Official Title: Oxygen Reserve Index (ORi) Validation of INVSENSOR00014

Date of Protocol: May 14, 2018

NCT Number: NCT03500341

Oxygen Reserve Index (ORi) Validation of INVSENSOR00014

Protocol/Test Procedure Title	Oxygen Reserve Index (ORi) Validation of INVSENSOR00014
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Other Investigators	[redacted]
Expected Start Date	Based on IRB Approval Certification Approval Date
Expected End Date	Based on IRB Approval Certification Expiration Date
IRB	E&I West Coast Board – IRB00007807
Date Submitted To IRB	

Protocol Test Abstract:

The objective of this study is to validate the performance of Oxygen Reserve Index (ORi) as computed by the Masimo device in healthy volunteers. The changes in ORi measurements are compared to changes in PaO2 values obtained from arterial blood samples analyzed by a laboratory CO-oximeter reference instrument.

APPROVALS

Author	Date	Engineering	Date
Quality Assurance	**Date**	**Manufacturing**	**Date**

Oxygen Reserve Index (ORi) Validation of INVSENSOR00014

STATEMENT OF COMPLIANCE

This document is a protocol for a clinical research study sponsored by Masimo Corporation. The study will be conducted in compliance with all stipulations of this protocol, the conditions of IRB approval, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 812, ISO-14155, and International Conference on Harmonization E6 Good Clinical Practice (ICH GCP).

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study.

1. PURPOSE

This test procedure describes the method used to validate the performance of Oxygen Reserve Index (ORi) as measured by the Masimo INVSENSOR00014 sensors connected to the Masimo Radical-7 pulse oximeter and Masimo Root monitor in healthy volunteers. The changes in ORi measurements are compared to changes in PaO2 values obtained from arterial blood samples analyzed by a laboratory CO-oximeter reference instrument.

Outcome Measure:

This study reports ORi specificity, sensitivity and concordance for Masimo's ORi measurement system as compared to PaO2 from blood samples.

2. BACKGROUND

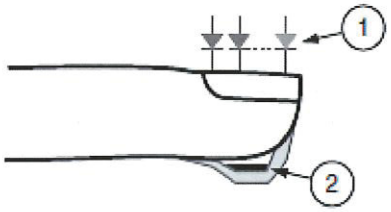
Masimo Corporation develops non-invasive medical technologies. These devices have applications in the operating room, critical care unit, emergency room, emergency transport vehicles, as well as physician's offices.

An invasive blood sample analyzed by a CO-oximeter reference instrument gives the best measure of arterial oxygen concentration as well as other blood solutes, but cannot measure these parameters continuously and requires skin puncture, arterial line placement and subsequent risk of infection, hematoma, and other physiological damage. Masimo SET and Masimo Rainbow technologies allow real-time, non-invasive monitoring of oxygen saturation (and other blood solutes) and has the potential to improve clinical outcomes while reducing the cost of care and risks to both patients and clinicians associated with arterial and venous punctures.

2.1. Technology Background

Pulse oximetry is governed by the following principles:

- Oxyhemoglobin (oxygenated blood) and deoxyhemoglobin (non-oxygenated blood) differ in their absorption of red and infrared light (spectrophotometry).
- The amount of arterial blood in tissue changes with arterial pulses (photoplethysmography). Therefore, the amount of light absorbed by the varying quantities of arterial blood changes as well.
- The CO-Oximeter utilizes a sensor with various light-emitting diodes (LEDs) that pass light through the site to a photodiode (detector). See figure below.



1. Light Emitting Diodes (LEDs) (2+ wavelengths)
2. Detector

- Signal data is obtained by passing various visible and infrared lights through a capillary bed (for example, a fingertip, a hand, a foot) and measuring changes in light absorption during the blood pulsatile cycle. The maximum radiant power of the strongest light is limited to ≤ 25mW. The detector receives the light, converts it into an electronic signal and sends it to the Masimo hardware (e.g. Rad-57, Radical-7) for calculation. Once the oximeter receives the signal from the sensor, it utilizes Masimo SET signal extraction technology for calculation of the patient's functional oxygen saturation, pulse rate and other blood parameters.

2.2. Parameter Background

A continuous supply of oxygen is essential for normal cell function. Failure of a patient's oxygen supply to meet metabolic needs is common to all forms of circulatory failure, tissue acidosis, and ultimately mortality. Like all essential commodities for body functions, optimal quantities of oxygen are required. A patient's oxygen status can be largely classified into 3 ranges: Hypoxia (less than normal), Normoxia (normal) and Hyperoxia (more than normal). The three states are typically classified using dissolved oxygen levels in the plasma (PaO_2), instead of arterial hemoglobin oxygen saturation (SaO_2), due to sensitivity of PaO_2 in all three states including hyperoxia (unlike SaO_2). Figure I.[1] shows the three oxygen states based on PaO_2 values along with the relationship between PaO_2 and SpO_2 (which is a proxy for SaO_2)

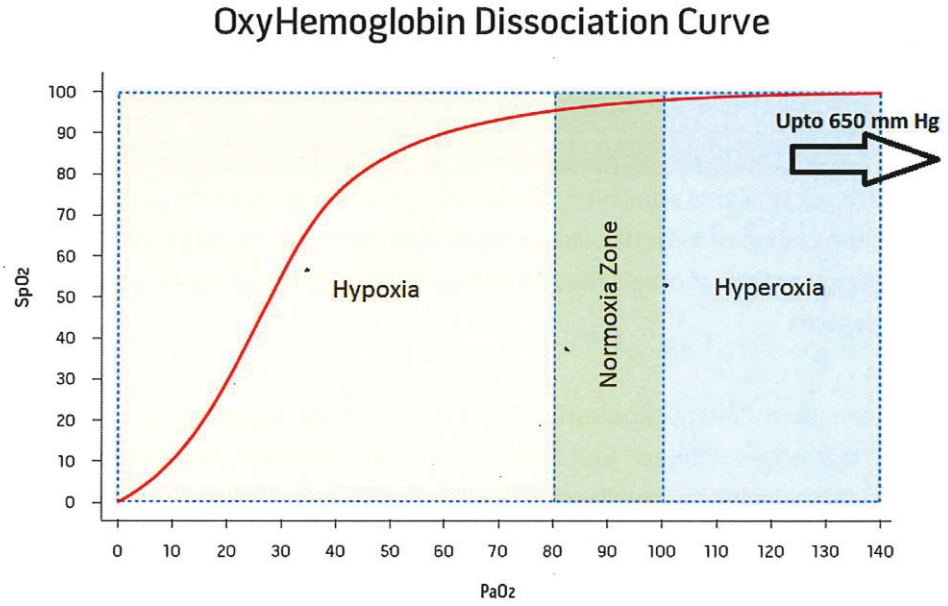


Figure 1: The oxygen dissociation curve with the three oxygen states

[1] Martin, L. (1999). *All you really need to know to interpret arterial blood gases*, Page 73, Lippincott Williams & Wilkins.

In order to prevent episodes of hypoxia, patients in critical care are administered a certain amount of surplus oxygen to prevent hypoxia even when oxygen supply may be lost intermittently. However this excess supply should be in moderation as large amounts of oxygen may result in potential lung damage. Hence it becomes imperative to monitor the amount of surplus oxygen in blood.[2]

Currently, in order for clinicians to monitor a patient's oxygen status, both continuously and non-invasively, they utilize a pulse oximeter to obtain SpO_2 (a proxy for SaO_2) levels. However, SpO_2 is sensitive in the normoxic and hypoxic regions and largely remains flat in the hyperoxic region (Figure 1) clinicians generally resort to invasive blood draws to obtain PaO_2 values which provide oxygen status within the hyperoxic zone. This method has multiple drawbacks such as intermittent samples to potential delay between time of blood draw to the time when the PaO_2 value is obtained through blood gas machines.

The ORi Parameter may help provide clinicians with a convenient noninvasive method for reference information in regards to PaO_2.While not a direct measurement of PaO_2, ORi provides a continuous and non-invasive index which correlates with changes in PaO_2 values (in the range of 100 to 200mmHg).

2.3 Investigational Study Devices

The investigational devices to be used in this study are the Masimo INVSENSOR00014 rainbow disposable sensor, Masimo Radical-7 Pulse CO-Oximeter, and Masimo Root Patient Monitoring and Connectivity Platform. [redacted]

INVSENSOR00014 is similar to existing FDA cleared Masimo rainbow disposable sensors. [redacted]

Investigational sensor is equivalent to the FDA cleared sensors with regard to intended use on the surface of the skin, the choice of materials, biocompatibility, manufacturing process and risk of exposure to the subject to any energy or light source. They do not pose any additional risk to patients as compared to the FDA cleared sensors.

The Masimo Root Patient Monitoring Platform is an FDA-cleared patient monitoring and connectivity platform that offers rainbow® and Masimo SET® measurements with other parameters in an integrated platform. With docking capabilities for the Radical-7® handheld monitor and multiple networking/connectivity options, Root integrates multiple streams of data into one display monitor. The Masimo Radical-7 pulse oximeter is an FDA-cleared noninvasive monitoring platform featuring Masimo SET Measure-through Motion and Low Perfusion™ pulse oximetry with the option to measure multiple additional blood constituents and physiologic parameters. [redacted]

[2] D. S. Martin and M. P. W. Grocott III. , Oxygen therapy in anaesthesia: the yin and yang of O2 Br. J. Anaesth. (2013) 111 (6): 867-871 doi:10.1093/bja/aet291

[2] Habre W1, Peták F2. Perioperative use of oxygen: variabilities across age. Br J Anaesth. 2014 Dec;113 Suppl 2:ii26-ii36. doi: 10.1093/bja/aeu380

3. REFERENCE

Consent To Be A Research Subject Oxygen Reserve Index (ORi) Validation of INVSENSOR00014
Post Care Instructions
_ Oxygen Reserve Index (ORi) Validation of INVSENSOR00014 Case Report Form (CRF)
Oxygen Reserve Index (ORi) Validation of INVSENSOR00014 Healthy Volunteers Needed Advertisement
_ Oxygen Reserve Index (ORi) Validation of INVSENSOR00014 Recruitment Script
_ Health Assessment Questionnaire Health Assessment Questionnaire Oxygen Reserve Index (ORi) Validation of INVSENSOR00014
- Confidentiality Agreement
Volunteer payment form
Informed Consent Process
Clinical Study Request Form (CSRF)

4. LOCATION

Masimo Corporation

Clinical Laboratory

52 Discovery

Irvine, CA 92618

5. STUDY POPULATION

5.1. Inclusion Criteria

- Subject is 18-50 years of age.
- Subject weighs a minimum of 110 lbs and no more than 250 lbs unless subject is over 6 feet tall.
- Hemoglobin value is greater than or equal to 11 g/dL.
- Baseline heart rate $\geq$ 45 bpm and $\leq$ 85 bpm.
- CO value $\leq$ 2.0% FCOHb
- Subject has a physical status of ASA I or II (American Society of Anesthesiology Class 1; Healthy subjects without any systemic disease at all. American Society of Anesthesiology Class II; subjects with mild systemic disease) as it applies to the systemic disease portion of the classification.
- Systolic Blood Pressure $\leq$ 140 mmHg and Diastolic Blood Pressure $\leq$ 90 mmHg.
- Subject is able to read and communicate in English and understands the study and risks involved.

5.2. Exclusion Criteria

- Subject is pregnant.
- Subject smokes (smoking includes e-cigarette use)
- Subject has a BMI > 35 and has been classified as morbidly obese or at an increased risk for participation by a medical professional.
- Subject has open wounds, inflamed tattoos or piercings or any visible healing wounds.
- Subject experiences frequent or severe headaches and/or migraine headaches.
- Subject has known drug or alcohol abuse or uses recreational drugs.
- Subject has experienced a concussion or head injury with loss of consciousness within the last year.
- Subject has any chronic bleeding disorders (i.e. hemophilia)
- Subject has any history of a stroke, myocardial infarction, seizures or heart attack.
- Subject has any cancer or history of cancer (not including skin cancer).
- Subject has a chronic neurological disease (i.e. multiple sclerosis, Huntington's disease).
- Subject has any cardiac dysrhythmia(s) (i.e. atrial fibrillation) and has not received clearance from their physician to participate.
- Subject has known neurological and/or psychiatric disorder (i.e. schizophrenia, bipolar disorder) that interferes with the subjects' level of consciousness.
- Subject has any medical condition which in the judgment of the investigator and/or medical staff, renders them ineligible for participation in this study (Discretion of investigator).
- Subject has Wolff-Parkinson-White Syndrome or Stokes - Adams syndrome.
- Subject who has taken anticoagulant medications within the last 30 days.
- Subject has taken opioid pain medication within 24 hours of start of study.
- Subject has either signs or history of peripheral ischemia or carpal tunnel syndrome.
- Subject has had invasive surgery within the past year- including but not limited to major dental surgery, gallbladder, heart, appendix, major fracture repairs (involving plates/ screws), jaw surgery, urinary tract surgery, plastic surgery, major ENT surgery, joint replacement or gynecological surgeries, heart surgery or thoracic surgery.
- Subject has donated blood within the last 2 weeks.
- Subject has symptoms of congestion, head colds, flu or other illnesses.
- Subject experiences claustrophobia or has generalized anxiety disorder.

- Subject has been in severe car accident(s) or a similar type of accident(s) requiring hospitalization within the last 12 months.
- Subject has had a concussion within the past 12 months.
- Subject has chronic unresolved asthma, lung disease or respiratory disease.
- Subject is allergic to lidocaine, latex, adhesives, or plastic.
- Subject has heart conditions, insulin-dependent Diabetes or uncontrolled hypertension.
- Subject has given vaginal delivery, had a pregnancy terminated, a miscarriage with hospitalization, or had a C-section within the past 6 months.
- Subject intends to participate in any heavy lifting, repetitive movement of their wrist (including riding a motorcycle) or exercise (working out, riding a bike, riding a skate board etc.), or any activity that will put additional stress on the wrist within 24 hours of the study.
- Discretion of investigator/study staff.

5.3. Withdrawal of subjects

Subjects must be withdrawn under the following circumstances:

5.3.1 The subject withdraws consent.

5.3.2 Discretion of investigator, for example:

- The investigator feels that the subject is too money motivated.
- The investigator feels that the subject does not fully comprehend and understand the consent form.
- The subject is ill-mannered and/or shows aggressive behavior towards study staff.
- Malfunction of the device for greater than 30 minutes that prevents accurate collection of optical data.
- Subject displays or communicates signs of discomfort or distress so that the study may not be continued.

5.4. Replacement of subjects

In case a subject is withdrawn from the study, another subject may be recruited.

6. EQUIPMENT AND MATERIALS

Equipment and Materials: All lab analyzers and equipment will be maintained per manufacturer specifications and all study personnel will be trained on the use of relevant equipment. Equivalent equipment and materials to those listed below may be used.

Safety Equipment (FDA-Cleared)

- Blood pressure monitoring system
- A-line pressure transducer
- Electrocardiogram (ECG)
- Masimo Pulse Oximeters (Radical-7) - for subject safety monitoring
- Pulse oximeter sensors and cables (Masimo SET, Masimo rainbow)
- Masimo Patient Monitoring Platform (Root®)- for subject safety monitoring

- Medical-grade Oxygen tank and mask
- Crash cart

Test Devices

- Masimo INVSENSOR00014 Rainbow sensor – Investigational

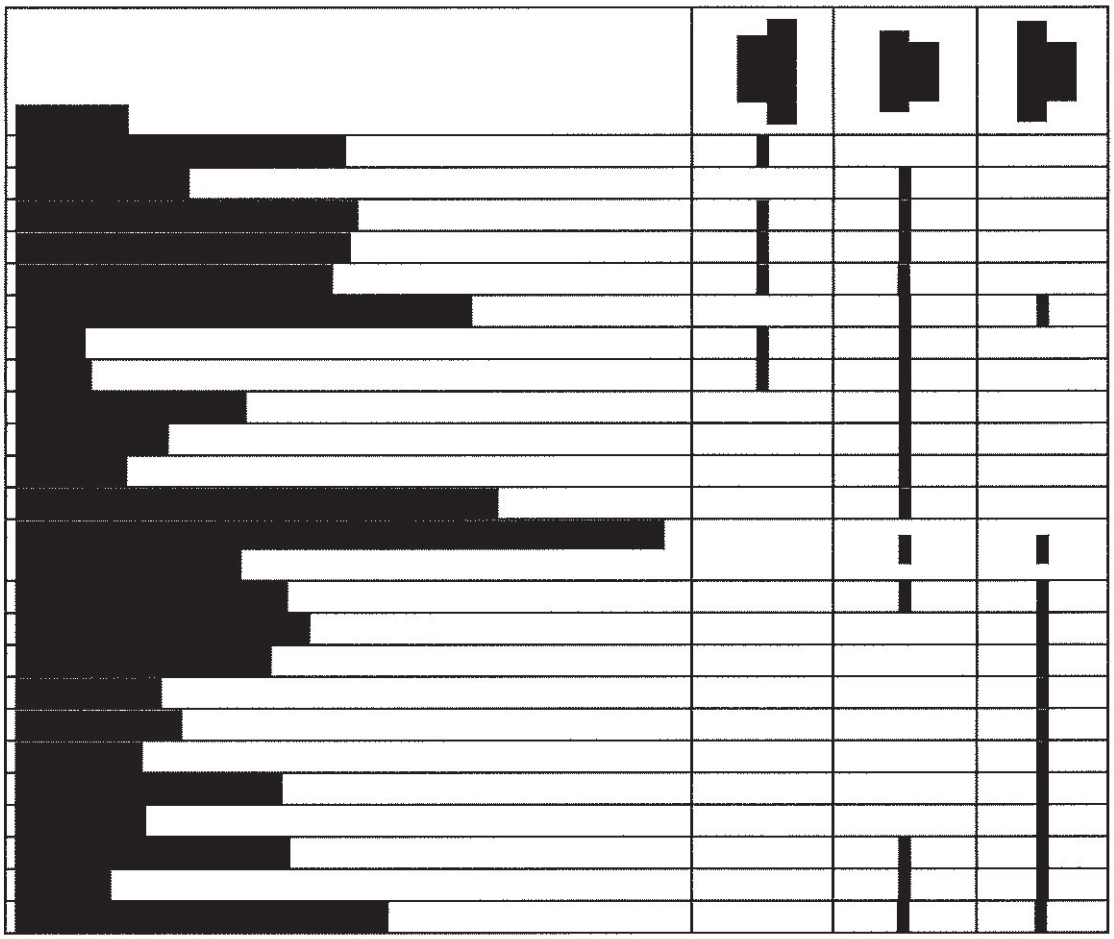
Research Equipment

Passive Data Collection Research Equipment

- Laboratory co-oximeters/blood analyzers

7. PROCEDURE

7.1 SCHEDULE OF ACTIVITIES



[redacted]

7.2. **RECRUITMENT AND PRESCREENING**

Subjects will be recruited using IRB-approved advertisements. Subjects may be referred to the study by previous subjects. Subjects are contacted via phone call to conduct a prescreening interview to determine their initial eligibility for the study. Potential eligible subjects are scheduled for a study visit to the clinical laboratory.

7.3 **CONSENTING AND SCREENING**

7.3.1. Study staff will discuss the informed consent process and the study with the potential subjects. The subjects will be provided with enough time to read and understand the informed consent document and their questions will be answered by study staff prior to the subject signing the informed consent form. No study related activities will be conducted until consent is signed.

7.3.2. The subject's weight and height are self-reported, however the subject may be weighed on a scale for verification.

7.3.3. Subjects will be asked to provide a copy of their valid government photo ID and/or Social Security Number (SSN) card to verify subject identity. The copies of these forms of identification will be stored along with the subject's consent. The confidentiality and retention of these documents will be protected to the extent provided and required by law.

7.3.4. Subjects will be asked a brief series of health questions to ensure their eligibility for this study. Subjects who do not meet the inclusion and exclusion criteria will not be eligible to participate in the study.

7.3.5. Subject demographic information including age, sex, skin tone, ethnicity, height and weight will be collected. These may be recorded for data analysis and/or subject safety monitoring purposes.

7.3.6. In addition, a medical history will be recorded after the initial screening questionnaire.

7.3.7. Pre-procedure vital signs will be recorded for subject safety monitoring. Spikes in blood pressure and heart rate can be expected during line placement, needle sticks, blood draws etc. and may also be attributed to anxiety/nervousness relating to a new environment. Only the initial recorded blood pressure and/or heart rate determines a subject's qualification for the study.

7.3.8. Female subjects will be required to take a pregnancy test. Results will be noted in study documentation. If the pregnancy test is positive, the subject will be notified and removed from the study.

[redacted]

7.3.9. A venous sample will be obtained via needle stick or by placement of an IV and analyzed to verify that the subject meets the inclusion criteria for hemoglobin level and HbCO. The subject will be excluded from the study if the values from the blood draw fall outside the ranges stated in the inclusion criteria.

7.3.10. Subjects may have a blanket placed on them for their comfort.

7.3.11. Subjects may be offered a snack (e.g., granola bar) and/or beverage (e.g., water, juice) due to the amount of time their involvement in this study may take.

7.4. PROCEDURES

7.4.1. Standard hospital-type monitors will be placed on the subject, including ECG, blood pressure, and a reference pulse oximeter for safety monitoring by medical staff.

7.4.2 Proprietary Masimo data collection software will be used to verify all oximeters are reading. If not, proper sensor positioning will be checked and sensors may be repositioned, as needed.

7.4.3 Rainbow parameter output values (e.g., SpO_2, pulse rate, PI) along with ORi will be recorded using the proprietary Masimo data collection software. These values match the values calculated by the instrument at runtime.

7.4.4 A peripheral venous line will be placed in the subject's hand or arm. This line may be used for the qualifying venous blood draw and for safety or clinical intervention required during the study.

7.4.5 Local anesthetics such as lidocaine, ethyl chloride spray, or Pain Ease skin refrigerant spray may be used in the event that an IV is placed to numb the site. Subjects will be given the option to have lidocaine or numbing spray be used during IV placement for the purpose of making catheter placement more comfortable for the subjects.

7.4.6 After intravenous access is established, one or more intra-arterial catheter(s) (arterial line or A-line) will be placed in the radial artery of the subject's wrist. The A-line is placed to facilitate continuous blood pressure measurement for subject safety monitoring, and/or to enable repeated removal of blood aliquots for reference arterial blood gases (ABG), Hgb, Hct, as well as other non-infectious blood solutes.

7.4.7 After arterial access is established, sensors will be placed on the required sensor sites.

[redacted] Arterial blood samples will be drawn at specified targeted increments. [redacted]

[redacted] Upon indication the subject is comfortable, a gas mixture will be administered [redacted]. The proportion of inspired oxygen (FiO_2) will be increased in specified targeted increments [redacted]

7.4.9 After reaching the desired targeted FiO2 levels during hyper-saturation, the proportion of inspired oxygen (FiO2) will be decreased in specified targeted increments until reaching room air; samples should be drawn at each targeted saturation level. After reaching room air, [redacted] the subject may be allowed to breathe room air [redacted]

[redacted] After hyper-saturation and return cycle, the volunteer is desaturated until SpO_2 drops to approximately [redacted] The lowest allowable value will be [redacted] oxygen saturation. Readings near [redacted] will be immediately verified [redacted] to ensure that levels are within the targeted oxygen saturation range and to minimize time that the subject may drop below the targeted range. Note: At any point in the study, if the subject feels uncomfortable, the subject will be given 100% oxygen [redacted]

7.4.11 The study will end with several minutes at a FiO_2 greater than or equal to room air (≥21%) to help the subject re-saturate after the procedures.

[redacted]

7.4.17 If at any point the subject is uncomfortable with the study, the study will be stopped.

[redacted]

7.4.18 At the conclusion of the procedure, the sensors/devices, IV(s), and arterial line(s) will be removed and the subject will be allowed to leave after medical personnel determine it is safe to do so.

7.4.19 The total procedure time will be approximately [redacted].

7.4.20 All subjects will be encouraged to remain in the study area until they feel fit to leave; subjects should feel safe and able before returning to work directly after participation in the study.

7.4.21 Subjects will be given instructions on wound care. All subjects will be instructed to contact the principal investigator or study staff in the event of any potential complication.

7.4.22 Subjects will be paid for their time.

7.4.23 Subjects will be provided with information related to any significant new findings that develop at any time during the study which may relate to their willingness to continue their participation.

8. ACCEPTANCE CRITERIA

For validation studies, acceptance criteria is determined by Masimo specifications for each design.

9. SAMPLE SIZE JUSTIFICATION

[redacted] we need 22 completed subjects for this study. The subjects should be both male and female with varying skin pigmentation.

10. DATA ANALYSIS PROCEDURE TO BE USED

Data from subjects who did not go through the full protocol are excluded from data analysis. Specificity, sensitivity and concordance will be computed for changes in ORi with respect to changes in PaO2 as described below:

ΔPaO_2 vs ΔORI

ΔPaO_2 and ΔORI are defined below.

$$\Delta PaO_2 = PaO_2(t) - PaO_2(t_{ref})$$

where t_{ref} is the time of the sample closest to $PaO_{2threshold}$ in a ± 10 mmHg (see footnote⁺) window. A ± 10 mmHg window is used as it is not possible to draw a blood sample at the exact desired value of $PaO_{2\ threshold}$. PaO_2 can be any value from 110 to 190 in steps of 10mmHg (see footnote) to cover the range of 100 to 200mmHg..

$$\Delta ORI = ORI(t) - ORI(t_{ref})$$

Samples with ΔPaO_2 of ± 10 mmHg are ignored (see footnote⁺).

[redacted]

[5] Bedford, Robert F. MD, (1978), Long-term radial artery cannulation: effects on subsequent vessel function, *Critical Care Medicine, 6 (1),* 1-71.

[5] Slogoff S, Keats AS, Arlund C, (1983), On the safety of radial artery cannulation, *Anesthesiology,59 (1),* 42-47.

1) As per Figure 2, specificity is defined as

   Specificity = N1 / (N1 + N4)

2) As per Figure 2, sensitivity is defined as

   Sensitivity = N3 / (N2 + N3)

3) As per Figure 2, concordance is defined as

   Concordance = (N1 + N3) / (N1 + N2 + N3 + N4)

The relationship between Concordance, Specificity and Sensitivity is as shown below.

Let $N = (N1 + N2 + N3 + N4)$

$$\text{Concordance} = \frac{N1}{N} + \frac{N3}{N}$$

$$= \frac{N1\ (N1+N4)}{N\ (N1+N4)} + \frac{N3\ (N2+N3)}{N\ (N2+N3)}$$

$$= \frac{N1+N4}{N} * Specificity + \frac{N2+N3}{N} * Sensitivity$$

$$\text{Concordance} = \alpha * Specificity + (1-\alpha) * Sensitivity$$

where $0 \leq \alpha \leq 1$.

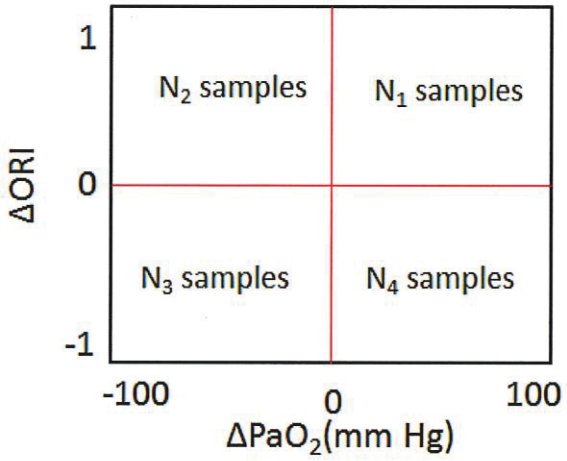


Figure 2: Specificity and Sensitivity Illustration for ΔPaO_2 vs ΔORI

11. ADVERSE EVENTS

Definitions:

Adverse event: Any untoward medical occurrence in a subjects, users or other persons, whether or not related to the medical device under study.

Device-related adverse event: Adverse event related to, associated with, or caused by, the use of a medical device under study, including but not limited to events that may have been attributed to the device because of device failure or malfunction, improper or inadequate design, manufacture or user error.

Device deficiency: Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, use errors and inadequate labeling.

Device deficiencies will be reported according to department procedures.

Serious adverse event: Adverse event that: a) led to death, b) led to serious deterioration in the health of the subject, that resulted in: (i) a life-threatening illness or injury, (ii) a persistent or significant impairment of a body structure or a body function, (iii) in-patient or prolonged hospitalization, or (iv) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, or c) led to fetal distress, fetal death or a congenital abnormality or birth defect. NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered a serious adverse event.

All adverse events, including inter-current illnesses will be reported and documented as described below.

10.1 Adverse Events

All adverse events that occur during the study shall be recorded on the Case Report Form even if the investigator/study staff assesses the adverse event as unlikely to be causally related to the test device or study procedures.

10.2 Serious Adverse Events

The investigator/study staff shall promptly report both serious adverse events and unanticipated adverse device effects to the sponsor within 48 hours. All serious adverse events will also be reported to the IRB per IRB reporting requirements.

At the time of discharge from the study, any unresolved serious adverse event(s) will be followed up by the investigator/study staff until the event(s) are resolved, stabilized or the patient is lost to follow-up or the adverse event is otherwise explained. The investigator/study staff will also instruct the subject to report any subsequent events occurring in the next 30 days, which the subject or the subject's physician believes might reasonably be regarded as caused by or have a reasonable possibility of being caused by the test device or procedures involved in the study.

10.2. Unanticipated Problems

Any unanticipated problem involving subjects will be reported to the IRB, such as protocol violations or deviations as required by the IRB reporting procedures.

11. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

11.1 Measures Taken to Protect the Rights and Welfare of Subjects

11.1.1 All subjects will be monitored closely throughout the study. There will be an ACLS certified medical doctor present in the study area throughout the study.

11.1.2 The following measures will be taken to ensure the confidentiality of the subjects:

11.1.2.1 A code (identification) number for each subject will be kept on file.

11.1.2.2 Only their corresponding identification number will identify subjects.

11.1.2.3 Access to identifying documents (IC, SSN, photo ID) and data will only be made to the principal investigators in the study and study staff.

11.1.2.4 The confidentiality and retention of these documents will be protected to the extent provided and required by the law.

11.2 Vulnerable Populations

11.2.1 Employees are considered to be a vulnerable population.

Participation is not a condition of employment. There will be no repercussions in the workplace in the case that the employee refuses to participate in the study or withdraws at any point during the study. Neither supervisors nor superiors will be involved in the recruitment of employees for participation in the study.

11.2.2 Economically disadvantaged or unemployed and educationally disadvantaged.

Reasonable compensation will be provided for economically disadvantaged subjects to eliminate possibility of undue influence due to financial incentive. Educationally disadvantaged subjects will be provided ample time to ask questions and comprehend information.

11.3 Documents and Database

11.3.1 Documents will be kept [redacted] after the specific product/tested for is no longer being made. If destroyed, these documents will be shredded and done by a certified company used for destroying medical and clinical data.

[redacted]

[redacted]

12. DEVICE ACCOUNTABILITY

12.1 Receipt of Study Device

Upon receipt of the study device supplies, an inventory must be performed and the device accountability log filled out and signed by the person accepting the shipment. It is important that the designated study staff counts and verifies that the shipment contains all the items noted in the shipment inventory. Any damaged or unusable study devices in a given shipment will be documented in the study files.

12.2 Use of Study Device

Use of devices and sensors will be documented on Case Report Forms for each subject.

12.3 Return or Destruction of Study Device

At the completion of the study, there will be a final reconciliation of study devices and sensors shipped, devices/sensors used, and devices/sensors remaining. This reconciliation will be logged on the device accountability log. Any discrepancies noted will be investigated, resolved, and documented prior to return or destruction of unused study devices. Devices destroyed on site will only be upon written instruction from the sponsor and will be documented in the study files.

13. RISKS AND BENEFITS

13.1. Benefits: There will be no benefit to the subject. Other possible benefits would be to society as a whole. Evaluation of the accuracy of this new device could enable healthcare workers to more appropriately treat potentially life threatening conditions.

13.2. Device Risks: The noninvasive devices used in this study are similar in technology and design to some commercially available pulse oximeters and other non-invasive devices and hence have the same risks. Pulse oximeters and other non-invasive devices are commonly used and are considered to be minimal risk. There is an extremely small risk of damage to the subject's fingers, or other locations where sensors are placed, from the device including temporary skin irritation or discomfort associated with exposure to the sensor as well as potential temporary mechanical irritation or discomfort. There is a remote, yet possible, risk of a burn from the sensor. In the case of a sensor burn there is the potential for permanent skin damage (scar/discoloration).

13.3. Venous Cannulation Risks: swelling, infection, infiltration of fluids/ blood into area surrounding IV, bruising, hematoma, lightheadedness, fainting, feeling flush/warm, feeling nauseated, throwing up, sudden drop in blood pressure/sudden increase in blood pressure, sudden drop in heart rate/sudden increase in heart rate, tingling sensation of face, arms and/or legs, sweating, mouth dryness, damage to the blood vessel and surrounding nerves or tissue.

13.4. Arterial Cannulation risks: decreased blood supply, blood clot, embolization, infection, hematoma, damage to the blood vessel and surrounding nerves, tendons or tissue; loss of feeling in hand and/or arm and even the loss of hand due to rare complications of the study.

13.5. Blood Draw risks: discomfort is generally associated with needle puncture. The most common complications associated with blood draws and capillary sticks are hematomas or bruising. All blood

[redacted]

draws will be performed by qualified personnel. An ACLS certified physician will be in attendance throughout the entire procedure, and the study will be completed under their general supervision. Other anticipated adverse events that may occur, include but are not limited to: vasovagal (passing out/fainting), infection to the skin or area right below the skin, lightheadedness, feeling flush/ warm, feeling nauseated, throwing up, seizures, sudden drop in blood pressure/ sudden increase in blood pressure, sudden drop in heart rate/ sudden increase in heart rate, tingling sensation of face/arms and/or sweating, and mouth dryness. These anticipated adverse events are expected to be temporary.

13.6. Risk From Oxygen Administration: There are no risks associated with high oxygen/oxygen administration for less than 24 hours as long as subjects do not have any cardiac conditions, COPD or any other lung diseases. Subjects' answers on the health questionnaire will help the medical staff decide if they can safely participate in this study; subjects are encouraged to let the study staff know if they have any concerns.

13.7. Low Oxygen Concentration Risks: Risks associated with hypoxia include dizziness, shortness of breath, drowsiness, or headache. If or when this occurs, the study can be stopped. There is an extremely small risk of loss of consciousness, damage to vital organs, or death from lack of oxygen. The study shall be stopped by the subject or clinical staff long before this could occur. Other anticipated adverse events that may occur, include but are not limited to: vasovagal (passing out/fainting), lightheadedness, feeling nauseated, throwing up, seizures, sudden drop in blood pressure/sudden increase in blood pressure, sudden drop in heart rate/sudden increase in heart rate, tingling sensation of face, arms and/or legs, sweating, mouth dryness. These anticipated adverse events are expected to be temporary.

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13.9. Risk from Inflicted Knowledge: The risk of inflicted medical knowledge to subjects is negligible since we de-identify all associated sample information including those relevant to our clinical and engineering parameter studies. The monitoring and test results are not examined for diagnostic purposes and do not reflect an attempt to ascertain any subject's medical condition. The attending physician's role during this study is to ensure the safety of the subject during the study. Subjects are informed that these are not diagnostic tools, if observations are made using FDA cleared devices we will refer them to their primary care physician.

13.10. Risk From Loss of Confidentiality: Masimo upholds the highest standards to protect hard and electronic data however, a complete promise for confidentiality cannot be guaranteed due to unforeseeable events.

13.11. Risk From Additional Testing:

13.11.1. During the conduct of the study, it is possible, but not likely, that someone could become exposed to the sample of blood drawn from the subject through an inadvertent needle stick or by contact with an open cut. In such circumstances, it will be important to the exposed individual to know whether the blood to which he or she was exposed contained Hepatitis B virus (HBV), Human immunodeficiency virus (HIV), or Hepatitis C virus (HCV) and additional testing of the sample will be performed.

13.11.2. Within the consent, subjects will agree to permit the company to test the blood sample (or samples) by signing the consent. The test results will be maintained as confidential and will only be used by healthcare professionals for the diagnosis and treatment of the exposed individual as appropriate.

13.11.3. In the case that Masimo needs to contact a subject regarding additional testing they will be contacted by a Masimo employee and medical personnel can be available for further counsel if requested.

13.11.4. The cost for the initial testing and compensation for their time/travel to the testing facility will be the only things paid for by Masimo.

13.12. Lidocaine (injection) Risks: Insertion of the Lidocaine may be discomforting and can feel like a slight pinch along with a warm/burning sensation. Other anticipated adverse events that may occur, include but are not limited to: Flushing or redness of the skin, itching skin, small red or purple spots on the skin, unusually warm skin, bruising, bleeding at the application site, and swelling. These adverse events are expected to be temporary.

13.13. Although not common, it is also possible to have an allergic reaction to injectable lidocaine. Subjects should not take part in this study if they are allergic to lidocaine injection or other types of numbing medicine, or if they have a heart rhythm disorder such as Wolff-Parkinson-White Syndrome or Stokes-Adams syndrome. Subjects are instructed to tell the study staff right away if they experience hives; difficulty breathing; swelling of your face, lips, tongue or throat.

13.14. Ethyl Chloride (Lidocaine Spray): Ethyl Chloride is a topical anesthetic which is used to prevent pain by cooling the skin. Although unlikely, the anticipated adverse events that may occur, include but are not limited to: changes in skin color (i.e. Flushing or redness of the skin), delayed wound healing, rash, itching and swelling. These adverse events are expected to be temporary.

14. EMERGENCY RESPONSE PLAN FOR MEDICAL EMERGENCIES

The physician and nurse present during the study will be ACLS certified and will respond to any medical emergency involving a subject with the ACLS approved protocol for intervention. A crash cart is on site and full emergency services are within 3 miles.

15. MONITORING PLAN

A separate document for the study monitoring plan will be developed and followed to ensure subject safety and GCP compliance.

16. PROTOCOL DEVIATIONS AND AMENDMENTS

Deviations to the protocol will be documented on the Case Report Form or a separate document. Protocol deviations will be reported to the sponsor and IRB per IRB reporting guidelines.

Modifications to the protocol, informed consent materials, recruitment materials, or any other materials provided to subjects must be reviewed and approved by the IRB.