Accuracy of the NICCI™ monitor in providing beat-to-beat non-invasive blood pressure readings in children and adolescents

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PROTOCOL TITLE: Accuracy of the NICCI™ monitor in providing beat-to-beat non-invasive blood pressure readings in children and adolescents

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REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?

1.0 Study Summary

Study Title	Accuracy of the NICCI™ monitor in providing beat-to-beat non-invasive blood pressure readings in children and adolescents
Study Design	Prospective, non-blinded comparative study
Primary Objective	The primary objective of this study is to compare the blood pressure reading (systolic, diastolic, and mean) from an arterial cannula with the readings obtained from the non-invasive continuous blood pressure monitoring, NICCI™
Secondary Objective(s)	None
Research Intervention(s)/ Investigational Agent(s)	Measuring beat-to-beat blood pressure non-invasively with the NICCI™ monitor. There will be no change in anesthetic management or use of investigational pharmacological agents.
IND/IDE #	Not applicable
Study population	Patients who are scheduled for elective, urgent or emergent surgery
Sample size	150 (50 in each of 3 weight groups 10-20 kg, 20-40, and ≥ 40 kg)
Study duration for individual participants	Duration of the surgical procedure (2-10 hours)
Study Specific Abbreviations/ Definitions	BP = blood pressure sBP = systolic blood pressure dBP = diastolic blood pressure MAP = mean arterial pressure NIBP = non-invasive blood pressure IBP = intra-arterial blood pressure

2.0 Objectives

2.1 The primary objective of this study is to compare blood pressure (BP) readings obtained from an invasive arterial cannula and a non-invasive continuous BP device. The hypothesis is that this novel non-invasive device will provide an accurate and continuous estimation of BP.

3.0 Background

3.1 BP is one of the most important parameters in several clinical settings. Particularly during the perioperative period, BP needs to be monitored repeatedly or even continuously to facilitate the best care for patients. This is done either intermittently using an oscillometric non-invasive blood pressure device (NIBP) or continuously by an invasive arterial line (IBP). A number of clinical studies show that both methods may have pitfalls and at times be inaccurate. Since the NIBP provides discontinuous pressure readings with the current recommendations for intraoperative monitoring stating that the BP should be monitored every 5 minutes, hemodynamic events may be missed or there may be a delay in recognition of alterations in BP. Therefore, during major intraoperative procedures in patients with co-morbid cardiac diseases or during procedures with significant blood loss, invasive arterial monitoring of BP is chosen with placement of an intra-arterial cannula. Although generally safe and effective, the placement of an intra-arterial cannula may be

associated with complications including artery occlusion with distal ischemia, hematoma formation, blood loss due to unintended disconnection, infection or nerve damage with sensory disturbance. More importantly, arterial cannulation takes time and may at times be impossible. Therefore, a method that non-invasively allows the continuous measurement of BP would be clinically useful.

3.2 The NICCI, Pulsion/GETINGE uses novel technology to provide a continuous estimation of BP displayed as a waveform similar to that seen with an invasive arterial cannula (information attached). Infrared (IR) light, emitted from a Light Emitting Diode, is sent through the finger. The light is partly absorbed by the arterial blood, which is changing according to the heart activity (pulse). A light detector receives the remaining light on the other side of the finger and thus detects the continuous pulse signal. Counter pressure is exerted from the outside in such a way that the arterial wall is totally unloaded. This continuously changing outside pressure keeps the arterial blood volume constant at all times and directly corresponds to the arterial pressure. The intra-arterial pressure is therefore measured indirectly. To calibrate the continuous pulse-contour curve with the correct absolute blood pressure values, an automatic non-invasive blood pressure (NIBP) measurement is either performed on the patient's upper arm or provided by the user. This device is based on technology original developed as the CNAP™ monitor which has been tested and validated by us previously in other IRB-approved trials.

21 Dewhirst E, Corridore M, Klamar J, Beebe A, Rice J, Barry S, Tobias JD. Accuracy of the CNAP™ monitor, a noninvasive continuous blood pressure device, in providing beat-to-beat blood pressure readings in the prone position. J Clin Anesth 2013;25:309-313.

22 Kako H, Corridore M, Rice J, Tobias JD. Accuracy of the CNAP™ monitor, a non-invasive continuous blood pressure device, in providing beat-to-beat blood pressure readings in pediatric patients weighing 20 to 40 kilograms. Pediatric Anesth 2013;23:989-993.

23 Tobias JD, McKee, Herz D, Teich S, Sohner P, Rice J, Barry N, Michalsky M. Accuracy of the CNAP™ monitor, a non-invasive continuous blood pressure device, in providing beat-to-beat blood pressure measurements during bariatric surgery in severely obese adolescents and young adults. J Anesth 2014;28:861-865.

4.0 Study Endpoints

4.1 The primary study endpoint is to compare the BP readings from the non-invasive NICCI device with those obtained from an arterial cannula.

5.0 Study Intervention/Investigational Agent

5.1 The only novel intervention is the use of the NICCI device to monitor blood pressure. No change in the anesthetic technique will be required during the study. The study will include only patients scheduled for a surgical procedure that requires invasive monitoring of arterial blood pressure (placement of an arterial cannula).

6.0 Procedures Involved*

6.1 This is a prospective study that will compare the blood pressure readings from an arterial cannula with those obtained non-invasively by the NICCI device. The study will enroll 50 patients into each of three weight ranges: 10-20 kg, 20-40 kg, and 40-80 kg.

6.2 The study cohort will include patients requiring anesthetic care and in whom an indwelling arterial cannula will be placed for the surgical procedure. The arterial cannula will not be placed for the purpose of the study. The NICCI™ monitor will be attached to the patient and simultaneous readings from the NICCI™ monitor and the invasive arterial cannula will be downloaded every minute into a laptop computer for later analysis.

6.3 Exclusion criteria:

- Patients with history of a peripheral neurologic or neuropathic disorder
- Patients in whom the upper extremity cannot be used for blood pressure monitoring
- Patients in whom an invasive arterial cannula cannot be placed
- Patients with vascular implants at the sites of non-invasive blood pressure measurement (fingers and upper arm of the examined arm)
- Edematous patients

6.4 There are no foreseeable risks associated with the use of NICCI™ device.

6.5 The data (BP readings) will be downloaded into a bedside NCH laptop in the operating room and stored on our password-secured server.

7.0 Data and Specimen Banking*

N/A

8.0 Sharing of Results with Subjects*

8.1 Results will not be shared with subjects.

9.0 Study Timelines*

9.1 An individual study subject's participation in the study should last 2-10 hours depending on the duration of the surgical procedure.

9.2 All study subjects should be enrolled within 1 year of the start of the study.

9.3 The study data will be analyzed, a manuscript written, and the study completed within 18 months of the start of the study.

10.0 Inclusion and Exclusion Criteria*

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

10.2 Inclusion criteria: ASA 1-4 patients, weighing 10 to 80 kg undergoing a surgical procedure with general anesthesia and requiring an invasive arterial cannula.

10.3 Exclusion criteria:

- Patients with history of a peripheral neurologic or neuropathic disorder
- Patients in whom the upper extremity cannot be used for blood pressure monitoring
- Patients in whom an invasive arterial cannula cannot be placed
- Patients with vascular implants at the sites of non-invasive blood pressure measurement (fingers and upper arm of the examined arm)
- Edematous patients

11.0 Vulnerable Populations*

11.1 We will include children, and will not include adults, pregnant woman, and prisoners as they are not part of our usual patient population.

12.0 Local Number of Subjects

12.1 150 (50 in each weight range of routine, urgent, and emergent cases).

13.0 Recruitment Methods

13.1 Potential subjects will be recruited in the surgical preoperative area on the day of the surgery. The research team will contact the guardian/parents and obtain consent. Assent will also be obtained from age appropriate patients.

13.2 The patients to be recruited are those who are scheduled for surgery under general anesthesia in the NCH operating rooms.

13.3 Using Epic, the research team will check the patients scheduled for planned surgery in the NCH operating rooms.

14.0 Withdrawal of Subjects*

Patients may withdraw from the study at any time.

15.0 Risks to Subjects*

15.1 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. All study related procedures are non-invasive.

15.2 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.

16.0 Potential Benefits to Subjects*

16.1 There are no specific immediate benefits to the patient.

17.0 Data Management* and Confidentiality

17.1 Statistical analysis and data presentation will include a calculation of the absolute difference of the sBP, dBP and MAP values of the two devices. To avoid biasing the data, the absolute not directional difference will be used. For example, if the reading from NICCI™ device was 10 mmHg above or below the reading from the AL, a value of 10 mmHg was used, not -10 or +10 mmHg. Additionally, a determination will be made of the percentage of values from the NICCI™ device that are ≤ 5 mmHg and more than 10 mmHg from the IBP values. A Pearson correlation coefficient will be calculated comparing the sBP, dBP and MAP values between the arterial cannula and the NICCI™ device. A Bland-Altman analysis with multiple measurements per subject will be performed to determine the bias and 95% level of agreement for the three groups.

17.2 De-identified data will be shared with the manufacturer of the monitor, Getinge. They will be assisting with data analysis, as well as, using the data for a 510(K) submission to the FDA.

17.3 Research records will be stored in a locked cabinet and password protected computer. Only certified research personnel will be given access to identifiable subject information

17.4 Following publication of study results, research records will be stored for a period of 5 years and then will be destroyed by placing in a secure shredding bin.

18.0 Provisions to Monitor the Data to Ensure the Safety of Subjects*

The study will only be monitored by the study investigators.

19.0 Provisions to Protect the Privacy Interests of Subjects

19.1 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.

20.0 Compensation for Research-Related Injury

Not applicable

21.0 Economic Burden to Subjects

None

22.0 Consent Process

22.1 The consent process will begin in the preoperative surgery unit on the day of surgery, by PI, Sub-Investigators, Study Coordinators, and/or trained research staff.

22.2 The study will be thoroughly explained to the patient and their family. There will be ample time allotted for questions and answers. An explanation of voluntary participation will take place, and the family will be asked if they are interested in participating in the study. If the patient and their parent(s), or legal guardian agrees to participate they will be asked to sign consent and assent form. The patient will then be enrolled in the study with the understanding that they can elect to stop the study and be withdrawn from the study at any time.

23.0 Process to Document Consent in Writing

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

24.0 Setting

Research procedures will be performed in the operating room during anesthetic care.

25.0 Resources Available

25.1 We will need approximately 30 minutes per patient to explain the research protocol, obtain consent, and enroll patients. The Department of Anesthesiology and Pain Medicine has 2 research coordinators/RNs and 2 research associates that will be enrolling subjects for this study. All study staff will be trained regarding the study procedures. Before the study starts, the study protocol, the

research procedures, research member's duties, and functions will be informed by e-mail and during a pre-study meeting.

26.0 Multi-Site Research*

Not applicable

27.0 Protected Health Information Recording

1.0 Indicate which subject identifiers will be recorded for this research.

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

2.0 Check the appropriate category and attach the required form* on the Local Site Documents, #3. Other Documents, page of the application. (Choose one.)

☒ Patient Authorization will be obtained. (Include the appropriate HIPAA language (see Section 14 of consent template) in the consent form OR attach the HRP-900, HIPAA AUTHORIZATION form.)
☐ Protocol meets the criteria for waiver of authorization. (Attach the HRP-901, WAIVER OF HIPAA AUTHORIZATION REQUEST form.)
☐ Protocol is using de-identified information. (Attach the HRP-902, DE-IDENTIFICATION CERTIFICATION form.) (Checked "None" in 1.0 above)
☐ 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 IRB Website Library, Templates.**

Attach the appropriate HIPAA form on the "Local Site Documents, #3. Other Documents", page of the application.

3.0 How long will identifying information on each participant be maintained?
Following publication of study results, research records will be stored for a period of 5 years and then will be destroyed by placing in a secure shredding bin.

4.0 Describe any plans to code identifiable information collected about each participant.
Not applicable.

5.0 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**

6.0 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. 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.

Confidential Health Information

1.0 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)

☒ Diagnosis

☐ Laboratory reports

☐ Radiology reports

☐ Discharge summaries

☒ Procedures/Treatments received

☒ Dates related to course of treatment (admission, surgery, discharge)

☐ Billing information

☐ Names of drugs and/or devices used as part of treatment

☐ Location of treatment
☐ Name of treatment provider
☐ Surgical reports
☒ Other information related to course of treatment
☐ None

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

Demographics need to be recorded to describe the patient characteristics of the study cohort for publication of these data in scientific journals. Diagnosis and procedures need to be assessed for inclusion criteria.

3.0 Is the health information to be accessed and reviewed the minimal necessary to achieve the goals of this research? ☒ Yes ☐ No

4.0 Will it be necessary to record information of a sensitive nature? ☐ Yes ☒ No

5.0 Do you plan to obtain a federally-issued Certificate of Confidentiality as a means of protecting the confidentiality of the information collected? ☐ Yes ☒ No