PennState

HRP-591 - Protocol for Human Subject Research

Protocol Title: A volunteer study to determine the anatomical distribution of injectate, the extent of sensory block, and the pharmacokinetics of ropivacaine following Erector Spinae Plane (ESP) blocks.

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Table of Contents

1.0 Objectives

1.1 Study Objectives

The **primary objectives** of this study are to define the extent of dermatomal anesthesia and anatomical spread of injectate (as defined by MRI imaging) that is provided by an ESP block at the T5 level, using twenty milliliters of 0.5% ropivacaine. MRI data will not be collected after May 2023

The **secondary objectives** include: 1) the measurement of changes in hemodynamic parameters associated with the ESP block, 2) the duration of sensory effects provided by ropivacaine with or without epinephrine, 3) the venous plasma concentration of ropivacaine at various time intervals after completion of the ESP block.

1.2 Primary Study Endpoints

Outcomes to be assessed

1. Extent of dermatomal sensory loss
2. Duration of sensory loss
3. Anatomical extent of injectate spread using MRI imaging. MRI data will not be collected after May 2023
4. Venous plasma concentration of ropivacaine at periodic time intervals

We are comparing these outcomes between

1. 20ml ropivacaine 0.5% with epinephrine vs no epinephrine

1.3 Secondary Study Endpoints

1. Hemodynamic parameters at periodic time intervals
2. Any adverse effects or side effects related to injection of the medications

2.0 Background

2.1 Scientific Background and Gaps

Thoracic surgery is associated with significant postoperative pain and providing adequate analgesia in these patients is essential for enhanced recovery protocols[1]. Regional anesthesia

techniques, such as thoracic epidural and thoracic paravertebral blockade, are therefore commonly employed [2]. These techniques have limitations however; they require a high degree of technical expertise, are contraindicated if the patient has a coagulopathy, and are associated with significant adverse effects and risk of complications. These include, but are not limited to hypotension, pneumothorax, and epidural abscess or hematoma formation. We recently described a novel ultrasound-guided regional anesthetic technique for providing thoracic analgesia, the ultrasound-guided Erector Spinae Plane (ESP) block. The ESP block involves injection of local anesthetic into the musculofascial plane deep (anterior) to the erector spinae muscle and superficial (posterior) to the tip of the transverse processes of the thoracic spine. Our radiological and anatomical investigation in fresh adult cadavers has shown that injection of a clinically-relevant volume (20ml) at the T5 vertebral level produces extensive spread of injectate within the erector spinae musculofascial plane, along the Para spinal and posterior chest wall, and extending between C4 and T12 vertebral levels [3]**.** This corresponds with early clinical experience indicating that the ESP block is effective in treating chronic thoracic pain[3], acute post-thoracic surgical pain [4-6], and pain from rib fractures [7]. It thus appears to provide similar analgesia to a thoracic paravertebral block, while being technically simpler and safer to perform. The ESP block therefore has promise as a simple, safe, yet highly effective method of providing thoracic analgesia, and one that can be learned and performed by the majority of anesthesiologists.

2.2 Previous Data

Ultrasound-guided ESP injections of a clinically relevant volume (20 mL) of normal saline (with iodinated contrast and methylene blue) at the T5 vertebral level were performed in fresh cadavers. The cadavers underwent computed tomography imaging and anatomical dissection. The radiological and anatomical findings demonstrated a distribution of injectate within the erector spinae musculofascial plane, along the Para spinal and posterior chest wall, and extending between C4 and T12 vertebral levels [4]**.** It is unclear how the extent of spread may have been influenced by the state of preservation of the cadaver, post mortem tissue desiccation, temperature difference, and lack of perfusion and respiratory motion that would be present in a living subject. Even though the ESP block has not been studied extensively for evaluation of mechanism of action, there are a number of case reports and case series that have been published in the last year, where ESP has been shown to be safe in different conditions of use. [4-6] To date, there are 39 manuscripts that have been published and indexed in PubMed, and no associated complications or side effects have been reported. A list of those publications can be found using the following link: https://www.ncbi.nlm.nih.gov/pubmed/?term=erector+spinae+plane+block**.** Here at the Penn State Hershey Medical Center, more than two hundred of these blocks have been performed for different procedures, without any complications or side effects.

2.3 Study Rationale

At present, no systematic investigation has been published that describes first, the spread of injectate following the ESP block in live human subjects; second, the extent of sensory blockade that can be reliably expected; and third, the pharmacokinetics of local anesthetic injected into this location. It is also unknown what effect additives such as epinephrine, might have on these parameters. Epinephrine is commonly used for erector spinae plane blocks (ESP) or similar peripheral fascial plane injections to produce local vasoconstriction in order to prolong the action of the ropivacaine. The current evidence for the mechanism of action and efficacy of the ESP block in providing sensory blockade of the thorax comes from cadaveric studies and small patient case series.[4-6] For this potentially valuable regional anesthesia technique to be adopted more widely in clinical practice, it is essential to determine, with more precision, the mechanism of action in live human subjects, and the extent of sensory blockade that can be reliably achieved

with clinically significant volumes of injectate boluses. Local anesthetic systemic toxicity, although rare, is always a concern in regional anesthesia and it is, therefore, also important from a safety perspective to determine the pharmacokinetics associated with the ESP block, so as to provide appropriate guidelines for maximum dose, volume and concentration of local anesthetic to be injected. In addition, this knowledge will provide baseline data from which to embark upon comparative studies with other more established techniques for regional anesthesia of the thorax, such as thoracic epidural or thoracic paravertebral blocks. A volunteer study in non-anesthetized subjects offers the most controlled setting to study these factors, as it eliminates the confounding effects of concomitant analgesic and anesthetic medications, surgical trauma, and patient co-morbidities.

3.0 Inclusion and Exclusion Criteria

3.1 Inclusion Criteria

- Healthy adults, male or female, aged 18 to 60 inclusive
- Weight between 55 and 100 kg inclusive
- Height 160 to190 cm inclusive
- Normal baseline creatinine result

3.2 Exclusion Criteria

- Pregnant females
- Chronic medical condition requiring medication
- History of previous major spinal, abdominal or thoracic surgery
- Congenital abnormalities of the spine, back, thorax or abdomen
- History of major trauma to the thorax or abdomen;
- Allergy to ropivacaine or other amide local anesthetics
- The presence of any metallic implant in their body
- Any contraindication to magnetic resonance imaging as determined by completion of a standard questionnaire administered to all patients undergoing magnetic resonance imaging. (Does not apply after May 2023)
- Individuals with any clinically relevant history or the presence of neurological deficits or cardiovascular disease
- Trainees actively involved within the Department of Anesthesiology (e.g., fellows, students and residents)

3.3 Early Withdrawal of Subjects

3.3.1 Criteria for removal from study

- Subject does not complete the study
- Develop any complications or side effects due to injections.
- Abnormal Creatinine level following baseline blood test
- Subject does not follow fasting rules

3.3.2 Follow-up for withdrawn subjects

Any subject withdrawn from the study due to complications or side effects of the injection will be seen immediately by the PI and a course of treatment will be determined.

4.0 Recruitment Methods

4.1 Identification of subjects

We will hang recruitment flyers

4.2 Recruitment process

Healthy volunteers aged between 18yrs to 60 of both genders will be recruited with Recruitment Flyers. Interested subjects will be interviewed by the project coordinator from the Department of Anesthesia over the phone and will be advised to meet them at the Anesthesia clinic at a scheduled time. The informed written consent for the study will be obtained from them at the Anesthesia Clinic.

4.3 Recruitment materials

- Recruitment Flyer

4.4 Eligibility/screening of subjects

Interested subjects will be interviewed by the project coordinator from the department of Anesthesia over phone using the attached IRB approved phone script and will be advised to meet them at the Anesthesia clinic at a scheduled time.

5.0 Consent Process and Documentation

5.1 Consent Process

5.1.1 Obtaining Informed Consent

5.1.1.1 Timing and Location of Consent

Consent to participate will be obtained from eligible patients after preoperative evaluation in the Anesthesia Preoperative Evaluation Clinic (APEC), during this visit blood will be drawn and sent to the clinical laboratory for measurement of kidney function as base line creatinine level. If the creatinine level is higher than normal they will be informed about it and excluded from the study.

5.1.1.2 Coercion or Undue Influence during Consent

The patient will be advised that participation in research studies is voluntary and that their decision to participate or not participate will not affect the level of care at this institution.

5.1.2 Waiver or alteration of the informed consent requirement

Not applicable

5.2 Consent Documentation

5.2.1 Written Documentation of Consent

We will obtain a consent form signed by the patient and the person obtaining the consent. An original signed copy will be retained by the patient and the research team and a copy will be placed in the patient's medical record.

5.2.2 Waiver of Documentation of Consent (Implied consent, Verbal consent, etc.)

A waiver of documentation of consent is being requested for use of the phone screening process. During phone contact with a potential participant, verbal consent is obtained from the caller in order for the study coordinator to continue explaining the research study and asking pertinent eligibility questions. If the caller is interested in participating in this study, a study visit will be scheduled.

5.3 Consent – Other Considerations

After the consent is obtained, 1 ml of blood will be drawn and sent to the clinical laboratory for measurement of kidney function as base line creatinine level. Once the creatinine level is known and found to be within normal limits, they will be included in to the study. Once included they will be informed of the date and time of the study and advised to fast from solids for at least 6 hours prior to the study, with clear liquid permitted until 2 hours before the procedure.

6.0 HIPAA Research Authorization and/or Waiver or Alteration of Authorization

6.1 Authorization and/or Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

Check all that apply:

☐ **Not applicable, no identifiable protected health information (PHI) is accessed, used or disclosed in this study.** *[Mark all parts of sections 6.2 and 6.3 as not applicable]*

☒ **Authorization will be obtained and documented as part of the consent process.** *[If this is the only box checked, mark sections 6.2 and 6.3 as not applicable]*

☐ **Partial waiver is requested for recruitment purposes only (Check this box if patients' medical records will be accessed to determine eligibility before consent/authorization has been obtained).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Full waiver is requested for entire research study (e.g., medical record review studies).** *[Complete all parts of sections 6.2 and 6.3]*

☒ **Alteration is requested to waive requirement for written documentation of authorization (verbal authorization will be obtained).** *[Complete all parts of sections 6.2 and 6.3]*

6.2 Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

6.2.1 Access, use or disclosure of PHI representing no more than a minimal risk to the privacy of the individual

6.2.1.1 Plan to protect PHI from improper use or disclosure

Information is included in the "Confidentiality, Privacy and Data Management" section of this protocol.

6.2.1.2 Plan to destroy identifiers or a justification for retaining identifiers

Identifiers will be destroyed when the study has been completed and the results published.

6.2.2 Explanation for why the research could not practicably be conducted without access to and use of PHI

Information must be obtained either from the subject's electronic medical record or self-reported physical history during recruitment to determine eligibility

6.2.3 Explanation for why the research could not practicably be conducted without the waiver or alteration of authorization

The waiver is requested only for recruitment to determine subject eligibility to ensure that no medical conditions that fall into the exclusion criteria are present and would thus preclude enrollment. This waiver will minimize the enrollment of subjects' who may ultimately fail to meet the study inclusion/exclusion criteria.

6.3 Waiver or alteration of authorization statements of agreement

Protected health information obtained as part of this research will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other permitted uses and disclosures according to federal regulations.

The research team will collect only information essential to the study and in accord with the 'Minimum Necessary' standard (information reasonably necessary to accomplish the objectives of the research) per federal regulations.

Access to the information will be limited, to the greatest extent possible, within the research team. All disclosures or releases of identifiable information granted under this waiver will be accounted for and documented.

7.0 Study Design and Procedures

7.1 Study Design

This will be a randomized, blinded, controlled study.

This study will examine the effects of **single injections** of 0.5% ropivacaine with epinephrine or without epinephrine (20 ml of each) injected at ESP at the T5 vertebra level.

7.1.1 Randomization process

The subjects enrolled will be randomized into two groups (6 participants in each group) by a computer-generated randomization list using SAS software (SAS Institute, Cary, NC):

Randomization groups
1. Group RE will have 20mL of **0.5% Ropivacaine with epinephrine** injected at the left or right T5 transverse process.
2. Group R will have 20mL of **0.5% Ropivacaine without epinephrine** injected at the left or right T5 transverse process.

The randomization will be performed, using a sealed envelope technique, and will be stratified according to the side of the injections (either left or right) so that each arm will have equal number of left and right sided ESP blocks. This will be done by the investigational pharmacy while preparing the medications. All subjects, the anesthesiologist performing the procedure, the radiologist, and the research coordinator collecting the data will be blinded and will not be aware of the details of the injection and allocation of the participants. In the event that the patient has a concerning reaction or becomes unstable in any fashion, the patient will be immediately unblinded and removed from the study.

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The conduct of the study will be as follows.

7.2 Study Procedures

7.2.1 Pre-Procedure Visit

This visit will take place at the Anesthesia Preoperative Evaluation Clinic (APEC) for pre-procedural evaluation.

At this visit:

- Consent to participate will be obtained from eligible patients
- Blood will be drawn for baseline creatinine level
- All subjects will be instructed to fast from solids for at least 6 hours prior to the study, with clear liquid permitted until 2 hours before the procedure.

The blood collected for the creatinine level will be taken in person by the research coordinator to the clinical lab of Hershey Medical center. The samples will be destroyed immediately after the required amount of blood is tested. The results of the creatinine test will be sent to PI and that will determine the inclusion of the subject in the study.

Day of Procedure - (n=12)

The procedure will be scheduled at least 24 hr. after the pre-procedure visit. On the day of the procedure, the investigational pharmacy will prepare the syringe according to the randomization. The appropriate study medication will be picked up by the coordinator at the investigational pharmacy. The appearance of the syringe will be the same regardless of the medication that is inside. The study physician will use the randomization number as generated by investigational pharmacy to determine on which side to place the block and allocate a study number. Subjects and outcome assessors will be blinded to randomization allocation.

Study subjects will report to the Clinical Research Center (CRC) of Milton S. Hershey hospital on the day of their scheduled study procedure. Once they are checked in to CRC and ascertained that they followed fasting instructions, the female participants will be asked to take pregnancy test using a urine sample and a standardized pregnancy testing kit. Once the pregnancy test is determined to be negative, they will be considered to be a study participant. If pregnancy test is positive, they will be excluded from the study. Once the participant is included in to the study, an intravenous access and continuous monitoring of vital signs (ECG, non-invasive blood pressure every 5 minutes, and pulse oximetry) will be established. 3 ml of blood will be obtained from the Intravenous line already placed in the subject prior to performing the block. These samples will be repeated at 20, 40, 60, 90, 120, and 240 minutes after completion of the injection of active drug. A member of the research team will manually transport the appropriately-

labeled blood collection tube to a storage freezer in the Perioperative Genomics Laboratory (C2813, C2848) during the transport, blood samples will be placed in Category A sealed triple packaging. During transport, the specimen tubes will be placed in splash-proof and leak-proof containers. These primary containers are placed inside of secondary containers which will be sealed. The blood samples will be processed and analyzed for ropivacaine level using HPLC at genomic laboratory of department of Anesthesia, Hershey medical center at a later date. The results of the level of the ropivacaine level will be used for analysis of the results for the study. The subjects will not receive the results of these tests. However, if any of the subjects if specifically request for the results of these test that will be given to them. The blood samples will be immediately destroyed after the results of the ropivacine conc. in the samples is obtained. The additional blood from samples, if any, will be destroyed.

The subject will be placed in a sitting position, the skin over their upper back will be disinfected with chlorhexidine 2%, and the tip of the T5 transverse process on one side will be identified using a low-frequency curvilinear ultrasound transducer (Sonosite, Bethesda, USA) placed in a longitudinal parasagittal orientation as previously described. [4] The skin over the needle insertion site will be anesthetized with 2ml of lidocaine 1% conc. for patient comfort. A 22-gauge 10cm Tuohy needle (Stimuplex, BBraun, and Bethlehem, USA) will be inserted in-plane with the ultrasound beam to contact the T5 transverse process. One ml of 0.9% normal saline will be injected to confirm correct needle tip placement separating the ESP from transverse process, as evidenced by visible linear fluid spread deep to the erector spinae muscle. Injection of the specific volume and type of fluid according to the randomization group (see above) will then take place. MRI part of study stopped May 2023. After the completion of the assigned injection they will be transported to the MRI suite at the MRI core facility on the Hershey campus in a wheel chair. The subject will undergo two MRI's to determine the spread of the anesthetic. These will take place at approximately 30 and 90 minutes following the completion of the assigned block.

Following the Block injection (completion of the MRI data May 2023), the subjects will be allowed to sit, stand or lay down for the remainder of the study. Continuous monitoring and recording of vital signs will take place as, blood pressure and heart rate will be measured every 5 minutes, starting prior to performing the block, till 60 minutes after the block is performed and every 15 minutes thereafter for the duration of the study. A member of the research team blinded to the randomization allocation will perform a sensory assessment for loss of sensation to cold using ethanol on the skin at 20, 60, 120, 240, and 360 mins after the injection of active drug. The extent of sensory loss to cold will be marked on the body using a water-soluble color marker each time and will be photographed each time interval. A binary scoring system will be used for both assessments: 1 = reduced sensation; 2 = normal sensation.

Once the final sensory assessment has been completed (360 minutes following block), the subject will remain for an additional 30 minutes of observation. The intravenous cannula will be removed and the subject will then be discharged to return home. The subjects will be discharged from the research facility with a note to inform the PI or Research coordinator if they feel anything different or abnormal. The subject should not drive for 24 h after receiving the block, and will need to have someone to drive them home after the procedure.

7.3 Duration of Participation

It will take three days to complete this research study. For two consecutive days following the procedure they will be asked to participate in a follow-up phone call to discuss how they are feeling. The script for the follow-up phone call is attached.

7.4 Test Article(s) (Study Drug(s) and/or Study Device(s))

7.4.1 Description

The group receiving the ropivacaine 0.5% will receive 1 syringe containing 20mLs of ropivacaine 0.5%, and the group receiving the ropivacaine/epinephrine will receive 1 syringe containing 19.9mLs of ropivacaine 0.5% and 0.1 mLs of Epinephrine 1mg/mL for a total volume of 20mLs. The medications will be injected between muscle planes in the back using real time ultra sound guidance. Both medications have been approved by the FDA for many years, for this specific use, as well as for injection around nerve fibers. These medications have been used in billions of people in the world already, with a very robust safety record. In our institution, we use these medications routinely every day for a number of procedures, including ESP blocks.

7.4.2 Treatment Regimen

There will be no adjustment to dose. Every participant will receive the same amount of medications as prepared by the investigational Pharmacy. The medications will be injected using real time ultra sound guidance between two muscle planes in the back of the body, using a 22gauge needle.

7.4.3 Method for Assigning Subject to Treatment Groups

The subjects enrolled will be randomized into two groups by a computer-generated randomization list using SAS software (SAS Institute, Cary, NC):

Randomization groups

1. Group RE will have 20mL of **0.5% Ropivacaine with epinephrine** injected at the left or right T5 transverse process.
2. Group R will have 20mL of **0.5% Ropivacaine without epinephrine** injected at the left or right T5 transverse process.

7.4.4 Subject Compliance Monitoring

The study will be done in the CRC of the Penn State College of Medicine. (and the MRI suit of the Department of Radiology, where the MRI will be done. Completed May 2023) Once the participant is included in to the study, an intravenous access and continuous monitoring of vital signs (ECG, non-invasive blood pressure every 5 minutes, and pulse oximetry) will be established. Continuous monitoring and recording of vital signs will take place as follows: blood pressure and heart rate will be measured every 5 minutes, starting prior to performing the block, till 60 minutes after the block is performed, and every 15 minutes thereafter for the duration of the study.

7.4.5 Blinding of the Test Article

The randomization will be performed, using a sealed envelope technique, by the investigational pharmacy while preparing the medications. All subjects, the anesthesiologist performing the procedure, the radiologist, and the research coordinator collecting the data will be blinded and will not be aware of the details of the injection and allocation of the participants. In the event that the patient has a concerning reaction or becomes unstable in any fashion, the patient will be immediately unblinded and removed from the study.

7.4.6 Receiving, Storage, Dispensing and Return

7.4.6.1 Receipt of Test Article

The study drug will be prepared and dispensed in standard sterile way by the Investigational Pharmacy of the Milton S. Hershey medical center. The medications will be collected, by the study coordinator, in a container with the participant's number, and will be brought to the CRC on the day of the study prior to the administration of medications for the study.

7.4.6.2 Storage

Investigational Pharmacy personnel, study coordinator and investigator will only have access to the medications and there will not be any storage of the medications.

7.4.6.3 Preparation and Dispensing

The randomization will be performed, using a sealed envelope technique, by the investigational pharmacy while preparing the medications.

7.4.6.4 Return or Destruction of the Test Article

NA

7.4.6.5 Prior and Concomitant Therapy

None

8.0 Subject Numbers and Statistical Plan

8.1 Number of Subjects

12 subjects are needed to follow the study protocol through to completion. Up to 35 subjects may be enrolled to allow for loss of participants who complete the enrollment step, but do not proceed to receive the ESP block procedure.

8.2 Sample size determination

This is a pilot study and will use descriptive results of this study to plan for a larger randomized clinical trial in the future.

8.3 Statistical methods

Statistics: The statistical analysis will be performed using STATA 14.1 statistical software (StataCorp LP, College Station, TX) and Wilcoxon matched-pairs U test will be utilized for different MRI measurements and calculations. The χ^2 test will be used to analyze the differences between dermatomal anesthesia on hemi-thorax and abdomen.

9.0 Confidentiality, Privacy and Data Management

See the Research Data Plan Review Form.

10.0 Data and Safety Monitoring Plan

10.1 Periodic evaluation of data

The PI and research coordinator will review cumulative adverse events, early termination of study participation, and accrual every six months and report any issues requiring modification of the study or alteration of the risk: benefit ratio to the IRB immediately. A summary of adverse events, study progress and protocol modifications will be included for IRB review in the continuing review.

10.2 Data that are reviewed

The data to be reviewed will be:

- Safety data
- Untoward events
- Efficacy data

10.3 Method of collection of safety information

Safety information will be collected by the research coordinator at study visits and follow-up phone call.

10.4 Frequency of data collection

See table below

	Frequency of data collection, including when safety data collection starts							
		Consent	Placement of IV	Collection of blood samples	MRI Remove May 2023	Monitoring of Vitals	Phone calls	Sensory Evals
	Pre Procedure Visit	X		X				
The day of Procedure	On Arrival		X	X		X		
	5mts					X		
	10					X		
	15					X		
	20			X		X		X
	25					X		
	30				X	X		
	35					X		
	40			X		X		
	45					X		
	50					X		
	55					X		
	60			X		X		X
	75					X		
	90			X	X	X		
	105					X		
	120			X		X		X
	135					X		
	150					X		
	165					X		
	180					X		
	195					X		
	210					X		
	225					X		

	240			X		X		X
	255					X		
	270					X		
	285					X		
	300					X		
	315					X		
	330					X		
	345					X		
	360					X		X
	Post Procedure Day 1						X	
	Post Procedure Day 2						X	

10.5 Individuals reviewing the data

Oversight for the conduct of the study will be provided by the PI and the research coordinator will monitor the data. They will ensure that all eligible criteria and consent requirements are met prior to a subjects' participation in the study and that the procedures and adverse event reporting occur according to the IRB approved protocol.

10.6 Frequency of review of cumulative data

The PI and research coordinator will review cumulative adverse events, early termination of study participation, and accrual every six months and report any issues requiring modification of the study or alteration of the risk: benefit ratio to the IRB immediately. A summary of adverse events, study progress and protocol modifications will be included for IRB review in the continuing review.

10.7 Statistical tests

Not applicable

10.8 Suspension of research

The study will be immediately suspended if there is any report or occurrence of serious side effect to any of the subjects. The serious side effects include but not limited to Infection, sepsis, severe hypotension, severe hypertension, any condition requiring to air way management,

11.0 Risks

The risks to you include:

Venipuncture: The discomfort associated with removing blood by venipuncture (by needle from a vein) is a slight pinch or pin prick when the sterile needle enters the skin. The risks include mild discomfort and/or a black and blue mark at the site of puncture. Less common risks include a small blood clot, infection or bleeding at the puncture site, and on rare occasions fainting during the procedure.

Regional Anesthesia - Possible complications and discomforts from regional anesthesia include:

- Common – local/pain and/or discomfort, infection, and/ or headache
- Uncommon – shock or extreme fall in blood pressure, convulsions and/or seizures
- Rare – nerve damage resulting in numbness, tingling and/or paralysis which may be temporary or permanent. Respiratory arrest, cardiac arrest, and/or allergic reaction to drugs. Death.

Ropivacaine Hydrochloride: Possible complications and discomforts from ropivacaine hydrochloride include:

- Incidence 5% or greater – High blood pressure, nausea, vomiting, fever, headache, back pain, low blood pressure, and slow heartbeat.
- Incidence 1% to 5% - Urinary retention, dizziness, shaking or exaggerated shivering, rapid heart rate, anxiety, production of abnormally small amounts of urine, reduced sense of touch or sensation, chest pain, deficiency of potassium in the bloodstream.

Epinephrine:

- Side effects of epinephrine include: Fast heartbeat, sweating, headache, weakness, shakiness, paleness, and dizziness.

Procedural risks:

- It will involve the similar procedural risk as other peripheral regional anesthesia procedures. This procedure has not been studied very extensively so the literature of its safety is not known completely. However, there are a number of case reports and case series that have been published in the last year, where ESP has been shown to be safe in different conditions of use.[4-6] Here at the Penn State Hershey Medical Center, more than two hundred of these blocks have been performed for different procedures, without any complications or side effects.
- There is a rare risk of pneumothorax, which is getting air or gas in the cavity between the lungs and the chest wall, causing collapse of the lung.
- Venipuncture: Any time we insert a needle in your body there is a minimal risk for bruise, infection or extravasation of blood.

MRI removed May 2023

MRI discomfort and risks -- Because the MRI scanner contains a very strong magnet, you may not be able to have the MRI if you have certain kinds of metal in your body (for example, a heart pacemaker, a metal plate, certain types of heart valves or brain aneurysm clips). Someone will ask you questions about this before you have the MRI. Having a MRI may mean some added discomfort to you. In particular, you may be uncomfortable inside the MRI scanner if you do not like to be in closed spaces ("claustrophobia"). You may also be bothered by the loud banging noise during the study. Temporary hearing loss has been reported from the loud noise. This is why you will be asked to wear earplugs. During the procedure, you will be able to talk with the MRI staff through a speaker system. You can tell them to stop the scan at any time.

You should not expect to get your results from the MRI scan since the scan done during this study is not designed to detect or evaluate any medical condition you may have. The MRI scan is intended solely for research purposes and will not provide the same detailed information as an MRI done for clinical reasons. There is a small chance that researchers could find something that might be important to your health. If this happens, a member of the study team may contact you to find out if you would like to learn more. However, even if we find something important to your health, we cannot guarantee that you will be contacted.

Risk of loss of confidentiality: There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of your electronic data, created by you or by the researchers, will be maintained to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

12.0 Potential Benefits to Subjects and Others

12.1 Potential Benefits to Subjects

You will not experience any direct benefit from this research.

12.2 Potential Benefits to Others

Presently there is no outcome and other related data available for this procedure. The results of this research may guide the future use of ESP Blocks by providing providers with a better understanding of the technique and its associated effect and may help improve the practice of ESP blocks for patients in the future.

13.0 Sharing Results with Subjects

Results will not be shared with the participants.

14.0 Subject Stipend (Compensation) and/or Travel Reimbursements

Participants will receive $300 for the time they have given for participation in this research study. If they do not complete the study for any reason, they will be paid for the visits they have completed:

15.0 Economic Burden to Subjects

15.1 Costs

There is no cost to participants for taking part in this study.

15.2 Compensation for research-related injury

It is the policy of the institution to provide neither financial compensation nor free medical treatment for research-related injury. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. Costs for the treatment of research-related injuries will be charged to subjects or their insurance carriers.

16.0 Resources Available

16.1 Facilities and locations

The research will be conducted at the Hershey Medical Center‘s Clinical Research Center.

16.2 Feasibility of recruiting the required number of subjects

We will be using flyers to recruit patients.

16.3 PI Time devoted to conducting the research

PI has academic time that he can use to perform the research, and he is available when onsite.

16.4 Availability of medical or psychological resources

Not applicable.

16.5 Process for informing Study Team

Meetings will be held periodically as needed to ensure all research team members are informed about the protocol and their duties. Team emails will also be used to keep team members updated.

17.0 Other Approvals

17.1 Other Approvals from External Entities

Not applicable

17.2 Internal PSU Committee Approvals

Check all that apply:

☐ Anatomic Pathology – Hershey only – Research involves the collection of tissues or use of pathologic specimens. Upload a copy of HRP-902 - Human Tissue For Research Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ Animal Care and Use – All campuses – Human research involves animals and humans or the use of human tissues in animals

☒ Biosafety – All campuses – Research involves biohazardous materials (human biological specimens in a PSU research lab, biological toxins, carcinogens, infectious agents, recombinant viruses or DNA or gene therapy).

☐ Clinical Laboratories – Hershey only – Collection, processing and/or storage of extra tubes of body fluid specimens for research purposes by the Clinical Laboratories; and/or use of body fluids that had been collected for clinical purposes, but are no longer needed for clinical use. Upload a copy of HRP-901 - Human Body Fluids for Research Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☒ Clinical Research Center (CRC) Advisory Committee – All campuses – Research involves the use of CRC services in any way.

☐ Conflict of Interest Review – All campuses – Research has one or more of study team members indicated as having a financial interest.

☐ Radiation Safety – Hershey only – Research involves research-related radiation procedures. All research involving radiation procedures (standard of care and/or research-related) must upload a copy of HRP-903 - Radiation Review Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ IND/IDE Audit – All campuses – Research in which the PSU researcher holds the IND or IDE or intends to hold the IND or IDE.

☒ Scientific Review – Hershey only – All investigator-written research studies requiring review by the convened IRB must provide documentation of scientific review with the IRB submission. The scientific review requirement may be fulfilled by one of the following: (1) external peer-review process; (2) department/institute scientific review committee; or (3) scientific review by the Clinical Research Center Advisory committee. NOTE: Review by the Penn State Hershey Cancer Institute Scientific Review Committee is required if the study involves cancer prevention studies or cancer patients, records and/or tissues. For more information about this requirement see the IRB website at: http://www.pennstatehershey.org/web/irb/home/resources/investigator

17.0 Multi-Site Research

Not applicable

19.0 Adverse Event Reporting

19.1 Reporting Adverse Reactions and Unanticipated Problems to the Responsible IRB

In accordance with applicable policies of The Pennsylvania State University Institutional Review Board (IRB), the investigator will report, to the IRB, any observed or reported harm (adverse event) experienced by a subject or other individual, which in the opinion of the investigator is determined to be (1) unexpected; and (2) probably related to the research procedures. Harms (adverse events) will be submitted to the IRB in accordance with the IRB policies and procedures.

20.0 Study Monitoring, Auditing and Inspecting

20.1 Auditing and Inspecting

The investigator will permit study-related monitoring, audits, and inspections by the Penn State quality assurance program office(s), IRB, the sponsor, and government regulatory bodies, of all study related documents (e.g., source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g., pharmacy, diagnostic laboratory, etc.).

21.0 Future Undetermined Research: Data and Specimen Banking

Not applicable.

22.0 References

1. Romero, A., J.E. Garcia, and G.P. Joshi, The state of the art in preventing postthoracotomy pain. Semin Thorac Cardiovasc Surg, 2013. **25**(2): p. 116-24.

2. Bottiger, B.A., S.A. Esper, and M. Stafford-Smith, Pain management strategies for thoracotomy and thoracic pain syndromes. Semin Cardiothorac Vasc Anesth, 2014. **18**(1): p. 45-56.
3. Joshi, G.P., et al., A systematic review of randomized trials evaluating regional techniques for postthoracotomy analgesia. Anesth Analg, 2008. **107**(3): p. 1026-40.
4. Forero, M., et al., The Erector Spinae Plane Block: A Novel Analgesic Technique in Thoracic Neuropathic Pain. Reg Anesth Pain Med, 2016. **41**(5): p. 621-7.
5. Forero M. Rajarathinam M. Adhikary S, C.K., Continuous Erector Spinae Plane Block for Rescue Analgesia in Thoracotomy After Epidural Failure. Anesthesia & Analgesia case reports, 2017.
6. Chin, K.J., et al., The analgesic efficacy of pre-operative bilateral erector spinae plane (ESP) blocks in patients having ventral hernia repair. Anaesthesia, 2017. **72**(4): p. 452-460.
7. Borglum, J., et al., Distribution patterns, dermatomal anesthesia, and ropivacaine serum concentrations after bilateral dual transversus abdominis plane block. Reg Anesth Pain Med, 2012. **37**(3): p. 294-301.
8. Rifai, N., et al., Simultaneous measurement of plasma ropivacaine and bupivacaine concentrations by HPLC with UV detection. Ther Drug Monit, 2001. **23**(2): p. 182-6.
9. Tanaka, E., et al., Simultaneous determination of three local anesthetic drugs from the pipecoloxylidide group in human serum by high-performance liquid chromatography. J Chromatogr B Analyt Technol Biomed Life Sci, 2006. **834**(1-2): p. 213-6.
10. American College of Radiology, Manual on Contrast media. 2017. ISBN: 978-1-55903-012-0
11. Schulte-Altedorneburg G et al. MR arthrography: pharmacology, efficacy and safety in clinical trials.Skeletal Radiol. 2003;32 (1):1-12
12. Hunt H et al. Frequency and severity of adverse effects of iodinated and gadolinium contrast materials: Retrospective review of 356, 930 doses. AJR 2009; 193: 1124-1127.
13. Wittich C. et al. Ten Common Questions (and Their Answers) About Off-label Drug Use. Mayo Clin Proc. 2012;87:982-990