Train-of-four monitoring using the Tetragraph Neuromuscular Transmission Monitor and comparison to standard (visual) train-of-four assessment with a peripheral nerve stimulator in patients less than 1 year of age.

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July 9, 2024

PROTOCOL TITLE:

Train-of-four monitoring using the Tetragraph Neuromuscular Transmission Monitor and comparison to standard (visual) train-of-four assessment with a peripheral nerve stimulator in patients less than 1 year of age.

PRINCIPAL INVESTIGATOR:

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VERSION NUMBER/DATE:

Version: 4

Date: July 9, 2024

Revision History

Version Date	Summary of Changes	Consent Change?
3	Changing this to a multi-center study to add OU summer research student	No
4	Adding gestational age to the demographics	Yes

PROTOCOL TITLE: Train-of-four monitoring using the TetraGraph in patients less than 1 year of age**.**

1.0 Study Summary

Study Title	Train-of-four monitoring using the TetraGraph Neuromuscular Transmission Monitor and comparison to standard (visual) train-of-four assessment with a peripheral nerve stimulator in patients less than 1 year of age.
Study Design	Prospective, non-blinded comparative study
Primary Objective	The primary objective of this study is to evaluate the use of the Tetragraph Neuromuscular Transmission Monitor in pediatric patients less than 1 year of age and compare it to standard qualitative train-of-four (TOF) monitoring.
Secondary Objective(s)	None
Research Intervention(s)/ Investigational Agent(s)	TetraGraph Neuromuscular Transmission Monitor
IND/IDE #	Not applicable
Study Population	Patients less than 1 year of age who are scheduled for surgery requiring administration of a neuromuscular blocking agent.
Sample Size (finite #, no estimates) (Other sites + Local = TOTAL)	100
Study End Date	December 31, 2027
Study Specific Abbreviations/ Definitions	TOF = train-of-four NMBA = neuromuscular blocking agent MAP = muscle action potential EMG = electromyograpy

2.0 Objectives

- Describe the purpose, specific aims, or objectives.
- State the hypotheses to be tested.

The primary objective of this study is to evaluate the efficacy of TOF monitoring using the TetraGraph Neuromuscular Transmission Monitor in pediatric patients less than 1 year of age and when feasible to compare it to standard TOF monitoring using a qualitative monitor.

3.0 Background

- Describe the relevant prior experience and gaps in current knowledge.
- Describe any relevant preliminary data.
- Provide the scientific or scholarly background for, rationale for, and significance of the research based on the existing literature and how will it add to existing knowledge.

The neuromuscular junction consists of the nerve terminal, the postsynaptic muscle end plate (sarcolemma), and the intervening gap. An action potential reaching the end of the neuron triggers the release of acetylcholine from synaptic vesicles. Acetylcholine then diffuses across the gap to the postsynaptic end plate, where nicotinic acetylcholine receptors are clustered. These receptors convert the chemical signal into an electrical impulse, causing depolarization in the postsynaptic membrane, release of calcium from the sarcoplasmic reticulum, and muscle contraction. The action of acetylcholine is terminated by its passive dissociation from receptors, diffusion away from the end plate, and enzymatic degradation by acetylcholinesterase.

Neuromuscular blocking agents are commonly used during anesthetic care to facilitate endotracheal intubation or provide muscle relaxation during surgical procedures. These agents (non-depolarizing NMBAs) competitively inhibit the binding of acetylcholine to the sarcolemma thereby inhibiting skeletal muscle function. During clinical care, when neuromuscular blockade is no longer required, these agents are reversed, most commonly with a medication known as sugammadex which encapsulates the NMBA, resulting in cessation of its pharmacological effects.

The dosing of these medications is guided by monitoring neuromuscular transmission by use a peripheral nerve stimulator. This monitor stimulates the nerve (two impulses per second for two seconds) generating what is known as a TOF response. This monitor is routinely used during anesthetic care when NMBAs are in use. The electrodes are placed over a peripheral nerve and the number of twitches in the distal innervated muscle groups (hand) are noted when the device is activated. The number of twitches (0-4) is based on the receptor occupancy ratio of the NMBA. The response (number of twitches of the TOF) is used to judge the need for redosing of NMBAs as well as efficacy of reversal when sugammadex is administered. In clinical practice, the TOF is viewed by visual observation thereby leading to concerns that its use may be relatively inaccurate. Additionally, since up to 70-80% of receptors must be occupied before any change in the TOF is noted, the device is relatively insensitive. Standard qualitative monitoring is notoriously difficult in smaller pediatric patients especially those less than 1 year of age Although easy to use and part of our current clinical care, it has been shown that newer devices may be more accurate and useful in clinical care.

The TetraGraph provides an electrical stimulation of the peripheral nerve in the same way as a standard peripheral nerve stimulator, but instead of relying on visual observation of the twitch response, it directly measures the amplitude of the evoked response of the muscles (Muscle Action Potential or MAP), thereby providing a quantitative and automatic measurement of muscle response to a stimulus using electromyography (EMG). This avoids the visual observation of the twitch response and its potential inaccuracy. The device also allows a more sensitive measure of the EMG thereby providing information with less receptor occupancy than is needed to result in changes in the standard TOF. The device has been tested, validated, and approved for use in adults. We have previously used this monitoring in IRB-approved studies and have published our results.

4.0 Study Endpoints

- Describe the primary and secondary study endpoints.
- Describe any primary or secondary safety endpoints.

The primary study endpoint is to evaluate the efficacy and feasibility of using the TetraGraph monitor in pediatric patients who are less than 1 year of age. The study will evaluate the ability of the monitor to generate, record, and evaluate the EMG. When feasible, we will compare the new device with standard visual TOF monitoring (qualitative monitoring) using a peripheral nerve stimulator.

5.0 Study Interventions/ Investigational Agent

- Describe the study intervention and/or investigational agent (e.g., drug, device) that is being evaluated.

The only novel intervention is the use of the Tetragraph device to monitor neuromuscular blockade. No change in the anesthetic technique will be required during the study. When NMBAs are administered,

standard practice includes the use of a peripheral nerve stimulator with visual TOF monitoring. The study will include only patients scheduled for a surgical procedure that requires uses of NMBAs. The Tetragraph will be placed on one extremity and the standard peripheral nerve stimulator will be placed on a different extremity.

- Drug Device Handling: If the research involves drugs or device, describe your plans to store, handle, and administer those drugs or devices so that they will be used only on subjects and be used only by authorized investigators.
    - *If the control of the drugs or devices used in this protocol will be accomplished by following an established, approved organizational SOP (e.g., Research Pharmacy SOP for the Control of Investigational Drugs, etc.), please reference that SOP in this section.*

The monitors and sensors are kept in a locked cabinet in the Anesthesia Research office.

- If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:
    - Identify the holder of the IND/IDE/Abbreviated IDE.
    - Explain procedures followed to comply with sponsor requirements for FDA regulated research for the following:

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	***X***	***X***	
21 CFR 54	***X***	***X***	
21 CFR 210	***X***		
21 CFR 211	***X***		
21 CFR 312	***X***		
21 CFR 812		***X***	***X***
21 CFR 820		***X***	

The FDA has given 510(k) approval for both the device and the pediatric sensors.

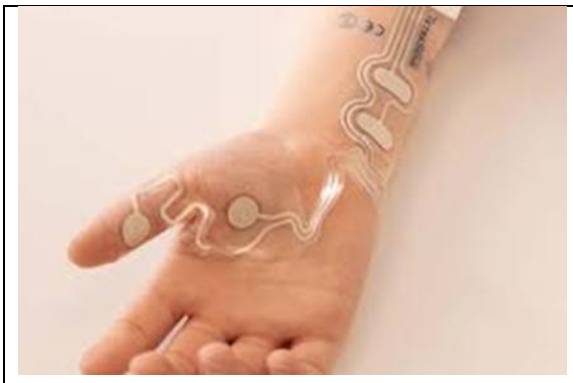
6.0 Procedures Involved

- Describe and explain the study design.

This is a prospective study that will evaluate the feasibility of using the Tetragraph in pediatric patients who are less than 1 year of age.

- Provide a description of all research procedures being performed and when they are performed, including procedures being performed to monitor subjects for safety or minimize risks.

The device, which is FDA-approved for use, will be attached to an extremity and data recorded by the device as it stimulates the nerve and generates the EMG from the muscle. Data is recorded every 20 seconds by the TetraGraph based on its normal functioning parameters. We will enroll 25 patients into each of 4 age ranges under 1 year of age.



We will also compare data from the standard peripheral nerve stimulator and the TetraGraph. Specifically, we will compare the visual TOF ratio obtained from the peripheral nerve stimulator and the one recorded from the Tetragraph at 5-15 minute intervals and at the time that reversal of neuromuscular blockade is required (administration of sugammadex).

- Describe:
  - Procedures performed to lessen the probability or magnitude of risks.
  - All drugs and devices used in the research and the purpose of their use, and their regulatory approval status.
  - The source records that will be used to collect data about subjects. (Attach all surveys, scripts, and data collection forms.)

There are no foreseeable risks associated with the use of Tetragraph device.

- What data will be collected during the study and how that data will be obtained.

- Patient demographics - MRN, date of birth, date of surgery, sex at birth, race, ethnicity, ASA, height, weight, gestational age
- Time of sensor placement
- Preoperative and intraoperative medications administered
- The EMG readings from the TetraGraph will be uploaded to TetraConnect, a secure server

- If there are plans for long-term follow-up (once all research related procedures are complete), what data will be collected during this period.

No plans for long-term follow-up.

- For Humanitarian Use Device (HUD) uses provide a description of the device, a summary of how you propose to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests or procedures.

Not applicable.

7.0 Study Timelines

- Describe:
  - The duration of an individual subject's participation in the study.
  - The duration anticipated to enroll all study subjects.
  - The date for the investigators to complete this study (complete primary analyses, study closure in eIRB2).

An individual study subject's participation in the study should last 2-8 hours depending on the duration of the surgical procedure.

All study subjects should be enrolled within 36 months of the start of the study.

The study data will be analyzed, a manuscript written, and the study completed within 6 months of the last subject enrollment.

8.0 Inclusion and Exclusion Criteria

- Describe how individuals will be screened for eligibility.
- Describe the criteria that define who will be included or excluded in your final study sample.
  - Please include the age range that will be used ("birth to adult" or specify age range (e.g. 2 years old to 10 years old)

Potential subjects will be identified by reviewing the surgery schedule in Epic and will be recruited from the pre-operative area the day of their surgery.

Inclusion criteria: ASA 1-4 patients ≤ 1 year of age undergoing a surgical procedure with general anesthesia and requiring the administration of an NMBA.

Exclusion criteria:

- Patients less than 28 days old
- Patients with history of a peripheral neurologic or neuropathic disorder
- Patients in whom the upper extremity cannot be used for TOF monitoring
- Patients undergoing a surgical procedure in which neuromuscular blockade is not required
- Edematous patients

- Indicate specifically whether you will include or exclude each of the following special populations: (You may not include members of the below populations as subjects in your research unless you indicate this in your inclusion criteria.)
  - Adults unable to consent
  - Individuals who are not yet adults (infants, children, teenagers)
  - Pregnant women
  - Prisoners

We will be including children but will be excluding all others as they are not part of our target population for this study.

9.0 Vulnerable Populations

If the research involves individuals who are vulnerable to coercion or undue influence:

- Check the box for the vulnerable population(s) involved.
- Review the appropriate checklist (do *not* include in submission).
- Describe additional safeguards included to protect their rights and welfare.

☐ Research involving pregnant women, reference "CHECKLIST: Pregnant Women (HRP-412)"

Not applicable.

☐ The research involves neonates of uncertain viability or non-viable neonates, review "CHECKLIST: Neonates (HRP-413)" or "CHECKLIST: Neonates of Uncertain Viability (HRP-414)" to ensure that you have provided sufficient information.

Not applicable.

☐ The research involves prisoners, review "CHECKLIST: Prisoners (HRP-415)" to ensure that you have provided sufficient information.

Not applicable.

☒ The research involves persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children"), review the "CHECKLIST: Children (HRP-416)" to ensure that you have provided sufficient information.

The research involves no greater than minimal risk to children. Permission will be obtained from one parent/guardian after thorough explanation of the study. Wards of the state or county will not be included in the research study.

☐ The research involves cognitively impaired adults, review "CHECKLIST: Cognitively Impaired Adults (HRP-417)" to ensure that you have provided sufficient information.

Not applicable.

10.0 Local Number of Subjects

- Indicate the total number of subjects to be accrued locally.
- If applicable, distinguish between the number of subjects who are expected to be enrolled and screened, and the number of subjects needed to complete the research procedures (i.e., numbers of subjects excluding screen failures.)

100 (25 in each of 4 age ranges: 28 days-3 months; 4-6 months; 7-9 months; and 10-12 months).

11.0 Withdraw of Subjects

- Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent.
- Describe any procedures for orderly termination.

- Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection.

Subjects will be withdrawn from the study if the sensors cannot be applied or there is an unexpected change in anesthetic plan (e.g. rocuronium is not being administered).

Parents may withdraw their child at any time.

There will be no further data collection or contact required following withdrawal.

12.0 Risks to Subjects

- List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research. Include as may be useful for the IRB's consideration, a description of the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, and economic risks.

Although not likely, there may be a potential risk for breach of patient health information. There is no study related physical risk to study subjects associated with this study.

- Describe what actions will be taken to minimize the risks (listed above).

Subject information will not be given to any other investigators. Subjects and their information will be closely monitored and guarded by study staff; there will be limited access to patients and their information by trained study staff; and subject information will only be shared and discussed between study staff specific to this study. Subject PHI will be stored in a locked cabinet, and will be stored and maintained in password protected computer files.

- If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable. (Include what actions will be taken to minimize the risks.)

Not applicable.

- If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant. (Include what actions will be taken to minimize the risks.)

Not applicable.

- If applicable, describe risks to others who are not subjects. (Include what actions will be taken to minimize the risks.)

Not applicable.

13.0 Potential Benefits to Subjects

- Describe the potential benefits that individual subjects may experience from taking part in the research. (Consider and include the probability, magnitude, and duration of the potential benefits).

OR

- Indicate if there is no direct benefit. Do not include benefits to society or others.

There are no specific benefits to the subjects by participating in this study.

14.0 Data Management and Confidentiality

- Describe the data analysis plan, including any statistical procedures or power analysis.

Statistical analysis and data presentation will be a descriptive analysis of the feasibility of using the device in patients of various weight ranges. Feasibility, for the purpose of using this monitor intraoperatively, will defined as the generation of appropriate EMG for monitoring with ≥ 75% of the nerve stimulations. This will depend on the ability of the device to stimulate a peripheral nerve and generate the EMG of the muscle. We will compare the TOF from the Tetragraph with that from the standard peripheral nerve stimulator.

- Describe the steps that will be taken to secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission.

All data collected during this study will be stored in secure password protected computer files and a locked cabinet to which only trained members of the research team and collaborators directly involved with this research project will have access.

- Describe any procedures that will be used for quality control of collected data.

Data will be entered into a REDCap database which will be created with built in quality control elements.

- Describe how data or specimens will be handled study-wide:
  - What information will be included in that data or associated with the specimens?
  - Where and how data or specimens will be stored?
  - How long the data or specimens will be stored? (Must be kept for a minimum of 6 years, once deidentified may be kept longer if specified)
  - Who will have access to the data or specimens?
  - Who is responsible for receipt or transmission of the data or specimens?
  - How data or specimens will be transported?

All data collected during this study will be stored in a secure password protected computer files and a locked cabinet to which only trained members of the research team and collaborators directly involved with this research project will have access.

15.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

*****This section is required when research involves more than Minimal Risk to subjects.***

- Describe:
  - The plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe. The plan might include establishing a data monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor.

- What data are reviewed, including safety data, untoward events, and efficacy data
- How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).
- The frequency of data collection, including when safety data collection starts.
- Those responsible to review the data.
- The frequency or periodicity of review of cumulative data.
- The statistical tests for analyzing the safety data to determine whether harm is occurring.
- Any conditions that trigger an immediate suspension of the research.

Since this is a minimal risk study, it will only be monitored by the study investigators.

16.0 Provisions to Protect the Privacy Interests of Subjects

- Describe the steps that will be taken to protect subjects' privacy interests. "Privacy interest" refers to a person's desire to place limits on whom they interact or whom they provide personal information.
- Describe what steps you will take to make the subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject might experience in response to questions, examinations, and procedures.
- Indicate how the research team is permitted to access any sources of information about the subjects.

Subject information will not be given to any other investigators. Subjects and their information will be closely monitored and guarded by study staff; there will be limited access to patients and their information by trained study staff; and subject information will only be shared and discussed between study staff specific to this study.

17.0 Data and Specimen Banking

Data and/or Tissue "banking" refers to data and/or tissue that will be stored in large databanks or tissue banks for future research. This does not refer to storage of data during a specific ongoing study that is not going to be shared with a large data bank. Data for one study is stored by the investigator in a secure manner can be described in the Data Management section in the protocol.

- If data or specimens will be banked for future use (*not* for use with this study only), describe where the data and/or specimens will be stored, how long they will be stored, how the data and/or specimens will be accessed, and who will have access to the data and/or specimens.
- List the data to be stored or associated with each specimen.
- Describe the procedures to release data or specimens, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

There will be no data or specimens banked for future use.

18.0 Sharing of Results with Subjects

- Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject's primary care physicians) and if so, describe how the results will be shared.

Study results will not be shared with subjects or others. Results will be uploaded to ClinicalTrials.gov at the completion of the study.

19.0 Recruitment Methods

- Describe when, where, and how potential subjects will be recruited.
- Describe the source of subjects.
- Describe the study team member's relationship to the potential participant.
- Describe the methods that will be used to identify potential subjects.
- Describe materials that will be used to recruit subjects. (Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)

Potential subjects will be recruited in the surgical preoperative area on the day of surgery. The research team will explain the study to the parents/guardians and obtain written permission.

The patients to be recruited are those who are scheduled for surgery under general anesthesia in the NCH operating rooms and will be identified using EPIC.

20.0 Process to Document Consent in Writing

- Describe whether you will be following "SOP: Written Documentation of Consent (HRP-091)." If not, describe whether and how consent of the subject will be documented in writing.

***If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent.*

***If you will document consent in writing, attach a consent document. If you will obtain consent, but not document consent in writing, attach a consent script. Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information. You may use "TEMPLATE CONSENT DOCUMENT (HRP-502)"to create the consent document or script.*

We will be following "SOP: Written Documentation of Consent (HRP-091).

21.0 Consent Process

- Indicate whether you will be obtaining consent, and if so describe:
  - Where will the consent process take place.
  - Any waiting period available between informing the prospective subject and obtaining the consent
  - Any process to ensure ongoing consent.
  - Whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." If not, describe:
    - The role of the individuals listed in the application as being involved in the consent process.
    - The time that will be devoted to the consent discussion.
    - Steps that will be taken to minimize the possibility of coercion or undue influence.
    - Steps that will be taken to ensure the subjects' understanding.

Consent will take place in the surgery pre-op area on the day of surgery. We will be following SOP: Informed Consent Process for Research (HRP-090).

Considerations for Consent Process

☐ ***Waiver or Alteration Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)***

- Provide a justification for the waiver or alteration in the response box below.
- Review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure you have provided sufficient information for the IRB to make these determinations.
- If the research involves a waiver the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations.

There will be no waiver or alteration of the consent process.

☐ ***Waiver of Written Documentation of Consent (verbal, virtual, and/or eConsent without signature)***

- Review the "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure you have provided sufficient information for the IRB to make these determinations.

There will be no waiver of written documentation of consent.

Non-English Speaking Subjects- (if not known, skip)

- Indicate what language(s) other than English are understood by prospective subjects or representatives.
- If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language. Indicate the language that will be used by those obtaining consent.

It is not known what other languages will be understood by prospective subjects.

Subjects who are not yet adults (infants, children, teenagers)

- Describe the criteria that will be used to determine whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted. (E.g., individuals under the age of 18 years.)

All of the potential subjects for this study will be under the age of legal consent. Parental permission will only be obtained from one parent.

○ For research, conducted in the state, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children." ○ For research, conducted outside of the state, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)." • Describe whether parental permission will be obtained from: ○ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. ○ One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child. • Describe whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. Describe the process used to determine these individuals' authority to consent to each child's general medical care. • Indicate whether assent will be obtained from all, some, or none of the children. If assent will be obtained from some children, indicate which children will be required to assent. • When assent of children is obtained describe whether and how it will be documented.	
Cognitively Impaired Adults • Describe the process to determine whether an individual is capable of consent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely	Cognitively impaired adults will not be enrolled.

require cognitively impaired adults to sign assent documents.	
Adults Unable to Consent • List the individuals from whom permission will be obtained in order of priority. (E.g., durable power of attorney for health care, court appointed guardian for health care decisions, spouse, and adult child.). o For research conducted in the state, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "legally authorized representative." o For research conducted outside of the state, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)." • Describe the process for assent of the subjects. Indicate whether: o Assent will be required of all, some, or none of the subjects. If some, indicate which subjects will be required to assent and which will not. o If assent will not be obtained from some or all subjects, an explanation of why not. o Describe whether assent of the subjects will be documented and the process to document assent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require subjects to sign assent documents.	Adults unable to consent will not be enrolled.
Consent for HUD • For HUD uses provide a description of how the patient will be informed of the potential risks	HUD will not be used in this study.

and benefits of the HUD and any procedures associated with its use.	

22.0 Compensation for Research-Related Injury

- If the research involves more than Minimal Risk to subjects, describe the available compensation in the event of research related injury.
- *Provide a copy of contract language, if any, relevant to compensation for research-related injury.*

This is a minimal risk study.

23.0 Compensation to Subjects

- Describe the amount and timing of any payments to subjects.

Subjects will not be paid for participation in this study.

24.0 Economic Burden to Subjects

- Describe any costs that subjects may be responsible for because of participation in the research, e.g., fuel, parking, childcare.

There will be no costs to participants in this study.

25.0 Setting

- Describe the local sites or locations where your research team will conduct the research.
  - Identify where your research team will identify and recruit potential subjects.
  - Identify where research procedures will be performed.
  - Describe the composition and involvement of any community advisory board.
  - For research conducted outside of the organization and its affiliates describe:
  - Site- specific regulations or customs affecting the research for research outside the organization.
  - Local scientific and ethical review structure outside the organization.

Potential subjects will be identified from the OR schedule in EPIC and recruited from the Surgery Unit on the day of surgery. All research procedures will be performed in the OR.

26.0 Resources Available

- Describe the resources available to conduct the research. For example, as appropriate:
  - Justify the feasibility of recruiting the required number of suitable subjects within the agreed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?
  - Describe the time that you will devote to conducting and completing the research.
  - Describe your facilities.
  - Describe the availability of medical or psychological resources that subjects might need as a result of an anticipated consequences of the human research.
  - Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

We will need approximately 20 minutes per patient to explain the research protocol, obtain consent, and enroll patients. The Department of Anesthesiology & Pain Medicine has 2 research coordinators and 4 research associates who will be enrolling subjects for this study. All study staff will be trained regarding the study procedures. Before the study starts, the involved personnel will be informed by e-mail and during a pre-study meeting about the study protocol, the research procedures, research member's duties, and functions.

27.0 Confidentiality of Data Collection

- How long will identifying information on each participant be maintained? (Study data and identifiers must be stored for at least six years after study closure; a longer period may be used. A specific date or number of years must be listed.)

Following completion of study, research records will be stored for a period of 6 years and then will be destroyed by placing in a secure shredding bin and deleted from REDCap.

- Describe any plans to code identifiable information collected about each participant.

There are no plans to code identifiable information collected about each participant.

- Check each box that describes steps that will be taken to safeguard the confidentiality of information collected for this research:
  - ☒ Research records will be stored in a locked cabinet in a secure location
  - ☒ Research records will be stored in a password-protected computer file
  - ☐ The list linking the assigned code number to the individual subject will be maintained separately from the other research data
  - ☒ Only certified research personnel will be given access to identifiable subject information.

- Describe the provisions included in the protocol to protect the privacy interests of subjects, where "privacy interests" refer to the interest of individuals in being left alone, limiting access to them, and limiting access to their information. (This is not the same provision to maintain the confidentiality of data.)

Subject information will not be given to any other investigators. Subjects and their information will be closely monitored and guarded by study staff; there will be limited access to patients and their information by trained study staff; and subject information will only be shared and discussed between study staff specific to this study.

- Will it be necessary to record information of a sensitive nature?
  "Sensitive information includes but is not limited to 'information relating to sexual attitudes, preferences, or practices; information relating to the use of alcohol, drugs, or other addictive products; information pertaining to illegal conduct; information that, if released, might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information or tissue samples.'"

  ☐ Yes ☒ No

- Do you plan to obtain a federally-issued Certificate of Confidentiality as a means of protecting the confidentiality of the information collected? (If the study is NIH funded, Certificate of Confidentiality will be issued; please mark "Yes").

  "Certificate of Confidentiality (Certificate) protects the privacy of research participants enrolled in biomedical, behavioral, clinical, or other types of health-related research that collect or use identifiable, sensitive information. With limited exceptions, researchers may not disclose names or any information, documents or biospecimens containing identifiable, sensitive information. The Certificate prohibits disclosure in response to legal demands, such as a subpoena."

  ☐ Yes ☒ No

28.0 Protected Health Information (PHI) Recording

PHI: individually identifiable health information transmitted or maintained in any form (electronic means, on paper, or through oral communication) that relates to the past, present or future physical or mental health or conditions of an individual plus any of the following 18 identifiers.

Are you accessing or recording information related to the provision of healthcare or payment for healthcare services (medical records, lab test results, diagnoses, etc.)?
Consider sources such as the medical record, clinic schedules, billing statements, etc. This includes screening for potential subjects for recruitment purposes.

☒ If yes, complete section 28.0.
☐ If no, skip section 28.0.

Indicate which subject identifiers will be ACCESSED for this research.

☒ Name	☐ Account Numbers
☐ Address *(including street, city, state, zip code and county)*	☐ Certificate/License Numbers
☒ Dates *(treatment dates, birth date, date of death)*	☐ Vehicle Identifiers and Serial Numbers
☐ Telephone	☐ Device Identifiers and Serial Numbers
☐ Fax Number	☐ URL
☐ Email address,	☐ IP address
☐ Social Security Number *(do not check if only used for ClinCard)*	☐ Biometric identifiers, including finger and voice prints
☒ Medical Record Number or other account number (specify below)	☐ Full face photographic images and/or any comparable images
☐ Health Plan Beneficiary Identification Number	☐ Other number, characteristic or code that could be used to identify an individual (specify below)
	☐ None *(Complete De-identification Certification Form)*

If the "Medical Record Number or other account number" and/or "Other number, characteristic or code that could be used to identify an individual" identifiers are selected, please respond below.

The Medical Record Number is required to locate the potential subject's health records to assess for inclusion/exclusion criteria.

Indicate which subject identifiers will be RECORDED for this research.

☒ Name	☐ Account Numbers
☐ Address *(including street, city, state, zip code and county)*	☐ Certificate/License Numbers
☒ Dates *(treatment dates, birth date, date of death)*	☐ Vehicle Identifiers and Serial Numbers
☐ Telephone	☐ Device Identifiers and Serial Numbers
☐ Fax Number	☐ URL
☐ Email address,	☐ IP address
☐ Social Security Number *(do not check if only used for ClinCard)*	☐ Biometric identifiers, including finger and voice prints
☒ Medical Record Number or other account number (specify below)	☐ Full face photographic images and/or any comparable images
☐ Health Plan Beneficiary Identification Number	☐ Other number, characteristic or code that could be used to identify an individual (specify below)
	☐ None *(Complete De-identification Certification Form)*

If the "Medical Record Number or other account number" and/or "Other number, characteristic or code that could be used to identify an individual" identifiers are selected, please respond below.

The Medical Record Number will need to be recorded so that study data can be collected from the medical record following enrollment.

29.0 Confidential Health Information Recording

Please mark all categories that reflect the nature of health information to be ACCESSED and USED as part of this research.

☒ Demographics *(age, gender, educational level)*	☒ Names of drugs and/or devices used as part of treatment
☐ Diagnosis	☐ Location of treatment
☐ Laboratory reports	☐ Name of treatment provider
☐ Radiology reports	☐ Surgical reports
☐ Discharge summaries	☒ Other information related to course of treatment
☒ Procedures/Treatments received	☐ None
☐ Billing information	

If the information you are collecting does not match any of the options listed above, please list what information you will be gathering.

Not applicable.

30.0 Waiver or Alteration of HIPAA Research Authorization

1. **Check the appropriate category and attach the required form on the Local Site Documents, #3. Other Documents, page of the application. (Mark all that apply.)**

   ☒ Protocol meets the criteria for waiver of authorization. (Continue filling out section 30.)
   ☒ Patient Authorization will be obtained. (Include the appropriate HIPAA language (see the "How Will My Study Information Be Kept Private?" section of the consent template or information sheet template) in the consent form OR attach the HRP-900, HIPAA AUTHORIZATION form.)
   ☐ Protocol is using de-identified information. (Attach the HRP-902, DE-IDENTIFICATION CERTIFICATION form.)
   ☐ Protocol involves research on decedents. (Attach the HRP-903, RESEARCH ON DECEDENTS REQUEST form.)
   ☐ Protocol is using a limited data set and data use agreement. (Contact the Office of Technology Commercialization to initiate a Limited Data Use Agreement.)

Find the HIPAA forms in the eIRB2 Website Library, Templates.

2. Please indicate the type of waiver or alteration needed for this study.
   Note: If the research involves more than one type of waiver, check the appropriate box.

   ☒ A. Partial Waiver (to access PHI for recruitment purposes only)
   ☐ B. Full Waiver (entire research study)
   ☐ C. Alteration (waiver of written documentation of authorization; obtaining verbal authorization to use PHI)

3. Please discuss why it is necessary to access and review the health information noted in your response above.

A partial waiver is required so that we can screen for inclusion/exclusion criteria prior to recruitment.

4. Is the health information to be accessed and reviewed the minimal necessary to achieve the goals of this research? Please provide an explanation, as well.

☒ Yes ☐ No
We will only be looking at information related to the inclusion/exclusion criteria.

5. Explain how the access, use, or disclosure of PHI presents no more than a minimal risk to the privacy of the individual.

Only certified research personnel will be given access to identifiable subject information.

6. Describe your plan to protect the identifiers (or links to identifiable data) associated with the PHI from improper use and disclosure, including where PHI will be stored, what security measures will be applied, and who will have access to the information. Describe the safeguards for electronic and/or hard copy records.

All PHI will be stored in a locked cabinet, and a password protected computer file in the Dept. of Anesthesiology and only the department investigators and study coordinators will have access to the cabinets and computer system. The PHI may also be accessed by the IRB or the Research Compliance Office (RCO) upon request and both the entities are NCH trusted bodies governing research investigations.

7. Will identifiers (or links to identifiable data) be destroyed? Provide a justification for your answer.

☒ Yes – Describe the plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research. Include **when** (consistent with section 27) and **how** identifiers will be destroyed.

☐ No – Provide the legal, health, or research justification for retaining the identifiers. Legal justification should include a brief description/citation of the legal requirement.

☐ N/A – Will not record identifiers or create links or codes to connect the data.

Following completion of study, research records will be stored for a period of 6 years and then will be destroyed by placing in a secure shredding bin and deleted from REDCap.

8. Explain why a waiver/alteration (instead of written authorization) is needed to conduct the research.

We require the partial waiver to be able to review the surgery schedule for potential subjects.

NOTE: Only those personnel listed on the IRB-approved application may access PHI and medical information.

Reminder: Protected Health Information obtained as part of this research will not be reused or disclosed to any other person or entity other than those listed (except as required by law for authorized oversight of the research project) without additional approval. IRB/Privacy Board approval must be obtained for other research involving the use or disclosure of this PHI.

31.0 Multi-Site Research

****This section is required when research will be conducted at multiple sites. Check the appropriate box.***

☒ NCH **IS** participating in multi-site research.

☐ NCH **IS NOT** participating in multi-site research. No further information is needed in this section.

- TOTAL Number of Subjects to be Enrolled Study-Wide
- List the locations of the additional sites. Please indicate which sites are International.

100
OU will be a relying site solely for the purpose of adding their medical student as study staff for the summer. No subjects will be enrolled at OU.

- Study-Wide Recruitment Methods

** If this is a multicenter study and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods here. Local recruitment methods are described earlier in the protocol (Section 19.0).

- Describe when, where, and how potential subjects will be recruited.
- Describe the methods that will be used to identify potential subjects.
- Describe the materials that will be used to recruit subjects. (Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)

Subjects will only be recruited and enrolled at NCH.

- Multi-Site Data Management
  - Check all applicable boxes below.
    - ☐ NCH will SEND data to other sites
    - ☐ NCH will RECEIVE data from other sites

  - Describe the procedures for maintenance or confidentiality of data at non-NCH sites.
    - Where and how data or specimens will be stored?
    - How long the data or specimens will be stored?
    - Who will have access to the data or specimens?
    - Who is responsible for receipt or transmission of the data of specimens?
    - How data specimens will be transported?

No data will be exchanged with OU. All data will be maintained at NCH.

☒ NCH investigator **IS** the LEAD investigator in the study.
☐ NCH **IS NOT** the LEAD investigator in the study. No further information needed in this section.

- Review "WORKSHEET: Communication and Responsibilities (HRP-830)"
- Describe the processes for communication among sites to conduct the study in accordance with applicable federal regulations and local laws.
- Describe the method for reporting the following:
  - Problems (inclusive of reportable events)
  - Non-compliance with the study protocol of applicable requirements
  - Interim results
  - The closure of the study

.

OU will be notified in writing when the study closes.