PROTOCOL TITLE:

Utilization of Near-Infrared Spectroscopy Technology to Determine Normative Cerebral Regional Oxygen Saturation in a Preterm Population Born at Altitude

PRINCIPAL INVESTIGATOR:

Dr. Jessie Maxwell, MD
Department of Pediatrics and Neurosciences
Division of Neonatology

ADMINISTRATIVE CONTACT:

Name Sandra Beauman

Department Pediatrics

VERSION NUMBER:

Version 5

DATE:

5/26/21

REGULATORY FRAMEWORK:

Please indicate all that apply:

☐	DOD (Department of Defense)
☐	DOE (Department of Energy)
☐	DOJ (Department of Justice)
☐	ED (Department of Education)
☐	EPA (Environmental Protection Agency)
☐	FDA (Food and Drug Administration)
☒	HHS (Department of Health and Human Services)
☐	VA
☐	Other:

FUNDING:

This pilot project is not currently funded; however, we will be applying for internal funding to cover the cost of the NIRS leads and a NIRS monitor. IRB approval is required to apply for the internal funding, which is why it has not yet been received.

CLINICAL TRIALS

Is this a clinical trial per the NIH definition of a Clinical Trial? ☒ Yes ☐ No

NIH Definition of a Clinical Trial:

A research study in which one or more human subjects are prospectively assigned to one or more interventions. An "intervention" is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related

biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

Use the following four questions to determine the difference between a clinical study and a clinical trial:

1) Does the study involve human participants? ☒ Yes ☐ No
2) Are the participants prospectively assigned to an intervention? ☒ Yes ☐ No
3) Is the study designed to evaluate the effect of the intervention on the participants? ☒ Yes ☐ No
4) Is the effect being evaluated a health-related biomedical or behavioral outcome? ☒ Yes ☐ No

Note that if the answers to the 4 questions are yes, your study meets the NIH definition of a clinical trial, even if…

- You are studying healthy participants
- Your study does not have a comparison group (e.g., placebo or control)
- Your study is only designed to assess the pharmacokinetics, safety, and/or maximum tolerated dose of an investigational drug
- Your study is utilizing a behavioral intervention

If yes to all 4 questions, please confirm that the research team is familiar with and agrees to comply with the investigator requirement to register the study on the ClinicalTrials.gov database. Additionally, the approved consent document(s) must be uploaded to the ClinicalTrials.gov database ☒ Yes ☐ No

For any assistance with registration of your trial or the requirements, please contact HSC-CTSCResearchConcierge@salud.unm.edu

PROTOCOL TITLE:

Table of Contents

Deleted: 6
Deleted: 6
Deleted: 9
Deleted: 11
Deleted: 12
Deleted: 13
Deleted: 13
Deleted: 13
Deleted: 14
Deleted: 14
Deleted: 15
Deleted: 15
Deleted: 15
Deleted: 18
Deleted: 19
Deleted: 19
Deleted: 20
Deleted: 21
Deleted: 21
Deleted: 21
Deleted: 22
Deleted: 22
Deleted: 24
Deleted: 24
Deleted: 25
Deleted: 25
Deleted: 26
Deleted: 27
Deleted: 28
Deleted: 28
Deleted: 29
Deleted: 29

Deleted: 35
Deleted: 36
Deleted: 36
Deleted: 37

1. Objectives

The objective of this study is to obtain the cerebral regional oxygen saturation ($cRSO_2$) in a preterm population that is born at altitude to determine if the range of "normal" values is different than those obtained at sea level. **We hypothesize that the $cRSO_2$ will be lower than the normative values that have been previously described**. As more clinical studies are being performed, and the use of NIRS becomes more common, it is imperative that we assess if other factors such as altitude must be considered prior to general implementation.

Aim 1: We will prospectively obtain $cRSO_2$ for the first 96 hours of life in infants born <32 weeks' gestation. The data obtained will not be interrupted clinically as the clinicians will not be able to view the data obtained from the NIRS monitoring.

Aim 2: Outcome measures including death, intraventricular hemorrhage, necrotizing enterocolitis, sepsis, duration of supplemental oxygen required, time to taking full volume feeds via nippling, and hospital length of stay will be collected. This will be compared with the infant's average $cRSO_2$ as well as the fluctuation in $cRSO_2$ that was observed. This may provide supportive evidence for clinical use of NIRS in future trials at UNMH.

2. Background

Near-infrared spectroscopy (NIRS), is a technology that can provide continuous, non-invasive monitoring of oxygenation in tissue[1]. Light absorption is measured at a few discrete wavelengths which can provide information for the tissue oxygen saturation in multiple organs[2], with cerebral, renal and splanchnic oxygenation being the most commonly measured in neonates[1]. NIRS technology was first available in 1977, however different sensors and manufacturers resulted in a large range of regional oxygen saturation (RSO_2), making it difficult to establish normative values within a specific population[1]. Thus, improvements in the technology has resulted in the ability to consider more clinical uses for the NIRS technology.

Infants with congenital heart disease is a population in which the NIRS technology has been applied. The use of cerebral oximetry measurement has provided the first indication of a clinical problem in 23% of the procedures in which the technology was utilized[1]. While some initial studies have shown a negative correlation between cerebral regional oxygen saturation ($cRSO_2$) and gestational age[3], routine use in the preterm infant has not been established.

Infants born prematurely (<37 weeks' gestation), and especially those born extremely preterm (<28 weeks' gestation), have organs that are immature and vulnerable. There are fluctuations in cerebral blood flow due to limitations in autoregulation, which may be exacerbated by routine care of the infant[4]. Previously there was a limitation in the ability to monitor these changes in blood flow and saturations, however NIRS now provides the technology needed. There are clinical trials ongoing to assess $cRSO_2$ immediately after birth in an attempt to improve outcomes[5] as well as monitoring in the first 72 hours of life in extremely preterm infants[4]. While these studies will likely provide support for applying NIRS as routine care for preterm infants, there is data lacking when infants are born at altitude. It is unknown if the increased altitude in places such as Albuquerque and Denver would result in a different range of expected values with NIRS monitoring. Thus, we proposed a prospective observational study in which we apply NIRS monitoring to

infants born <32 weeks' gestation for the first 96 hours of life to assess the $cRSO_2$ as well as outcome information for the infant.

3. Study Design

The study will be a prospective observational study, in which any infant consented to participate in the study will have the NIRS applied for the first 96 hours of life. It will be the goal to apply the NIRS sensors in the first 12 hours of life. All infants will have the same treatment if in the study, but clinicians will not be able to see the data obtained so that there is no clinical interpretation during this time.

4. Inclusion and Exclusion Criteria

Inclusion Criteria:

- Infant must be <32 weeks' gestational age at time of delivery.
- Consenting mother/guardian of the infant must speak English. Other languages are not being included due to the need of a translator being brought into the unit, which adds risk to the vulnerable population. Additionally, as the time to consent is a narrow window, adding the complexity of getting a translator may delay the ability to get consent and thus make it more difficult to enroll patients.
- Infants that require blood transfusions during the monitoring time may be included.

Exclusion Criteria:

- Any known cardiac anomaly or other anomaly which may impair perfusion and blood flow.
- Infant born after placental abruption or concern for extreme blood loss immediately after birth.
- Unable to consent the mother/guardian due to maternal health issues after delivering (eg requiring intubation or sedation after the delivery).
- Mothers/guardians that are prisoners, as the study team would like to have continuing communication with the mother during the study period as needed.
- Mothers/guardians that are <18 years of age will not be approached for consent.
- Any mother/guardian that is not able to consent due to having a legal representative will not be approached for consent in this study.
- Any infant that is planned to be placed for adoption
- Infant is greater than 24 hours of age at time of consent.

Individuals will be screened for eligibility by reviewing the Newborn Intensive Care Unit (NICU) census twice daily.

Any infant that has been consented for participation and completes at least 48 hours of NIRS monitoring will be included in the final study sample.

5. Number of Subjects

This is a single site, observational study. The goal number of patients to be recruited is 100. A similar study that evaluated an older cohort (30 weeks' gestation to 42 weeks' gestation) was able to find significant differences with a sample size of 100[3]. Given the number of extremely preterm infants (<28 weeks' gestation) born at UNMH varies from 18-30 per year, we expect to reach goal enrollment within a 2-year period, as we are including up to 32 weeks' gestation.

6. Study Timelines

An individual will participate in the study if the guardian consents for participation. The NIRS device will be applied after consent has been obtained (ideally within the first 12 hours of life). The device will remain in place, with routine skin care management during care times, for the first 96 hours of life and then removed. No further interventions will occur during the study period. Data on relevant outcomes will be extracted from the hospital chart during the birth hospitalization.

The duration of time to enroll subjects is 2 years. If the goal enrollment is reached sooner, then enrollment will be stopped. Upon completion of enrollment, data will then be analyzed. This is expected to be completed 6 months after enrollment is complete; thus, the study duration is expected to be 2.5 years.

7. Study Endpoints

The primary endpoint of the study will be upon completion of goal enrollment of 100 infants. During the enrollment period, a safety review will be completed every 5 subjects to ensure there are no adverse effects from the NIRS equipment. Specifically, skin integrity will be assessed. Given the use of this technology in multiple other studies at this gestational age, this is not expected to be a common finding. However, this will be routinely checked. Additionally, a data safety monitoring board (consisting of neonatologist Dr. Maxwell and co-investigators) will review the findings every 10 infants to ensure no safety concerns exist; any concerning findings will be immediately reported to the IRB (please see section 14 for additional information).

At this time, no exploratory endpoints are expected beyond the Aims presented.

8. Research Setting

The research would be conducted in the NICU at the University of New Mexico Hospital (UNMH). Patients would be identified after admission to the NICU. The application of the NIRS would occur in the NICU as well.

9. Resources Available

Dr. Maxwell is a neonatologist who conducts basic, translational and clinical research when not on service in the NICU. She has dedicated research time, and thus has the availability to complete the proposed project. She is well experienced in caring for this patient population. Her involvement on an IRB committee has significantly increased her knowledge in regard to ensuring that all research is conducted in the highest quality possible.

Dr. Novak is a neonatologist and the fellowship director for the neonatology fellowship at UNMH. She has experience providing care for this patient population, as well as

experience in education that will be crucial in ensuring that all training is completed for all providers involved.

Dr. Enright is a neonatology fellow who is developing experience providing care for this patient population and has dedicated time reserved for research and participation in this project.

Dr. Rockholt-Smith is a pediatric resident who is interested in pursuing a fellowship in neonatology.

All research persons will remain up to date on CITI training, as well as be expected to remain updated on the most recent version of the IRB approved protocol for this study. Additionally, research persons have availability to all patients admitted to the NICU that meet inclusion criteria, making the goal recruitment of 100 infants over 2 years obtainable.

10. Prior Approvals

The departmental approval has been obtained and is uploaded for review.

11. Multi-Site Research – N/A

12. Study Procedures

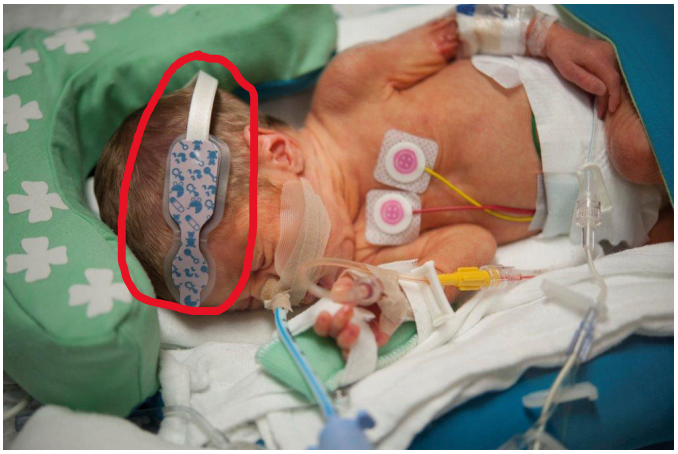
Any infant that is born at <32 weeks' gestational age and does not meet exclusion criteria as described above will be considered for the study. The mother/guardian must speak English as we do not have the resources to translate the documents, nor could we obtain consent appropriately. If an infant is born at another hospital and transferred to UNMH, they will be considered for the study only if the mother/guardian is physically present.

The study will be described following the consent script (attached) and if consent is obtained, the infant will then be given a study identifier (ex. NIRS-1). The "NIRS-1" component of the identifier will be the infant's number used so that identifying information can be removed. For sub-analysis, the infants will be divided into 3 groups to assess the impact of gestational age on the measurements. Specifically, the 3 groups will be divided into the following ages: Group 1: 23 to ≤26 weeks' gestation; Group 2: >26 weeks' gestation to ≤29 weeks' gestation; Group 3: >29 weeks' gestation to 31 6/7 weeks' gestation.

The NIRS device will be applied after the infant is admitted to the Newborn Intensive Care Unit (NICU) at UNMH (ideally within the first 12 hours of life). The device will remain in place, with routine skin care management during care times, for the first 96 hours of life and then removed. This will allow 72-96 hours of data collection, depending on the timing of the placement of the NIRS device in relation to the birth time. The SpO2 (routine oxygen saturation monitoring) information will be collected at the same time so that the relative cerebral fractional tissue oxygen extraction can be calculated. The data output will not be visible to the clinical team, so there will not be any incidental clinical interpretation of this data.

To apply the devise, a trimmed piece of Mepitel (MoInlycke), which is a translucent skin dressing, will be placed with the hydrocolloid adhesive-backed NIRS sensor placed

directly onto the Mepitel. The sensor will then be placed with the skin dressing onto the central forehead of the infant. The sensor will be plugged in to ensure that signal strength is appropriate. There will be daily inspection of the sensor site by the research team, with the area monitored by the bedside nurse with each care-time (usually every 3 hours). The area will be monitored for erythema or irritation of the skin around the sensor, and the sensor will be removed or replaced if necessary. We will avoid lifting up the sensor unless necessary for removal or repositioning. Care will be taken to avoid pressure on top of the sensor. After the infant is 96 hours of age, the sensor will be removed. Adhesive remover or a warm moist cloth will be used to slowly remove the sensor from the skin. The sensor will then be discarded after use. The NIRS probe (circled in red) is shown below in this sample image taken from van Bel, et al[6]. Additionally, the NIRS probe is plugged into a NIRS monitor, which is then plugged into the Phillips monitor if desired. We currently have 6 of the devices which connect the NIRS to the Phillips monitor, however need to purchase the NIRS monitor and the NIRS probes.



Information will be collected from the medical record at time of enrollment as well as at the time of infant discharge. This information will include: gestational age at birth, birth weight, mode of delivery, sex of infant, maternal complications during pregnancy (including pre-eclampsia, chorioamnionitis, hypertension, diabetes, thyroid disease, and cervical insufficiency), maternal medications during pregnancy, resuscitation required at birth including if chest compressions were done, length and type of respiratory support infant required, intraventricular hemorrhage, necrotizing enterocolitis, patent ductus arteriosus and if treatment was used, chronic lung disease, retinopathy of prematurity, any surgeries that were completed during the hospitalization, sepsis, hospital length of stay, time to full volume nippling of feeds, and death if applicable. The data obtained during the NIRS recording will be collected and analyzed to determine the average cerebral regional oxygen saturation. The relative cerebral fractional tissue oxygen extraction will be calculated. The blood pressure and heart rates of each infant that are normally obtained for clinical purposes will be extracted from the patient charts during the time of the NIRS monitoring.

13. Data Analysis

The cerebral regional oxygen saturation data will be averaged for each infant. All male and female data will be analyzed separately and the compared to determine any statistical differences that are present between sexes. NIRS parameters will be summarized as median and interquartile ranges. The relative cerebral fractional tissue oxygen extraction will be calculated using the following equation: (SpO2 – rScO2)/SpO2.

As described above, there will be a sub-analysis of the infants enrolled based on gestational age. Specifically, the 3 groups will be divided into the following ages: Group 1: 23 to ≤26 weeks' gestation; Group 2: >26 weeks' gestation to ≤29 weeks' gestation; Group 3: >29 weeks' gestation to 31 6/7 weeks' gestation. Comparisons among different groups will be analyzed by one-way ANOVA followed by Dunn's method. Categorical data will be analyzed using Fisher's test. Spearman's rank correlation coefficient will be used to calculate correlations between cerebral regional oxygen saturation, relative cerebral fractional tissue oxygen extraction and gestational age. Values of $p<0.05$ will be considered statistically significant.

14. Provisions to Monitor the Data to Ensure the Safety of Subjects

This study is seen as no more than minimal risk to the patient population, however, given that the patient population is at high risk for adverse outcomes, the information collected on each patient will be reviewed each time 10 patients have completed the NIRS component of the study. The neonatologists involved in the study, Dr. Maxwell, Dr. Zamora and Dr. Novak, will review the data. They will also review the scientific literature at these meetings to ensure that the study protocol remains appropriate for this patient population. Any concerns or SAEs will be reported to the IRB immediately.

15. Withdrawal of Subjects

If at any time there are concerns that the NIRS is interfering with routine care (although not expected to occur), the subject will be withdrawn from the research without their consent. If withdrawal from the study needs to occur, the NIRS equipment will be removed and any data collected to that point will be utilized. Collection of information will be obtained from the medical record as previously described, even if the NIRS monitoring is discontinued early. A subject can voluntarily withdrawal at any time from the study with no consequence or change in routine medical management. If a parent decides to withdraw the participant from the study, then any data that has already been collected will be kept for analysis (unless the PI is contacted as described in the next sentence). If the parent / guardian wishes to remove the data collected, then they can contact the PI , Dr. Maxwell, at 630-864-9422 to request all data to be removed and it will be removed. No additional data will be collected.

16. Data Management/Confidentiality

All data will be kept on a password protected computer in Dr. Maxwell's office (BRF 137D), which has a locked office door and a locked ante-room door. All paper records will be kept in a locked cabinet in Dr. Maxwell's office (BRF 137D), which has a locked office door and a locked ante-room door. All electronic data will be de-identified as soon as

possible with identifying information destroyed. All de-identified information will be kept until the youngest subject reaches the age of 22, as required by UNM HSC Research Policy, and then destroyed.

Each patient will be assigned a code at time of enrollment (NIRS-1, NIRS-2, etc). This will allow for de-identification of the patient. As protected health information and identifying information will be collected, this de-identification will allow for added confidentiality. The date of birth and medical record number will be the identifying information that is removed from the data collection once the study ID is assigned and the medical chart has been reviewed for the additional information (see attached excel file for additional information that will be collected). The electronic link between the study ID and the patient identifiers will be kept on Dr. Maxwell's UNM issued computer, which is password protected. This is stored in her locked office, which also has a locked anteroom. This will not be stored in the same computer folder as any other documents pertaining to this study (it will be separated from the data). If the research team needs any of the patient information, they will be required to utilize the computer in Dr. Maxwell's office. The data will not be publicly available unless requested with publication. No sensitive information will be collected, and a certificate of confidentiality is not required. As this is a single site study, there will be no transfer of the data required. REDCap will be used to maintain the data in a secured manner. All data will be electronically collected and stored. All data will be kept per the policy HSC-R-801 PR.1, in which research records of minors (under 18 years) must be retained until the minor turns 22 years old; thus, all data will be stored until the youngest participant has reached 22 years of age.

17.Data and Specimen Banking – N/A

18. Risks to Subjects

We expect the risks to the subjects to be minimal in relation to the NIRS device. The infants in this study, particularly in group 1, are at high risk of serious adverse events not related to NIRS. Specifically, this gestational age group is at high risk of death, severe brain injury, necrotizing enterocolitis, chronic lung disease, retinopathy of prematurity and sepsis. These will be included as outcome measures for the assessment, but the presence of any of these conditions would not be related to the use of NIRS.

The risks that may be present related to NIRS sensor placement include erythema and irritation of the skin around the sensor. If this is noted, the sensor will be removed. If the area appears to have erythema and/or irritation after removal, no sensor will be replaced, and the data collected to that point will be used in analysis. We will use adhesive remover or a warm moist cloth to gently remove the sensor to avoid any discomfort during this process.

As protected health information will be gathered, there is the risk for loss of privacy and/or confidentiality. We will minimize these risks by giving each participant a study ID and removing the identifiers at that time. Per policy, records of participants under the age of 18 years must be stored until the youngest participant receives 22 years of age. All records will be stored either electronically on Dr. Maxwell's UNM issued password protected computer that is stored in her locked office, or paper copies will be stored in a locked cabinet in Dr. Maxwell's office in BRF137D.

Additionally, there is the possibility of unforeseen risks. Any concerns or SAE from the study will be reported to the IRB immediately.

19. Potential Benefits to Subjects

The infants in this study will likely not receive direct benefit from this study. The benefit of this project will potentially be for extremely preterm infants that are born at UNMH in the future. The information obtained from this study will likely result in information that would allow the routine use of NIRS in infants born preterm. The infants in this study will likely not receive direct benefit from this study.

20. Recruitment Methods

Any infant that meets the inclusion / exclusion criteria will be considered for enrollment. The mother / guardian will be approached by one of the study personnel that are included on this IRB, and the study will be discussed if they are interested in the study. The consent script has been included to show what the study personnel would verbally state to the mother / guardian. The mother / guardian may be approached at the infant's bedside or in her hospital room. If approached at the infant's bedside, the mother / guardian will be given the option to go into a family room to discuss the study further for additional privacy. The Powerchart census will be reviewed twice daily to monitor for admission of infants that would meet criteria. There will be no additional recruitment materials used for this study.

21. Provisions to Protect the Privacy Interests of Subjects

To protect the privacy of the subjects in this study, consent will be obtained in the mother's hospital room if possible. However, if the mother / guardian is present at the bedside in the NICU, they will be approached and asked if the study can be discussed in a private location (utilizing a family room or conference room) or at the bedside if the mother / guardian desires. If the mother / guardian states they do not want to participate in a study, they will be informed that the infant will continue to receive all appropriate medical care and consent for use of NIRS will not be obtained.

22. Economic Burden to Subjects

There is no expected economic burden to the subject. Participation in the study will result in an added mode of monitoring, at no cost to the subject. The information collected from the medical record will be obtained through electronic medical record access. There are no samples that will be obtained, and no cost expected to the participants or a 3rd party payer.

23. Compensation

No compensation will be provided to infants and the mothers/guardians in the study.

24.Compensation for Research-Related Injury

As this technology is used routinely in some NICUs, the study is not expected to be more than minimal risk. Therefore, no research-related injury is expected to occur, and no compensation will be offered.

25.Consent Process

Investigators included on the IRB protocol will be responsible for obtaining consent, and include Dr. Maxwell, Dr. Zamora and Dr. Novak. All are neonatologists with extensive experience in caring for this patient population as well as participating in clinical research studies. The consent process will take place in the mother's hospital room if possible, to allow for privacy. The consent process can also take place in a family room in the NICU; the consent would only be obtained at the infant's bedside if that mother / guardian requested the conversation to occur in that location. It will be stated during the consent process that participation is voluntary and will have no impact on the infant's medical care or treatment to minimize the possibility of coercion or undue influence. Once the study has been described (using the consent script that has been attached), the mother / guardian will be offered additional time to consider participation in the study. As the goal is to place the sensors within 12 hours of life, the time to consider will be dependent on the infant's age at time of initial discussion. The mother / guardian will be contacted during the study period to ensure they continue to consent to the study. During the consent process, it will be requested that the mother / guardian is able to describe the study with the sensor placement to ensure understanding.

As this study does not involve greater than minimal risk, one parent is able to give consent. If there is a guardian in place, that one guardian would be required to provide consent. This study involves neonates, so they will not be able to provide assent. Consent will be obtained for all neonates participating in the study. A partial waiver or alteration of consent is being requested in order to review the medical records to determine which infants may qualify for participation in the study.

26.Documentation of Consent

We will use a consent form that is modified from the HRPO website. It has been attached for review. The signed consent forms will be stored in a locked cabinet in Dr. Maxwell's office, which is locked and has an ante-room that is locked in non-business hours. We will obtain consent from the mother / guardian by providing them a written document that will be signed (attached). The study personnel that is obtaining consent will use the consent script to guide the review of the study (attached).

27.Study Test Results/Incidental Findings

Test results will not be specifically shared with the participant's families; however, they will be able to see the monitor and the readings while at the bedside. If at any time there are significant results which support or do not support the use of the NIRS, the study will be stopped, and families will be notified immediately.

The infant will still have all routine monitoring in place with the NIRS being an additional tool. As the NIRS is a means of continuous, non-invasive monitoring of oxygenation in tissue, and the infant will have the pulse oximeter in place as part of routine monitoring, we do not expect any incidental findings.

28.Sharing Study Progress or Results with Subjects

There will not be a summary of the trial progress provided while the study is underway. Also, there will not be a summary of the study results after the study is complete.

29. Inclusion of Vulnerable Populations

This study will include the vulnerable population of neonates. As some of the neonates will be uncertain viability (using the federal research regulations which states "viable, as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration) due to continued need for ventilatory support to maintain respiration, that checklist has been completed.

The population proposed in this study is necessary, as they are the population that has the potential to achieve benefit from this study.

30. Community-Based Participatory Research – N/A

31. Research Involving American Indian/Native Populations

This study will not exclude American Indian / Native populations, nor will it target the population for inclusion. If a woman and infant otherwise meet criteria, they will be approached for consent.

32. Transnational Research – N/A

33. Drugs or Devices

The device that will be used is an approved NIRS for clinical use in infants. The sensors will be new for each patient and discarded after use. The sensors have a hydrocolloid adhesive-backing, and they will be placed on a translucent skin dressing. Mepitel (MoInlycke) will be used as a protective barrier for the skin.

34. Principal Investigator's Assurance

By submitting this study in the Click IRB system, the principal investigator of this study confirms that:

☒ The information supplied in this form and attachments are complete and correct.

☒ The PI has read the Investigator's Manual and will conduct this research in accordance with these requirements.

☒ Data will be collected, maintained and archived or destroyed per HSC Data Security Best Practices, including:

1. **Best Practice for data collection** is for it to be directly entered onto a data collection form that is in a secured access folder on an HS drive behind a firewall, or in a secure UNM Data Security approved system such as RedCap.
2. **Data collection of <u>de-identified data</u>**, if done in a clinical setting or other setting that does not allow direct entry into a secured system, may be done temporarily using a personal or university owned electronic storage device or hard copy document. **The important security safeguard is that no identifiers be include if the data is entered or stored using an untrusted device or storage.**

3. **Permanent (during data analysis, after study closure**) storage must reside on HSC central IT managed storage. Processing of data (aggregation, etc.) are to be carried out in such a way as to avoid creating/retaining files on untrusted storage devices/computers. Trusted devices are HSC managed and provide one or more of following safeguards: access logs, encryption keys, backups, business continuity and disaster recovery capabilities.
4. **Alternate storage media** must be approve by HSC IT Security as meeting or exceeding HSC central IT provided security safeguards.

35.CHECKLIST SECTION

This section contains checklists to provide information on a variety of topics that require special determinations by the IRB. Please complete all checklists relevant to your research.

36.Partial Waiver of Consent for Screening/Recruitment

Complete this checklist if you are requesting a partial waiver of consent so that you can review private information to identify potential subjects and/or determine eligibility prior to approaching potential subjects for consent or parental permission.

A. Describe the data source that you need to review (e.g., medical records):

The medical records for the NICU census will need to be reviewed twice daily to monitor for infants that meet inclusion criteria. The partial waiver of consent is to identify the patients that could be included in the study.

B. Describe the purpose for the review (e.g., screening):

The purpose of the review is to identify the gestational age of the infant and the time of birth. This will allow for the initial screening. The additional screening will then be completed to determine if the infant meets inclusion criteria.

C. Describe who will conducting the reviews (e.g., investigators, research staff):

Only the investigators included on this proposal will be conducting the reviews.

D. Do all persons who will be conducting the reviews already have permitted access to the data source?

☒ Yes

☐ No. Explain:

i. Verify that each of the following are true or provide an alternate justification for the underlined regulatory criteria:

1. <u>The activity involves no more than minimal risk to the subjects</u> because the records review itself is non-invasive and the results of the records review will not be used for any purposes other than those described above.

☒ True

☐ Other justification:

2. <u>The waiver or alteration will not adversely affect the rights and welfare of the subjects</u> because eligible subjects will be approached for consent to participate in the research and are free to decline. Further, the information accessed during the records review will not be disclosed to anyone without a legitimate purpose (e.g., verification of eligibility).

☒ True

☐ Other justification:

3. The research could not practicably be carried out without the waiver or alteration because there is no other reasonably efficient and effective way to identify who to approach for possible participation in the research.

   ☒ True

   ☐ Other justification:

4. Whenever appropriate, potentially eligible subjects will be presented with information about the research and asked to consider participation. *(Regulatory criteria: Whenever appropriate, the subjects will be provided with additional pertinent information after participation.)*

   ☒ True

   ☐ Other justification:

37.Partial Waiver of HIPAA Authorization for Screening/Recruitment

Complete the following additional questions/attestations if the records you will review to identify potential subjects and/or determine eligibility include Protected Health Information (PHI).

A. Will you be recording any PHI when conducting the records review to identify potential subjects and/or determine eligibility?

☒ Yes. Describe: *The study team will review the medical records of the infants admitted to the newborn intensive care unit to determine which infants may qualify for the study. This will include looking at the following items:*

Inclusion Criteria:

- *Infant must be <32 weeks' gestational age at time of delivery.*
- *Consenting mother/guardian of the infant must speak English.*
- *Infants that require blood transfusions during the monitoring time may be included.*

Exclusion Criteria:

- *Any known cardiac anomaly or other anomaly which may impair perfusion and blood flow.*
- *Infant born after placental abruption or concern for extreme blood loss immediately after birth.*
- *Unable to consent the mother/guardian due to maternal health issues after delivering (eg requiring intubation or sedation after the delivery).*
- *Mothers/guardians that are prisoners, as the study team would like to have continuing communication with the mother during the study period as needed.*

- *Mothers/guardians that are <18 years of age will not be approached for consent.*
- *Any mother/guardian that is not able to consent due to having a legal representative will not be approached for consent in this study.*
- *Any infant that is planned to be placed for adoption*
- *Infant is greater than 24 hours of age at time of consent.*

If the infant is found to meet inclusion criteria, the study personnel will then approach the mother / guardian for consent.

☐ No

B. If you answered "Yes" to question 6 above, please describe when you will destroy identifiers (must be the earliest opportunity consistent with the conduct of the research) or provide justification for why they must be retained:

The identifying information will be separated from the rest of the study data once a patient is consented for participation. At that time, the participant will be given a study ID, and the identifiers will be removed. The link for the study ID and identifiers will be kept on Dr. Maxwell's UNM issue password protected computer, stored in her locked office with a locked anteroom. Upon completion of the study, all data will be stored per policy until the youngest participant reaches age 22 years. All identifying information will be destroyed upon completion of the study.

C. The PHI accessed or recorded for identification/screening purposes will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

☒ True

☐ False

38. Vulnerable Populations (Checklist)

A. Children

Complete this checklist if the subject population will include children.

1. Select the category of research that you believe this research falls within and provide justification for any associated criteria. If there are different assessments for different groups of children or arms (e.g., placebo vs. drug), include a memo to provide an assessment for each group.

   ☒ Research not involving greater than minimal risk. *(Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.)*

B. Neonates of Uncertain Viability or Nonviable Neonates

Complete this checklist if the subject population will include neonates of uncertain viability.

Provide justification for each of the following:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

   Prior research has been conducted using the NIRS technology in this patient population. There have been minimal risks noted to the neonates that have the sensor in place. However, the use of this technology has not been reported at high altitude, which has the potential to directly impact the results.

2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

   Each mother / guardian will provide consent and be fully informed. We expect there to be no direct benefit to the neonates in the study, however the results may inform future use in the NICU that may become routine.

3. Individuals engaged in the research will have no part in determining the viability of a neonate.

   The use of this technology will not impact the viability of the neonate, and the research team will not be determining the viability of the neonate in relation to this study.

4. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, ***or***, the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research

   The results from this study have the potential to impact the routine use of this technology in the NICU and may have the ability to note if/when an infant is having an acute change in cerebral blood flow which may reflect an intraventricular hemorrhage. The purpose of this research cannot be obtained by other means and there will be no added risk to the neonate resulting from the research.

Verify each of the following:

1. The research will not terminate the heartbeat or respiration of the neonate

   ☒ True

   ☐ False

2. There will be no added risk to the neonate resulting from the research

   ☒ True

☐ False

39.Medical Devices (Checklist) – N/A

Complete this checklist if the research evaluates the safety or effectiveness of a medical device. If more than one medical device is being evaluated, provide the requested information for each.

40. Data Transfer/Sharing (Checklist)

Complete this checklist if the research involves transferring/sharing of data with an external entity (institution, company, etc.).

A. Will data be transferred/shared with an external entity (institution, company, etc.)?

☐ Yes

☒ No. **The remainder of this section does not apply.**

41.Specimen Transfer/Sharing (Checklist)

Complete this checklist if the research involves transferring/sharing of specimens with an external entity (institution, company, etc.).

A. Will specimens be transferred/shared with an external entity (institution, company, etc.)?

☐ Yes

☒ No. **The remainder of this section does not apply.**

References

1. Sood, B.G., K. McLaughlin, and J. Cortez, *Near-infrared spectroscopy: applications in neonates.* Semin Fetal Neonatal Med, 2015. **20**(3): p. 164-72.
2. Kewin, M., et al., *Evaluation of hyperspectral NIRS for quantitative measurements of tissue oxygen saturation by comparison to time-resolved NIRS.* Biomed Opt Express, 2019. **10**(9): p. 4789-4802.
3. Tina, L.G., et al., *Near Infrared Spectroscopy in healthy preterm and term newborns: correlation with gestational age and standard monitoring parameters.* Curr Neurovasc Res, 2009. **6**(3): p. 148-54.
4. Hansen, M.L., et al., *Cerebral near-infrared spectroscopy monitoring versus treatment as usual for extremely preterm infants: a protocol for the SafeBoosC randomised clinical phase III trial.* Trials, 2019. **20**(1): p. 811.
5. Pichler, G., et al., *Cerebral regional tissue Oxygen Saturation to Guide Oxygen Delivery in preterm neonates during immediate transition after birth (COSGOD III): an investigator-initiated, randomized, multi-center, multi-national, clinical trial on additional cerebral tissue oxygen saturation monitoring combined with defined treatment guidelines versus standard monitoring and treatment as usual in premature infants during immediate transition: study protocol for a randomized controlled trial.* Trials, 2019. **20**(1): p. 178.
6. van Bel, F. and J.P. Mintzer, *Monitoring cerebral oxygenation of the immature brain: a neuroprotective strategy?* Pediatr Res, 2018. **84**(2): p. 159-164.