RESEARCH SUBJECT
INFORMED CONSENT FORM

Protocol Title: ***Protocol for a Single Center Randomized Controlled Trial of Liposomal Bupivacaine Intercostal Nerve Blockade versus Continuous Thoracic Epidural for Regional Analgesia in Patients with Multiple Rib Fractures***

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Why am I being invited to volunteer?

You are being invited to participate in a research study. "Research" designates an activity designed to test a hypothesis, permit conclusions to be drawn and thereby to develop or contribute to generalizable knowledge, whereas "practice of medicine" refers to interventions designed solely to enhance the well-being of an individual patient. Research subjects may or may not benefit from research procedures. Federal regulations require that you are informed of the research you are being invited to volunteer for and your signature indicating that you have been informed about the research. You are being invited to volunteer since you meet the requirements for enrollment into this study. Your participation is voluntary which means you can choose whether or not you want to participate. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being

in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be invited to sign this form. Your signature on this form is voluntary and does not waive any of your legal rights or make any institutions or persons involved in this research any less responsible for your well-being. You are free to refuse to participate or to withdraw from the study at any time without penalty or loss of benefits to which you would otherwise be entitled.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

Who is the Principal Investigator for this Study?

Dr. Chadrick Evans
UICOMP Department of Surgery
North Building, 2nd Floor
624 NE Glen Oak Avenue
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(309) 655-2383

What is the purpose of this research study?

The purpose of this study is to compare epidural pain relief to a nerve block with liposomal bupivacaine to determine which one provides better pain relief in patients with rib fractures.

How long will I be in the study?

You will be actively participating in this study for up to 96 hours after your enrollment. Active participation means we will collect data related to your pain and injuries for 96 hours or less. This does not mean you will only be in the hospital for 96 hours. We will also analyze other data collected passively from you during your entire hospital stay. You will remain in the hospital as long as required based on your level of injury and care needs. We expect the enrollment period for this study to be open for a minimum of one year.

How many other people will be in the study?

Our study will ideally enroll a minimum of 44 patients.

What is involved in this study?

Upon agreeing to participate in this study, the study team will assign you to one of two study arms for pain relief. This assignment is random and unknown to the team at the time you sign this consent form.

If you are assigned to the first study arm, you will receive pain relief for your rib fractures through an epidural. Once assigned, a specialist will be consulted. This specialist will then place the epidural in your upper back. This epidural will remain in place for an uncertain amount of time. The decision to remove the epidural will be determined by your physician and will be based on your level of pain and injury. However, only your pain scores during the first 96 hours after the epidural is placed will be used for analysis. You can request intravenous and oral pain medications for breakthrough pain. After the epidural is removed, you will remain in the hospital until discharged by your attending physician.

If you are assigned to the second study arm, you will receive a nerve block with the medication liposomal bupivacaine, also called Exparel®. Once assigned, a University of Illinois surgeon, or resident surgeon, will administer the nerve block. The nerve block is expected to provide pain relief from 72 to 96 hours. During this time, you may request oral or intravenous pain medication for breakthrough pain. You will remain in the hospital until discharged by your attending physician.

What about Confidentiality?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Federal government regulatory agencies
- The Peoria Institutional Review Boards (the committees charged with overseeing research on human subjects)
- The Office of Human Research Oversight (the office which monitors research studies)

Your enrollment paper work will be kept in a locked office and filing cabinet in the Surgery Department offices located in the North Building of OSF ST. Francis Medical Center. Your name, age, and medical record number will be shared with the research team and the OSF St. Francis research office to allow review of your clinical data for purposes of this study only. Your information will not be shared with any other individuals or organizations outside of those listed above, apart from clinical staff at OSF St. Francis that may need to know your name and enrollment status to appropriately care for you.

Data collected during your participation in this study will remain confidential to Dr. Chadrick Evans, Dr. Melissa Medina, and sub-investigators deemed appropriately qualified by Dr. Evans and the Peoria IRB. This data will be kept in a password protected file shared between the previously listed individuals. This data will be shared through the encrypted server system provided to University of Illinois College of Medicine faculty and staff called *Sharepoint*.

What are the possible risks or discomforts?

There may be unexpected or unanticipated problems that may arise during your participation in this study. Most of the anticipated or know side effects are listed below, but they will vary from person to person. You should discuss these with the research team and/or your regular physician. Other drugs may be given to make side effects less serious and discomforting. Many side effects will go away after the epidural is removed, or the liposomal bupivacaine nerve block wears off. However, in some cases side effects can be serious or long-lasting or permanent. Risks and side effects related to the epidural and liposomal bupivacaine nerve blocks we are studying include:

Epidural

Likely

- Altered sensation, numbness, and weakness in regions of the body supplied by nerves at the level of the epidural. These effects may extend to regions adjacent, and nerves above or below, the epidural due to diffusion of the anesthetic contained in the epidural.
- Discomfort during and after the insertion of the epidural

Less Likely

- Urinary retention
- Low blood pressure
- Itching
- Slow heart rate
- Infection at the site of administration

Rare but serious

- Epidural hematoma
- Epidural abscess
- Dural and subarachnoid puncture leading to injection of anesthesia into spinal fluid

- Spinal cord injury
- Meningitis
- Respiratory failure
- Intravascular injection of anesthesia
- Toxic effects on your heart and central nervous system from the anesthesia

Liposomal Bupivacaine (as reported on the drug label from clinical trial experience)

Likely

- Altered sensation and numbness in your back and chest over the regions supplied by the nerves we block
- Nausea
- Vomiting
- Constipation

Less Likely

- Dizziness
- Itching
- Low heart rate
- Fast heart rate
- Increased body temperature
- Edema or swelling in your extremities
- Anemia postoperatively
- Low blood pressure
- Headache
- Difficulty sleeping
- Muscle spasm
- Back Pain
- Excessive sleepiness
- Pain from your rib fractures and application of the nerve block

Rare

- chills, erythema, bradycardia, anxiety, urinary retention, pain, edema, tremor, dizziness postural, paresthesia, syncope, incision site edema, procedural hypertension, procedural hypotension, procedural nausea, muscular weakness, neck pain, pruritus generalized, rash pruritic, hyperhidrosis, cold sweat, urticaria, bradycardia, palpitations, sinus bradycardia, supraventricular

extrasystoles, ventricular extrasystoles, ventricular tachycardia, hypertension, pallor, anxiety, confusional state, depression, agitation, restlessness, hypoxia, laryngospasm, apnea, respiratory depression, respiratory failure, body temperature increased, blood pressure increased, blood pressure decreased, oxygen saturation decreased, urinary incontinence, vision blurred, tinnitus, drug hypersensitivity, and hypersensitivity

You may also experience these rare but serious adverse effects from the nerve block itself

- Pneumothorax
- Hemothorax
- Intravascular injection
- Infection at the site of administration

It is important to call the staff caring for you, the researcher, and/or your regular physician when you think you are having problems, even if they are not included on the above list.

Reproductive Risks

My physician has explained that this research may be hazardous to an unborn child. If I become pregnant while undergoing this research treatment/therapy, there may be injury to my baby. It is understood that by my agreement to participate in the clinical trial I will continue to take acceptable means to avoid pregnancy throughout the duration of the study.

If you are pregnant, or think you may be pregnant, please let the clinical staff and research staff know. You will still receive pain control for your injuries. However, pregnancy is a criterion for exclusion since liposomal bupivacaine has not been adequately studied in pregnant women, and animal studies have shown increased rates of fetal losses.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

There may be no direct benefit to you if you decide to participate in this research. The value of liposomal bupivacaine for treating pain caused by rib fractures is unproven.

A clinical trial is one of the most exact ways to test whether the liposomal bupivacaine nerve block is effective at providing extended pain relief in multiple rib fractures. Published studies evaluating conventional nerve blocks to epidural for pain relief in patients with rib fractures have provided equivocal results. This means that nerve blocks have not been proven to be better or worse at relieving pain in patients with multiple rib fractures. Therefore, we expect a nerve block consisting of liposomal bupivacaine will provide you with at least equal pain relief based on the current available data.

The new knowledge gained from this study will benefit future patients and medical investigators. If the liposomal bupivacaine nerve block is found to be equally effective or better, you may not receive the improved pain relief provided if you are assigned to the epidural, or "control," group.

What other choices do I have if I do not participate?

Instead of being in this study, you have these options:

- You may choose not to participate in this study
- You may choose no therapy at this time
- You may choose to receive only care to help you feel more comfortable, such as oral or intravenous nonsteroidal anti-inflammatory drugs (Tylenol or acetaminophen, and ibuprofen), oral or intravenous opioid analgesics (morphine, and hydromorphone)
- You may choose to receive a nerve block with a non-liposomal preparation of local anesthetic
- You may choose to receive a liposomal bupivacaine nerve block without participating in the study
- You may choose to receive an epidural without participation in the study
- You may receive treatment from another center

Will I be paid for being in this study?

You will receive no payment for taking part in this study.

What are the costs for participating in this research?

We do not expect this research will lead to any additional costs. Epidural analgesia and nerve blocks are common procedures used for pain relief in patients with rib fractures and after surgical procedures. You will be receiving the usual medical care regardless of which trial arm you are in.

You or your insurer will be responsible for paying for the cost of your care, including the following:

- Epidural placement and management
- Administration of the nerve block

The liposomal bupivacaine used in the nerve block is what is considered the "experimental" drug. However, this drug has been approved by the FDA for use as a local anesthetic. It has been studied retrospectively as nerve blocking agent postoperatively for surgeries involving the rib cage with efficacy equal to that of an epidural. Therefore, you or your insurance company will be charged for the actual cost of the drug.

If you have questions about whether specific clinical services are research related or usual medical care, please speak to your physician or research contact person.

If you have health insurance, the insurance company may or may not pay for your participation in the research. You may have to pay for any co-payments, deductibles or co-insurance amounts that your insurance coverage requires. We encourage you to determine your health insurer's policy about paying for standard medical treatment while in a research study. Again, this is because you or your insurance company will be charge for your usual care.

If you do not have insurance, you will be billed for the amount you have to pay.

What happens if I am injured or hurt during the study?

If you get ill or injured from being in the study, you should let the study doctor know right away. You should contact Dr. Chadrick Evans at telephone number 309-287-2077.

You should let any health care provider who treats you know that you are in a research study. If you do seek medical treatment, please take a copy of this document with you because it may help the doctors where you seek treatment to treat you. It will also provide the doctors where you seek treatment with information they may need if they want to contact the research doctors.

You or your health insurance plan will be billed. No money has been set aside to pay the costs of this treatment. Health insurance plans may or may not cover costs of research-related injury or illness. You should check with your insurance company before deciding to participate in this research study. Costs not covered by insurance could be substantial. Please ask about any added costs or insurance problems

The University of Illinois College of Medicine Peoria (UICOM-P) has not set aside any money to pay you or to pay for your treatment if you get ill or injured from being in the study. There are no plans for the University to provide other forms of

compensation (such as lost wages or pain and suffering) to you for research related illnesses or injuries.

By signing this form, you are not giving up any legal rights to seek compensation of injury.

When does the Study end?

This study is expected to end after all participants have been discharged from the hospital, and all information has been collected your inpatients stay.

You can stop participating at any time. However, if you decide to stop participating in this study, we encourage you to talk to the researcher and your regular physician first. If you decide to stop participating, you may still be invited to provide the researcher with information through telephone calls or clinic visits.

We do not foresee any adverse effects occurring should you withdraw from the study early. You will receive the appropriate care for your rib fractures regardless of your participation status. This includes intravenous or oral pain medications commonly used.

This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Principal Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

Although the study is ongoing, you may discontinue participation or the principal investigator may ask you to withdraw from the study at any time. If you decide not to participate, you are free to leave the study at any time. Withdrawal will not interfere with your future care.

Who can see or use my protected health information? How will my protected health information be protected?

Your privacy and the protection of your health information are important to us. This section of the consent will cover:

- What protected health information about you will be collected in this study

- Who will use your information and why
- Who may disclose your information and to whom
- Your rights to access research information about you
- Your right to withdraw your authorization (approval) for any future use of your protected health information

1. Protected health information about you that will be collected in this study

The following personal health information will be collected, used for research and may be disclosed or released during your involvement with this research study:

- Name
- Medical Record Number
- Medical History
- Allergies
- Current and past medications or therapies
- Information from a physical examination that generally also includes body mass index, blood pressure reading, heart rate, breathing rate, and temperature.
- Information from the tests and procedures described earlier in this document

2. Why your protected health information is being used

Your personal information is important for the study team to communicate with you during the study. Your health information and results of tests and procedures are being collected as part of this research study and for the advancement of medicine and clinical care. The Principal Investigator and your attending physician will also use the results of these tests and procedures outside the context of this study to care for you.

3. Who may use or disclose your personal health information

By signing this document, you are giving permission to Dr. Chadrick Evans and his study team to use the protected health information described above for the purposes of this study. You are also giving OSF St. Francis Medical Center and University of Illinois College of Medicine at Peoria permission to disclose or release your protected health information for purposes of this study only.

4. Who might receive your personal health information?

As part of the study, the Principal Investigator, Food and Drug Administration, study team and others listed above in item number 3 may disclose your protected health information, including the results of the research study tests and procedures to the following:

- **The Peoria Institutional Review Boards (the committees charged with overseeing research on human subjects)**
- **The Office of Human Research Oversight (the office which monitors research studies)**
- **Authorized members of the University of Illinois College of Medicine Peoria (UICOM-P) workforce who may need to access your information in the performance of their duties, for example: to provide treatment, to ensure integrity of the research, accounting or billing matters, etc.**
- **UICOMP Center for Outcomes Research: Representatives of this office will assist the Primary Investigator in data analysis for publishing in an academic journal. The data forwarded to the UICOMP Center for Outcomes Research will not contain any of your personal health information.**

The Principal Investigator or study team will inform you if there are any changes to the list above during your active participation in the trial. Once information is disclosed to others outside this institution, the information may no longer be covered by the federal privacy protection regulations. However, in all disclosures outside of this institution's system, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law.

5. How long will this institution be able to use or disclose your personal health information?

Your authorization for use and disclosure of your personal health information for this specific study does not expire. This information may be maintained in a research repository (database).

6. Access to your records

During your participation in this study, you will have access to your medical record and any study information that is part of that record. The investigator is not required to release to you research information that is not part of your medical record.

7. Changing your mind

You have the right to refuse to sign this HIPAA Authorization.

You do not have to sign this form. If you do not, you will not be allowed to join the research study. Your decision to not sign this permission will not affect any other treatment, health care, enrollment in health plans or eligibility for benefits to which you are normally entitled.

You may withdraw from the study for any reason simply by explaining this to the Principal Investigator or a member of the study team. If you decide not to participate, you are free to leave the study at any time. Withdrawal will not interfere with your future care.

You may also withdraw your permission for the use and disclosure of any of your protected health information for research, **but you must do so in writing** to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected health information that was collected prior to your written request if that information is necessary to the study. If you withdraw your permission to use your protected health information that means you will also be withdrawn from the research study.

Who can I call about my rights as a research subject?

If you have questions regarding your participation in this research study or if you have any questions about your rights as a research subject don't hesitate to speak with the Principal Investigator listed on page one of this form. Concerning your rights as a research subject, you may also contact the Peoria Institutional Review Board by calling (309) 680-8630.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting this institution to use your personal health information collected about you for research purposes. You are also allowing this institution to disclose that personal health information to outside organizations or people involved with the operations of this study.

A **signed** copy of this consent form will be given to you.

A1. Signature Block for Capable Adult: I have read this document or it was read to me. I have been encouraged to ask questions and all my questions were answered. I agree to take part in this research study.

_____
Printed Name of Research Participant

_____
Signature of Research Participant

_____
Date

A2. Signature Block for Researcher/Designee: I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

_____
Printed Name of Person Obtaining Consent

_____
Signature of Person Obtaining Consent

_____
Date

The Impartial Witness signature lines should be included when the subject speaks and understands English, but cannot read and write or is visually impaired. Persons who cannot read and write are considered illiterate. Visual impairments include blindness and other visual defects in which changes to the consent document, such as increased font size, are insufficient to allow the subject to read it. It is important to emphasize that use of an Impartial Witness is limited to situations in which the subject comprehends spoken English and is able to communicate.

_____
Printed Name of Impartial Witness

_____
Signature of Impartial Witness

_____

Date

B1. Signature Block for ADULT UNABLE TO CONSENT to participation and unable to provide authorization to use and disclose his/her personal health information: I have read this document or it was read to me. I have been encouraged to ask questions and all my questions were answered.

_____

Printed Name of Subject

_____

Printed Name of Authorized Subject Representative

_____

Signature of Authorized Subject Representative

_____

Date

Please designate Authorized Subject Representative's relationship to the subject*:

_____

***For Adult Subjects ONLY:** According to Illinois law, unless there is a court-appointed proxy or guardian, the following persons are authorized to make health care decisions on behalf of an incapacitated or otherwise incompetent patient (listed in order of priority): spouse; adult child; either parent; adult sibling; adult grandchild; close friend; and guardian of the estate.

The Impartial Witness signature lines should be included when the subject's legally authorized representative (LAR) speaks and understands English, but cannot read and write or is visually impaired. Persons who cannot read and write are considered illiterate. Visual impairments include blindness and other visual defects in which changes to the consent document, such as increased font size, are insufficient to allow the LAR to read it. It is important to emphasize that use of an Impartial Witness is limited to situations in which the subject's LAR comprehends spoken English and is able to communicate.

_____

Printed Name of Impartial Witness

_____

Signature of Impartial Witness

_____

Date

B2. Signature Block for Researcher/Designee: I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

_____

Printed Name of Person Obtaining Consent

_____

Signature of Person Obtaining Consent

_____

Date