Transesophageal echocardiography (TEE) to guide and confirm epidural catheters in pediatric patients

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Form Content

I. Project Introduction

I.1 ***Project to be reviewed by:***
IRB-01

I.2 ***Project Title:***
Transesophageal echocardiography (TEE) to guide and confirm epidural catheters in pediatric patients

I.3 ***Short Title (optional):***

I.4 ***Provide a short summary of the purpose and procedures of the study proposed in this IRB application.***
DO NOT include information on studies not proposed in this application.
Use LAY terminology only. This must be easily understandable by IRB community members and nonscientists.
DO NOT cut and paste technical abstracts from funding applications that may not be understood by a general audience.
The aim of this study is to assess whether transesophageal echocardiography (TEE) can be used to successfully guide an epidural catheter to a targeted thoracic level in pediatric patients. The catheter will be placed in the epidural space under real-time TEE imaging and assistance by a trained TEE operator (this could include an anesthesiologist or cardiologist).

I.5 ***Specify your research question(s), study aims or hypotheses (do not indicate "see protocol")***
The primary outcome is to determine the success rate achieved using TEE guidance to thread an epidural catheter to a targeted thoracic spinal level. Post-operative radiograph will be used to confirm catheter position.
The secondary outcomes include analysis of catheter tip position within the epidural space as anterior, lateral or inferior to the spinal cord. Further, efficacy of the catheter will be determined using the following criteria from previous studies [1]: Hemodynamic response at skin incision analyzed by heart rate and systemic blood pressure changes using the no change in HR or BP or changes < 20% from baseline were considered “sufficient block” to surgical stimulation, while HR or BP changes > 20% from baseline were considered “not sufficient block” to surgical stimulation.

I.6 ***Background and significance and/or Preliminary studies related to this project. (do not indicate "see protocol")***
Epidural block has been utilized extensively in pediatric patients [2], however, blind advancement of epidural catheters to the thoracic space can be technically

challenging. In pediatric patients, thoracic catheter threading exhibits failure rates as high as 32% [3] and 48% [4] from caudal levels and 85% [5] from lumbar levels due to catheter curling and arrest [3].
The inability to verify catheter tip placement at the targeted vertebral level could lead to an inappropriately high spinal level of catheter placement and this is especially critical in upper thoracic epidural catheterization [6].
To overcome these issues, a number of confirmatory techniques have been described including radiological fluoroscopy, epidural electrocardiography (ECG) [7], electrical stimulation [8], and surface ultrasound sonography (US) [9] [1]. Problematically, these methods may require unnecessary exposure to ionizing radiation and contrast [10] or exhibit limitations in confirming exact catheter tip placement [7] [11].

We suggest the use of TEE as a minimally invasive, real-time imaging technique for verification of thoracic epidural catheters threaded blindly. Given the nearly universal use of TEE in cardiac surgical operating rooms as well as its low risk of complications [12] potential outcomes of this study include the use of TEE in placing epidural catheters and visualizing injected drug distribution. Ultimately, TEE as a confirmatory tool could improve the precision, success and safety of regional anesthesia in children.

I.7 ***Literature cited / references (if attaching a grant or protocol enter N/A).***

1. Willschke H, Marhofer P, Bosenberg A, Johnston S, Wanzel O, Sitzwohl C, Kettner S, Kapral S: Epidural catheter placement in children: comparing a novel approach using ultrasound guidance and a standard loss-of-resistance technique. British journal of anaesthesia 2006, 97(2):200-207.
2. Hassan SZ: Caudal anesthesia in infants. Anesthesia and analgesia 1977, 56(5):686-689.
3. Valairucha S, Seefelder C, Houck CS: Thoracic epidural catheters placed by the caudal route in infants: the importance of radiographic confirmation. Paediatric anaesthesia 2002, 12(5):424-428.
4. Blanco D, Llamazares J, Rincon R, Ortiz M, Vidal F: Thoracic epidural anesthesia via the lumbar approach in infants and children. Anesthesiology 1996, 84(6):1312-1316.
5. Baidya DK, Pawar DK, Dehran M, Gupta AK: Advancement of epidural catheter from lumbar to thoracic space in children: Comparison between 18G and 23G catheters. Journal of anaesthesiology, clinical pharmacology 2012, 28(1):21-27.
6. Chawathe MS, Jones RM, Gildersleve CD, Harrison SK, Morris SJ, Eickmann C: Detection of epidural catheters with ultrasound in children. Paediatric anaesthesia 2003, 13(8):681-684.
7. Tsui BC, Seal R, Koller J: Thoracic epidural catheter placement via the caudal approach in infants by using electrocardiographic guidance. Anesthesia and analgesia 2002, 95(2):326-330, table of contents.
8. Tsui BC, Tarkkila P, Gupta S, Kearney R: Confirmation of caudal needle

placement using nerve stimulation. Anesthesiology 1999, 91(2):374-378.
9. Rapp HJ, Folger A, Grau T: Ultrasound-guided epidural catheter insertion in children. Anesthesia and analgesia 2005, 101(2):333-339, table of contents.
10. Tsui BC, Berde CB: Caudal analgesia and anesthesia techniques in children. Current opinion in anaesthesiology 2005, 18(3):283-288.
11. Roberts SA, Galvez I: Ultrasound assessment of caudal catheter position in infants. Paediatric anaesthesia 2005, 15(5):429-432.
12. Owall A, Stahl L, Settergren G: Incidence of sore throat and patient complaints after intraoperative transesophageal echocardiography during cardiac surgery. Journal of cardiothoracic and vascular anesthesia 1992, 6(1):15-16.

II. Research Team

II.1 ***Principal Investigator***

Name	E-mail	College
Kenichi Ueda	kenichi-ueda@uiowa.edu	Carver College of Medicine

UI Team Members

Name	E-mail	Contact	Key Prsn	Consent Process Involvement	Deactivated	
Kenichi Ueda, MD	kenichi-ueda@uiowa.edu	Yes	Yes	No	Yes	No

Nothing found to display.

II.3 ***The Principal Investigator of this study is:***
Faculty

III. Funding/Other Support

III.1 ***Funding Sources***

Type
Departmental / PI Discretionary

III.3 ***Does any member of the research team have a financial conflict of interest related to this project according to the Conflict of Interest in Research policy? If yes, please indicate which members below.***

Name	Has Conflict of Interest
Kenichi Ueda, MD	No

IV. Project Type

IV.1 ***Do you want the IRB to give this project***
Regular (expedited or full board) review

IV.2 ***Enter the date you will be ready to begin screening subjects/collecting data for this project. (If you do not have a specified date, add "upon IRB approval")***

IV.3 ***Are you requesting a waiver of informed consent/authorization (subjects will not be given any oral or written information about the study)?***
No

V. Other Committee Review

V.1 ***Does this project involve any substance ingested, injected, or applied to the body?***
Do not answer yes, if the involvement includes a device, wire, or instrument
No

V.2 ***Are any contrast agents used for any purpose in this study?***
No

V.9 ***Will any subject be asked to undergo a diagnostic radiation procedure (including radiographic, nuclear medicine, DEXA)?***
Yes

V.10 ***Are all diagnostic radiation procedures routine, standard, clinical procedures?***
Yes

V.11 ***Will all subjects who receive the diagnostic radiation procedure(s) require the exact same procedure for clinical purposes?***
Yes

V.12 ***For all subjects, would the clinical diagnostic radiation procedure(s) always be required as frequently as is required for the research project?***
Yes

V.13 ***For all subjects, would the clinical diagnostic radiation procedure(s) always be required at the same timepoints as is required for the research project?***
Yes

V.14 ***Will any subject be asked to undergo a radiation therapy procedure (including external beam therapy, brachytherapy, or nuclear medicine therapy)?***
No

V.20 ***Does this project involve the deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules, into one or more human research participant?***
No

V.21 ***Will any portion of this project be conducted in the CRU, or does it use any CRU resources?***
No

V.22 ***Will this project use any resource/patients of the HCCC?***
No

V.25.a ***Will the study involve any of the following activity at UI Health Care, even if subjects or their insurance will not be billed for the item or service, and regardless of the study funding source (including studies with departmental***

or no funding)?
Procedures, tests, examinations, hospitalizations, use of Pathology services, use of clinic facilities or clinical equipment, or any patient care services, including services conducted in the Clinical Research Unit; or
Physician services or services provided by non-physicians who are credentialed to bill (ARNPs, Physician Assistants, etc.)
No

V.26 ***The study involves Department of Nursing Services and Patient Care nursing, nursing resources or evaluates nursing practices at UI Health Care.***
No

VI. Subjects

VI.1 ***How many adult subjects do you expect to consent or enroll for this project?***
0

VI.6 ***How many minor subjects do you expect to consent or enroll for this project?***
25

VI.7 ***What is the age of the youngest minor subject?***
0.0

VI.8 ***What is the age of the oldest minor subject?***
17.0

VI.9 ***What is the percentage of minor male subjects?***
50

VI.10 ***What is the percentage of minor female subjects?***
50

VI.11 ***Will any of the minors enrolled be in foster care or Wards of the court?***
No

VI.13 ***Describe EACH of your subject populations***
Include description of any control group(s)
Specify the Inclusion/Exclusion criteria for EACH group
The study population will include 25 pediatric patients scheduled to undergo cardiothoracic surgery or interventional cardiology diagnostic procedures under general anesthesia. All subjects will also be scheduled to undergo post-operative chest x-ray as a routine part of their clinical care, so no additional exposure to ionizing radiation will occur due to this study. We will exclude any patients with known esophageal abnormalities, lesions or disease that would disqualify the patient for the use of TEE as standard procedure. We will further exclude any patients that are solely undergoing TEE diagnostic procedures and only include patients that are already scheduled to undergo procedures where TEE is used as part of routine surgical preparation. There is no control population needed because all patients will receive the same treatment, three attempts at TEE guided catheter placement.

VI.14 ***Provide an estimate of the total number of subjects that would be eligible for***

inclusion in each of your study populations (include your control population if applicable)

25 pediatric patients. There is no control population needed. We expect to complete this study in one year.

VI.15 ***Describe how you will have access to each of your study populations in sufficient number to meet your recruitment goals.***

Outpatient pediatric cardiac surgery patients will be recruited at the pediatric cardiology clinic when patients visit for the preoperative evaluation. Inpatient cardiac patients will be identified initially by using the EPIC operating room schedule on the day before surgery. We will have access to these populations by working within the Department of Anesthesiology and by monitoring the OR schedule for patients scheduled to undergo cardiothoracic or interventional cardiac diagnosis or surgery. The use of TEE and post operative x-ray are already standard procedure for each of these cases. A trained TEE operator (anesthesiologist or cardiologist) will be available to control the TEE probe and assist in catheter guidance. Patients will be recruited until data has been collected in 20 pediatric patients.

VI.16 ***Do you plan to recruit/enroll non-English speaking people?***

No

VI.18 ***Do you propose to enroll any of the following in this study as subjects?***
Employee of the PI or employee of a research team member
Individual supervised by PI or supervised by member of research team
Individual subordinate to the PI or subordinate to any member of the research team
Student or trainee under the direction of the PI or under the direction of a member of the research team

No

VI.20 ***Will subjects provide any information about their relatives?***

No

VI.23 ***Will anyone (other than the subject) provide you with information about the subject (e.g. proxy interviews)?***

No

VI.26 ***Is this project about pregnant women?***

No

VI.27 ***Will this project involve fetuses?***

No

VI.28 ***Does this project involve adult subjects who may be incompetent or have limited decision-making capacity on initial enrollment into the study?***

No

VI.32 ***Does this project involve subjects whose capacity to consent may change over the course of the study?***

No

VI.37 ***Does this project involve prisoners as subjects?***

No

VII.A. Project Description (A)

VII.A.1 ***Where will project procedures take place (check all that apply)?***

UIHC - Main Operating Rooms, Pediatric Catheter Laboratory, Pediatric Cardiac Surgery Clinics

VII.A.2 ***Is this project also being conducted by other researchers at their own sites (e.g. a multi-site collaborative project)?***

No

VII.B. Project Description (B)

VII.B.1 ***Does this project involve any of the following (Check all that apply):***

☐ **Registry** – The collection and maintenance of data (not including biologic samples) in which: (1) the individuals in the registry have a common or related condition(s), and/or (2) the individuals in the registry are interested in being contacted for future studies by investigators other than those listed in Section II of this project.(UI Guide)

☑ **Repository** – The collection, storage, and distribution of human biologic samples and/or data materials for research purposes. Repository activities involve three components: (i) the collection of data and/or specimens such as blood, tissue, saliva, etc.; (ii) the storage of data or specimens, and data management function; and (iii) the sharing of data/specimens with recipient investigators other than the original investigators. (paraphrased from OHRP)

☐ **Expanded Access** – A process regulated by the Food and Drug Administration (FDA) that allows manufacturers to provide investigational new drugs to patients with serious diseases or conditions who cannot participate in a clinical trial. Examples of expanded access include non-protocol access to experimental treatments, including protocol exception, single-patient IND, treatment IND, compassionate use, emergency use, continued access to investigational drug, and parallel track (ClinicalTrials.gov & FDA).

☐ **Clinical (or Treatment) trial** – A prospective biomedical or behavioral research study of new treatments, new drug or combinations of drugs, new devices, or new approaches to surgery or radiation therapy. (NIH and ClinicalTrials.gov & FDA)

☐ **Physiology intervention/study** – A pharmacologic or measurement study aimed at understanding basic mechanisms of disease and/or of normal human physiology, often without any therapeutic intent (though a clinical trial could include such components, often labeled as “translational” or “basic science” aims.) Measurements in such studies could include, but are not limited to, a

blood draw, EKG, EEG, MRI, auditory or sensory testing, checking vital signs, DEXA scans, eye tracking, specimen collection, exercise, fasting, special diets, etc.

☐

Behavioral intervention/study – May be used to refer to studies of individual or group behavior. This option does not include drugs, biologics, or devices but could include psychotherapy, lifestyle counseling, behavior modification, etc.

☐

Diagnostic trial – Protocol designed to evaluate one or more interventions aimed at identifying a disease or health condition (ClinicalTrials.gov & FDA)

☐

Non-clinical – any college/department that would regularly submit to IRB-02

☑

Other – Describe:

The project is a new approach to intervention. Non randomized observational study.

VII.B.1.b ***Provide the NCT (National ClinicalTrials.gov Identifier) number***

NCT02415998

VII.B.2 ***Does this project involve a drug washout (asking subject to stop taking any drugs s/he is currently taking)?***

No

VII.B.6 ***Will any subjects receive a placebo in this study when, if they were not participating, they could be receiving an FDA-approved treatment for their condition?***

No

VII.B.11 ***Is there a separate, written protocol that will be submitted in addition to this IRB New Project form? (Note: a grant application is not considered to be a protocol)***

No

VII.B.18 ***Does this project involve testing the safety and/or efficacy of a medical device?***

Yes

VII.B.19 ***Describe in detail procedures in place for maintaining device shipment and receipt records:***

This device is already onsite being used in the UIHC Main Operating Room and Pediatric Catheter Laboratory of alternative purposes, thus, no device shipping or receipt will occur.

VII.B.20 ***Who will be responsible for maintaining these shipment and receipt records?***

N/A

VII.B.21 ***Describe in detail procedures in place for tracking use and disposition of devices described in this study:***

N/A

VII.B.22 ***Who will be responsible for maintaining these use and disposition tracking records?***
N/A

VII.B.23 ***Describe in detail procedures in place to limit access to authorized study personnel for the storage, control, and dispensing of the investigational devices. (For example, investigational devices are kept in a locked area away from approved devices or have a keyed interlock, and only study personnel authorized to dispense the device have the keys)***
N/A

VII.B.24 ***Is the device FDA-approved for the way it will be used in this study?***
No

VII.B.25 ***Is there an IDE (Investigational Device Exemption) for this device in this research project?***
No

VII.B.29 ***Indicate the appropriate FDA status you and/or the sponsor are requesting for the use of this device in this study.***
Non-Significant Risk (NSR) device/software

VII.B.31 ***Provide a detailed rationale for why this device meets the FDA definition of a Non-Significant Risk Device (NSR)***
Because it is not intended as an implant nor is it to be used in supporting or sustaining human life. At this time it is not of substantial importance in diagnosing, curing, mitigating or treating disease.

VII.B.32 ***Provide a summary of prior investigations with this device.***
Transesophageal echocardiography is a semi-invasive, monitoring and analytic tool used to generate reproducible images of the heart and mediastinum. TEE is routinely used in cardiothoracic and interventional surgeries as well as in detecting thromboses, valvular defects and congenital heart disease. There has been expanding utilization of TEE outside of cardiac surgery as a potential haemodynamic monitor both intraoperatively and postoperatively (Pissarra 2012). While TEE is not regularly used to visualize the spinal column, it can be done with relative ease when consciously attempted (Chitilian 2006). Given the nearly universal use of TEE in cardiac surgical operating rooms, in combination with the low risk of complications (Daniel 1991), potential outcomes include the use of TEE in the placement of thoracic epidural catheters, in identification of spinal cord trauma or as a monitor of intraoperative perfusion and pressure surrounding the spinal cord (Godet 1994). This could lead to improved precision, success and safety of regional anesthesia.

VII.B.33 ***Have there been any prior IRB reviews (at UI or elsewhere) and/or determinations made with regard to this device?***
Yes

VII.B.34 ***Provide a discussion of these reviews/determinations.***
Yes, as TEE is a standard intraoperative monitor, multiple studies have

demonstrated a low rate of complications associated with TEE, deeming it safe for use in surgery (Daniel 1991).

VII.B.35 ***Has the FDA made an assessment of risk with regard to this device?***
No

VII.B.36 ***Has this device/software been approved by the FDA for another indication or in another form from its use in this project?***
Yes

VII.B.37 ***Describe differences between approved device/software and its use in this study:***
TEE is routinely used in cardiothoracic and interventional surgeries as well as in detecting thromboses, valvular defects and congenital heart disease. TEE is used nearly universally in cardiac surgical operating rooms and exhibits a low risk of complications (Daniel 1991). While it has been shown that TEE can be used to visualize the spinal column when attempted (Chitilian 2006), TEE has never been used to confirm the placement of epidural catheters using this new window of view. Because epidural catheters are usually blindly threaded, we would like to assess the sensitivity and specificity achieved by TEE in correlating confirmation of an epidural catheter at targeted thoracic spinal levels and the efficacy of that catheter.

VII.C. Project Description (C)

VII.C.1 ***Does this project involve any research on genes or genetic testing/research?***
No

VII.D. Project Description (D)

VII.D.1 ***Check all materials/methods that will be used in recruiting subjects (you will need to attach copies of all materials at the end of the application):***
Use of any information available to the researchers or their colleagues because this person is a patient OR use of any information considered to be Protected Health Information (PHI) OR review of patient/clinic records - Operating room schedule
Referral from colleague - Thoracic surgery physicians and nurses may identify potential patients. Also, some patients may be identified by Pre-Anesthesia Evaluation Clinic staff.

VII.D.2 ***List the individual data elements you will need to access/use from the patient or clinic records to identify potential subjects for recruitment***
We will need to access patient records to check the patient's eligibility for the study by checking their surgical procedure, past medical history, counter indications for TEE use intra-operatively (esophageal trauma, lesion or disease) and age.

VII.D.3 ***Describe why you could not practicably recruit subjects without access to and use of the information described above***
Many patients may be unaware that they are eligible for the study because they do not understand the routine use of TEE in the operating room. They

may not realize counter indications for the use of TEE and may not report any esophageal trauma, lesion or disease. Also, patients coming to UIHC for this type of surgery come from all over Iowa and surrounding states. Recruitment of eligible patients outside of Iowa City for such a specific study population would be extremely difficult.

VII.D.4 ***Describe why you could not practicably obtain authorization from potential subjects to review their patient or clinic records for recruitment purposes.***
We will not know of potential subjects unless we view the OR schedule with the surgery date. It would not be feasible due to time restraints to consent patients the day of surgery and then identify inclusion/exclusion criteria. If we assessed this by the OR schedule a day in advance, we would then have time the morning of surgery to discuss potential participation in the study.

VII.D.5 ***Describe plans to protect the identifiers from improper use or disclosure***
The only people who will have access to the data collected for this study will be members of the research team that are screening, entering or analyzing data. The subject's initials and the last 4 digits of their medical record number and date of surgery is all that will be utilized to identify potential subjects. Once a subject has been excluded, that information will be placed in a confidential shred bin. If they are eligible, we will proceed with that identifier in able to offer consent. After data collection, the data will be immediately transferred electronically to a password protected file on a password protected computer with their initials and last four of their medical record number. A separate enrollment log will identify subject name, MRN, and date of surgery on a password protected computer in a locked office, within a password protected file. Paper files will be kept in a locked filing cabinet in a locked office.

VII.D.6 ***Describe plans to destroy identifiers at the earliest opportunity consistent with conduct of the research***
Paper identifiers will be shredded and electronic identifiers will be completely cleared from computers at the earliest opportunity possible, consistent with the conduct of this project. This typically occurs once a manuscript has been accepted or rejected for publication.

VII.D.7 ***Does the research team agree that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the study, or for other research for which the use or disclosure of the requested information would be permitted by the HIPAA Privacy Rule***
Yes

VII.D.8 ***Will a member of the research team discuss the study with the subject in person prior to the subject agreeing to participate?***
Yes

VII.D.9 ***Describe the physical location where the consent process will take place:***
In most cases the (because patients are pediatric) parents of the patients will

be approached in the Thoracic Surgery Clinic, Pediatric Intensive Care Unit or Anesthesia Pre-Surgical Evaluation Clinic approximately 24 hours before surgery. Those approached in the Thoracic Surgery Clinic will recieve a copy of the consent form to take home with them. Those parents who consent for patients on the day of surgery will have 1-2 hours before the surgery begins. Parents of patients will be consented before they receive any sedation.

VII.D.10 ***Will a member of the research team discuss the study with the subject by phone prior to the subject agreeing to participate?***
Yes

VII.D.11 ***Describe:***
If subjects have questions for the research team they are able to contact team members by phone as provided on the consent.

VII.D.12 ***Who will be involved in the consent process (including review of consent document, answering subjects' questions)?***

Name	Consent Process Involvement
Kenichi Ueda, MD	Yes

VII.D.15 ***Check all materials that will be used to obtain/document informed consent:***
Consent Document

VII.D.16 ***Are you requesting a waiver of documentation of consent (either no subject signature or no written document)?***
No

VII.D.19 ***Before the subject gives consent to participate are there any screening questions that you need to directly ask the potential subject to determine eligibility for the study?***
Yes

VII.D.20 ***List any screening questions you will directly ask the potential subject to determine eligibility.***
We will ask if the subject has any known esophageal abnormalities, lesions, disease or other issues that would increase risks associated with transesophageal echocardiographic imaging.
We will ask the subject if they are pregnant or incarcerated. All subjects are pediatrics.

VII.D.21 ***Will you keep a screening log or other record that would include information on people who do not enroll in the study?***
No

VII.D.25 ***After the subject agrees to participate (signs consent), are there any screening procedures, tests, or studies that need to be done to determine if the subject is eligible to continue participating?***
No

VII.D.27 ***Discuss how much time a potential subject will have to agree to consider***

participation and whether or not they will be able to discuss the study with family/friends before deciding on participation.

Patients who are approached in the Pediatric Intensive Care Clinic or Thoracic Surgery Clinic pre-operatively will have at least 24 hours to consider participation in our study. These patients will recieve a consent form to take home for further discussion. Patients who are approached on the day of surgery will have 1-2 hours to agree to consider participation in the study. All patients will have the opportunity to discuss with family/friends and ask questions before deciding on participation.

VII.D.28 ***How long after the subject agrees to participate do study procedures begin?***

Patients who are consented in the pre-operative clinic will have at least 24 hours between agreeing to participate and their surgery. Patients who are consented the morning of surgery will have between one and two hours from the time of consent until their surgery. Patients will be consented before they receive any sedation. All patients will consent by parent or guardian as all patients are pediatric.

VII.D.30 ***Describe how you will obtain the consent of the parents or legal guardians for child/minor subjects in this study***
Describe each study population separately including control population
Include when recruitment and consent materials are used
Use FIRST person, and provide detail as to order of events
Describe the steps that will be taken by the research team to minimize the possibility of coercion or undue influence during the consent process

We will identify patients who meet the inclusion criteria by reviewing the pre-operative clinic patient list and operating room schedule. All patients will be consented in the same manner.

In most cases we will approach the patients, and their parents, in the Thoracic Surgery Clinic, Pediatric Intensive Care Clinic or Anesthesia Pre-Surgical Evaluation Clinic at least 24 hours before surgery. We will introduce ourselves as members of the anesthesia team. We will explain the study and standard TEE procedure, including benefits and risks to the patient and provide them a copy of the consent document. This discussion would take place in a private room or exam room. The patients will have the opportunity to ask questions and discuss their participation with family or friends. Patients will also receive a copy of the consent form to take home with them. Patients who agree to participate will sign the consent document and will be provided with a copy of the consent. The consent document will contain contact information that the patient may use to contact the research team with any questions or concerns.

Those patients who are consented the day of surgery will be approached by a nurse and handed a card which states that the patient is eligible to participate in a research study. If they are interested in participating, a member of the

research team will explain the study to the patient, in a private Day of Surgery room. We will explain the study, including benefits and risks, to the patient and provide them with a copy of the consent document. The patients will have the opportunity to ask questions and discuss their participation with family or friends. Patients who agree to participate will sign the consent document and will be provided with a copy of the consent. The consent document will contain contact information that the patient may use to contact the research team with any questions or concerns. Patients will have between one and two hours after consent is obtained before their surgery. All pediatric patients will consent by parent or guardian.

Further, in order to minimize the possibility of coercion or undue influence during the consent process, potential subjects will be reminded that participation is voluntary and choosing not to participate will not affect their surgery/care when they discuss the consent for with the research team.

VII.D.31 ***What are the plans for the assent process for children/minors in this study? (You may choose more than one procedure if you have different child populations in your study)***

No assent procedure because some or all of the children/minors do not have the capability to assent or their capability is so limited that they cannot reasonably be consulted to provide assent -
Children/minors will be given only a verbal description of the study and asked to assent verbally -
Children/minors will sign an assent or consent document -

VII.D.36 ***Provide a detailed description and rationale for each of the procedures chosen above and describe the child/minor populations to which they apply in your study.***

Because our study population includes children/minors who are too young (younger than 7 years old) to assent on their own or their capability is so limited they cannot reasonably do so, their parent or guardian will consent on their behalf. All procedures and information will be explained by a member of the research team and all questions will be answered before consent is obtained.
For those children/minors that are old enough to sign an assent (7-12 years old) or consent (>12 years old) document, they will also have all procedures and information explained by a member of the research team and will be given the opportunity to ask questions before assent/consent is obtained.

VII.D.37 ***Does the study include any form of deception (e.g., providing participants with false information, misleading information, or withholding information about certain study procedures)?***

Examples:
Procedure includes a cover story that provides a plausible but inaccurate account of the purposes of the research.

Participants will be provided with false information regarding the particular behaviors of interest in the research.
Procedures include a confederate pretending to be another participant in the study.
Participants will be told that the research includes completion of a particular task, when in fact, that task will not be administered.
Study is designed to introduce a new procedure (or task) that participants are not initially told about.
If yes, a waiver of informed consent must be requested under question IV.3.
No

VII.E. Project Description (E)

VII.E.1 ***Will subjects be randomized?***
No

VII.E.3 ***Will any questionnaires, surveys, or written assessments be used to obtain data directly from subjects in this study?***
No

VII.E.5 ***Does this project involve creating any audiotapes, videotapes, or photographs?***
Yes

VII.E.6 ***Provide a detailed description in sequential order of the study procedures following the consent process - DO NOT cut and paste from the Consent Document.***

Describe study populations separately if they will be participating in different procedures - include CONTROL population if applicable.

DESCRIBE:
What subjects will be asked to do/what happens in the study (in sequential order)
The time period over which procedures will occur
The time commitment for the subject for individual visits/procedures
Long-term followup and how it occurs
The subjects of the study, pediatric patients scheduled to undergo cardiothoracic surgery or interventional cardiology diagnostic procedures under general anesthesia, will be asked to come to their surgery. The day of surgery the patients will not be required to do anything different from standard anesthesia and surgical practice at the hospital. Subjects will come to the operating room suite and the usual monitors (electrocardiogram, non-invasive blood pressure, and oxygen saturation) will be placed.
Following the routine induction of anesthesia, the Mini-Multi TEE probe (Model T6207 (21381A), Philips, Bothell, WA, USA) will be advanced to mid esophageal level in order to visualize the heart, this is standard surgical procedure in these cases. The probe will be rotated by approximately 180

degreestowardthedescendingaorta,withadjustedgainanddepthinorder toobtainthebestimageofthespinalcordandepiduralspacepossible.A trainedTEEoperator(eitherananesthesiologistorcardiologist)will control themachineandobtainani mageofthespinalcanalatthetargetedvertebral level.Theywillthencaptureanimageofthespinalcanalatthislevel.A differentanesthesiologistwillbeginplac ementofathoracicepiduralcatheter, asisstandard protocolforanesthesia,however, thesecathetersarenormally threadedblindly.Inourstudy,catheterplacementwilloccurwiththe assistanceoftheTEEoperatortoconfirmthecatheterasitisadvancedto targetlevel.Thereal -timeTEEimagegenerat edwillallowforconfirmationof thecatheterwithintheepiduralspaceatthispoint.Further,whenthe anesthesiologistbelievestheyhavereachedthet argetedthoraciclevel,they willinject1mLofnormalsalinetoassessintra -epiduralspreadinthe epidural space.Whenthecatheter isthreadedtosufficienttargetedlevel,as determinedbytheanesthesiologist,abolusdosageofanestheticwillbegiven (0.4mL/kgof1.5%Li docaine)again,thisisallstandardprocedureinthese surgeries.Because itisstandardprocedureforepidur alcath eterstobeplaced blindlypriortosurgery,wehopetodeterminewhethertheuseofTEEfor guidanceandconfirmationwillactuallyimprovetheresultsanddecreasethe timeneededtoensureadequateplacement.A nesthesiologistswillbegiven threeattemptstouseTEEforconfirmation.Theanesthesiologistwillbeable toseetheimageonTEE,andthetrainedTEEmonitorbeallowedtodiscuss imagesseenontheultrasoundscreen.

Atthistime,thetrainedTEEop eratorwillassessthelocationof theepidural catheterwithintheepiduralspaceattargetlevelonreal -timeTEEimageas anterior,posteriororlateraltothespinalcord.Further,theTEEoperatorwill takeimagesofthecatheterconfirmedatthetarg etspinallevelinorderto laterc omparewiththeimagestakenpriortocatheterthreading.

Atthispoint,theTEEprobewillbereturnedtomidesophageallevelto visualizetheheartandtheoperationwillproceedasusual.Becausethisstudy willoccu rwhilethepatientisbeingprepar edforsurgerybytheanesthesia teamasusualinthesesurgeries,noadditionaltimeintheoperatingroomor catheterlaboratorywillberequired.Infact,itispossiblethatTEEguidance coulddecreasetimespentunde ranesthesiaandimproveconfidence inthe catheterposition.Duringtheprocedure,atthetimeofsurgicalincision,the anesthesiologistwillbeaskedtonotewhetherthepatientexhibitsa hemodynamicresponsetoincision.Thiswillbedeterminedbyth ecriteria usedinpreviousstudies (Willschke2006)analyzedbyheartrateandsystemic bloodpressurechangesusingnochangeinHRorBPorchanges<20%from baseline were considered “sufficient block” to surgical stimulation, while HR orBPchanges> 20% from baseline were considered “not sufficient block” to surgicalstimulation.Thesechangeswillcorrelatewiththeefficacyofthe epiduralblock.

Following surgery, a post-operative x-ray will be taken as is standard procedure to visualize the heart. Because this study will occur only in pediatric patients, the x-ray will also capture and exhibit catheter placement around the spinal cord. This is currently the gold standard confirmatory technique for epidural catheters and this will be used to compare with the success of pre-operative TEE guided catheter placement.

Following all procedures, the success rate achieved by TEE in threading a catheter to the epidural space of targeted spinal levels as compared to confirmation by post-operative x-ray. Further the efficacy of that catheter will be determined with correlation to catheter position (anterior, lateral or posterior to the spinal cord). When looking at patient medical records, we will only collect the following data: height, weight, age, any known history of esophageal abnormalities, lesions or disease, current procedure, hemodynamic markers, FLACC score immediately after surgery when the patient is in the post-anesthesia care unit ** or pediatric intensive care unit ** postoperatively 24 hours after surgery and total morphine used within 24 hours after surgery.

The time period for the pre-operative procedure will require approximately thirty minutes but will not extend patient time in the operating room or catheter laboratory as all procedures will occur as the patient is being prepared for surgery and this would occur normally by the anesthesia team.

No additional visits or extra time is required of the subject. There will be no necessary long-term follow up or data collection. When the patient leaves the operating room, nothing additional is required.

VII.E.7 ***Will you attempt to recontact subjects who are lost to follow-up?***
No - followup is not required in this study

VII.E.9 ***Will subjects be provided any compensation for participating in this study?***
No

VIII. Risks

VIII.1 ***What are the risks to subjects including***
- emotional or psychological
- financial
- legal or social
- physical?
The care the patient will receive is standard practice at UIHC for cardiothoracic surgery or interventional cardiology diagnostic procedures under general anesthesia and are necessary procedures regardless of this research study. The postoperative x-ray would occur to visualize the heart, regardless of study participation thus, no additional exposure to ionizing radiation is incurred by participation. The only potential additional physical

risk involved is an increased risk of esophageal trauma as the TEE probe may be maneuvered more than normal to observe catheter entry and anesthetic spread. The low risk of esophageal injury associated with TEE makes this unlikely but it is still a possibility that must be noted. Patients **(and parents)** may be under slightly elevated emotional stress knowing that they are part of a research study. There is a very low risk of loss of confidentiality of the patient's medical information, yet this is unlikely as patients will be given identification numbers at the earliest date possible and these will only be accessed by members of the research team. Only the data necessary to answer the research question will be collected upon reviewing patient information. There are no other known financial, physical or legal risks to the patient.

VIII.2 ***What have you done to minimize the risks?***
If applicable to this study ALSO include:
How you (members of your research team at Iowa) will monitor the safety of individual subjects.
Include a description of the availability of medical or psychological resources that subjects might require as a consequence of participating in this research and how referral will occur if necessary (e.g. availability of emergency medical care, psychological counseling, etc.)
Healthcare professionals will monitor the subject at all times during the operation. The patient will be reassured that although they are participating in the study, everything that happens during the case is already standard practice at UIHC for cardiothoracic surgery or interventional cardiology diagnostic procedures under general anesthesia. TEE probe maneuvering will only be done as necessary to minimize any physical trauma beyond what is already standard procedure in these patients. All patients will be given an identification number and be referred to by such. To prevent loss of confidentiality of the patient's medical information, we will keep all records used for this study in a locked office or on password protected computer system. Only members of the research team will have access to the records used in this study. No key will be kept as patients will not need to be contacted in the future.

VIII.3 ***Does this study have a plan to have an individual or committee review combined data from all subjects on a periodic basis (such as summary or aggregate safety and/or efficacy data)?***
No

IX. Benefits

IX.1 ***What are the direct benefits to the subject (do not include compensation or hypothesized results)?***
There are no direct benefits to the subject.

IX.2 ***What are the potential benefits to society in terms of knowledge to be gained as a result of this project?***

This novel method to visually confirm epidural catheter placement and anesthetic spread within the epidural space could greatly increase the safety and success rate of epidural analgesia. Further, it provides an alternative to the ionizing radiation and contrast injection used in current methods of fluoroscopy to confirm catheter placement. By determining the success rate achieved using TEE as an alternative method to thread and confirm epidural catheter placement, it will allow us to compare with current techniques already in use and potentially improve patient safety and care.

X. Privacy & Confidentiality

X.1 ***What are you doing to protect the privacy interests of the subjects?***

To protect patient privacy, researchers will be conducting the consent and study procedures in a private setting. Further, the research team will only be collecting the information necessary to complete the study.

X.2 ***Are you collecting the Social Security Number of any subjects for any purpose?***

No

X.4 ***How will information/data be collected and stored for this study (check all that apply):***

Paper/hard copy records (hard copy surveys, questionnaires, case report forms, pictures, etc.) - Paper/hard copy records, including consent documents and any other material printed for the study, will be stored in the primary investigator's office in a locked file cabinet. Further, patients will be assigned a unique identification number. They will always be referred to by this number. The patient's hospital number and day of surgery will be recorded, but will not be disclosed to anyone outside the research team. We will record the hospital number only to access the patients' chart later if needed. The database that contains the identifiers will be password protected so that the only the investigators needing it can access it. No unnecessary patient identifiers will be recorded, and those that are needed will be deleted at the earliest possible time. Only data necessary to collect for the study will be recorded.

Electronic records (computer files, electronic databases, etc.) - Electronic records will be kept on the password protected Anesthesia department server. The members of the research team will be the only people with access to the files. No records will be kept on personal computers. Further, patients will be assigned a unique identification number. They will always be referred to by this number. The patient's hospital number and day of surgery will be recorded, but will not be disclosed to anyone outside the research team. We will record the hospital number only to access the patients' chart later if needed. The database that contains the identifiers will be password protected so that the only the investigators needing it can access it. No unnecessary patient identifiers will be recorded, and those that are needed will be deleted at the earliest possible time. Only data necessary

to collect for the study will be recorded.
Name -
Title - System Administrator and System Programmer II
University Job Classification - IT Security Officer

X.5 ***Do the confidentiality protections indicated above allow only members of the research team to access the data/specimens?***
Yes

X.7 ***Does your study meet the NIH criteria for a Certificate of Confidentiality or will you be applying for Certificate of Confidentiality?***
No

XI. Data Analysis

XI.1 ***Describe the analysis methods you will use, including, if applicable, the variables you will analyze***
We are planning to determine the success rate achieved using TEE guidance to thread an epidural catheter to a targeted thoracic spinal level. Post-operative radiograph will be used to confirm catheter position for comparison. Thus, we will only use exploratory descriptive statistics for analysis.

XI.2 ***Provide the rationale or power analysis to support the number of subjects proposed to complete this study.***
Because this is a novel technique, we have no base for the ability to use TEE to guide and confirm thoracic epidural catheters. We assume that twenty pediatric patients will provide adequate power to confirm a high success rate for this novel technique in both imaging and guiding the catheter. Therefore, total of 25 subjects will be needed due to account for subjects who may withdraw or become ineligible.

XII. Future Research

XII.1 ***Do you wish to keep any information about subjects involved with this research project so that members of the current research team may contact them in the future for your own research projects?***
No

XII.2 ***Do you wish to keep any information about subjects involved with this research project so that other researchers may contact them for future research?***
No

XII.4 ***Does this project involve storing any data, tissues or specimens for future research?***
Yes – contribution for future use is mandatory for participation in the study

ROC. Record of Consent

ROC.1 ***Select which option applies to address the University of Iowa Health Care policy IM-MR-06.21 titled "Documentation of patient participation as a subject in a research protocol or use of an investigational medication,***

study medication, investigational device, or biologic."

The research related activities proposed in this study **does meet** the registration requirements under the University of Iowa Health Care policy IM-MR-06.21 titled "Documentation of patient participation as a subject in a research protocol or use of an investigational medication, study medication, investigational device, or biologic." **The below information must be completed and approved as part of the IRB application. This information contained within this page will be used to create the Epic Research Study Application Form.**

ROC.2 ***Select a publicly viewable title for this study. (This title will be visible in EPIC)***

Release full title

ROC.3 ***Select research team member who has taken Epic Training***

ROC.4 ***Who is a 24/7 contact person for projects involving treatment(s) or procedures that result in complications or side effects?***

Kenichi Ueda

Other contact information that may be relevant to a subject's clinical care (i.e. may be important if the contact person is not available 24/7 or an alternate contact may be required.)

ROC.5 ***Describe the key complications from the study drug(s) listed below or study procedure(s):***

The patient might experience sore throat from TEE manipulation for a few hours after the surgery.

ROC.6 ***Any other information that may be important to emergency personnel:***

None

XIII. Other Mod and/or Comments

XIII.1 ***Most modifications should be made in the appropriate section (see Index) of the project itself. If you need to describe other changes, or wish to add comments about something you changed, please do so here.***

CR I. Project Summary

CR I.1 ***Summarize your progress to date in conducting the study at Iowa. Address each of the bulleted items below in your response.***
Describe any problems or delays
Describe any significant changes to the study design(previously approved by the IRB) since the study began (requests for new changes should be described on a Modification form)
Describe any significant subject experiences (benefits, adverse events/adverse reactions) since the last IRB review.

No problems or delays in the study. No changes were made since the study began. No significant subject experiences noted since the last IRB review.