UNIVERSITY OF SOUTH FLORIDA

USF RESEARCH & INNOVATION

Informed Consent to Participate in Research and Authorization to Collect, Use, and Share your Health Information

Information to Consider Before Taking Part in this Research Study

Title: Use of Smart Knee Implant to Evaluate Efficacy and Superiority of Liposomal Bupivacaine and Bupivacaine with Meloxicam in Early TKA recovery

Study # 010693

Overview: You are being asked to take part in a research study. The information in this document should help you to decide if you would like to participate. The sections in this Overview provide the basic information about the study. More detailed information is provided in the remainder of the document.

Study Staff: This study is being led by Dr. Steven Lyons who is an Orthopaedic Surgeon at/in Florida Orthopaedic Institute. This person is called the Principal Investigator. Other approved research staff may act on behalf of the Principal Investigator.

Study Details: This study is being conducted at Florida Orthopaedic Institute and is not financially supported/sponsored. The purpose of the study is to determine the impact that different knee injection medications have on early recovery in patients undergoing Total Knee Arthroplasty. The three injections are Exparel (Liposomal Bupivacaine), Zynrelef (Bupivacaine with Meloxicam), and Marcaine (Bupivacaine hydrochloride). The Exparel and Zynrelef groups are considered experimental for this study, and Marcaine is considered the Control group. All three products are FDA approved and have been used in humans. These injections are part of the standard of care for Total Knee Arthroplasty. 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 a *one in three* chance of being given each treatment. You will not be told which treatment you are getting; however your study doctor will know.

Subjects: You are being asked to take part because you are planning to have your knee replaced in the near future. We want to determine which of the three medications can help patients recover faster following knee replacement surgery.

Voluntary Participation: Your participation is voluntary. You do not have to participate and may stop your participation at any time. There will be no penalties or loss of benefits or opportunities if you do not participate or decide to stop once you start. If you choose not to participate in this study, you will still receive an injection, but it will be decided by your surgeon, rather than being randomized to one of the three groups.

Benefits, Compensation, and Risk: We do not know if you will receive any benefit from your participation. There is no cost to participate. You will not be compensated for your participation. This research is considered minimal risk. Minimal risk means that study risks are the same as the risks you face in daily life. Participation in this study carries the same risk as undergoing Total Knee Arthroplasty outside of the study. The most common risks include transient local numbness or weakness and injection-site reaction. The most serious risks that may be related to taking part in this research include rare systemic local-anesthetic toxicity.

Confidentiality: Even if we publish the findings from this study, we will keep your study

information private and confidential. Anyone with the authority to look at your records must keep them confidential.

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

Why are you being asked to take part?

The purpose of this study is to determine the effect that each of three injections have on early recovery following knee replacement surgery. This study includes the use of a knee injection during Total Knee Arthroplasty. Exparel, Zynrelef, and Marcaine are approved by the Food and Drug Administration (FDA) for the injection during Total Knee Arthroplasty.

Study Procedures: What will happen during this study?

At the time of surgery, each participant receives an injection of either liposomal bupivacaine (Exparel), bupivacaine mixed with meloxicam (Zynrelef), or bupivacaine hydrochloride (Marcaine) alone as part of surgical care and is followed through the first postoperative year. Receiving an injection is part of the standard of care. The purpose of this study is to determine which of the three injections will help patients recover better within the first three days following surgery.

At the pre-operative visit, the provider will document knee range of motion, functionality, and pain. The participant will also fill out the Patient Reported Outcome Measures (PROMs) forms being used for this study. These forms look at levels of activity, pain, and functionality.

At each visit, you will be asked to fill out the following PROMs forms. Additionally, our research team will ask about your use of post-operative opioids for pain. These visits and surveys will be conducted at 3 days, 1 week, 2 weeks, 6 weeks, 3 months, 1 year, and 2 years post-surgery. These visits are part of standard of care and the data will be collected for research purposes.

- VAS – pain scale
- KOOS – pain, functionality, symptoms
- KSS – pain, stability, function
- UCLA – Activity scale
- Tegner – Activity scale
- EQ-5D-5L – Quality of Life survey

Data from your knee implant will tell us about function, movement, and motion at 3 days and 7 days post-operatively. This is part of the standard of care, and the data will be collected for research purposes.

- During your surgery, you will receive one of three periarticular injections (an injection placed into the tissues around the knee) as part of your pain control: liposomal bupivacaine (Exparel), bupivacaine and meloxicam (Zynrelef), or standard bupivacaine (control). You will be assigned to one of these three groups by chance, like flipping a coin. The injection is given one time, in the operating room during your knee replacement, by your surgeon.

- The only experimental part of this study is which of the three pain injections you receive and the additional activity, pain, and function questionnaires you complete. All three injections are used in routine knee replacement care; the research is the head-to-head comparison between them. Your knee replacement surgery itself is standard care and is not experimental.
- Your surgery, anesthesia, physical therapy, and overall recovery care will follow the usual standard of care and will not be changed by taking part in this study. The one difference is that the specific pain injection you receive is decided by chance rather than chosen by your surgeon.
- At your final study visit, 2-yearspost-operatively you will complete the same activity, pain, and function questionnaires as at earlier visits. No additional study procedures are performed at the final visit, and after it your participation in the study is complete; you will continue routine follow-up with your surgeon as normal.

Total Number of Subjects

A total of 200 individuals will participate in the study at all sites.

Alternatives / Voluntary Participation / Withdrawal

You do not have to participate in this research study.
You should only take part in this study if you want to volunteer. You should not feel that there is any pressure to take part in the study. You are free to participate in this research or withdraw at any time. There will be no penalty or loss of benefits you are entitled to receive if you stop taking part in this study.

You can decide after signing this informed consent document that you no longer want to take part in this study for any reason at any time. If you decide you want to stop taking part in the study, tell the study staff as soon as you can, and make sure to document the decision to withdraw from the study, in writing.

- We will tell you how to stop safely.
- If you decide to stop, you can continue getting care from your regular doctor.
- If you decide to stop, we will ask your permission to keep the information already collected about you up to that point, and to record why you stopped if you wish to tell us. You will not need to complete any further study questionnaires or visits, and your decision will not affect your surgery, your recovery care, or your relationship with your surgeon or this institution.

Please note, even if you want to stay in the study, there may be reasons we will need to withdraw you from the study. You may be taken out of this study if we find out it is not safe for you to stay in the study or if you are not coming for the study visits when scheduled. We will let you know the reason for withdrawing you from this study.

Benefits

Participants may or may not receive a direct benefit; whether either injection yields faster early functional recovery is the hypothesis under investigation and cannot be guaranteed. All

participants receive standard high-quality surgical care and standardized multimodal analgesia.

Risks or Discomfort

This research is considered to be minimal risk. That means that the risks associated with this study are the same as what you face every day. There are no known additional risks to those who take part in this study.

The following risks may occur:

- Foreseeable risks include those associated with the study drugs and the periarticular injection (e.g., transient local numbness or weakness, injection-site reaction, and rare systemic local-anesthetic toxicity) and the general risks of TKA surgery and anesthesia, which are present regardless of study participation.
- There is a small risk that information collected about you could be seen by someone outside the study team. We protect against this by storing your data in secure, password-protected files, using a study ID number in place of your name, and limiting access to approved study staff. The information collected in this study (activity, pain, and knee function) is not the type expected to affect your employability, insurability, or legal standing.

Compensation

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

Costs

There will be no additional costs to you as a result of being in this study. However, routine medical care for your condition (care you would have received whether or not you were in this study) will be charged to you or your insurance company. You may wish to contact your insurance company to discuss this further.

Privacy and Confidentiality

We will do our best to keep your records private and confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. Certain people may need to see your study records. These individuals include:

- The research team, including the Principal Investigator, study coordinator, research nurses, and all other research staff.
- Certain government and university people who need to know more about the study. For example, individuals who provide oversight on this study may need to look at your records. This is done to make sure that we are doing the study in the right way. They also need to make sure that we are protecting your rights and your safety.
- Any agency of the federal, state, or local government that regulates this research. This includes the Department of Health and Human Services (DHHS) and the Office for Human Research Protection (OHRP).
- The USF Institutional Review Board (IRB) and its related staff who have oversight responsibilities for this study, and staff in USF Research Integrity and Compliance.

Your information or samples collected as part of the research, even if identifiers are removed, will NOT be used or distributed for future research studies.

We may publish what we learn from this study. If we do, we will not include your name. We will not publish anything that would let people know who you are.

If completing an online survey, it is possible, although unlikely, that unauthorized individuals could gain access to your responses. Confidentiality will be maintained to the degree permitted by the technology used. No guarantees can be made regarding the interception of data sent via the Internet. However, your participation in this online survey involves risks similar to a person's everyday use of the Internet. If you complete and submit an anonymous survey and later request your data be withdrawn, this may or may not be possible as the researcher may be unable to extract anonymous data from the database.

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

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 this study. We will notify you as soon as possible if such information becomes available.

You can get the answers to your questions, concerns, or complaints.

If you have any questions, concerns or complaints about this study, call Dr. Steven Lyons at 813-978-9700. If you have questions about your rights, complaints, or issues as a person taking part in this study, call the USF IRB at (813) 974-5638 or contact by email at RSCH-IRB@usf.edu or call Florida Orthopaedic Institute at (813) 978-9700 or by email at anguyen@foreonline.org.

Authorization to Use and Disclose Protected Health Information (HIPAA Language)

The federal privacy regulations of the Health Insurance Portability & Accountability Act (HIPAA) protect your identifiable health information. By signing this form, you are permitting the Florida Orthopaedic Institute to use your health information for research purposes. You are also allowing us to share your health information with individuals or organizations other than FOI who are also involved in the research and listed below.

In addition, the following groups of people may also be able to see your health information and may use that information to conduct this research:

- The medical staff that takes care of you and those who are part of this research study;
- Any laboratories, pharmacies, or others who are part of the approved plan for this study;
- The USF Institutional Review Board (IRB) their related staff who have oversight responsibilities for this study, including staff in USF Research Integrity and Compliance;

- All designated review committees such as the USF Institutional Review Board and Florida Orthopaedic Institute research oversight;
- Data Safety Monitoring Boards or others who monitor the data and safety of the study;
- There may be other people and/or organizations who may be given access to your personal health information, including USF Research Integrity and Compliance, the study sponsor and its representatives,

Anyone listed above may use consultants in this research study, and may share your information with them. If you have questions about who they are, you should ask the study team. Individuals who receive your health information for this research study may not be required by the HIPAA Privacy Rule to protect it and may share your information with others without your permission. They can only do so if permitted by law. If your information is shared, it may no longer be protected by the HIPAA Privacy Rule.

By signing this form, you are giving your permission to use and/or share your health information as described in this document. As part of this research, USF may collect, use, and share the following information:

- Your research record.
- All of your past, current or future medical and other health records held by USF, other health care providers or any other site affiliated with this study as they relate to this research project. This may include but is not limited to records related to HIV/AIDs, mental health, substance abuse, and/or genetic information.
- Your medical and health records held by the Florida Orthopaedic Institute and any site affiliated with this study as they relate to this research project, including records of your knee replacement surgery, the study medication you received, your pain and pain-medication use, your activity and knee function assessments, and related clinical and imaging information.

You can refuse to sign this form. If you do not sign this form you will not be able to take part in this research study. However, your care outside of this study and benefits will not change. Your authorization to use your health information will not expire unless you revoke (withdraw) it in writing. You can revoke your authorization at any time by sending a letter clearly stating that you wish to withdraw your authorization to use your health information in the research. If you revoke your permission:

- You will no longer be a subject in this research study;
- We will stop collecting new information about you;
- We will use the information collected prior to the revocation of your authorization. This information may already have been used or shared with others, or we may need it to complete and protect the validity of the research; and
- Staff may need to follow-up with you if there is a medical reason to do so.

To revoke your authorization, please write to:

Dr. Steven Lyons
For IRB Study # *010693*

4115 West Spruce Street Suite 201
Tampa, Florida 33607

While we are conducting the research study, we cannot let you see or copy the research information we have about you. After the research is completed, you have a right to see the information about you, as allowed by USF policies.

Consent to Take Part in Research and Authorization for the Collection, Use and Disclosure of Health Information

I freely give my consent to take part in this study and authorize that my health information as agreed above, be collected/disclosed in this study. I understand that by signing this form I am agreeing to take part in research. I have received a copy of this form to take with me.

_____ _____

Signature of Person Taking Part in Study Date

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Printed Name of Person Taking Part in Study

Statement of Person Obtaining Informed Consent and Research Authorization

I have carefully explained to the person taking part in the study what he or she can expect from their participation. I confirm that this research subject speaks the language that was used to explain this research and is receiving an informed consent form in their primary language. This research subject has provided legally effective informed consent.

_____ _____

Signature of Person Obtaining Informed Consent Date

_____

Printed Name of Person Obtaining Informed Consent