STUDY TITLE: *Quadratus Lumborum Block versus Intrathecal Morphine for Postoperative Pain Control after Cesarean Delivery*

Principal Investigator: Nicholas J. Schott, MD

Source of Support: UPMC Department of Anesthesiology and Perioperative Medicine

NCT: 03261193

Date of Approval: 08/14/2017

University of Pittsburgh OSIRIS

!section: Triage!

[reviewer notes,]

Provide a short title for this study (200 characters or less):

QL block for post-cesarean delivery pain

Tl.O

Select the type of application:
New Research Study

T2.0

Is the proposed research study limited to the inclusion of deceased individuals?
* No

T2.1

Are any research activities being conducted at the VA Pittsburgh Healthcare System or with VA funds?

* No

[reviewer notes,]

T3.0 **What is the anticipated risk to the research participants?**

Greater Than Minimal Risk

!section: Cover Sheet!

[reviewer notes-,]

CS1.0 What is the reason for this submission?

New Research Protocol Submission

CS1.1

Has this research study been approved previously by the University of Pittsburgh IRB?

* No

CSI.1.1

Has this research study (or a substantially similar research study) been previously disapproved by the University of Pittsburgh IRB or, to your knowledge, by any other IRB?

* No

[reviewer notes-,]

CS2.0

Title of Research Study:

Quadratus Lumborum Block for Postoperative Pain Control after Cesarean Delivery

CS2.0.1

Requested approval letter wording:

CS2.1 Research Protocol Abstract:

Effective post-cesarean delivery analgesia is important to achieving functional recovery after cesarean delivery, and it is an influential factor shaping the patient experience. Currently, neuraxial morphine (e.g., Intrathecal Morphine, ITM) is an integral component of multimodal post-cesarean delivery analgesia. It is considered a standard of care in the administration of neuraxial anesthesia for cesarean delivery. ITM is also associated with side effects, including nausea, vomiting, respiratory depression, urinary retention and pruritus, although these side effects are dose-dependent and weighed by patients to be less important than pain after cesarean delivery.

Supplemental peripheral nerve blocks have been studied extensively for post-cesarean delivery pain and have focused primarily on local infiltration with or without catheters, transversus abdominis plane (TAP) blocks, and ilioinguinal iliohypogastric (IIIH) blocks. These blocks and have not shown superiority to ITM for dynamic pain outcomes, but may have a role in supplemental or "rescue" analgesia whenever ITM cannot be given (e.g., general anesthesia for cesarean delivery; contraindication to ITM). The ultrasound-guided quadratus lumborum block (QLB) is a regional anesthetic technique that has shown some promise in improving pain following cesarean delivery compared to placebo, though no randomized studies have directly compared it to the current gold standard, multimodal analgesia with ITM. Furthermore, QLB may have advantages over the TAP block in terms of its more superficial location (easier ultrasound visualization thereby theoretically conferring improved safety). In this context, the utility of QLB as part of a multimodal analgesic approach that includes ITM for post-cesarean delivery pain warrants investigation.

Objectives:
The objective of this study is to determine if the QLB adds benefit to a multimodal analgesia regimen that includes ITM for patients after scheduled elective cesarean delivery.

Study Design:

Prospective, single center, randomized control trial !section: Cover Sheet!

Setting/Participants:
This study will be limited to patients presenting to Magee Women's Hospital (MWH) for scheduled, elective cesarean delivery under spinal anesthesia. We plan to enroll a total of 60 patients for this study. Inclusion criteria include elective cesarean delivery under spinal anesthesia, singleton pregnancy, American Society of Anesthesiologists (ASA) classification score of 2 or less, and term gestational age of at least 37 weeks. Exclusion criteria include: contraindications to neuraxial blockade; anatomical abnormalities affecting spinal or QLB placement (i.e. scoliosis, conversion to general anesthesia); contraindications or true allergies to morphine, NSAIDs, acetaminophen, other oral opioids, or local anesthetics; presence of chronic pain history or opioid dependence on or off maintenance therapy.

Study Interventions and Measures:
Subjects will be randomized to one of two groups: ITM plus sham (saline) QLB and ITM plus true (bupivacaine) QLB. The primary outcome is pain on movement at 24 hours post-cesarean delivery. Other outcome measures that will be assessed and evaluated include:
• VAS pain scores at rest and with movement (VAS pain score with movement at 24 hrs will be the primary outcome)
• Time to first request for PRN oral or parenteral opioid
• Total opioid pain medications required throughout hospital stay
• Presence/absence of sedation, itching, and nausea/vomiting
• Vital signs - heart rate (HR), blood pressure (BP), respiratory rate (RR), and oxygen saturation (SpO2)
• Signs of local anesthetic toxicity including perioral numbness, ringing in the ears, or metallic taste in the mouth within 4 hours of block (assessed at 15 min, 30 min, 45 min, 1 hour and 4 hours by nursing or study personnel)
• Breastfeeding success and quality

The primary outcome will be measured at baseline (entry to post-anesthesia care unit) and at 1 hr, 4 hrs, 24 hrs, and 48 hrs following the completion of the QLB (true or sham)

CS2.2

Select the category that best describes your research:
Biomedical research

[reviewer notes,]

CS3.0 **Name of the Principal Investigator:**

Nicholas Schott

Note: Adjunct faculty of the University, including lecturers and instructors, are not permitted to serve as a PI or Faculty Mentor but may serve as co-investigators. Refer to Chapter 4 on the HRPO website for more information.

CS3.1 **Affiliation of Principal Investigator:**

UPP or UPMC staff member

If you chose any of the **Pitt options,** please indicate the specific campus:

If you chose the UPitt faculty member option, provide the PI's **University Faculty Title:**

CS3.2

Address of Principal Investigator:

Department of Anesthesiology

Magee-Womens Hospital
300 Ha ket Street
Pittsburgh, PA 15213

!section: Cover Sheet!

CS3.3 Recorded Primary Affiliation of the Principal Investigator:

UPMC | Other

CS3.4 Identify the School, Department, Division or Center which is responsible for oversight of this research study:

U of Pgh | School of Medicine | Anesthesiology

CS3.S Telephone Number of Principal Investigator:

412-641-4260

CS3.6 Recorded Current E-mail Address of Principal Investigator to which all notifications will be sent:

schottnj@u pmc.edu

CS3.7 Fax Number:

412-641-4766

CS3.8 Does this study include any personnel from Carnegie Mellon University, and/or use any CMU resources or facilities (e.g., Scientific Imaging and Brain Research Center (SIBR)?

* No

CS3.9 Is this your first submission, as PI, to the Pitt IRB?

* No

[reviewer notes-,]

CS4.0 List of Co-Investigators:

Last	First	Organization
Dalby	Patricia	U of Pgh | School of Medicine | Anesthesiology
Lim	Katherine Grace	U of Pgh | School of Medicine | Anesthesiology
Schott	Nicholas	UPMC | Other
Vernon	Thomas	Other | Other
Waters	Jonathan	U of Pgh | School of Medicine | Anesthesiology

!section: Cover Sheet!

[reviewer notes-,]

CSS.O **Name of Primary Research Coordinator:**

Nicholas Schott

CSS.1

Address of Primary Research Coordinator:

Department of Anesthesiology
Magee-Womens Hospital
300 Halket Street
Pittsburgh, PA 15213

CSS.2

Telephone Number of Primary Research Coordinator:

412-641-4260

CS6.0

Name of Secondary Research Coordinator:

CS6.1 **Address of Secondary Research Coordinator:**

CS6.2 **Telephone Number of Secondary Research Coordinator:**

CS6.3 **Key Personnel/Support Staff (Only list those individuals who require access to OSIRIS):**

Last First Organization
There are no items to display

[reviewer notes-,]

CS7.0 **Will this research study use any Pediatric PittNet or Clinical and Translational Research Center (CTRC) resources?**

No

[reviewer notes,]

CSS.O **Select the entity responsible for scientific review.**

Department Review - (a dean, department chair, division chief, or center head)
Note: **DoD funded studies** require departmental review

CSS.1

Select the school, department or division which is responsible for scientific review of this submission.

U of Pgh | School of Medicine | Anesthesiology

!section: Cover Sheet!

[reviewer notes-,]

CS9.0 **Does this research study involve the administration of an investigational drug or an FDA-approved drug that will be used for research purposes?**

* Yes

CS9.1 **Do you plan to utilize the Investigational Drug Service (IDS) to dispense the drug?**

* No

CS10.0 **Is this research study being conducted under a University of Pittsburgh-based, sponsor-investigator IND or IDE application?**

* No

If YES, you are required to submit the IND or IDE application and all subsequent FDA correspondence through the Office for Investigator-Sponsored IND and IDE Support (0315). Refer to applicable University policies posted on the 0315 website (www.0315.pitt.edu).

[reviewer notes-,]

CS11.0 **Use the 'Add' button to upload one or more of the following:**

- **the sponsor protocol (including investigator initiated studies) and/or other brochures**
- **the multi-center protocol and consent form template, *if applicable***

Name Modified Date

Is this research study supported in whole or in part by industry? This includes the provision of products (drugs or devices).

* No

Is this a multi-centered study?

* No

!section: Cover Sheet!

[reviewer notes-,]

CS12.0 **Does your research protocol involve the evaluation or use of procedures that emit ionizing radiation?**

* No

CS13.0 **Does this research study involve the deliberate transfer of recombinant or synthetic nucleic acid molecules into human subjects?**

* No

Upload Appendix M of NIH Guidelines:

Name	Modified Date

CS14.0 **Are you using UPMC facilities and/or UPMC patients during the conduct of your research study?**

* Yes

If Yes, upload completed Research Fiscal Review Form:

Name	Modified Date
Magee Fiscal Form- No costs to be occured	6/25/2017 5:30 PM

[reviewer notes-,]

CS15.0 **Indicate the sites where research activities will be performed and/or private information will be obtained.**

Choose all sites that apply and/or use **Other** to include sites not listed:

Sites:
UPMC

UPMC
Sites:
UPMC Magee Women's Hospital

If you selected **School, International or Other,** list the sites:

***For research being conducted at non Pitt or UPMC sites, upload a site permission letter granting the researcher permission to conduct their research at each external site:**

Name Modified Date

CS15.1 **Have you, Nicholas Schott, verified that all members of the research team have the appropriate expertise, credentials, and if applicable, hospital privileges to perform those research procedures that are their responsibility as outlined in the IRB protocol?** !section: Cover Sheet!

* Yes

CS15.2

Describe the availability of resources and the adequacy of the facilities to conduct this study:

* Magee Women's Hospital (MWH) sees nearly 9,000-10,000 patient encounters for deliveries a year. There are on average 3-4 elective C-sections taking place at MWH every weekday which would provide an ample and diverse sampling of patients to enroll for this study. MWH has all of the staff and resources necessary to provide complete care for laboring and delivering patients. An ultrasound machine as well as the other appropriate drugs and supplies area available at MWH to perform the quadratus lumborum block (QLB), and all blocks will be performed by people adequately trained in the procedure. The PI does have sufficient time to participate in and oversee the study, and does have access to UPMC password protected computers and servers by virtue of job responsibilities. Storage and distribution of data can be easily managed with any paper information being stored in locked file cabinets inside locked personal offices belonging to the PI or other listed co-investigators, and any electronic information being stored only on UPMC password protected computers. All disclosure of private information from patients will take place in a private pre-operative holding room, inside the operating room, or in the patient's private hospital room at MWH as is already the practice for obtaining such information for all elective procedures that are performed there everyday. MWH is fully equipped with both the staff and equipment necessary to handle any routine management or emergency situation that may arise related to this study.

[reviewer notes,]

CS16.0 **Special Research Subject Populations:**

Categories
Pregnant women, fetuses and/or neonates

[reviewer notes,]

CS17.0 **Does your research involve the experimental use of any type of human stem cell?**

* No

!section: Cover Sheet!

[reviewer notes-,]

NIH Definition of a Clinical Trial

A research study[1] in which one or more human subjects[2] are prospectively assigned[3] to one or more interventions[4] (which may include placebo or other control) to evaluate the effects of those interventions on health related biomedical or behavioral outcomes.[5]

[1] See Common Rule definition of research at 45 CFR 46.102(d).

[2] See Common Rule definition of human subject at 45 CFR 46.102(f) .

[3] The term "prospectively assigned" refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.

[4] An intervention is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.

[5] Health-related biomedical or behavioral outcome is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects' biomedical or behavioral status or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.

CS18.0 * **Based on the above information, does this study meet the NIH definition of a clinical trial?**

(•) **Yes** ( ) No

If Yes, click Save and then Click Here For Study Team's CITI Training Records . Please ensure all personnel's training is up to date

!section: Section 1 - Objective, Aims, Background and Significance!

[reviewer notes-,]

1.1 Objective: What is the overall purpose of this research study? (Limit response to 1-2 sentences.)

The purpose of this trial is to determine the effectiveness of a postoperative analgesia strategy that includes QLB added to a multi-modal post-cesarean analgesia strategy. We hypothesize that the QLB provides superior post-cesarean analgesia compared to the current standard of care, multi-modal analgesia.

1.2 Specific Aims: List the goals of the proposed study (e.g., describe the relevant hypotheses or the specific problems or issues that will be addressed by the study).

We will determine if the quadratus lumborum block (QLB) provides superior analgesia to patients following cesarean delivery compared to the current standard of care, multi-modal analgesia (i.e., ITM and scheduled post-operative non-opioid oral analgesics, with oral opioid analgesics reserved for breakthrough pain).

We will measure side-effects associated with each strategy: standard of care (ITM + care described *above,* plus sham QLB with saline), and standard of care plus true QLB.

We will measure and model economic ramifications associated with each strategy, modeling factors including drug costs, procedure costs, costs associated with length of stay and re-admissions.

1.3 Background: Briefly describe previous findings or observations that provide the background leading to this proposal.

The quadratus lumborum block (QLB) is similar to the transversus abdominis plane (TAP) block, but differs slightly in regards to the location where local anesthetic is injected. Because of the more posterior location of the QLB, it theoretically confers greater safety due to enhanced visualization (1). The TAP block has been studied extensively for post-cesarean delivery pain, consistently showing that it is not superior to ITM for post-operative analgesia, but that it may have a role in patients with breakthrough pain despite the use of ITM, or in patients who were unable to receive it (e.g. general anesthesia for cesarean, contraindications to neuraxial morphine). ITM is superior to TAP alone for post-cesarean analgesia, but it is associated with a dose-dependent increased risk for opioid related side effects (2,4,5). In 2015, Blanco et. al. published a study specifically using the QLB for postoperative pain after cesarean delivery (1). In this study, they compared a true QLB to a sham QLB all in patients who did not receive ITM, and found that the QLB provided improved pain control and decreased the need for post-operative opioids. Another study in 2016 demonstrated that the QLB is superior to the TAP block in regards to decreasing post-operative pain following c-section (3). Unfortunately, neither study compared the QLB to ITM (part of the current gold standard for post-cesarean delivery pain, multimodal analgesia).

References
(see supporting documentation)

1.4 Significance: Why is it important that this research be conducted? What gaps in existing information or knowledge is this research intended to fill?

This research is important to conduct because clinicans must constantly evaluate the medical management of patients to find ways that provide the most benefit with the least risk of harm. Post-operative pain control following cesarean delivery is an area that is important to patients and to providers, and the introduction of the QLB for this purpose has the potential to improve analgesic benefits.

!section: Section 2 - Research Design and Methods!

[reviewer notes-,]

2.1 **Does this research study involve the *use* or evaluation of a drug, biological, or nutritional (e.g., herbal or dietary) supplement?**

* Yes

2.1.1

Does this research study involve an evaluation of the safety and/or effectiveness of one or more marketed nutritional (e.g., herbal or dietary) supplements for the diagnosis, prevention, mitigation or treatment of a specific disease or condition or symptoms characteristic of a specfic disease or condition?

* No

[reviewer notes-,]

2.1.2

Does this research study involve the use or evaluation of one or more drugs or biologicals not currently approved by the FDA for general marketing?

* No

!section: Section 2 - Research Design and Methods!

[reviewer notes-,]

2.1.3 Does this research involve the *use* or an evaluation of the effectiveness and/or safety of one or more drugs or biologicals currently approved by the FDA for general marketing?

* Yes

2.1.3.1 Are the FDA-approved drugs or biologicals being evaluated in this research study for a new clinical indication, different population, or route of administration and/or dosage level that is not currently specified in the FDA-approved product labeling?

Drugs are often used **Off-Label** during routine practice. Before answering this question, review the FDA product labeling (http://labels.fda.gov) for the approved "Indications and Usage." If being used off-label, answer **Yes** to this question. You are required to provide information and/or upload the package insert for each drug that is administered for research purposes.

* No

If you respond **YES,** an IND number or the FDA written concurrence of IND exemption may be required.

Upload information on FDA approved indications/doses and FDA exemption letter if applicable:

Name	Modified Date

[reviewer notes,]

2.2 Will this research *use* or evaluate the safety and/or effectiveness of one or more devices?

* No

[reviewer notes-,]

2.3 Summarize the general classification (e.g., descriptive, experimental) and methodological design (e.g., observational, cross-sectional, longitudinal, randomized, open-label single-blind, double-blind, placebo-controlled, active treatment controlled, parallel arm, cross-over arm) of the proposed research study, as applicable.

Prospective, single center, randomized controlled trial

2.3.1 Does this research study involve a placebo-controlled arm?

* Yes

[reviewer notes-,]

2.3.1.1 Is there a commonly used diagnostic/treatment approach that is currently recognized as being effective for the proposed subjects' disease or condition, and that will be withheld from subjects assigned to the placebo arm of this research study?

No; subjects assigned to the placebo and experimental arms of the research study will continue to undergo a commonly used diagnostic/treatment approach

[reviewer notes-,]

2.4 Will any research subjects be withdrawn from known effective therapy for the purpose of participating in this research study?

* No

[reviewer notes.]

2.5 Will screening procedures (i.e., procedures to determine research subject eligibility) be performed specifically for the purpose of this research study?

* Yes

2.5.1

List the screening procedures that will be performed for the purpose of this research study. Do NOT include the inclusion/exclusion criteria in this section as they will be addressed in section 3; questions 3.13 and 3.14.

Potential patients will be assessed from the obstetrical operating room schedule the day prior. All scheduled cesarean deliveries will be screen for meeting inclusion criteria. Patients who are screened for inclusion will have discussion of informed consent to be involved in study.

[reviewer notes.]

2.6

Provide a detailed description of all research activities (e.g., all drugs or devices; psychosocial interventions or measures) that will be performed for the purpose of this research study.

This description of activities should be complete and of sufficient detail to permit an assessment of associated risks.

At a minimum the description should include:

- **all research activities**
- **personnel (by role) performing the procedures**
- **location of procedures**
- **duration of procedures**
- **timeline of study procedures**

A waiting period of 5-30 minutes will elapse between introduction of the study to the participant, and enrolling the participant into the study. At the time the participant has been enrolled into the study and the cesarean delivery is confirmed to occur, the pharmacist will be instructed to open an opaque, sealed, numeric envelope labeled only with a study

number. The envelope will contain the randomi e s!a+ ea> itD and Methods!
Participants wi| be assigned to either contra (ITM pus sham QLB with sa in e) or experimental (ITM plus QLB bupivacaine). The pharmacist will then dispense the blinded study drug to the investigator. Group assignment will not be revealed to the investigator, anesthesiology team, nursing team, obstetricians, nor participants, to achieve a double blind.

Spinal anesthesia will occur per institutional routine: either L3-4 or L4-5 consisting of 1.6 cc (12 mg) of 0.75% hyperbaric bupivacaine plus fentanyl 15 mcg and morphine 150 mcg in accordance with current institutional standards. Spinal anesthetics will be performed in the operating room (OR) by senior residents (CA2 or 3), fellows, or attendings only.

Following the cesarean delivery, bilateral QLB will be performed using the study drug (either saline or true drug). QLB will be performed under ultrasound guidance either in the operating room immediately after surgical drapes are lowered and prior to transfer to PACU, or immediately upon arrival to the PACU. Each unilateral QLB will consist of 40 cc of 0.25% bupivacaine (20 ml deposited per side). Prior to the QLB procedure, the patient will be prepped and draped in a sterile fashion. Sterile gloves, a hat, and a mask will be worn and sterility maintained throughout the procedure. Each unilateral QLB typically takes about 2-10 minutes to complete. The drugs used are FDA approved for the indication used in this research.

Post-operative analgesia protocol: patients in all groups will be given 30 mg IV ketorolac scheduled q6hrs x 3 doses (unless contraindications). Alter ketorolac, they will receive 600 mg PO ibuprofen q6hrs scheduled for mild pain (1-3) x 24 hours, as well as Tylenol 500 mg PO q4hrs scheduled for mild pain (1-3) x 24 hours (total acetaminophen dose not to exceed 3000 mg in 24 hours). For breakthrough pain, patients will have PRN oxycodone 5-10 mg PO q4hrs for moderate (4-6) or severe (7-10) breakthrough pain. If needed, some patients may also receive PRN IV morphine or other parenteral opioid if breakthrough pain is severe despite PRN oral oxycodone or if they are unable to take PO medications. All of these medications and doses are typical, standard post-operative orders commonly used for pain control in patients who have undergone a cesarean delivery.

The outcome measures that will be assessed and evaluated in all three groups include:
• VAS pain scores at rest and with movement (VAS pain score with movement at 24 hours will be the primary outcome)
• Time to first request for PRN oral or parenteral opioid
• Total opioid analgesics required throughout hospital stay
• Presence/absence of sedation, itching, and nausea/vomiting
• Vital signs - respiratory rate (RR), and oxygen saturation (SpO2)
• Signs of local anesthetic toxicity (e.g., perioral numbness, ringing in the ears, or metallic taste in the mouth, other non-specific neurological symptoms) within 4 hours of block (assessed at 1 5min, 30 min, 45 min, 1 hour and 4 hours by nursing or study personnel)
• Breastfeeding success and quality

The primary outcome will be measured at baseline (entry to post-anesthesia care unit, and immediately after QLB) and at 1 hour, 4 hours, 24 hours, and 48 hours following completion of the QLB. Follow-up will occur in the recovery room and in patient's rooms.

Post-operative scores for pruritus will be rated on a numeric 0-3 scale (0, none; 1, mild; 2, moderate; 3, severe), and nausea will be rated on a numeric 0-3 scale (0, none; 1, mild; 2, moderate; 3, severe or vomiting). Perioral numbness, ringing in ears, or metallic taste in mouth will be rates as either present or absent.

Following the final evaluation at 48 hours, participation in the study will be considered complete.

2.6.1

Will blood samples be obtained as part of this research study?

* No

*If submitting a protocol for expedited review, it should be clear that the planned blood draws are within the parameters described here:
http://www.hhs.gov/ohrp/policy/expedited98.html (see Expedited Research Category #2)

If **Yes,** address the frequency, volume per wit 8llt-1olii:t ctflN:i 2oll.ffi! 'i!l:IY si9 Ce Methodsl qualifications of the individual performing the procedure:

Study Flow Chart:

Name	Modified Date
QLB Study Flowchart	6/23/2017 7:32 PM

[reviewer notes-,]

2.7 **Will follow-up procedures be performed specifically for research purposes? Follow-up procedures may include phone calls, interviews, biomedical tests or other monitoring procedures.**

* Yes

See study flow chart in question 2.6

[reviewer notes-,]

2.8 **Does this research study involve the use of any questionnaires, interview or survey instruments?**

* Yes

Upload a copy of all materials except for the SCIO or KSADS which are on file at the IRB. The use of all instruments must be addressed in question 2.6 and/or question 2.7 (except for an exempt submission where they should be addressed on the appropriate uploaded exempt form).

Name	Modified Date
Data Collection Form	5/21/2017 5:37 PM

Previously the name and publisher for commercially available materials were listed in the textbox below but effective 9/1/2015, all materials (except for the SCID and KSADS) must be uploaded using the Add button above.

!section: Section 2 - Research Design and Methods!

[reviewer notes-,]

2.9 **If subjects are also patients, will any clinical procedures that are being used for their conventional medical care also be used for research purposes?**

* yes

If **Yes,** describe the clinical procedures (and, if applicable, their frequency) that will be used for research purposes:
Performing a spinal anesthetic consisting of intrathecal morphine is part of the routine, conventional medical care for patients undergoing an elective cesarean delivery. In this study, the benefits of the pain control and any associated side effects from spina l anesthesia with intrathecal morphine will be evaluated.

2.10 The blood sample question was moved to 2.6.1.

[reviewer notes-,]

2.11 **What is the total duration of the subject's participation in this research study across all visits, including follow-up surveillance?**

* 48 hours

[reviewer notes-,]

2.12 **Does this research study involve any type of planned deception?**
If Yes, you are required to request an alteration of the informed consent process (question 4.7)

* No

[reviewer notes-,]

2.13 **Does this research study involve the use of UPMC/Pitt protected health information that will be de-identified by an IRB approved "honest broker" system?**

* No

[reviewer notes-,]

2.14 **Will protected health information from a UPMC/Pitt HIPAA covered entity be accessed for research purposes or will research data be placed in the UPMC/Pitt medical record?**

* Yes

If you answer **Yes,** you are required to submit this study to the Center for Assistance in

Research using e-Record (CARe). Per UPMC P t!rlfuR **clll-rR ermlliJOO** Methods! access or invo ve UPMCle ectronic protected heath information (e-PHI) must be submitted to CARe, with the exception of clinical trials that are contracted through the UPMC Office of Sponsored Programs and Research Support (OSPARS).

Complete the online submission form at https://care.upmc.com/request.aspx. After the study is submitted in OSIRIS, a CARe representative will conduct a review. You will be notified once your CARe review is complete or if anything further is needed.

Studies that will access only paper-based medical records (not in combination with any electronic records) do not need to be submitted to CARe.

For additional information, please see https://care.upmc.com.

Describe the medical record information that will be collected from the UPMC/Pitt HIPAA covered entity and/or the research-derived information that will be placed in the medical records.

As part of this study, it will be necessary to review the patient's medical history to ensure that they have no contraindications to neuraxial anesthesia or a quadratus lumborum block. This typically involves briefly looking through the patients medical record to check their medical history and lab values, and a face to face discussion with the patient prior to their cesarean delivery. All patients presenting for an elective cesarean delivery are also routinely given a paper form that reviews their medical history. All of this information will be reviewed both for their routine care and also for the purposes of this study. No additional information other than what is reviewed for routine care for an elective cesarean will need to be obtained as a result of this study. For participants receiving QLB, data summarizing the procedure including exactly what medication and dose was given will be placed in the UPMC/Pitt medical record ("Study Drug" for the local anesthetic will be noted, to maintain blinding). Following the cesarean delivery, some follow-up measures (e.g. oral and parenteral pain medications) may be gleaned and recorded as it is routinely documented in the medical record.

2.14.1 **Will protected health information from a non-UPMC/Pitt HIPAA covered entity be obtained for research purposes or will research data be placed in the non-UPMC/Pitt medical record?**

* No

I, Nicholas Schott, **certify that any member of my research team accessing, reviewing and/or recording information from medical records have completed HIPAA Researchers Privacy Requirements (Formerly RPF Module 6) training. The HIPAA certificates must be available for review if audited but do not need to be uploaded into this OSIRIS application.**

* Yes

2.14.2

Are you requesting a waiver of the requirement to obtain written HIPAA authorization for the collection of the PHI?

* No

[reviewer notes-,]

2.15 Does this research study involve the long-term storage (banking) of biological specimens?

* No

[reviewer notes-,]

2.16 Will research participants be asked to provide information about their family members or acquaintances?

* No

[reviewer notes-,]

2.17 What are the main outcome variables that will be evaluated in this study?

The outcome measures that will be assessed and evaluated in all three groups include:
• VAS pain scores at rest and with movement (VAS pain score with movement at 24 hours will be the primary outcome)
• Time to first request for PRN oral or parenteral opioid
• Total opioid analgesics required throughout hospital stay
• Presence/absence of sedation, itching, and nausea/vomiting
• Vital signs - respiratory rate (RR), and oxygen saturation (SpO2)
• Signs of local anesthetic toxicity (e.g., perioral numbness, ringing in the ears, or metallic taste in the mouth, other non-specific neurological symptoms) within 4 hours of block (assessed at 1 5min, 30 min, 45 min, 1 hour and 4 hours by nursing or study personnel)
• Breastfeeding success and quality

The primary outcome will be measured at baseline (entry to post-anesthesia care unit, and immediately after QLB) and at 1 hour, 4 hours, 24 hours, and 48 hours following completion of the QLB. Follow-up will occur in the recovery room and in patient's rooms.

2.18 Describe the statistical approaches that will be used to analyze the study data.

* Addressed below:

The primary outcome is the mean numeric rating scale (NRS) pain scores with activity at 24 hours after completion of the quadratus lumborum block. The primary outcome will be compared between groups using the two-tailed unpaired Student t-test. Interval and ordinal data will be compared between groups using the two-tailed Student's t-test or the Mann-Whitney U-test after testing for normal distribution. Categorical data will be compared using a Chi-Square statistic or the Fisher's exact test.

We will apply Bonferroni correction for multiple comparisons. The time-to-first-supplemental opioid analgesic request will be compared by Cox proportional hazard modeling. Subjects who do not request additional analgesia will be censored at the time of delivery. $P < 0.05$ will be used to reject the null hypothesis.

!section: Section 2 - Research Design and Methods!

[reviewer notes-,]

2.19

Will this research be conducted in (a) a foreign country and/or (b) at a site (e.g., Navajo Nation) where the cultural background of the subject population differs substantially from that of Pittsburgh and its surrounding communities?

* No

Note that copies of training records, licenses, certificates should be maintained in the study regulatory binder and are subject to audit by the Research Conduct and Compliance Office (RCCO).

In addition, individuals planning to conduct human subject research outside the United States must complete an optional module on the CITI training website: International Studies. Click here to access the instruction sheet for accessing optional CITI modules.

[reviewer notes-,]

2.21

Will this research study be conducted within a nursing home located in Pennsylvania?

* No

[reviewer notes-,]

Section 3 - Human Subjects

3.1 What is the age range of the subject population?

Women of childbearing age >/= 18 years of age will be enrolled

3.2 What is their gender?

* Females only - Provide a justification for limiting enrollment to only one gender.

Provide a justification if single gender selected:
Because we are looking at post-operative pain control after cesarean , this study must be limited to women as only women can become pregnant and thus have the need to undergo a cesarean for delivery.

3.3 Will any racial or ethnic subgroups be explicitly excluded from participation?

* No

If **Yes,** identify subgroups and provide a justification:

3.4

For studies conducted in the U.S., do you expect that all subjects will be able to comprehend English?

* Yes

[reviewer notes,]

3.5 Participation of Children: Will children less than 18 years of age be studied?

* No

If **No,** provide a justification for excluding children:
While it is possible for children under the age of 18 to become pregnant, this age range is not typically representative of the population that we wish to evaluate in this study. It is also more challenging for children under the age of 18 to provide accurate medical histories, comprehend the risks and benefits of the study and interventions, be cooperative during spinal or peripheral nerve block procedures (such as the QLB), and provide accurate feedback regarding their participation in the study.

[reviewer notes-,]

3.6 Does this research study involve prisoners, or is it anticipated that the research study may involve prisoners?

* No

[reviewer notes,]

3.7 Will pregnant women be knowingly and purposely included in this research study?

* Yes

General Requirements: The Federal Policy **[45 CFR 46, Subpart B]** specify that research involving pregnant women and/or fetuses must also confirm to each of the

following criteria. Describe how your study meets each of th jlg)irfi l'E@ n 3 - Human Subjects!

3.7.1 **Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses.** ***[45 CFR 46.204 (a)]*** [Include references]

*

The experimental intervention in this study will be performing a quadratus lumborum block (QLB). This block will be performed at the conclusion of an elective cesarean section, thus at that time the baby will have already been delivered and the mother will no longer technically be pregnant. Furthermore, the risk of withholding intrathecal morphine from some patients will only affect pain control following delivery when the mother is no longer pregnant. There should therefore be no risks to the fetus at all as a result of this study. Any risks to the mother such as the potential for increased pain when not receiving intrathecal morphine and any possible side effects as a result of the QLB will occur after delivery and thus pose no risks to her pregnancy.

3.7.2 **The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the women or the fetus; or, if there is no such prospect of direct benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.** ***[45 CFR 46.204 (b)]***

*

For the reasons described above in section 3.7.1, there should be no risks to the fetus as a result of this study.

3.7.3 **Any risk is the least possible for achieving the objectives of the research.** ***[45 CFR 46.204 (c)]***

*

All efforts are being taken during the design of this study, and will be during implementation, to ensure that any risks associated with this study are minimized as much as possible.

3.7.4 **No inducements, monetary or otherwise, will be offered to terminate the pregnancy.** ***[45 CFR 46.204 (h)]***

*

No inducements of any type will be offered to terminate the pregnancy.

3.7.5 **Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.** ***[45 CFR 46.204 (i)]***

*

No individual engaged in this research will have any part in anything related to the termination of pregnancy. The goal of all patients in this study will be the delivery of a living and healthy infant.

3.7.6 **Individuals engaged in the research will have no part in determining the viability of a neonate.** ***[45 CFR 46.204 (j)]***

*

No individuals engaged in this research will have any role in determining the viability of any neonate. Viability of neonates is determined at Magee by neonatologists specialized in neonatal intensive care.

!section: Section 3 - Human Subjects!

[reviewer notes-,]

3.8 Does this research study involve neonates of uncertain viability or nonviable neonates?

* No

[reviewer notes.]

3.9 Fetal Tissues: Does this research involve the use of fetal tissues or organs?

* No

!section: Section 3 - Human Subjects!

[reviewer notes-,]
--->

3.10

What is the total number of subjects to be studied at this site, including subjects to be screened for eligibility?

Note: The number below is calculated by summing the data entered in question 3.11. Any additions or changes to the values entered in 3.11 will be reflected in 3.10.

* 60

3.11

Identify each of the disease or condition specific subgroups (include healthy volunteers, if applicable) that will be studied.

Click on the "Add" button and specify for each subgroup:

1) how many subjects will undergo research related procedures at this site; and

2) if applicable, how many subjects will be required to undergo screening procedures (e.g., blood work, EKG, x-rays, etc.) to establish eligibility. Do Not include subjects who will undergo preliminary telephone screening.

*

	Subgroup	Number to undergo research procedures	Number to undergo screening procedures
View	Control (ITM plus sham QLB)	26	30
View	Experimental (ITM plus upl•vacai•ne QLB)	26	30

3.12 **Provide a statistical justification for the total number of subjects to be enrolled into this research study at the multicenter sites or this site.**

* Described below:

The primary outcome is the mean numeric rating scale (NRS) pain scores with activity at 24 hours after completion of the quadratus lumborum block. Previous work comparing dynamic pain outcomes among women undergoing cesarean delivery with and without quadratus lumborum block 1 reported median [IQR] pain scores at 24 hours of 2[0-3] in the intervention group and 4[2-5] in the control group. Mean and standard deviation were estimated from this data using mean=median and SD = IQR/1.35.2 For 2 groups, a total sample of 60 subjects (26 in each group completed) is estimated to achieve 80% power to detect differences among the NRS means versus the alternative of equal means using an F test with a 0.05 significance level. The size of the variation in the means represented by the standard deviation is assumed to be 1.00, with a common standard deviation within a group of 2.22. To account for subject dropout and/or ineligibility, 60 subjects will be screened for randomization into 2 groups, with 30 subjects to be screened for each group.

1. Blanco R, Ansari T, Girgis E. Quadratus lumborum block for postoperative pain after caesarean section: A randomised controlled trial. Eur J Anaesthesiol. 2015 Nov;32(11):812-8.
2. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol. 2005 Apr 20;5:13.

!section: Section 3 - Human Subjects!

[reviewer notes-,]

3.13 Inclusion Criteria: List the specific criteria for inclusion of potential subjects.

Elective cesarean planned under spinal anesthesia
Singleton pregnancy
American Society of Anesthesiologists (ASA) classification score of 2 (or less)
Gestational age of at least 37 weeks
Intention to breastfeed infant

3.14 Exclusion Criteria: List the specific criteria for exclusion of potential subjects from participation.

Contraindications to neuraxial blockade (such as clinically relevant coagulopathy, recent anticoagulant use, patient refusal, or localized skin infection overlying the site of needle entry)

Anatomical abnormalities contraindicating spinal or QLB placement

Received/Conversion to general anesthesia

Received supplemental parenteral anesthesia (sedation) for any reason (e.g. unanticipated prolonged surgical procedure)

History of chronic pain

History of chronic opioid use/abuse

History of Subutex, methadone, other maintenance therapy

3.15 Will HIV serostatus be evaluated specifically for the purpose of participation in this research study?

* No

If **Yes,** provide a justification:

!section: Section 4 - Recruitment and Informed Consent Procedures!

[reviewer notes-,]

4.1 Select all recruitment methods to be used to identify potential subjects:
Other Strategies: Described below

4.2

Provide a detailed description of your recruitment methods, including identifying and initiating contact with participants:

All subjects approached for enrollment into this study are patients being seen by investigators during the course of normal clinical care. Screening of potential patients will occur by obstetirical OR schedule. After review, potential patients will havetelephone contact with subjects 2-3 days prior to the scheduled elective surgery.

The day of surgery the Anesthesia care team sees the patient. The current process at Magee Women's Hospital is for the anesthesia team to see all patients who come in for scheduled, elective cesarean deliveries in the pre-op holding area approximately 20-60 minutes before the scheduled start of their cesarean. During this visit, we typically review their history with them, explain the anesthetic plan, and obtain consent for the anesthesia.

For this study, for eligible participants, we will also utilize this visit to also explain the study to them; the risks and benefits of QLB and of participation will be explained, and a waiting period achieved as previously described. Informed consent will then be obtained from accepting participants, as screened and addressed with prior phone call. The study will be described and consent obtained by either the PI or one of the listed co-investigators for the study.

Note: Questions jump from 4.2 to 4.6 as questions 4.3-4.5 have been removed and the information is now captured in 4.1

[reviewer notes-,]

4.6 **Are you requesting a <u>waiver to document</u> informed consent for any or all participants, for any or all procedures? (e.g., a verbal or computerized consent script will be used, but the subjects will not be required to sign a written informed consent document.** ***This is not a waiver to obtain consent.***

* No

!section: Section 4 - Recruitment and Informed Consent Procedures!

[reviewer notes-,]

4.7 **Are you requesting a waiver to obtain informed consent or an alteration of the informed consent process for any of the following?**

* No

4.7.1 If **Yes, select the reason(s) for your request:**
There are no items to display

General Requirements: The Federal Policy **[45 CFR 46.116 (d)]** specifies in order for a waiver of consent to be approved, the request must meet four criteria. For each request, you will be asked to provide a justification addressing how each of these criterion is met.

[reviewer notes-,]

4.8 **Are you requesting an exception to the requirement to obtain informed consent for research involving the evaluation of an 'emergency' procedure?**

Note: This exception allows research on life-threatening conditions for which available treatments are unproven or unsatisfactory and where it is not possible to obtain informed consent.

* No

!section: Section 4 - Recruitment and Informed Consent Procedures!

[reviewer notes-,]

4.9

Upload all consent documents for watermarking:

Draft Consent Forms for editing:

Name	Modified Date
Informed Consent Form track changes revision	7/26/2017 3:23 PM

Approved Consent Form(s):

Name	Modified Date
Informed Consent Form track changes revision	7/26/2017 3:23 PM

[reviewer notes-,]

4.10 **Will all potential adult subjects be capable of providing direct consent for study participation?**

*

Yes

!section: Section 4 - Recruitment and Informed Consent Procedures!

[reviewer notes-,]

4.11 **At what point will you obtain the informed consent of potential research subjects or their authorized representative?**

After performing certain of the screening procedures, but prior to performing any of the research interventions/interactions

4.11.1 **Address why you feel that it is acceptable to defer obtaining written informed consent until after the screening procedures have been performed.**

The "screening procedures" that will be involved in this study simply involve confirming that it is a singleton pregnancy at 37 weeks gestational age or greater and that there are no contraindications to neuraxial blockade or performing a quadratus lumborum block. All of this information will be easily obtained by talking to the patient during the routine anesthesia visit that occurs prior to any scheduled cesarean. If during this visit, the patient is noticed to meet all of the inclusion and exclusion criteria, then the study will be explained to them and consent for the study obtained. If during this visit, the patient is noticed to not meet the inclusion and exclusion criteria, then we will not explain the study to them and will instead just proceed with routine care for their cesarean. Whether patients participate in the study or not, investigators will still be part of their anesthesia care team.

4.11.2 **Taking into account the nature of the study and subject population, indicate how the research team will ensure that subjects have sufficient time to decide whether to participate in this study. In addition, describe the steps that will be taken to minimize the possibility of coercion or undue influence.**

All potential study participants will be contacted subjects will be contacted 2-3 days prior to the procedure. They will have discussion of the study to allow for decision for participation. This should give ample time to describe the study, answer any questions. The day of surgery, patients will also be approached and look over the consent. It will be made clear to the patients that their participation is completely voluntary and that any refusal to participate will not affect their care in any way. We perform a large number of elective cesareans at Magee, thus even if many refuse we still anticipate no challenges in getting the numbers we need for the study. Any coercion or undue influence to obtain participants would be neither ethically or morally desired, nor at all necessary to complete the study in a timely fashion.

[reviewer notes,]

4.12 **Describe the process that you will employ to ensure the subjects are fully informed about this research study.**

* Not applicable; see previous request for a waiver of informed consent for all aspects of this research study (question 4.7)

This description must include the following elements:

- who from the research team will be involved in the consent process (both the discussion and documentation);
- person who will provide consent or permission;
- information communicated; and
- any waiting period between informing the prospective participant about the study and obtaining consent

In addition, address the following if applicable based on your subject population:

- process for child assent and parental permission

- continued partici ll!>riif: **<Eebtl@ att.111!mMltchtftflD7 4N!i:m!;ent** Procedures!
- process for obtaining proxy consent and assent for decisionally impaired subjects
  - continued participation if subject regains capacity to consent

Once the patient has confirmed booking for a scheduled, elective cesarean, they will be contacted 2-3 days prior to the scheduled C-section. Then a discussion will be made to describe the study, answer questions related to procedures and, if the subject is interested, indicate the informed consent process will take place in the pre-op hold area the day of surgery.

The day of surgery, the patient will approached by either the PI or another physician listed as a co-investigator for this study, who will be responsible for both discussing the study and documenting the consent. The patients themselves will be the ones to provide the consent. PI and the other physician co-investigators are all part of the L&D anesthesia care team, and will be part of the team providing clinical care to the patient regardless of whether they choose to participate in the study or not. Information communicated will include the risks and benefits of spinal anesthesia for cesarean, including the risks and benefits of receiving the current standard of care for post-operative pain. The quadratus lumborum block (QLB) will also be discussed in detail including how the procedure is performed and the risks and benefits of having it done. The patient's medical history will be reviewed with them in the usual fashion as is already routinely done by the anesthesia team prior to any scheduled cesarean. Once the patient has been fully informed regarding the study and anesthetic plan, and all questions have been answered, they will be given the consent form with enough time to review it in its entirety. Once they are satisfied with the consent and all of the information they have received, and all of their questions have been answered, they will then be asked to sign the consent form if they wish to participate. Thus, informing them about the study and explaining the consent will both be done at the same visit, and the amount of time of time between them should be minimal (it will only be determined by how many questions the patient has and how much time they would like to spend looking over the consent form prior to signing). If they wish, they can keep the consent form to consider things for as long as they wish prior to signing, and the research team will respect that time.

4.13

Are you requesting an exception to either IRB policy related to the informed consent process?

- For studies involving a drug, device or surgical procedures, a *listed physician* investigator is required to obtain the written informed consent unless an exception to this policy has been approved by the IRB
- For all other studies, a *listed* investigator is required to obtain consent (Note: In order to request an exception to this policy, the study must be minimal risk)

* No

If **Yes,** provide a justification and describe the qualifications of the individual who will obtain consent:

4.14 **Will you inform research subjects about the outcome of this research study following its completion?**

* No

If **Yes,** describe the process to inform subjects of the results:

!section: Section 5 - Potential Risks and Benefits!

[reviewer notes-,]

5.1

Describe potential risks (physical, psychological, social, legal, economic or other) associated with screening procedures, research interventions/interactions, and follow-up/monitoring procedures performed specifically for this study:

*

	Research Activity:	Access to PHI
	Common Risks:	*No Value Entered*
	Infrequent Risks:	Breach of confidentiality
	Other Risks:	*No Value Entered*
View	**Research Activity:**	Bupivacaine
	Common Risks:	*No Value Entered*
	Infrequent Risks:	*No Value Entered*
	Other Risks:	Maternal: Restlessness, anxiety, dizziness, tinnitus, blurred vision, or tremors, depression of the myocardium, decreased cardiac output, heartblock, hypotension, bradycardia, ventricular arrhythmias, allergic type reactions. Newborn: Infant lethargy after breastfeeding.
	Research Activity:	Follow-up: Pain and Breastfeeding Questions
	Common Risks:	Inconvenience
	Infrequent Risks:	Loss of confidentiality
	Other Risks:	frustration or embarrassment (if breastfeeding is unsuccessful).
	Research Activity:	Research intervention -quadratus lumborum block
	Common Risks:	*No Value Entered*
	Infrequent Risks:	bleeding, infection, damage to surrounding structures
	Other Risks:	*No Value Entered*
	Research Activity:	Screening procedures
	Common Risks:	*No Value Entered*
	Infrequent Risks:	Loss of confidentiality
	Other Risks:	*No Value Entered*

5.1.1 **Describe the steps that will be taken to prevent or to minimize the severity of the potential risks:**

The quadratus lumborum block (QLB) will be performed by anesthesiology physicians trained in the procedure in the OR in a sterile fashion (sterile prep, sterile gloves, sterile field) to minimize any risk of infection. It will be performed under ultrasound guidance to minimize the risk of any damage to surrounding structures or bleeding. A low concentration of local anesthetic has been chosen for the block, and the total amount administered will be within the known safe total dosage.

To minimize the risks of loss of confidentiality, any data collected by any interactions with participants for the purpose of this research will be stored on departmental computers (password protected, secure servers) or in locked cabinets in faculty offices. Data will be

de-identified for name, **MRN,** date of birth, and other identifiers prior to analysis.

5.2

What steps will be taken in the event that a clinically significant, unexpected disease or condition is identified during the conduct of the study?

* **Addressed below:**

Any unexpected diseases or conditions identified during the conduct of this study will be handled in the usual, routine manner. The anesthesia team remains on the labor and delivery floor 24/7 and is responsible for following the patient throughout their delivery and identifying and managing any complications that may arise. This process will not change as a result of this study. Patients enrolled in this study will also have close follow-up, particularly in the firs 2 hours following their procedure, and any patients having a cesarean typically remain inpatient for at least two days. If anything comes up, there will be a trained anesthesia provider immediately available to assess and if necessary treat the patient. If any other specialties need to be consulted for any reason that can be easily done as well. Any complications that may arise after the patient has been discharged from the hospital are not anticipated, however, should they arise, the patient will have the contact information of the anesthesia service with the ability to contact us 24/7 with any questions or concerns.

5.3 All the risk questions (screening, intervention/interaction, follow-up) have been merged into one question (5.1).

[reviewer notes,]

5.4 **Do any of the research procedures pose a physical or clinically significant psychological risk to women who are or may be pregnant or to a fetus?**

* No

[reviewer notes,]

5.5 **Do any of the research procedures pose a potential risk of causing genetic mutations that could lead to birth defects?**

* No

[reviewer notes,]

5.6

Are there any alternative procedures or courses of treatment which may be of benefit to the subject if they choose not to participate in this study?

* Yes - Describe below:

If **Yes,** describe in detail:
If a subject chooses not to participate in the study, they will receive standard of care which includes spinal anesthesia with ITM, multimodal postoperative analgesia as described, and no QLB.

[reviewer notes-,]

5.7

Describe the specific endpoints (e.g., adverse reactions/events, failure to demonstrate effectiveness, disease progression) or other circumstances (e.g., subject's failure to follow study procedures) that will result in discontinuing a subject's participation?

* Describe below:

Discontinuing a subject's participation may result if the subject refuses to follow any of the study protocols (e.g. if they are assigned to the quadratus lumborum block group but then change their mind and do not allow the block to be performed), or if there is any other breach in protocol. They will also be withdrawn if there is an alteration in their clinical condition leading to a change in anesthetic plan such as the need to convert to general anesthesia. Study subjects may also voluntarily choose to withdraw from the study at any time without prejudice to their care.

[reviewer notes-,]

5.8

Will any individuals other than the investigators/research staff involved in the conduct of this research study and authorized representatives of the University Research Conduct and Compliance Office (RCCO) be permitted access to research data/documents (including medical record information) associated with the conduct of this research study?

* Yes

5.8.1

Identify the 'external' persons or entity who may have access to research data/documents and the purpose of this access:

Research data may be shared with secondary investigators with similar research interests as well as authorized representatives of UPMC hospitals, court of law and DHHS.

5.8.2

Will these 'external' persons or entity have access to identifiable research data/documents?

*

No; the research data/documents will be coded and subject identifiers removed prior to access by the external persons

If **Yes,** describe how they will protect the confidentiality of the research data:

5.9

Has or will a Federal Certificate of Confidentiality be obtained for this research study?

* No

5.10

Question has been moved to 5.17

5.11

Question has been moved to 5.16

[reviewer notes-,]

5.12 Does participation in this research study offer the potential for direct benefit to the research subjects?

Yes - Describe the direct benefit that subjects may receive as a result of study participation. Indicate if all, or only certain, of the subjects may derive this potential benefit.

Describe the benefit:
All patients participating in this study have the potential to receive direct benefit in the form of possible improved pain control following the procedure. Improved pain control can also lead to other direct benefits such as having an easier time breastfeeding, being better able to bond with and care for their newborn earlier, and potentially being ready for discharge from the hospital sooner.

5.13 Describe the data and safety monitoring plan associated with this study. If the research study involves multiple sites, the plan must address both a local and central review process.

The incidence of any adverse events including any potential complications related to the quadratus lumborum block or inadequate post-operative pain control in any study group will be monitored and documented daily. Any adverse events will be immediately reported to the PI. Any serious adverse event resulting from this study (which are extremely unlikely) would be immediately reported by the PI to the IRB and appropriate action taken. All collected data will be de-identified and stored on departmental computers on secure servers and accessible only by the PI. The PI will have full oversight of the data and safety monitoring plan (DSMP), and will participate along with the other listed co-investigators in the local data safety monitoring. The DSMP will include monitoring for breach of confidentiality, deviations, data safety, changes to risk / benefit ratio, progress of the study, recruitment and retention, timeliness and quality of the data, AEs, UAPs, and subject withdrawals. The monitoring will occur continually during the study with each enrollment of a new subject, and is being completed to maintain the safety of all participants. All Data and Safety Monitoring meeting reports will be submitted to the IRB at the time of study renewal.

[reviewer notes-,]

Section 5 - Potential Risks and Benefits of Study Participation

5.14

What precautions will be used to ensure subject privacy is respected? (e.g. the research intervention will be conducted in a private room; the collection of sensitive information about subjects is limited to the amount necessary to achieve the aims of the research, so that no unneeded sensitive information is being collected, drapes or other barriers will be used for subjects who are required to disrobe)

Data collection will be limited to the minimum amount necessary to achieve the aims of the research, and the large majority of the information that will be screened for in this study is information that is already routinely screened during routine care. All patient interactions including the initial screening and consenting, spinal placement, quadratus lumborum block placement, and follow-up evaluation will be conducted while the patient is admitted to the hospital in either the pre-op holding area, operating room, recovery room, or their private patient room. Any documented patient information will be de-identified at the time of it being recorded and only the key (accessible only by PI) will be able to link it to specific patients. Patient privacy/modesty during the spinal and quadratus lumborum block procedures will be handled in the same standard fashion as it routinely is and includes keeping the patient covered as much as is possible.

5.15

What precautions will be used to maintain the confidentiality of the research data during collection, transmission and storage? It **is important that you indicate the data security measures for all data types.**

Go to the A-Z Guidance, download the Data Security Assessment Form, complete, and upload using the Add button below. Depending on the data type, you may need to consult with your data manager to address some of the sections. Email irb@pitt.edu if you have any questions.

* **Upload Data Security Form:**

Name	Modified Date
Data Security Form	2/9/2017 11:53 AM

Address what precautions will be used to maintain the confidentiality of the research data collected in paper format if applicable:
The system for maintaining patient confidentiality will be to immediately code patient information. Once enrolled, each patient will be given a study ID number. Paper data collection forms will then be used which contain the study ID number and blank spaces to document the relevant data. Other than the study ID number, no other information that can identify the specific patient will be included on the data collection form. All paper data collection forms will be stored in a locked file cabinet in the locked UPMC office of the PI. A single electronic master list connecting each study ID number to the specific patient will be kept on a password protected spreadsheet on a password protected UPMC desktop computer with a secure server behind the UPMC firewall.

5.15.1

Does your research study require a data security review? Answer Yes if any of the following conditions are met:

- Identifiable or *coded data will be collected, stored, or transmitted using any of the following technologies: mobile app, web-based site or survey, wearable device, text messaging, electronic audio, photographic, or video recording or conferencing **and/or**
- The IRB requested a data security review during their review of the study

* Yes

***Coded:** Identifying information (such as name) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a code (number, letter, symbol, or any combination) and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens

5.16

If **the subject withdraws from the study, describe what, if anything, will happen to the subject's research data or biological specimens.**

If a subject withdraws from the study, they will be informed that any study data collected up to that point will be kept and reported, but that no new study data will be obtained or documented.

5.17

Following the required data retention period, describe the procedures utilized to protect subject confidentiality. (e.g., destruction of research records; removal of identifiers; destruction of linkage code information; secured long-term retention)

Following the required data retention period, the electronic key linking each individual patient to their collected data (stored in a secure, locked location) will be destroyed. Individual, coded, data collection sheets will be maintained indefinitely in a secure and locked location for a minimum of seven years after final reporting or publication of a project. Following the required retention period they too will be destroyed. No collected data will be kept longer than what is required.

!section: Section 6 - Costs and Payments!

[reviewer notes-,]

6.1 **Will research subjects or their insurance providers be charged for any of the procedures (e.g., screening procedures, research procedures, follow-up procedures) performed for the purpose of this research study?** *

No

[reviewer notes-,]

6.2 **Will subjects be compensated in any way for their participation in this research study?**

* No

!section: Section 7 - Qualifications and Source(s) of Support!

[reviewer notes-,]

7.1

Summarize the qualifications and expertise of the principal investigator and listed co-investigators to perform the procedures outlined in this research study.

The principal investigator, Nicholas Schott, MD is a staff anesthesiologist at Magee Women's Hospital o the OB team. He is fellowship trained in acute pain and regional anesthesia. As an acute pain doctor, he performs a wide variety of peripheral nerve blocks daily and has extensive experience performing the quadratus lumborum block.

Jonathan Waters, MD is an attending anesthesiologist and the chief at the department of anesthesiology at Magee Women's Hospital. He is also the director of the Clinical Trials Program at UPMC. He has extensive experience in all aspects of the anesthetic management of obstetric patients and has performed numerous spinal procedures and peripheral nerve blocks over his career.

Grace Lim, MD is an attending obstetric anesthesiologist and the current director of obstetrical anesthesia at Magee Women's Hospital. Her subspecialty training in clinical obstetrical anesthesia, coupled with additional formal research training toward a Master of Science in clinical research makes her well-suited to inform the study design and execution of this trial. She has a track record of successful protocol development, implementation, study team coordination, and/or publication for clinical studies and trials in the obstetric population.

Patricia Dalby, MD is a current attending obstetric anesthesiologist and the current director of the obstetric anesthesiology fellowship program at Magee Women's Hospital with extensive clinical obstetric anesthesia experience for >20 years. She has significant experience in the anesthetic management of obstetric patients throughout the puerperium.

Thomas Vernon, MD is a former Obstetrical Anesthesiology fellow who has completed training the the specifics and management of complex obstetrical anesthesia care. This includes a high risk procedures as well ad a grand expertise in preforming obstetrical anesthesia. He is also a contributor to this project from the start. His current association is as a staff anesthesiologist for the Arizona Anesthesiologists Consultants group in Arizona, USA.

!section: Section 7 - Qualifications and Source(s) of Support!

[reviewer notes-,]

7.2 Indicate all sources of support for this research study.

*

Selections

Internal: Department funds

If **Federal** support, provide the sponsor information:
Federal sponsor Grant Title Grant number Awardee institution Federal grant application

For projects not supported by a federal grant, upload the research plan that was submitted for funding:

Name Modified Date

If **Industry** support, provide the sponsor information and level of support:
N/A

If **Foundation** support, provide the sponsor information:
N/A

If **Other** support, provide the support information and level of support:
N/A

!section: Section 7 - Qualifications and Source(s) of Support!

[reviewer notes-,]

7.3

Is this study funded in part or whole by a PHS Agency?

* No

Does any investigator* involved in this study (select all that apply):

	Name
☐	**A.** Have equity in a **publicly-traded entity** that either sponsors** this research or owns the technology being evaluated or developed that exceeds a **5% ownership interest** or a current value of **$10,000?**
☐	**B.** Have equity in a **non-publicly-traded entity** that either sponsors this research or owns the technology being evaluated or developed?
☐	**C.** Receive salary, consulting fees, honoraria, royalties or other remuneration from an entity that either sponsors this research or owns the technology being evaluated or developed that is expected to exceed **$10,000** during the past or next 12 months?
☐	**D.** Have rights as either the author or inventor of **intellectual property** being evaluated or developed in this research that is the subject of an issued patent or has been optioned or licensed to an entity?
☐	**E.** Have an officer or management position**** with a **Licensed Start-up Company** overseen by the COI Committee that either sponsors this research or owns the technology being evaluated or developed?
☐	**F.** Receive compensation of any amount when the value of the compensation would be affected by the outcome of this research, such as compensation that is explicitly greater for a favorable outcome than for an unfavorable outcome or compensation in the form of an equity interest in the entity that either sponsors this research or owns the technology being evaluated or developed?
☑	**None of the above options apply and there are no other financial conflicts of interest in the conduct of this research.**

***Investigator** means the PI, co-investigators, and any other member of the study team, regardless of title, who participates in the design, conduct, or reporting of this research, as well as his/her spouse, registered domestic partner, dependents, or other members of his/her household. **The PI is responsible for ensuring that s/he and all other relevant members of the study team review the above questions describing Significant Financial Interests.**

**through the provision of funds, drugs, devices, or other support for this research

****Such as serving on the Board of Directors or Board of Managers or a position that carries a fiduciary responsibility to the company (e.g., CEO, CFO, CTO, or CMO).

!section: Supporting Documentation!

[reviewer notes-,]

Supporting Documentation Section

References and Other Attachments

Additional documents:

Name	Modified Date	Version
QLB Study References	12/20/2016 1:00 PM	0.01
Ramsay Sedation Scale	12/20/2016 4:46 PM	0.01

Please use the Add button to the left to upload additional documents if needed.

[reviewer notes-,]

Clinica/Trials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

"Applicable clinical trials" are required **by federal law** to be registered in ClinicalTrials.gov.

Applicable Clinical Trials (ACTs) are studies that meet the following criteria:

- The study is an interventional study AND
- The study intervention is a drug, biologic, medical device, radiation or genetic AND
- The Study is not Phase 0 or 1 AND
- The study has at least one site in the United States or is conducted under an investigational new drug application or investigational device exemption

NIH Policy

Effective January 18, 2017, revised NIH Policy requires that all clinical trials funded in whole or in part by the NIH be registered and results information posted on ClinicalTrials.gov.

As defined by the NIH, a clinical trial is:

> *A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health related biomedical or behavioral outcomes.*

The NIH Policy extends beyond the Food and Drug Administration Amendment Act (FDAAA 801) requirements in that it requires registration and results reporting of:

- clinical trials of behavioral, surgical and other types of health and medical interventions
- phase 1 studies of drugs and biological products
- small feasibility studies of device products

Failure to submit all required registration and results information requested on ClinicalTrials.gov can jeopardize University grant funding, the future funding of the grantee and subject the University of Pittsburgh to future monetary penalties.

In addition, to promote transparency of the clinical trials process, the International Committee of Medical Journal Editors (ICMJE) has established a policy requiring the entry of clinical trials in a public registry, such as ClinicalTrials.gov, prior to subject enrollment as a condition of consideration for publication of the trial results.

* **Based on the above information, will this study be registered in ClinicalTrials.gov?**

Yes !section: Supporting Documentation!

Who will serve as the Responsible Party? UPMC/Pitt Investigator or IND/IDE Pitt Sponsor

Why are you registering your study? (Check all that apply)

It is strongly encouraged by the NIH

It is required for publication by the **International Committee of Medical Journal Editors** (*Registration is required in a publically available, searchable database system prior to informed consent being obtained from the first study participant)*

If you are not yet registered and need to establish an account for the PI or other research staff that may need to access the record, please send an email to the University of Pittsburgh PRS administrator at ctgov@pitt.edu with the following information for each individual:

- **Full** name
- Telephone number
- Pitt or UPMC email address

If you have any questions or concerns, please email us at ctgov@pitt.edu.

To find out additional information about how to register your study go to:
https://www.clinicaltrials.gov/ ct2/manage-recs/how-register