Consent Form

Title of Research Study: ***Prospective Randomized controlled trial comparing liposomal bupivacaine to bupivacaine Interscalene blocks for total shoulder arthroplasty surgery***

Investigator Team Contact Information: Dr. James Flaherty

For questions about the research study, research results, or other concerns, call the study team at:

Investigator Name: Dr. James Flaherty Investigator Departmental Affiliation: Anesthesiology Phone Number: 612-624-9990 Email Address: jflahert@umn.edu	Study Staff: Jonah Pearson, Katherine Harmelink, Jessica Hatfield, Candace Nelson, Melissa Cohen, Ryan Eskuri Phone Number: 612-625-7116 Email Address: cohen045@umn.edu

Supported By: This research is not supported by any company.

Financial Interest Disclosure: The primary investigator does not have any financial interest.

Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

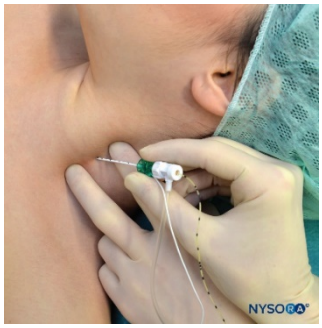
Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Your doctor, who is also responsible for this research study, is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Why am I being asked to take part in this research study?

You are being asked to take part in this research study because you are planning to receive an interscalene block as part of your surgical pain management plan. An interscalene block is an injection of numbing medication known as local anesthetic around the nerves that extend from your neck to your arm that allow you to feel sensation and pain of your arm.



What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The purpose of this study is to determine if liposomal bupivacaine plus bupivacaine compared to bupivacaine alone when given in an interscalene block provides better and longer pain control for total shoulder arthroplasty (TSA) surgery. Liposomal bupivacaine is a long acting anesthetic. It is liposome encapsulated bupivacaine which allows for prolonged release of bupivacaine over a 72-hour period. Bupivacaine is a medium acting local anesthetic, which provides between 6 and 24 hours of pain relief. Currently it is the standard of care to give either of these medications in an interscalene block at the University of Minnesota, however their effectiveness has not been adequately compared against one another in interscalene blocks for TSA patients.

How long will the research last?

We expect that you will be in this research study for 14 days following TSA surgery. However, we will continue to monitor your chart for adverse events up to 30 days post-procedure.

What will I need to do to participate?

You will be asked to consent to be randomized to receive either liposomal bupivacaine plus bupivacaine or bupivacaine alone in an interscalene block. In addition, we would ask you to have your pain scores and pain medication use evaluated by a member of the research staff at 2, 6, 24, 48, and 72 hours post procedure. This will be done in person or via telephone call. At 72 hours and 14 days post-procedure, you will be asked to complete a Quality of Recovery Survey and asked if you would undergo an interscalene block with your medication again or if you would opt for a different form of pain management. At 72 hours and 14 days you will also be assessed for any block related complications.

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

The foreseeable risks of the study are low and primarily relate to the nerve block and include things like infection, bleeding, nerve damage, and medication side effects. These risks are the standard risks of surgery and the interscalene injection. In addition there is always a risk of a data breach.

More detailed information about the risks of this study can be found under ***"What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include reduced pain following your procedure and shortened hospital stay. Other possible benefits include increased knowledge that may be applied to future patients.

What happens if I do not want to be in this research?

You do not have to participate in this research. Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. This means that your choice not to be in this study will not negatively affect your right to any present or future medical care. If you choose not to participate you would not be randomized to receive one treatment over another. An interscalene block is the standard of care for patients undergoing this procedure and you would still receive an interscalene block regardless of your participation in this study.

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

We expect up to 90 patients will be enrolled in this research study, with a goal of at least 35 per group.

What happens if I say "*Yes, I want to be in this research*"?

If you choose to take part in this research you will be randomized to receive an interscalene block with either liposomal bupivacaine plus bupivacaine or bupivacaine alone. The interscalene block is part of the standard of care and would be performed regardless of your participation in this study. The treatment you get will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose what treatment you get. You will have an equal chance of being given either treatment. You will not be told which treatment you are getting, however your study doctor will know.

You will receive standard oral pain medications once you are checked in for surgery. Following this, you will undergo the interscalene block with sedation provided to ensure your comfort. Your anesthetic care during surgery will not be affected by the block that you receive. You will receive a balanced general anesthetic which focuses on opioid sparing. While in the hospital you will receive a standardized pain medication regimen. You will be discharged with oral pain medications for postoperative pain control. You will be provided with a pain diary to help you track your pain levels and medication use at home.

You will be evaluated at 2, 6, 24, 48, and 72 hours following your procedure by a member of the research staff for your pain scores using a 0-10 point scale, and for opioid and any other use of pain medications. This will be done in person or via telephone call. The research assistant will be blinded to which medication you have received. At 24 hours, an ultrasound will be taken of your diaphragm. At 72 hours and at 14 days post-procedure you will be asked to complete a Quality of Recovery Survey and be assessed for any block related complications. Your chart will continue to be monitored up to 30 days post-procedure for any complications related to the procedure.

What are my responsibilities if I take part in this research?

You will be responsible for giving your pain scores and answering the questions of the Quality of Recovery survey to members of the research staff.

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

The foreseeable risks of the study primarily relate to the nerve block and possible medication side effects. These complications all fall within the standard risks of surgery and the performance of the interscalene injection. Either intervention being provided as a part of this study falls within the standard of care as both medication options are within the standard treatments for post-operative pain and are

currently used as analgesic (pain management) options at the University of Minnesota Medical Center. In addition to these risks described further below, you risk having your day interrupted by the anesthesia team to ask about your pain control and side effects as well as having your record looked at to see medication use during your hospitalization. There is also some risk of a data breach involving the information we have about you. We comply with the University's security standards to secure your information and minimize risks, but there is always a possibility of a data breach.

Risks from the nerve block are all estimated to be less than 1% and include infection, bleeding, nerve injury, cardiac arrhythmias (irregular heartbeat) and respiratory complications.

Serious side effects related to bupivacaine are not common, but may occur if too much is given or if it is accidentally injected into a blood vessel. When given incorrectly, side effects may involve the brain or the heart. The effects on the brain and central nervous system may include restlessness, anxiety, tinnitus (ringing in the ears), blurred vision, and tremors (shaking) possibly proceeding to convulsions. The effects on the heart appear when too much bupivacaine is given or when bupivacaine is injected in a blood vessel by accident. These effects cause a decrease of the heart function, including low heart rate or abnormal heart rhythm, decreased blood flow, low blood pressure, and, in extreme cases, heart attack.

The numbing sensation caused by bupivacaine may be persistent, with slow, incomplete, or no recovery. Sometimes a tingling sensation may appear in the area treated with bupivacaine. When injected next to a large nerve, bupivacaine may cause weakness or paralysis.

Allergic reactions are rare, but may include rash, itching and redness of the skin, sneezing, nausea, vomiting, dizziness, fainting, sweating, fever, and low blood pressure. If you have these symptoms, please call your study doctor.

Other side effects related to liposomal bupivacaine can include nausea (22.6%), constipation (8.7%), vomiting (6%), high temperature (5.5%), headache (5%), itching (2.4%), dizziness (<2%), low blood pressure (<2%), high heart rate (1.3%), swelling (<1%), and anemia (<1%).

What do I need to know about reproductive health if I am in this study?

The research may also hurt a pregnancy or fetus in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

Will it cost me anything to participate in this research study?

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services are performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the Institutional Review Board (IRB), the committee that provides ethical and regulatory oversight of research, and other representatives of this institution, including those that have responsibilities for monitoring or ensuring compliance.

The sponsor, monitors, auditors, the IRB, the University of Minnesota Research Compliance Office and

other University compliance units, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available at 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.

Will anyone besides the study team be at my consent meeting?

You may be asked by the study team for your permission for an auditor to observe your consent meeting. Observing the consent meeting is one way that the University of Minnesota makes sure that your rights as a research participant are protected. The auditor is there to observe the consent meeting, which will be carried out by the people on the study team. The auditor will not document any personal (e.g. name, date of birth) or confidential information about you. The auditor will not observe your consent meeting without your permission ahead of time.

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

Can I be removed from the research?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury

let the study physicians know right away.

Use of Identifiable Health Information

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the 1099 Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission. Please read the HIPAA Authorization form that we have provided and discussed.

The de-identified results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

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Signature of Participant Date

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Printed Name of Participant

_____ _____

Signature of Person Obtaining Consent Date

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Printed Name of Person Obtaining Consent