all sensors described below to appropriate locations on the patient's skin.
- Patients will already have undergone application of the ECG and pulse ox plethysmography disposables as part of normal clinical monitoring. These will be left in place and the ECG and plethysmography data will be shared with our prototype data collection system in a manner that does not interfere with the clinical monitor electrodes. The study monitor data will be acquired via iCollect software manufactured by GE. The software collects biometric data (e.g. EKG, SpO2) from clinical monitors without any imbedded PHI.

- Two SwissTom EIT arrays will be placed per subject: 1) around the thorax at the anatomic nipple line, and 2) the second alternating patient to patient between the upper abdomen at the level of the liver-spleen and the proximal thigh at the femur mid-shaft.
- **NIRS** – 3 locations, 1 probe per location: upper chest in region of thoracic EIT, and 1 either upper thigh or upper arm.
- Three sets of four ScioSpec EIS electrodes (I+, V+, V-, I-). V electrodes are placed medially to I electrodes.
    - 1st set – is applied on the torso just above the upper SwissTom arrays, I+ and V+ on the right mid-axillary line and V- and I- on the left mid-axillary line.
    - 2nd set – is applied between the upper and lower SwissTom arrays adopting the same positioning technique as set one with respect to the mid-axillary line. In patients with the 2nd SwissTom array on the thigh, the 2nd ScioSpec EIS is also applied in this same truncal location.
    - 3rd set – applied on the right upper arm, "+" leads on the outside of the arm and "-" leads on the inside, sandwiching the bicep.
- Please see device descriptions on pg. 12 for further detail

System Setup

CLINICAL MONITOR			
1. Clinical monitor: Open the desktop icon "iCollect - shortcut"			

2. At the following menu, ensure the settings in the orange box are as shown below and click “Online”		

Patient Case Methods

- Research team member will turn on device and enter study identifier data.
- Research team member applies the device sensors as per Appendix II
- Research team member will confirm that data is being acquired.
- Device will remain attached to each patient until any of the following:
    - Stable for 6 hours (no signs of hemodynamic deterioration)
    - Disposition via discharge from the ED or admission to a care unit
    - Development of change from baseline hypotension or tachycardia below or above limits respectively.
    - The patient wishes for the device to be removed.
- The following data will be collected from the sensors: heart rate and electrical activity via electrocardiogram, transcutaneous oxygen saturation, blood pressure and arterial waveforms via finger plethysmography. Lastly, sensor data will collect changing perfusion physiology via electrical impedance tomography system.
- The study coordinator will extract relevant data from the patient's chart to complete a case enrollment form.
    - Data points from chart-
        - Gender

        - Age (by decade)
        - Height
        - Weight
        - Medications given during the ED visit and admission (if patient is admitted)
        - Vital signs at triage and at "change in status."
- Based on clinical chart review, the PI and co-PI will independently adjudicate each patient into either the "likely ongoing hemorrhage" or "likely no ongoing hemorrhage" outcome categories without reference to the algorithm results. In the event of differing results, the PI and the co-PI will meet and discuss until consensus is reached.
- At the quarterly milestones the existing data will be used iteratively to refine the Phase II algorithm, creating an initial Phase III algorithm.

Data Acquisition and Storage:

SwissTom Impedance Tomography, NIRS Spectroscopy and ScioSpec Bioimpedance raw signals are all stored in a live, streaming fashion directly on an internal hard drive. All of this data is non-PHI and completely de-identified – only the subject number is incorporated into the file name. Similarly, any data collected by iCollect (mentioned above) has absolutely no PHI embedded within it and is live-captured and saved on an internal hard drive. At the end of the experiment all of this non-PHI, de-identified data will be uploaded to a secure cloud-based drive that has been approved by the participating institutions.

Data Analysis

At the completion of the study, the full data set will be used to define the performance of the Phase II algorithm with respect to the pre-specified performance criteria.
Data analysis will include the following steps:

1) **Data cleaning, filtering and validation**: All data will be processed to ensure that patterns are consistent with the underlying physiology. Any physiologically incorrect data will indicate issues related to loose electrodes, malfunctioning sensors,

etc. Such data will be filtered and cleaned to ensure that only meaningful data is used for algorithm testing.

2) **Data transformation and feature generation**: The cleaned, validated data will be transformed through a series of processing steps to generate the necessary features to be used in the supervised machine learning algorithms as predictors.
3) **Classification**: The features will then be used to generate machine learning-based predictions. These predictions will be compared against the ground reality of the patient's status to evaluate the algorithm performance.

Algorithm Performance Criteria: the algorithms developed will be trained to alarm under two circumstances indicating significant risk of ongoing hemorrhage progressing to shock: 1) a change from baseline, 2) development of prespecified patterns.

Performance will be judged on the basis of:

1. time of alarm before onset of deterioration
2. sensitivity, specificity, PPV, NPV for alarm/no alarm outcome
3. ROC curve and AUC for alarm/no alarm outcome
4. false-positive and false-negative rates

Power and Sample Size: We anticipate acquiring data from every enrolled subject. Power and sample size calculations indicate that a sample size of 480 subjects should be sufficient to: 1) further identify the minimal subset of noninvasive measurement technologies necessary for the desired diagnostic performance, 2) validate the existing algorithms, and 3) initially train a human clinical iteration of the algorithms, with a sufficient degree of accuracy ($p < 0.05$ for ROC-AUC).

Enrolled patients will undergo standard electrocardiogram (3-lead) and oxygen saturation continuous monitoring.

In addition to these standard physiologic measurements, as a part of research, we will also acquire the following non-invasive optical and impedance measurements. All of these devices have been previously validated as non-invasive and safe in humans.

The clinicians providing care to the patient will be blind with respect to the measurements from these devices.

General Approach to Minimize Risk

This protocol will be minimal risk to patients as all these technologies have been robustly demonstrated to be safe (see below). There is minimal risk associated with placement of these devices and they can be removed at any time. They don't interfere with standard equipment used in clinical management of trauma patients. As described above, clinical management of the patient will not be affected by the study intervention.

Protection: Each subject will give informed consent after all questions have been answered by a study team member. Confidentiality of data will be assured by study specific coding of subject identities. No identified individual data will be presented or published; rather, group mean data will serve as the basis for comparisons. Procedures used in this study are performed regularly in the clinical setting by the investigators.

Any original signed paper consent documents, as well as any hard copy of study documents will be stored in a locked cabinet at Baystate Medical Center. Any electronic patient information will be stored on REDCap, a secure online database that is password-protected and only accessible by study personnel.

Uploaded de-identified data is stored in a secure server room at the Thayer School of Engineering and backed up nightly to a secure offsite facility operated by Dartmouth College. Access is limited to authorized users, based on the security model of the share. Access to data is via SMB or kerberized NFS protocols and allowed only from on-campus locations or over VPN. For any data shares that store Level 3 data (according to Dartmouth DISC policy), access is only allowed via VPN or from properly secured on-campus systems to ensure two-factor security.

Potential Risks:

The adhesives used on the electrodes can cause skin irritation. This risk should not be greater than that caused by our hospital ECG monitor. Tomography (EIT) and Near Infrared Spectroscopy (NIRS) may carry a risk of electrical sensation/shock or light exposure to eyes if the equipment malfunctions or gets displaced. There may be additional risks in this study which are not yet known.

Benefits:
None beyond participation in biomedical research.

Inclusion of Women and Minorities:

These groups will not be excluded from screening or enrollment in this convenience sample.

Inclusion of Children:

Children less than 18 years of age are excluded.

Inclusion of Adults with Impaired Decision-making Capacity: Adults with impaired decision-making capacity will not be included in this study.

Safety monitoring:

As this is a minimal risk, non-invasive study, we do not anticipate major changes in risks and benefits. Continual and prompt monitoring by the Principal Investigator of any unanticipated problems will be reported to the IRB and the sponsor.

No Significant Risk

All modules within the prototype are designed to conform to the International Electrotechnical Commission (IEC) 60601-1 safety standard for medical devices. Specifically, all devices are below the safety limits defined for Patient Auxiliary Currents which specifies that the maximum injected current for a diagnostic device is:

1. **< 100 uA for frequencies < 1 kHz**
2. **< 100uA between 1 kHz and 100 kHz**
3. **< 10 mA for frequencies > 100 kHz**

All devices are operated so the patient is floating with respect to the circuitry of the devices; ensuring that the patient is not exposed to appreciable DC current levels.

Continuous-wave Near Infrared Spectroscopy (CW-NIRS) is non-significant risk (NSR) as proposed for use in this study. Specifically, the proposed use does not meet the criteria for significant risk defined under 21CFR812.3(m). The energy is below (IEC) 60601-1 safety standard for diagnostic medical devices.

ISX-3 (MultiChannel Electrical Impedance Spectroscopy System) is non-significant risk (NSR) as proposed for use in this study. Specifically, the proposed use does not meet the criteria for significant risk defined under 21CFR812.3(m). The energy is below (IEC) 60601-1 safety standard for diagnostic medical devices.

Pioneer Set (Electrical Impedance Tomography System), is non-significant risk

(NSR) as proposed for use in this study. Specifically, the proposed use does not meet the criteria for significant risk defined under 21CFR812.3(m).

Combination, even in combination the cumulative current of the impedance-based technologies does not surpass the minimum threshold level for NSR.

IDE Not Required: The Mark I meets all the requirements of CFR §812.2(c) for exemption.

Labeling - The devices will be labeled in accordance with the labeling provisions of the IDE regulations (§812.5) and will bear the statement "CAUTION - Investigational Device. Limited by Federal (or United States) law to investigational use."

IRB Approval – The Sponsor and Investigators will obtain and maintain Investigational Review Board (IRB) approval throughout the investigation as a nonsignificant risk device study

Informed Consent – The Sponsor and Investigators will assure that investigators obtain and document informed consent from each subject according to 21 CFR 50.

Monitoring – The Sponsor and Investigators will properly monitor the study so as to protect the human subjects and assure compliance with approved protocols (§812.46). An IRB approved monitor will be identified before enrollment begins.

Records and Reports - The Sponsor and Investigators will maintain specific records and make reports as required by the IDE regulations.

Investigator Records and Reports – The Sponsor and Investigators will assure that participating investigators maintain records and make reports as required.

Prohibitions – The Sponsor and Investigators will not engage in Commercialization, promotion, test marketing, misrepresentation of an investigational device, or prolongation of the study (§812.7).

ClincialTrials.gov – The Sponsor and Investigator have registered the study and maintain this registration up to date. **(ClinicalTrials.gov Identifier: NCT04912232)**

Appendix I

Description of Impedance and Infrared Subsystems of the Mark I

***SwissTom Electrical Impedance Tomography (EIT) System*:**

Name of device: Pioneer Set (Electrical Impedance Tomography System)
Device Manufacturer: SwissTom AG (Parent company SenTec AG)

This device monitors dynamically changing perfusion physiology. To record multiplexed impedance signature from two arrays of 16 electrodes, one array is placed around the thorax above the nipple line and the second array alternates patient to patient between the upper abdomen at the level of the liver-spleen, and the proximal thigh at the femur mid-shaft. The Impedances are recorded between multiple sets of electrodes.

SwissTom developed a clinical EIT system that is approved for pulmonary imaging. This Pioneer system is their research platform that has similar functionality and safety performance to their clinical system but provides research teams with access to raw data and additional functionality for specifying imaging parameters (e.g. control of frame rates, signal frequency acquisition, electrode drive patterns).

***Continuous-wave Near-Infrared Spectroscopy (CW-NIRS) Device, custom built*:**

The device is built on an Ocean Optics FLAME USB Spectrometers, with two OSRAM 4736 NIR LEDs in plastic holders meant to be taped or strapped to the patient on the chest/torso. Probe holders are designed to collect light from surface of skin by means of a mirror and collimator. The device will collect data on light attenuation of muscle in models of shock/trauma. The light output is below the ANSI limits for maximum permissible skin exposure.

***<u>ScioSpec MultiChannel Electrical Impedance Spectroscopy (EIS) System</u>*:**

Name of device: ISX-Mini (MultiChannel Electrical Impedance Spectroscopy System)
Device Manufacturer: ScioSpec

To record multiplexed impedance signatures- 3 arrays of 4 electrodes is placed around the thorax, arm, and thigh of the patient and impedance spectroscopy signatures are recorded. This device monitors dynamically changing intrathoracic and intra-abdominal physiology.

Appendix II

Multivariate Systems Inc.™ Mark I Prototype

Setup and Operation Instructions

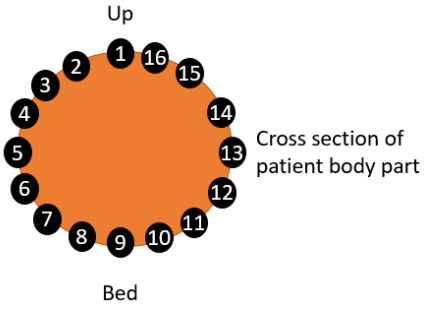
Patient and Wearables Setup

Patient preparation

1. Ensure patient documentation is completed
2. Patient is supine on the table
3. Ensure the device location is suitable to reach all test locations (within 10 feet of cable distance) and is plugged in
4. Shave electrode locations on the patient if there is excessive hair

Note: for applying electrodes, it may be more comfortable for the patient to connect the electrode pad to the snap fitting **before** affixing to the patient

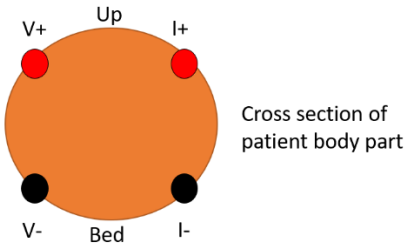
5. Apply Electrical Impedance Tomography (EIT) electrodes – two (2) sets of 16 electrodes each. Ensure each ring of electrodes set is installed in the same horizontal plane.



a. Apply electrodes 1-16 (branches A and B) as per protocol

b. Apply electrodes 17-32 (branches C and D) as per protocol
c. To improve even spacing of pads, place electrodes 1, 5, 9, and 13 at the 12, 3, 6, and 9 o'clock positions first, then fill in the three (3) electrodes between them

6. Apply Electrical Impedance Spectroscopy (EIS) electrodes as per protocol – three sets of 4 electrodes each



7. Apply Near Infrared Spectroscopy (NIRS) probes as per protocol – each probe is labeled according to the location on the patient. Place each probe with the cables directed away from the patient's head.

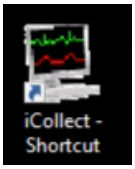
8. Apply the dedicated clinical monitor electrode stickers – three probes, white, black and red. The ECG cables can be connected after the electrode pads are placed. Place the plethysmography probe on a patient's finger.

System Configuration and Setup

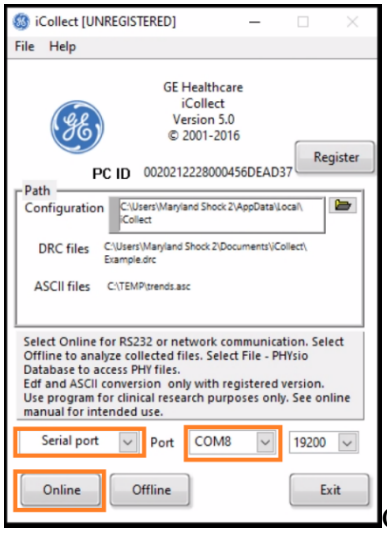
1. Turn the system on
    a. Ensure the overall system power switch (rear of right side of system enclosure) is turned to the "ON" position.
    b. Turn switch on the NIRS plate to the on (down) position.
    c. The monitor may need to be turned on by pressing the power button in rear of the lower right side.
    d. If power does not start, check that the uninterrupted power supply is on by viewing the power button through the hole in the front of the system.
2. Turn on the dedicated clinical monitor (do NOT interface with the existing clinical monitor) by pressing and holding the power button. ECG and plethysmography data should be displayed upon startup.
3. In the desktop folder, "Data Output," create a folder for the date and patient number using the following format: Month Day, Year Patient ###. Use the template folder, if desired.

Initialize software packages

3. Clinical monitor: Open the desktop icon "iCollect - shortcut"



    a. At the following menu, ensure the settings in the orange box are as shown below and click "Online"



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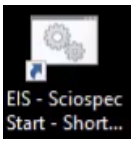
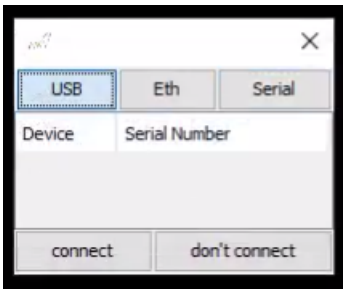
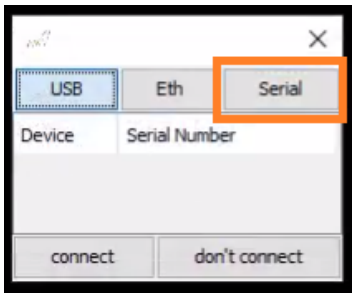
4. EIS: Open the desktop icon, “EIS - Sciospec Start – Shortcut”

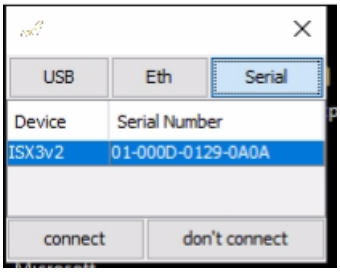


   a. On the following screen, make sure the “USB” icon is selected, then click “Serial”



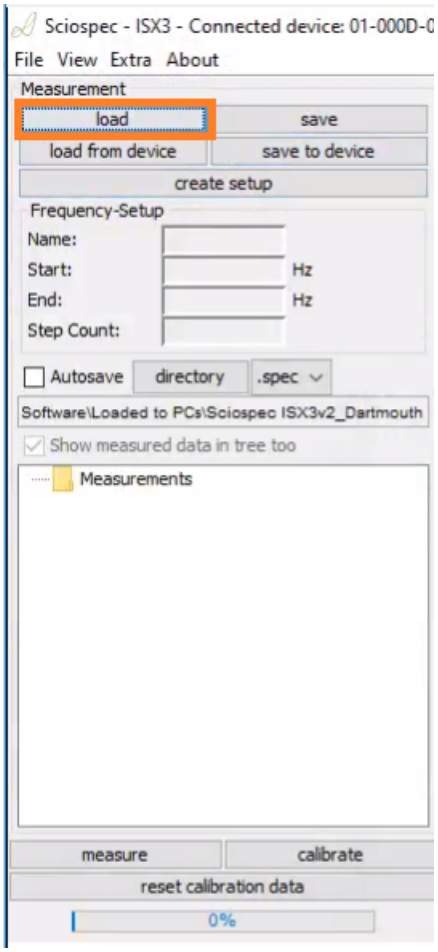


   b. In the subsequent menu, select “COM5.” If COM5 is not an option, it means the EIS device is not found.
      i. First try restarting the software
      ii. Next try restarting the computer
      iii. If neither of these allow COM5 to be found, check the connections on the ISX-3 mini – requiring removal of the REAR panel of the enclosure.
         1. Confirm the white USB cable is fully inserted into the device – the computer should make a sound when the connection is identified
         2. Confirm the power cable to the ISX-3 mini is plugged in (small black cable into ISX-3 mini, try unplugging and replugging in the power cable
         3. Cycle the power switch on the back of the ISX-3 mini
   c. Once you select the COM5 port, the device should appear in the list as shown below

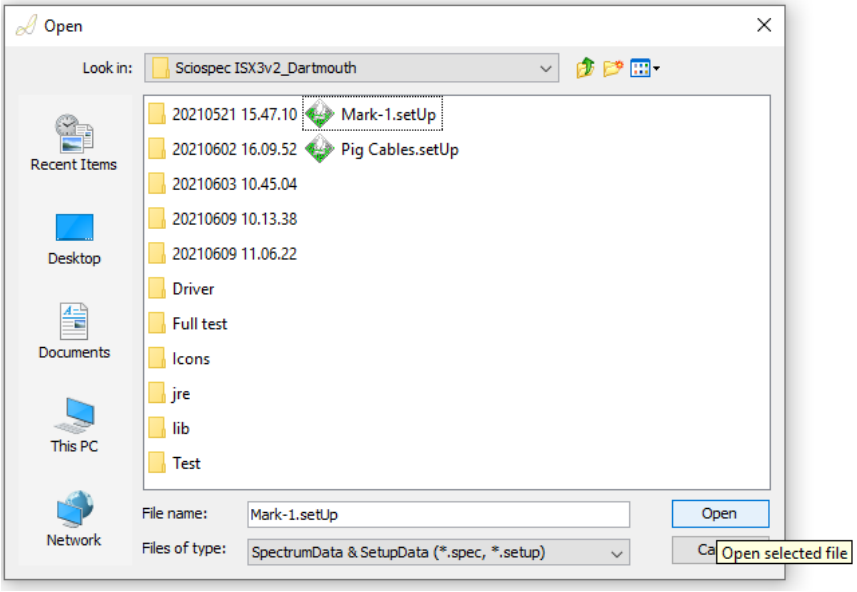


d. Click, “connect”

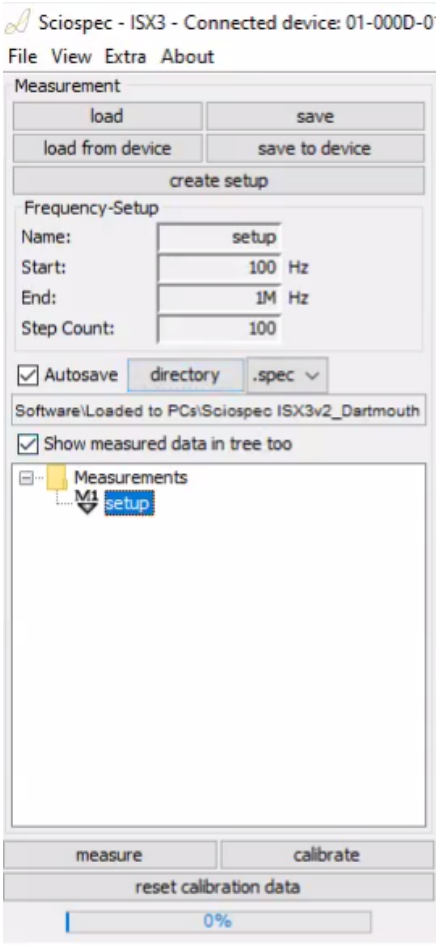
e. Once connected, the software will look like this. Click the “load” button, which will open the window to select the setup file (.setUp) to use.



f. Open the setup file, “Mark-1.setUp” located at the following directory: C:\Users\Mark-1\Desktop\Software\Loaded to PCs\Sciospec ISX3v2_Dartmouth



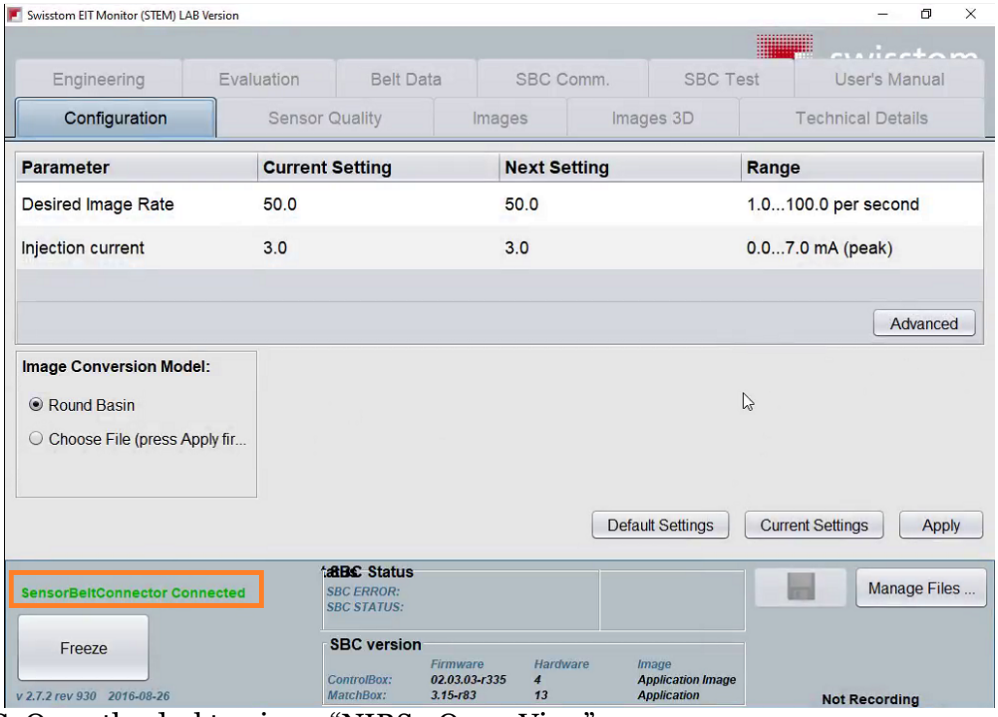
g. You should now see the setup in the measurement window, called “Mark-1.setUp.” Open this file.
h. Click on the “setup” under the measurements folder and it will load the frequency settings in the Frequency-Setup display just above it.



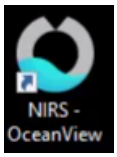
i. Click the Autosave option and set the directory to the data output directory you made for this patient: C:\Users\Baystate\Desktop\Data Output\ Month Day, Year Patient ###\EIS

5. EIT: Open the desktop icon, “EIT - STEM run - Shortcut”

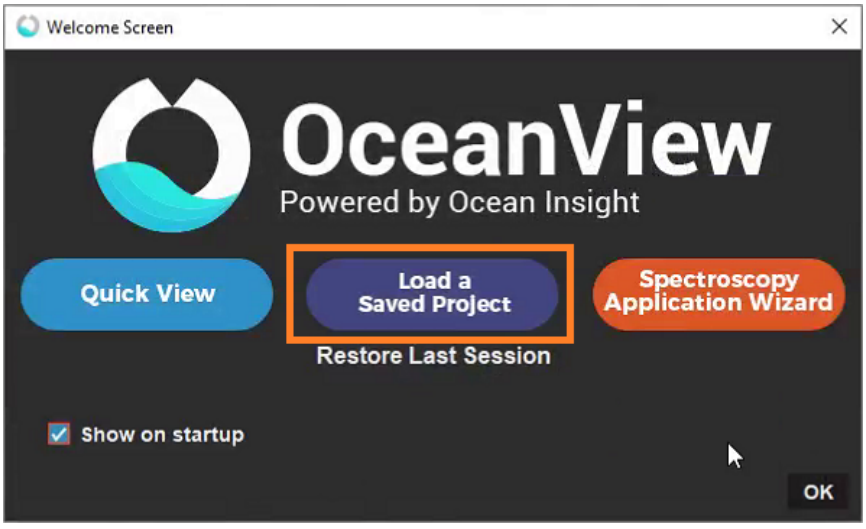
a. At the bottom left, confirm the software is showing the Sensor Belt Connector as Connected. If the software says the Sensor Belt Connector is disconnected, it indicates an internal power or connectivity problem, requiring the enclosure to be opened. Check if:
    i. The power cable to the Pioneer Interface Module is fully inserted
    ii. The cable connector on the front of the Pioneer Interface Module is connected



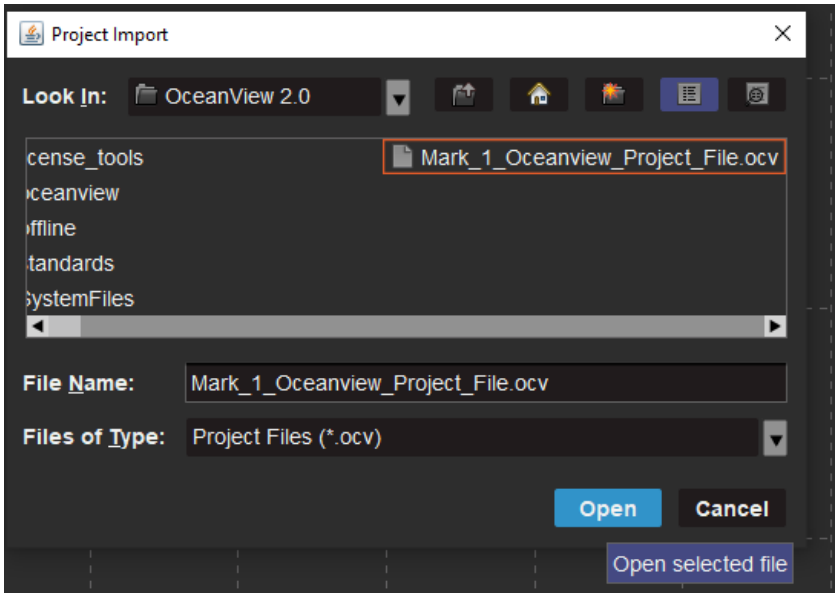
6. NIRS: Open the desktop icon, "NIRS - OceanView"



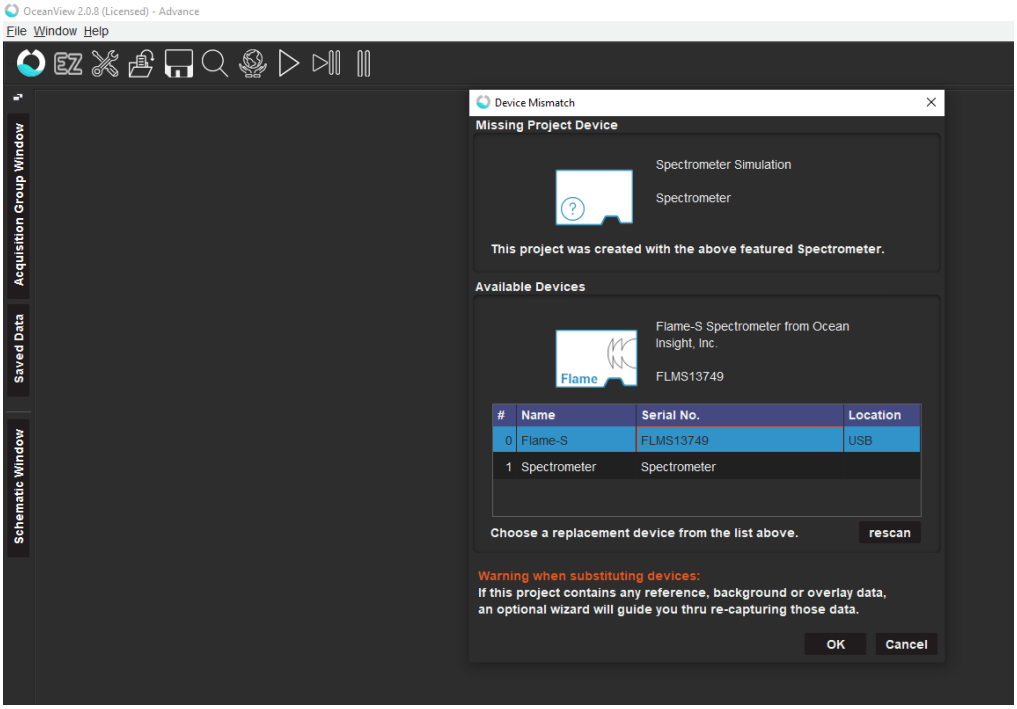
a. Upon initialization the Welcome Screen will look like this. Select Load a Saved Project.



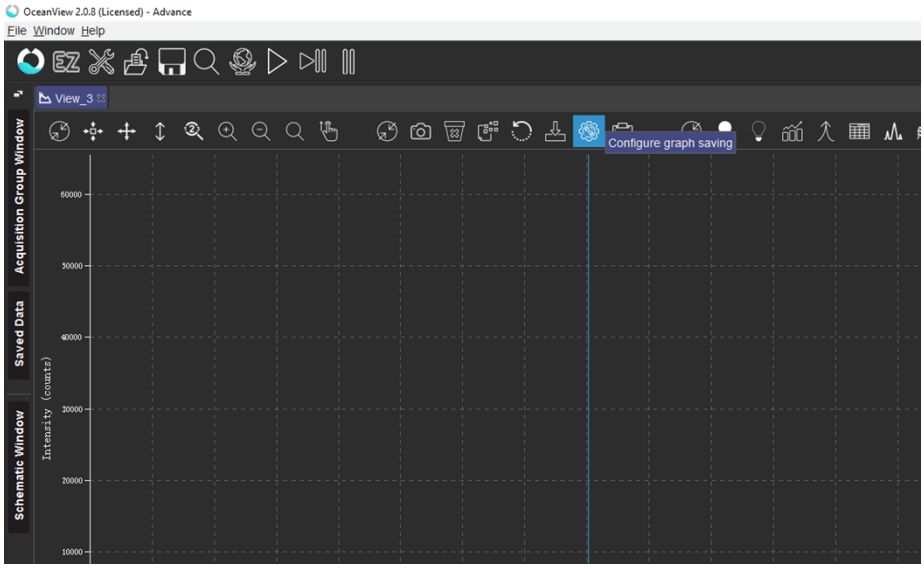
b. Select the file, "Mark_1_Oceanview_Project_File.ocv" located at the following directory (if the correct folder does not appear initially): C:\Users\Baystate \Desktop\Software\Loaded to PCs\OceanView 2.0



c. Select the Flame-S spectrometer as shown below and click OK

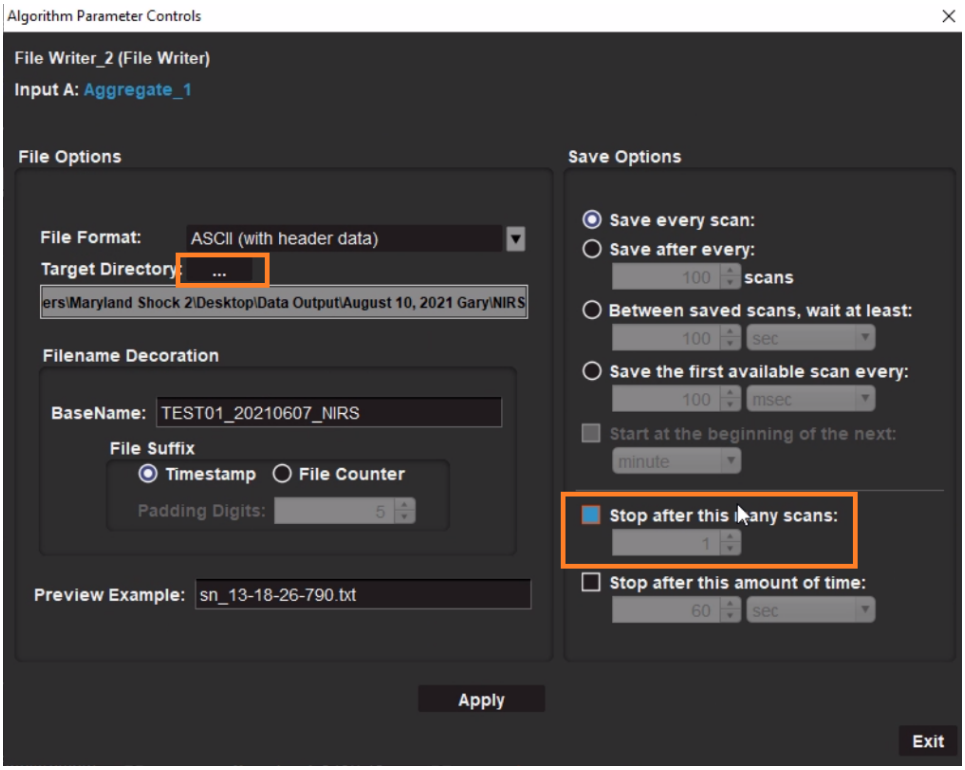


d. Open “Configure graph saving” icon.



e. **Uncheck** the option to stop after 1 sample.

f. Configure the destination folder (Target Directory) to the desired Data Output directory and click **Apply**, then **Exit**

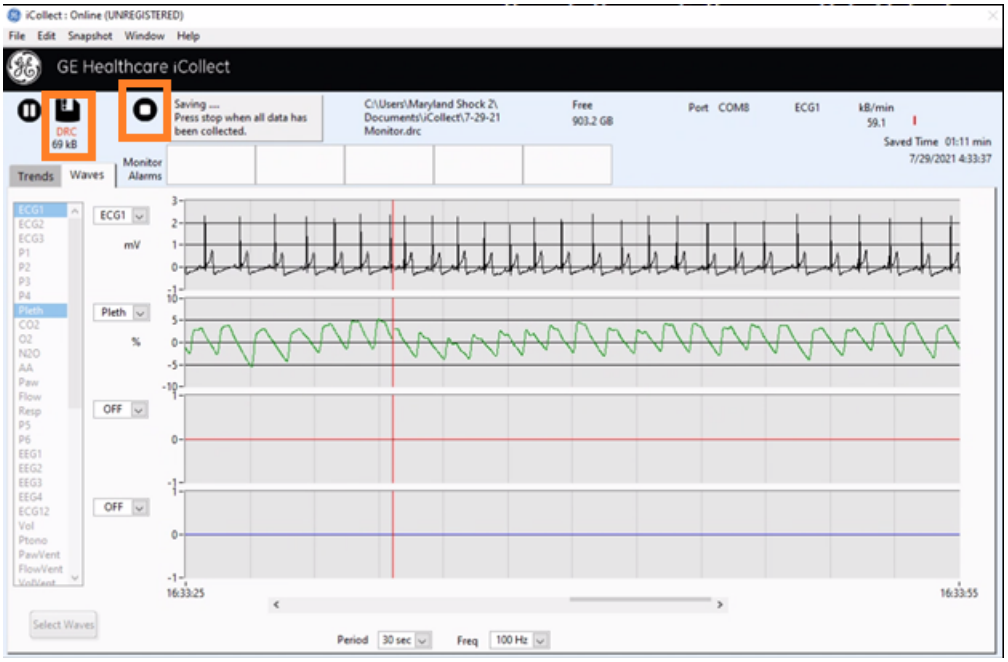


g. *Sensor calibration*: The NIRS probes require some level of calibration data, by connecting the probes to the calibration blocks and collecting data as you would on a patient. This data is not needed regularly if the probes are consistently used on the same body part or do not get damaged. Label calibration data accordingly.

Data Collection

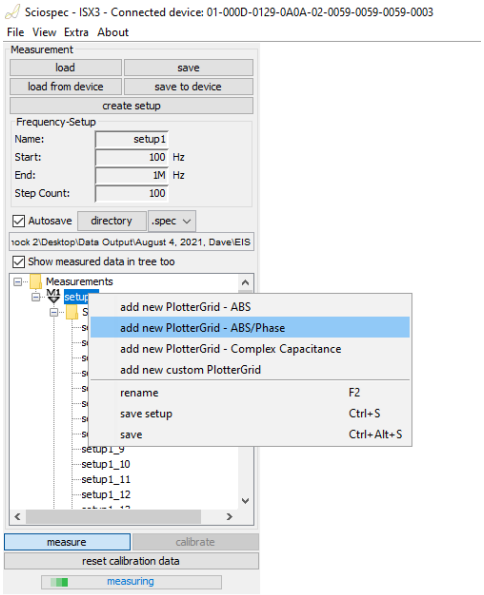
Prior to beginning data collection, quickly ensure all cables have been attached to the patient.

1. ***Clinical Monitor***:
    a. Click the save (looks like a floppy disk) icon to start data recording.
        i. A window will pop up asking where to save the file. Navigate to the "Clinical Monitor" folder in the Data Output directory. Name the file "Patient number, date" and click OK. Data is now being recorded and saved.



    b. Click the stop icon to stop and save data at the end of measurements.

2. ***EIS***:
    a. When ready to begin collecting data, click, "measure." You should see measurements begin in the window below the setup heading.
        i. To view data as it is collected, right click the setup and select, "add new PlotterGrid – ABS/Phase"



ii. There are six plots: two plots per set of electrodes. One plot measures impedance (Z) vs frequency (f), and the other plots phase (Φ) vs frequency. Each plot is labelled at the top, indicating which group of EIS cables it corresponds to (see below table).

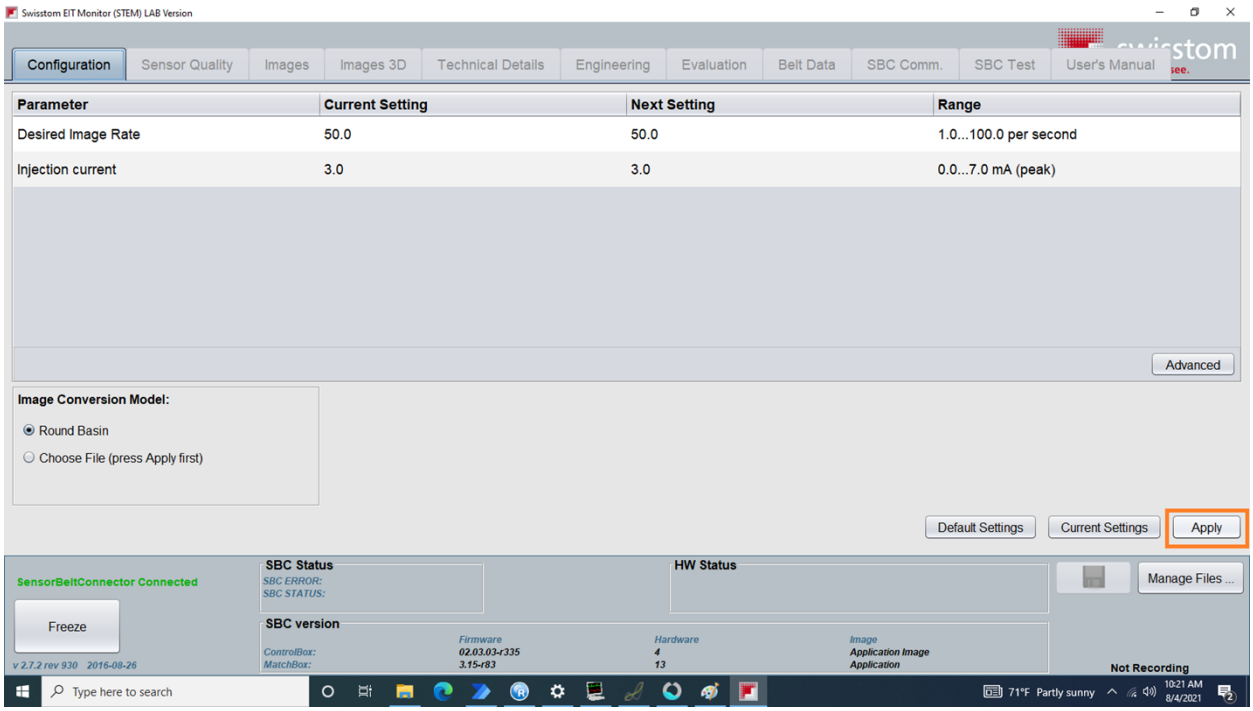
Slide Chip	Group Number	Probes Location
1 1 1 1	1	Arm
3 2 3 2	2	Chest
5 3 5 3	3	Leg

iii. Impedance is measured in Ohms (Ω), phase is measured as an angle (°), and frequency is measured in Hertz (Hz).

iv. For the Z vs f plots, right click on the plot area and select, "double-log" view

1. Impedance should be below 1,000 Ω. If the impedance is much higher, it likely means a poor connection at the electrode pad/patient interface
    a. See the above table to help identify which group has the poor connection
    b. After checking the electrode pad/patient connections (hair, peeling electrode pad, etc), the next place to check for connectivity problems if impedance is still high is the connection at the system enclosure. Remove and plug in the cable fittings of the problem group.

3. ***EIT***:
    a. Click "Apply" to begin data measurements – the computer will not record/save the data until you select the save icon.

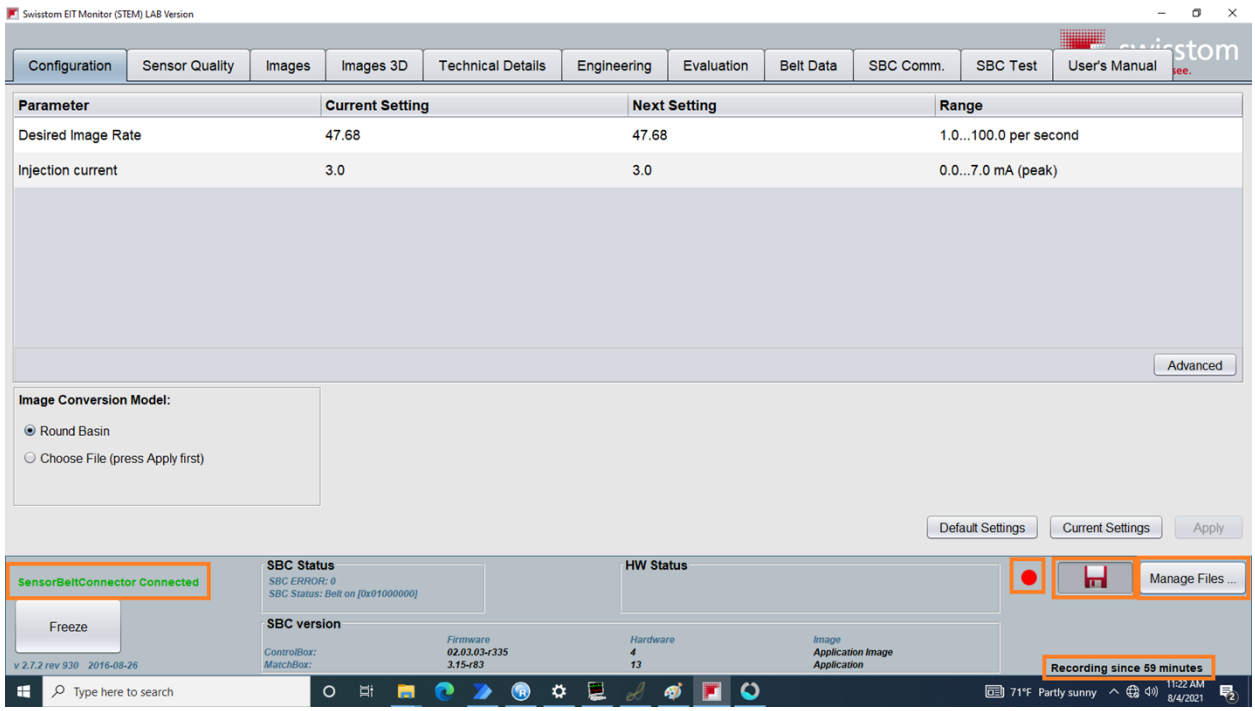


i. Once you click "Apply" the other tabs should be selectable to see measurements and electrode connectivity

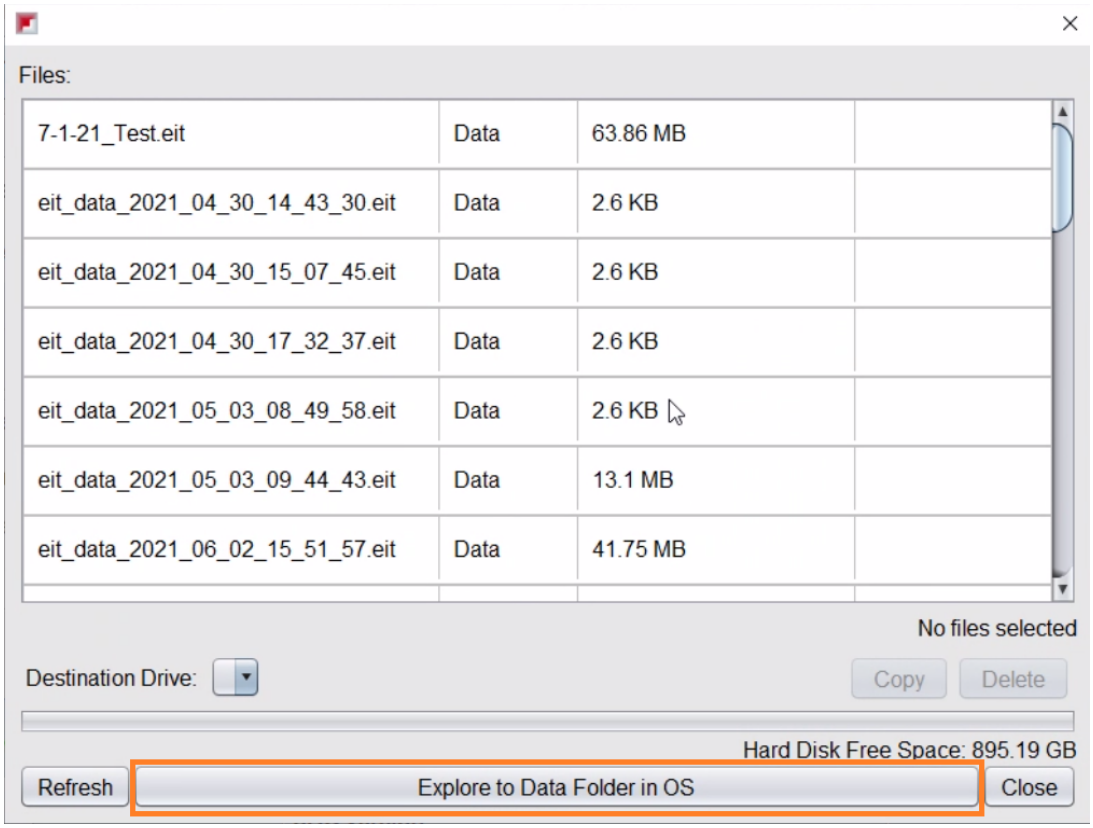
ii. Check the "Sensor Quality" tab to check for any connectivity issues with the electrodes or cables

1. The best way to identify problem probes is by looking at the individual impedance values of each electrode
2. Electrode connectivity problems usually occur at the electrode pad/patient connection

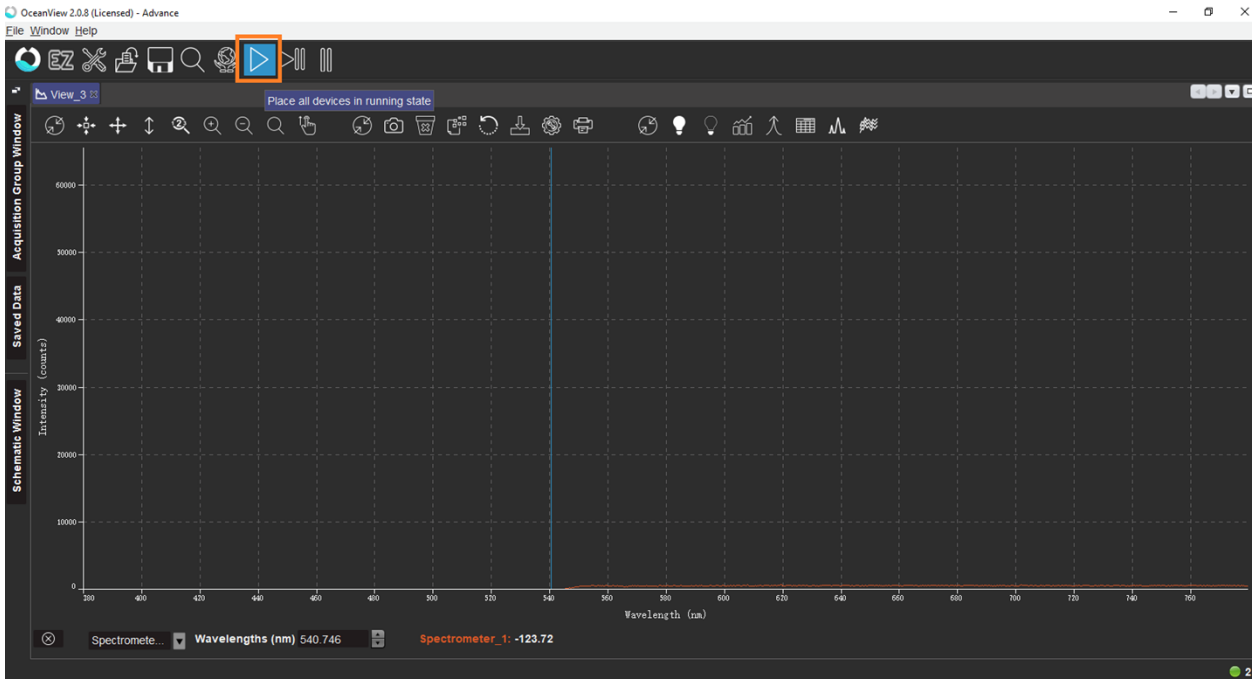
b. On the "Configuration" tab, click the green save icon to begin recording the data – the icon should turn red and the software will indicate data is recording



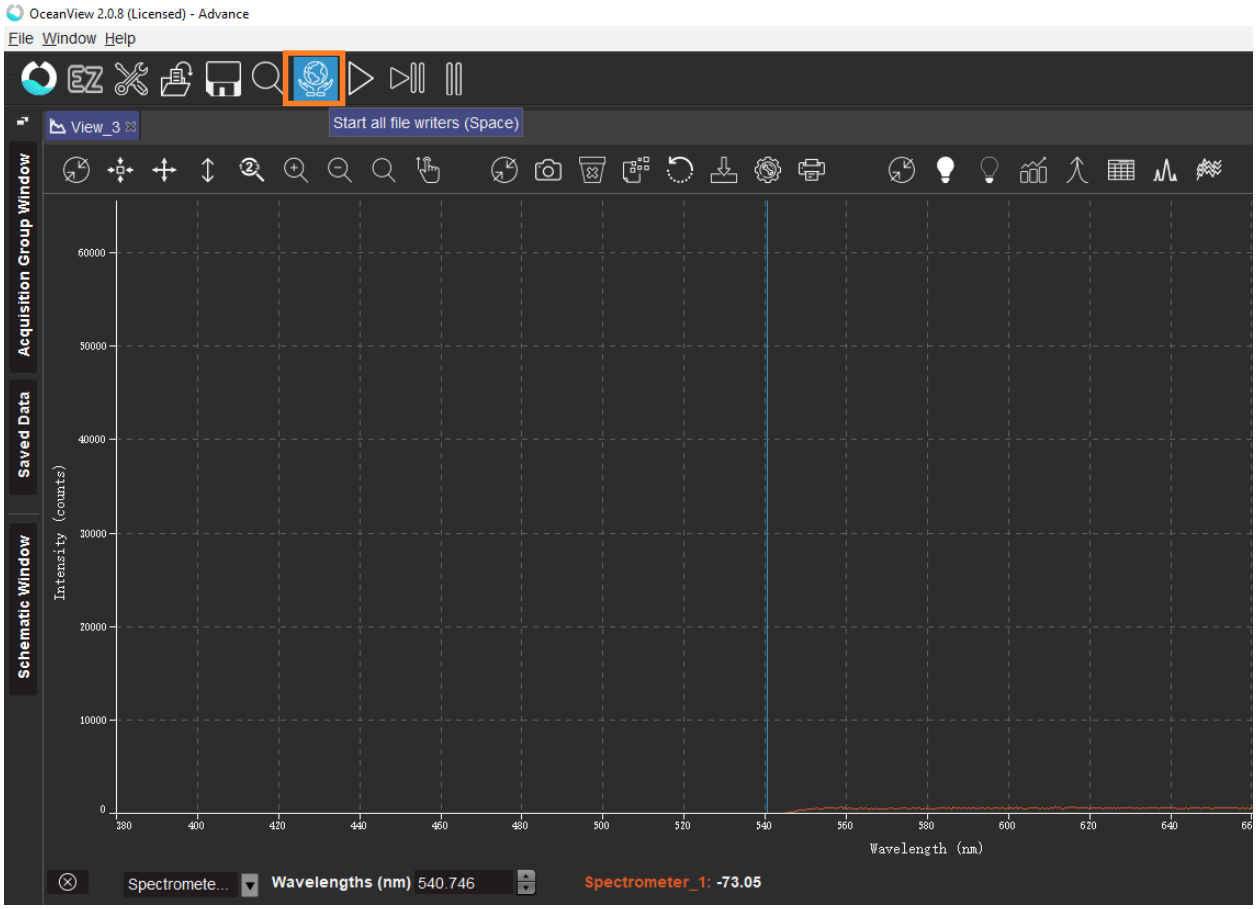
c. The "Manage Files" icon will bring up a screen allowing you to view and access saved data, ensuring data is being recorded, and later, for copying completed files to the Data Output directory. The "Explore to Data Folder in OS" opens the folder containing the EIT data files.



4. ***NIRS***:
    a. The probes should sequentially light up. If *not:*
        i. If one light on the NIRS panel stays illuminated, it is indicating an error with the probe itself or a setting within the software
            1. Before replacing or repairing probes, try cycling the NIRS system power by turning off the Uninterrupted Power Supply
    b. Press the play icon



c. “Start all file writer” (space) to start recording



d. “Pause graph saving” data recording (download icon) to stop

Data Saving and Transmission

NIRS

a. Should be saving as data is collected. Check the "saved data" tab in Oceanview, or the selected destination folder

EIT

a. Click the "Manage Files" icon, then "Explore to Data Folder in OS" which will bring you to the folder where the EIT data is stored. Cut/paste the file you just created to the "Data Output Directory"

EIS

a. Click "measure" again to stop data collection.
b. Check that the data has been autosaving in the desired directory. If not, click the "save" icon
c. In the popup window, select, "include sub-data"
d. Save to the EIS folder in the Data Output directory

Monitor

a. Select the "Stop saving" icon. Ensure the .drc file for your experiment is located in the Data Output directory

Data Transmission

a. There are multiple options for transmission of data to outside storage
    a. A UBS port is available in the rear of the enclosure where an external hard drive can connect. Copy the desired files from the prototype PC to the external drive.
    b. The PC is configured to be operated remotely (RemotePC software) so long as the PC is connected to the internet and turned on. An external user with the proper credentials can control the PC remotely to configure data transmission.
    c. The RemotePC software also has a data file transfer function, which can be accessed using the desktop version of the software. This method is not recommended for large data sets as the file transfer capability within the RemotePC software is unreliable for the time duration required to transmit these large files.

Shutdown

1. Switch off the NIRS switch on the faceplate
2. Place the NIRS probes in their holster or somewhere else where they are secure.
3. Close-down software once you have confirmed the data is properly saved in the Data Output directory.
4. Shut down the system by pressing the power button on the Uninterrupted Power Supply, then flipping the switch at the back right of the system enclosure.
5. Disconnect all probes and electrodes from the patient, storing them safely, minimizing any bending tension at the cable/enclosure connections.
6. Disconnect the power chord from the wall and unlock the wheels before moving.

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