1.0 General Information

***Please enter the full title of your protocol:**

Trigger Point Injections in Reducing Pain Following Total Knee Arthroplasty

***Please enter the Protocol Number you would like to use to reference the protocol:**

FDG20240079H
* This field allows you to enter an abbreviated version of the Protocol Title to quickly identify this protocol.

Is this a multi-site protocol (i.e. Each site has their own Principal Investigator)?

No

Does this protocol involve the use of animals?

○ Yes ◉ No

2.0 Add departments

2.1 List sites associated with this study:

Is Primary?	Site Name
◉	**P and R** - 60th Medical Group Clinical Investigation Facility (60th MDG)

3.0 ▪ Assign project personnel access to the project

3.1 * Please add a Principal Investigator for the study:

Name	Role	Training Record
Bennett, Dustin Lansing	**Principal Investigator**	**View Training Record**

Responsibility

- ☐ Student
- ☐ Resident
- ☐ Site Chair
- ☑ Fellow

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Name	Role	Training Record
Dalessandro, Ashley Marie, Capt	**Associate Investigator**	**View Training Record**

B) Research Support Staff

Name	Role	Training Record
No Research Support Staff have been added		

3.3 *Please add a Protocol Contact:

Name	Role	Training Record
Bennett, Dustin Lansing	**Study Contact**	**View Training Record**

The Protocol Contact(s) will receive all important system notifications along with the Principal Investigator. (i.e. The protocol contact(s) are typically either the Principal Investigator themselves).

3.4 If applicable, please select the Designated Site Approval(s):

Name	Role	Training Record
No Designated Department Approval have been added		

Add the name of the individual authorized to approve and sign off on this protocol from your Site (e.g. the Site Chair).

4.0 Project Information

4.1 * What department(s) will be associated with this protocol?

	Orthopedics

4.2 * Is the IRB of record for this study an IRB/HRPP that does NOT use EIRB? If Yes, complete the application according to the IRB/HRPP Determination.

If your Projects or Protocols are under the oversight of another IRB that does use EIRB, stop this submission and contact the core site and request an invitation as a performing site.

If your Project or Protocol is now being submitted for the first time to an IRB that does use EIRB, continue with this application and answer the questions to be reviewed by the IRB.

Answering yes means the board of record is an IRB that does NOT use EIRB.

○ Yes ◉ No

4.3 * Is this protocol research, expanded access, or humanitarian use device?

◉ Yes ○ No

4.4 * What type of protocol is this?

- [ ] Behavioral Research
- [x] Biomedical Research
- [ ] Clinical trial (FDA regulated)
- [ ] Educational Research
- [ ] Expanded Access
- [ ] Humanitarian Use Device (HUD)
- [ ] Psychosocial Research
- [ ] Oral History
- [ ] Other

4.5 Are you conducting this project in pursuit of a personal degree?

(•) Yes ( ) No

4.7 * Is this human subjects research? (As defined by 32 CFR 219) Human subject means a living individual about whom an investigator (whether professional or student) conducting research:
(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
(ii) Obtains, uses, studies, analyzes or generates identifiable private information or identifiable biospecimens.

(•) Yes ( ) No

4.8 * Do you believe this human subjects research is exempt from IRB review?

( ) Yes (•) No

5.0 Personnel Details

5.1 Does the Principal Investigator have a Permanent Change of Station (PCS) Date or Estimated Institutional Departure Date (EIDD)?

( ) Yes (•) No

5.2 List any Research Team members without EIRB access that are not previously entered in the protocol:

No results found

5.3 Are any Contractors or Subcontractors involved in this study? If yes, please list them and describe their role.

( ) Yes (•) No

No results found

5.4 Will you have a Research Monitor for this study?

- ○ Yes
- ○ No
- ◉ N/A

6.0 Data/Specimens

6.1 Does the study involve the use of existing data or specimens only (no interaction with human subjects)?

○ Yes ◉ No

7.0 Funding and Disclosures

7.1 Source of Funding:

Funding Source	Funding Type	Amount
No results found		

Total amount of funding:

0

7.2 Do you or any other Investigator(s) have a disclosure of a personal interest or financial nature significant with sponsor(s), product(s), instrument(s) and/or company(ies) involved in this study?

○ Yes ◉ No

All personnel engaged in research must complete and attach a Conflict of Interest (COI) form.

8.0 Study Locations

8.1 Is this a collaborative or multi-site study? (e.g., are there any other institutions involved?)

○ Yes ◉ No

8.2 Study Facilities and Locations:

Institution	Site Name	Site Role	FWA or DoD Assurance Number	Assurance Expiration Date	Is there an agreement?	IRB Reviewing for Site
No results found						

Other:

Other Institution Site	Site Role	FWA or DoD Assurance Number	FWA or DoD Expiration Date	Is there an agreement?	IRB Reviewing for Site
No results found					

8.3 Are there international sites?

Attach international approval documents, if applicable, when prompted. Note: Ensure local research context has been considered

○ Yes ◉ No

8.4 Is this an OCONUS (Outside Continental United States) study?

○ Yes ◉ No

Select the area of responsibility:

Have you obtained permission from that area of responsibility? (This is a requirement prior to study approval)

○ Yes ◉ No

9.0 Study Details

9.1 Key Words:

Provide up to 5 key words that identify the broad topic(s) of your study

Trigger point injections AND pain

9.2 Background and Significance:

Include a literature review that describes in detail the rationale for conducting the study. Include descriptions of any preliminary studies and findings that led to the development of the protocol. The background section should clearly support the choice of study variables and explain the basis for the research questions and/or study hypotheses. This section establishes the relevance of the study and explains the applicability of its findings

Opioid addiction and abuse have become a significant burden on the healthcare system since this class of medication was first used in the 1990s. Opioid medication's highly addicting properties have led to its classification as an epidemic by the CDC in 2011. Alternative means of pain control for highly invasive procedures need to be explored. Orthopedic surgery specifically accounts for an estimated 8.8% of iatrogenic opioid use disorder (Trasolini et al. 2018). More effort should be directed to explore non-opioid interventions in the post-operative setting of orthopedic surgery to reduce the use of opioids and risk of addiction.

In an orthopedic setting one of the most preformed surgeries is the total knee arthroplasty (TKA). This procedure is most commonly performed in cases of severe osteoarthritis; some other indications include rheumatoid arthritis, deformity, and trauma. There are several surgical techniques to achieve this operation; however, all include performing an arthrotomy which is creating a semi-permanent opening by dissecting the superficial soft tissue to expose the bony anatomy of the knee joint. Those bony structures include the distal aspect of the femur, the patella, and the superior aspect of the tibia. By performing the arthrotomy the surrounding muscles and fascia are manipulated and temporarily displaced leading to stiffness, trigger points, and pain. This constellation of symptoms makes up a condition called myofascial pain syndrome. Treatment of m

yofascial pain syndrome with use of trigger point injections has shown that inactivation of myofascial pain trigger points around the knee joint can promote structural remodeling of the surrounding skeletal muscle to regulate the biomechanical balance, thus improving the clinical symptoms of knee osteoarthritis (Lin et al, 2022).

There have been limited studies aimed at the treatment of myofascial pain syndrome in the acute setting of a TKA. Mayoral et al. (2013) conducted a randomized double-blinded, placebo-controlled clinical trial where patients who underwent a TKA had dry needling completed in the pre-operative and intra-operative setting. This study demonstrated an improvement in pain scores within the first month of surgery in the dry needling group compared to a sham group. This has been the only study to date to address direct intervention for myofascial pain syndrome around the operative time frame. Henry et al. (2012) conducted a prospective study in which patients on the waitlist for a TKA were treated with trigger point injections; patients reported an improvement in pain up until the TKA procedure could be completed. Although Henry et al. did not assess pain in the post-operative setting, this study nonetheless demonstrated that myofascial pain syndrome is a component of osteoarthritis.

Despite these favorable results there are no studies that look at trigger point injections in the post-surgical setting. The aim of this study is to perform trigger point injections with administration of a local anesthetic immediately following TKA to assess the effect on pain scores. The trigger point injection/experimental group will be compared to a sham injections/control group where a superficial injection will be made into the dermis and no anesthetic will be injected. Injections will include two injections to four muscle bellies: the vastus medialis, vastus lateralis, medial, and lateral gastrocnemius muscle belly. Injections will include 0.5 mL of lidocaine without epinephrine and will be outside of the operative area distal and proximal to the joint, the popliteal fossa and incision site. With each injection the plunger will be pulled back to ensure placement of the needle is outside vascular structures. To assess the primary outcome measures, patients will complete a Visual Analogue Scale (VAS) which ranges from 0 (no pain) to 100 (severe intolerable pain) on post operative day (POD) 1 and at follow-up visits during weeks 2 and 6. The secondary outcome will assess how much opioid medication (ie, MME) was used in the immediate post-operative period through the week 6 follow-up visit.

9.3 Objectives/Specific Aims/Research Questions:

Describe the purpose and objective(s) of the study, specific aims, and/or research questions /hypotheses

The aim is of this study is to explore the effect of a pain intervention (ie, trigger point injection) vs. a sham injection on managing post-surgical pain and reducing the reliance on systemic opioid analgesics. Outcomes include the VAS on POD1 and week 2 and week 6 follow-up appointments. Opioid use will also be evaluated during these intervals.

9.4 Study Design:

Describe study design in one to two sentences (e.g., prospective, use of existing records/data /specimens, observational, cross-sectional, interventional, randomized, placebo-controlled, cohort, etc.). Specify the phase – Phase I, II, III, or IV – for FDA-regulated investigational drug research

Prospective, interventional study comparing trigger point injections vs. sham injections on VAS pain scale ratings and opioid use.

9.5 Target Population:

Describe the population to whom the study findings will be generalized

DoD beneficiaries aged 45 years and older who will be receiving a TKA, on either knee.

9.6 Benefit to the DoD:

State how this study will impact or be of benefit to the Department of Defense

The purpose of this study is to explore a unique pain management modality to reduce the use of opioids following a routine surgery in the military hospital setting. This will benefit the Department of Defense by improving post surgical pain, decreasing overall opioid use which in turn may lead to decrease rate of opioid use disorders, shorter inpatient stays and decrease adverse medication side effects.

10.0 Study Procedures, Data Management, and Privacy

10.1 Study Procedures:

Describe step-by-step how the study will be conducted from beginning to end

Step 1: A HIPAA Waiver will be used to access MHS Genesis to obtain all joint surgeons' case lists for those patients scheduled for surgery, all those not scheduled for a TKA will be removed from the list. The principal investigator will review case lists to identify name, TKA procedure, date scheduled for TKA, and phone. Patients scheduled for a TKA will be contacted within two weeks of their surgery to discuss the study. Study inclusion and exclusion criteria will be reviewed with patients who are interested in participation to ensure they are eligible. Those who are eligible will be scheduled for an appointment with the principal investigator before TKA surgery, ideally at their pre-op visit (standard of care visit) but may occur on the day of their surgery, to review consent documents and answer any questions. In order to ensure patient understanding, a copy of the consent documents will be emailed (if email address is provided) to the patient prior to the appointment to allow him/her to review the consent in advance.

Step 2: Patients return for their appointment to review and sign the consent documents either at their pre-operative visit or day of surgery. Consents will be sign either during their pre-operative appointment in a clinic exam room or during the day of their surgery in the PACU. Consenting a patient in the PACU on the day of surgery is a last resort and all efforts will be made to complete consents during pre-operative clinic visit. During the consent phase the PI and/or AI will not be in military uniform and will not have their rank displayed. After consent documents are signed, participants are assigned to a study group. Due to academic time constraints (i.e. deadlines to complete and present the research), an alternating convenience sample approach will be taken for study group assignment. Each participant will be assigned a subject ID number based on their order of enrollment (e.g., the first participant enrolled will be assigned 1, second participant enrolled assigned 2, and so on). Every participant with an odd number will be placed in the trigger point injection group (experimental) and those assigned an even number will be placed in the sham injection group (control). Those in the trigger point injection group will have an E after the number and

those in the sham injection group an S. The study participants will not know which study group they will be assigned to. An equal number of participants will be included in each group (ie, trigger point injection vs. sham injection).

Step 3a: (Trigger point injection group) The principal investigator will identify relevant structures to include the vastus medialis, vastus lateralis, medial, and lateral gastrocnemius muscle bellies by utilizing anatomical landmarks. Once those structures are identified, each area will be prepped in an aseptic fashion with alcohol swabs. Two injections will be made in each muscle belly. Each injection will include 0.5 mL of 1% lidocaine without epinephrine. A total of eight injections will be administered with a total of 4 mLs of 1% lidocaine without epinephrine using a 1 ½" 25-gauge needle. A separate needle and syringe will be utilized for each of the four muscle bellies. Careful consideration to avoid neurovascular structures will be taken by retracting the plunger to ensure needle placement is outside vascular structures with each injection. A blind will be placed between the patient and the needle in order for the patient not to witness the injection, which is the same protocol as the sham injection. The blind used will be a drape or other soft item held by a person not involved with the study to obscure the vision of the subject during the injection and allow the investigator to use both hands to safely conduct the injection and aspiration procedure. The local anesthetic will be massaged into the area to ensure the medication disperses thoroughly into the muscle belly. After the needle is removed, the area will be cleaned with alcohol swabs and a bandage will be applied. This will be completed on POD 0 (ie, the day of the TKA procedure). Within the informed consent the consenting verbiage will ensure that the participants will not be able to identify injection technique that will identify whether they are in the sham or experimental group.

Step 3b: (Sham injection group) The principal investigator will identify relevant structures to include the vastus medialis, vastus lateralis, medial and lateral gastrocnemius muscle. Once those structures are identified using anatomical landmarks, each area will be prepped in an aseptic fashion with alcohol swabs. A needle with a syringe filled with sterile water will be inserted into the epidermis to mimic an actual trigger point injection. The needle will be left in place for 3-5 seconds to create the false perception of injection anesthetic into the muscle groups. No sterile water will be injected into the participant. Since the effects from the anesthetic block will still be active and the injections will be administered in a position that prevents the participant from viewing the procedure, participants will not know that there is nothing being injected into the area. This will occur by placing a blind between the patient and the needle in order for the participant not to see that no water will be injected. The blind used will be a drape or other soft item held by a person not involved with the study to obscure the vision of the subject during the sham injection and allow the investigator to use both hands to safely conduct the sham injection procedure. After the needle is removed the area will be cleaned with alcohol swabs and a bandage will be applied. Four separate needles and syringes will be utilized for each location. This will be completed on POD 0 (ie the day of the TKA procedure). Within the informed consent the consenting verbiage will ensure that the participants will not be able to identify injection technique that will identify whether they are in the sham or experimental group.

Step 4: On POD0 (after TKA surgery, the investigator will review MHS Genesis to obtain demographic information (age, sex, beneficiary status, BMI), morphine milligrams equivalents (MME) using the Medication Administration Record (MAR) Summary, prior pain medication history, diabetic history, tobacco use, anesthetic block type, surgical site, ICD codes, complications, and discharge disposition.

Step 5: On POD1, participants in each study group will be provided with the VAS and Opioid Use questionnaires. The VAS pain scale questionnaire will be used to report average pain scores by placing a hash mark (/) on the numbered scale

on the region that best represents their pain and writing the number (a whole number) on the form; scores range from 0 (no pain) to 100 (severe intolerable pain). The Opioid Use questionnaire will be used to document average opioid use following discharge. Both questionnaires will be completed by all participants at POD1, week 2 and week 6 visits. The VAS will be given to the participant with the intake form that is provided by the orthopedic technician, and the investigator will provide the Opioid Use questionnaire to the participant during the visit, and review the MAR Summary to obtain and calculate the total MME from POD0 to POD1 using MDCalc . Prior to ending the visit, the investigator will ask participants to bring in their opioids to be physically counted at their week 2 and week 6 visits.

Step 6: The investigator will provide a reminder phone call 1-2 days prior to the week 2 and week 6 appointments to ensure participants remember to bring in their medication.

Step 7: Participants return for the week 2 and week 6 visits. They are given VAS and Opioid Use questionnaires to complete, and opioid medication is counted. On ce opioids have been accounted for, MME will be calculated.

10.2 Data Collection:

Describe all the data variables, information to be collected, the source of the data, and how the data will be operationally measured.

Injection type: Dichotomous variable. Trigger point or sham injection.

Visual analogue scale: Discrete variable. Will be scaled from 0 (no pain) to 100 (severe intolerable pain) and will be measured at POD1, week 2, and week 6. The VAS will be presented to the participant on paper.

Morphine milligram equivalent (MME): Discrete variable. Will be measured from POD 0 to POD1, then a total MME will be calculated from POD1 to week 2 and week 2 to week 6. This will be calculated utilizing the MME calculator on MDCalc.

Block: Categorical variable. Spinal, adductor or femoral nerve block determined by anesthesiology.

Age: Continuous variable. Age stated in years at time of surgery as stated in EHR.

Prior Pain Medications: Categorical variable. Obtained from EHR.

Discharge disposition: Dichotomous variable. Discharge to skilled nursing facility or home, discharge disposition will be reviewed in the discharge summary.

Active Duty, Dependent, Retiree: Categorical Variable.

Sex: Categorical (male, female). Obtained from EHR.

BMI: Categorical variable. Obtained from EHR. Categories will be BMI of 24.9 or less, BMI 25-29.9, and BMI greater than or equal to 30.

Nicotine use: Dichotomous variable. Obtained from EHR. Current use at time of injury.

History of Diabetes: Dichotomous variable. Obtained from EHR.

ICD Code: Categorical Variable. Obtained from EHR.

Laterality: Categorical Variable. Left or Right TKA

Complications: Categorical Variable. Pulmonary embolism/deep vein thrombosis, surgical site infection, severe pain from the injections, other, and multiple for more than one complication.

10.3 At any point in the study, will you request, use, or access health information in any form, including verbal, hard copy and electronic?

○ Yes ○ No

11.0 Statistical/Data Analysis Plan

11.1 Data Analysis Plan and Statistical Considerations:

List the statistical methods to be used to address the primary and secondary objectives, specific aims, and/or research hypotheses. Explain how missing data and outliers will be handled in the analysis. The analysis plan should be consistent with the study objectives. Include any subgroup analyses (e.g., gender or age group). Specify statistical methods and variables for each analysis. Describe how confounding variables will be controlled in the data analysis.

Demographic (age at time of surgery, BMI, sex, active duty/dependent/retiree status), medical (ICD code, nicotine use, history of diabetes, prior pain medications), laterality of the TKA (left or right), discharge disposition, and anesthetic block type (spinal, adductor, or femoral nerve block) data will be summarized overall and as a function of injection group using descriptive statistics (eg, mean, standard deviation, median, minimum, maximum, frequency, percentages) and 95% confidence intervals to describe the sample. Appropriate inferential statistics (eg, independent samples t tests, chi square tests) will be performed to determine if there are statistically significant differences in any of these variables between the two injection groups. If so, multivariable techniques (eg, ANOVA or regression) including these potentially confounding variables in the analyses and/or stratification will be undertaken.

VAS pain scores and the dosage (MME) of opioids will be evaluated in patients as a function of injection type (ie, trigger point injection vs. sham injection) at each time point. Data will be assessed for normality and homogeneity of variance to determine whether parametric (eg, independent samples t tests, repeated measures ANOVAs) or nonparametric (eg, Wilcoxon Mann Whitney tests, Skillings-Mack tests) methods are appropriate.

In addition, the number of patients with a VAS>40 (indicating a “significant” level of pain) will be calculated and compared in each group and at each time point using the chi-square test (or the Fisher’s Exact test if assumption regarding minimum expected cell counts is not met) as well as McNemar’s tests.

The critical alpha level will be set at .05. Missing data will be handled using the “pairwise deletion” method; this method still includes patients with some missing data in the analyses when possible.

The plan is to use 10-15 participants per group, although if time and resources permit, we will include more patients to increase the power of the study and

account for possible dropouts up to a maximum of 50 patients per group. Recruitment and enrollment will end once the target sample size has been achieved.

11.2 Sample Size:

The plan is to use 10-15 participants per group, although if time and resources permit, we will include more patients to increase the power of the study and account for possible dropouts up to a maximum of 50 patients per group (maximum of 100 patients total).

11.3 Total number of subjects requested (including records and specimens):

100

11.4 If you are recruiting by study arm, please identify the arms of the study and how many subjects will be enrolled in each arm

Experimental (ie, trigger point injection) group will include 10-15 patients (up to a maximum of 50 patients) and placebo (ie, sham injection) group will include 10-15 patients (up to a maximum of 50 patients). Recruitment and enrollment will end on 31 December 2025.

11.5 Please provide a justification for your sample size

We used G*Power 3.1 (Dusseldorf Germany) to perform sample size calculations for our study. We designed these calculations using the primary outcome measure (ie, VAS pain scale rating in each injection group) which will be statistically compared using the independent samples t test or its nonparametric equivalent (ie, the Wilcoxon Mann Whitney test) if the assumptions for the independent samples t test (ie, normality and homogeneity of variance) are not met.

Using the more conservative Wilcoxon Mann Whitney test (Type 1 error/alpha level=.05 (two tailed) and power=.80), a sample size of 30 (ie, 15 in the trigger point group and 15 in the sham group) would allow us to detect a statistically significant difference in VAS pain scale ratings if a “large” effect size of 1.1 was obtained. A “large” effect size of 1.1 corresponds to an average difference (delta) in VAS scores between groups of >=28 units and an average standard deviation in each group of <= 25 units. This standard deviation is similar to Mayoral et al. (2013) who reported an average standard deviation of 25 units for the VAS at the 1 month follow up. Note that Mayoral et al. (2013) did not report VAS scores on POD1, although their average difference (delta) in VAS scores at 1 month was smaller than 28 units.

If up to 5 patients (eg, 30%) per group drop out of the study, a lower sample size of 20 (ie, 10 in the trigger point group and 10 in the sham group) would allow us to detect a statistically significant difference in VAS pain scale ratings if a larger effect size of 1.4 was obtained. This “larger” 1.4 effect size corresponds to an average difference (delta) in VAS scores between groups of >=35 units and an average standard deviation in each group was <= 25 units (again using the more conservative Wilcoxon Mann Whitney test (Type 1 error/alpha level=.05 (two tailed) and power=.80)).

In summary, our aim of including at least 10-15 patients per group would allow us to statistically detect a “large” effect of trigger point injections (relative to sham injections) on VAS pain ratings assuming our standard deviations were <= to the standard deviations in VAS pain scales reported by Mayoral et al. (2013). In addition, if statistically significant differences are not found, the data from our

study can be used to perform sample size calculations to power future larger studies that could potentially detect smaller effects. Our data can also be used for potential future meta-analyses (ie, the statistical combination of the results of multiple studies addressing a similar research question).

Addendum:
Sample sizes for other combinations of the standard deviation and difference in means (Delta) are
shown in the table below for illustrative purposes only. The “effect sizes” for these combinations are derived using Cohen’s D (Cohen, 1988). A larger sample size is necessary to detect a smaller “true effect.”

Delta	SD	n	Cohen_D	Effect_Size
20	18.5	15	1.08	large
25	18.5	10	1.35	large

12.0 Participant Information

12.1 Subject Population:

DoD beneficiaries aged 45 years and older who will be receiving a TKA, on either knee.

12.2 Age Range:

Check all the boxes that apply. if the age range of potential subjects (specimens, records) does not match the range(s) selected, please specify in the text box.

- [ ] 0-17
- [ ] 18-24
- [ ] 25-34
- [ ] 35-44
- [x] 45-54
- [x] 55-64
- [x] 65-74
- [x] 75+

12.3 Gender:

- [x] Male
- [x] Female
- [ ] Other

12.4 Special categories, check all that apply

- [ ] Minors /Children
- [ ] Students
- [ ] Employees - Civilian
- [ ] Employees - Contractor
- [ ] Resident/trainee
- [ ] Cadets /Midshipmen
- [x] Active Duty Military Personnel

- [ ] Wounded Warriors
- [ ] Economically Disadvantaged Persons
- [ ] Educationally Disadvantaged Persons
- [ ] Physically Challenged (Physical challenges include visual and/or auditory impairment)
- [ ] Persons with Impaired Decisional Capacity
- [ ] Prisoners
- [ ] Pregnant Women, Fetuses, and Neonates
- [ ] Non-English Speakers
- [ ] International Research involving Foreign Nationals - Headquarters Review is necessary

You must also consider the requirements of DoDI 3216.02, Enclosure 3, paragraph 7.e.

12.5 Inclusion Criteria:

Order Number	Criteria
1	• Aged 45 years or older • Planned to undergo primary total knee arthroplasty • Able to speak, read, and understand English • Willing to complete a study questionnaires • Willing to bring in their medications to be counted • DoD beneficiaries • No allergy to lidocaine • Not fearful of needles

12.6 Exclusion Criteria:

Order Number	Criteria
1	• Chronic opioid users (daily use of prescribed opioids for at least 90 days) • Diagnosed with Fibromyalgia • Non-English speaking • Unable to read English • Unable to understand English • Pregnant • Allergy to lidocaine/sulfite allergy • Not willing to complete study questionnaires • Not willing to bring in their medications to be counted • Not a DoD beneficiary • Fearful of needles

13.0 Recruitment and Consent

13.1 Please describe the recruitment process, including how subjects will be identified and selected for the study.

A HIPAA Waiver will be used to access MHS Genesis to obtain all joint surgeons case lists for those patients scheduled for TKA. The principal investigator will review case lists to identify name, type of surgical procedure (i.e., TKA), date

scheduled for surgical procedure, and phone. Patients scheduled for a TKA within two weeks will be contacted to discuss the study. Study inclusion and exclusion criteria will be reviewed with patients who are interested in participation to ensure they are eligible. Those who are eligible will be scheduled an appointment with the principal investigator before TKA surgery, ideally at their pre-op visit (consent will not on the same day as the surgery), to review consent documents and answer any questions. A copy of the consent documents may be emailed (if email address is provided) to the patient prior to the appointment to allow him/her to review them in advance.

13.2 Compensation for Participation:

No

13.3 Please describe the pre-screening process. If no pre-screening, enter Not Applicable in the text editor

No

13.4 Consent Process: Revised Common Rule, Section 219.116: General requirements for informed consent, whether written or oral, are set forth in this paragraph and apply to consent obtained in accordance with the requirements set forth in paragraphs (b) through (d) of this section. Broad consent may be obtained in lieu of informed consent obtained in accordance with paragraphs (b) and (c) of this section only with respect to the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens.

Are you requesting a waiver or alteration of informed consent?

○ Yes ◉ No

Please explain the consent process:

Patients will be recruited through use of a HIPAA Waiver to access joint surgeon case lists. Patients scheduled for a TKA will be contacted by the principal investigator and informed of the study. Those who desire to participate will have study inclusion/exclusion criteria reviewed to determine eligibility. Those eligible will be scheduled a consent appointment. The investigator will offer to email (or provide by hard copy) consent document to review prior to the appointment. When patients returns for consenting, they will be taken to a private room (clinic exam room or private room in the PACU) to conduct the consent procedures. Consent documents will be reviewed with patients and any questions asked with be answered. Patients who desire to enroll in the study will sign the consent documents. The investigator will sign the consent documents, then provide a copy to the patient. During the recruitment and consenting phase, the PI or AI will not be in military uniform or have their rank visible.

13.5 DoDI 3216.02 requires an ombudsman to be present during recruitment briefings when research involves greater than minimal risk and recruitment of Service members occurs in a group setting. If applicable, you may nominate an individual to serve as the ombudsman.

◉ N/A
○ Propose ombudsman

13.6 Withdrawal from Study Participation:

Explain the process for withdrawal and specify whether or not the subjects will be given the opportunity to withdraw their data their data/specimens in the event they wish to withdraw from the study

At any point in the study participants can self-withdrawal from the study if they have a poor response to the injections, are unable to tolerate all injections, not willing to complete questionnaires, intraoperative complications (pulmonary embolism, deep vein thrombosis, surgical site infection, multiple or other), not willing to bring in their medications or if they choose to no longer participate in the study. However, any data collected prior to withdrawal will still be analyzed.

14.0 Risks and Benefits

14.1 Risks of Harm:

Identify all research-related risks of harm to which the subject will be exposed for each research procedure or intervention as a result of participation in this study. Consider the risks of breach of confidentiality, psychological, legal, social, and economic risks as well as physical risks. Do not describe risks from standard care procedures; only describe risks from procedures done for research purposes

Risk of breach of confidentiality. Other risks of harm include allergy to the medication used in the trigger point injection, pain, bleeding, injury to neurovascular structures, and infection. Being selected for the sham can potentially increase a patient's risk for pain.

14.2 Measures to Minimize Risks of Harm (Precautions, safeguards):

For each research procedure or intervention, describe all measures to minimize and/or eliminate risk of harms to subjects and study personnel

Risk is limited by coding the data, security limiting access of the data set to investigators, password protected files, and lock and key.

Injections will be performed by a trained provider under an aseptic technique by prepping the site with alcohol swabs. All injection sites will be marked utilizing landmarks to identify each muscle belly. The plunger will be retracted prior to injecting medication to ensure needle placement is not within a vascular structure. One needle and plunger will be used for each muscle belly to limit risk of infection. After completion of all injections the injection site will be cleaned with alcohol swabs and a bandage will be applied.

14.3 Confidentiality Protections (for research records, data and/or specimens):

Describe in detail the plan to maintain confidentiality of the research data, specimens, and records throughout the study and at its conclusion (e.g., destruction, long term storage, or banking). Explain the plan for securing the data (e.g., use of passwords, encryption, secure servers, firewalls, and other appropriate methods). If data will be shared electronically with other team members/collaborators outside the institution, describe the method of transmission and safeguards to maintain confidentiality. Explain whether this study may collect information that State or Federal law requires to be reported to other officials or ethically requires action, e. g., child or spouse abuse

Risk is limited by coding of the data set, password protection, locked cabinet /drawer, and security limiting access of the data set to investigators.

14.4 Potential Benefits:

Describe any real and potential benefits of the research to the subject and any potential benefits to a specific community or society

If the individuals in the research are considered experimental subjects (per 10 USC 980), and they cannot provide their own consent, the protocol must describe the intent to directly benefit all subjects

The potential benefits of this study include a decrease in pain levels following TKA. This could result in decreased risk for opioid use disorder. Also, this may secondarily improve recovery and allow for easier participation in physical therapy.

14.5 Privacy for Subjects:

Describe the measures to protect subject's privacy during recruitment, the consent process, and all research activities, etc.

All consents and other information will be stored on a CAC enable computer that is password protected only accessible to investigators. All consents will be performed by either the PI and/or AI without official military uniforms or ranks displayed in a private exam or PACU room. Hard copy consent documents will be stored in a locked drawer, separate from other study documents, and saved for at least six years after study closure. After this period, the hard copy, and electronic study documents will be destroyed by shredding and/or files deleted.

14.6 Incidental or Unexpected Findings:

Describe the plan to address incidental findings and unexpected findings about individuals from screening to the end of the subject's participation in the research. In cases where the subject could possibly benefit medically or otherwise from the information, state whether or not the results of screening, research participation, research tests, etc., will be shared with subjects or their primary care provider. State whether the researcher is obligated or mandated to report results to appropriate military or civilian authorities and explain the potential impact on the subject

If any incidental unexpected findings are identified by the investigators during the medical record review (i.e., capturing medical or surgical history data), he/she will inform the participant and his/her primary care provider to facilitate follow-up.

15.0 Study Monitoring

15.1 Your study requires either Data and Safety Monitoring Plan (DSMP) or a Data and Safety Monitoring

Board (DSMB).

- ○ DSMP
- ○ DSMB
- ○ Both
- ◉ Not Applicable

16.0 Reportable Events

16.1 Reportable Events: Consult with the research office at your institution to ensure requirements are met. Describe plans for reporting unexpected adverse events and unanticipated problems. Address how unexpected adverse events will be identified, who will report, how often adverse events and unanticipated problems will be reviewed to determine if any changes to the protocol or consent form are needed and the scale that will be used to grade the severity of the adverse event.

Consult with the research office at your institution to ensure requirements are met

• Describe plans for reporting expected adverse events. Identify what the expected adverse events will be for this study, describe the likelihood (frequency, severity, reversibility, short-term management and any long-term implications of each expected event)

• Describe plans for reporting unexpected adverse events and unanticipated problems. Address how unexpected adverse events will be identified, who will report, how often adverse events and unanticipated problems will be reviewed to determine if any changes to the research protocol or consent form are needed and the scale that will be used to grade the severity of the adverse event

Pain – pain is anticipated given the type of intervention. However, pain is temporary and will improve after the local anesthetic takes effect.

Bleeding – another rare complication of trigger points. If a vascular structure is infiltrated the injection will be halted. Once the needle is removed will apply direct pressure for 3-5 minutes to ensure no continued bleeding. Likelihood of accessing vascular structures is minimal due to the location of arteries as they relate to musculature aimed at injecting.

Infection – very low risk for infection following trigger point injection, <0.05% of adverse side effects are reported. If infection takes place, then the patient will be treated with antibiotics. If infection includes an abscess will treat with incision and drainage.

Adverse events such as infection, damage to vascular structures that cause hematoma and excessive bleeding, injection of lidocaine into the blood stream are identified will be reported to the IRB. These adverse events will be monitored for during each visit through visually inspecting the injection sites and completing a neurovascular evaluation. The patient may also verbally inform the principal investigator of any of these potential adverse effects. The IRB will be notified by completing and submitting an eIRB Reportable Event Form (serious adverse event, unanticipated problem) or reporting at the time of continuing review (all others). The form will be routed to the DGMC C&T Board. The DGMC HRPP staff regularly monitor C&T Board notifications; they will notify the institution's HRPO of the reportable event by email, telephone, or in-person until it has been received and acknowledged. If any adverse event takes place the design of this study will be examined and determine is research protocol needs to be revised.

17.0 Equipment/non-FDA Regulated Devices

17.1 Does the study involve the use of any unique non-medical devices/equipment?

○ Yes ◉ No

18.0 FDA-Regulated Products

18.1 Will any drugs, dietary supplements, biologics, or devices be utilized in this study?

☑ Drugs
☐ Dietary Supplements
☐ Biologics
☐ Devices
☐ N/A

18.2 Drugs, Dietary Supplements and Biologics/Vaccines details:

☑ Are drug(s) in this research being used in accordance to the approved labeling?
☐ Are drug(s) in this research being used in a manner other than its approved labeling?

Enter Dietary Supplements and Biologics/Vaccines in the Drug Information table. Complete all relevant fields in the table ("Protocol Drug Details" screen). If the question is not relevant, leave the question blank and/or do not change the default selection.

View Details	Drug Name	FDA Approved	A new drug or a new use of an already approved drug:	IND Number
⊟	**Trade Drug Name:** lidocaine 1-2% with or without epinephrine **Generic Drug Name:** **Investigational Drug Name:**	Yes	No	

Trade Drug Name:	lidocaine 1-2% with or without epinephrine
Generic Drug Name:	
Investigational Drug Name:	
Identify the name of the manufacturer or source of investigational drug/biologic:	Hospira
Is the drug supplied at no cost?	Yes
Is the Drug FDA Approved:	Yes
Is this a new drug or a new use of an already approved drug	No
Is an IND necessary	No
IND Number	
Who holds the IND:	N/A
IND details:	
If FDA Approved and an IND is	

not required, Please provide a rationale for exemption:	
Are you currently using this IND in another research project?	No
If yes, list the IRB Number(s):	
Dose Range:	4mL
Frequency:	once
Route of administration:	intramuscular
Will the investigational pharmacy be dispensing?	Yes
If the source is not a FDA licensed facility, provide details regarding the purity, quality, stability and sterility of the investigational drug/biologic:	
Identify who will be preparing the investigational drug /biologic for administration and describe in detail how it will be prepared:	The PI will remove the lidocaine 1% without epinephrine from the pyxis within the orthopedics clinic. Once the medical is removed the PI will wear gloves and prepare 4 25-gauge needles and 4 5 mL syringes. Once all needles are attached to the syringes the cover to the lidocaine will be removed and cleaned with alcohol swabs before each draw. Once 1 mL of lidocaine 1% without epinephrine is prepared in each syringe the needles will be recapped and immediately go to the patient's room for injection.
Indication(s) under Investigation:	
Where will the drug be stored	Orthopedic clinic pyxis
Drug Storage Restrictions (including temperature, etc.):	Medication will be stored in the clinic pyxis at room temperature
Administration Instructions:	Prior to injection the PI will identify those anatomic landmarks meant for injection. Then the areas will be marked by indenting the skin with an empty pen, there will not be any ink on the injection site. The area will be prepped with chlorohexidine. Once the site is prepped the investigator will make two injections into the muscle belly and injection 0.5mL of lidocaine 1% without epinephrine. Once the needle is removed it will be discarded in the appropriate sharp's container. The area will then be cleaned with alcohol swabs and a band aid applied. These steps will be repeated for all 4-injection sites.
Possible Untoward Effects, Their Symptoms & Treatment:	
Potential or Actual Antidotes for Excessive or Adverse Drug Effect:	
Contraindications and Interactions, If Known:	Allergy to medication
Investigators Authorized to Prescribe:	PI and AI are authorized to prescribe lidocaine 1% without epinephrine

18.4 Reporting Requirements for FDA-regulated research under IND and IDE:

Describe the process for complying with FDA regulatory requirements for adverse event reporting and adverse device effects reporting to the sponsor

N/A

18.5 Sponsor (organization/institution/company):

☑ N/A

If applicable, provide sponsor contact information:

19.0 Research Registration Requirements

19.1 ClinicalTrials.gov Registration:

- ○ Registration is not required
- ○ Registration pending
- ○ Registration complete

19.2 Defense Technical Information Center Registration (Optional):

- ○ Registration is not required
- ○ Registration pending
- ○ Registration complete

20.0 References and Glossary

20.1 References:

1. Lin, X., Li, F., Lu, H., Zhu, M., & Peng, T. Z. (2022). Acupuncturing of myofascial pain trigger points for the treatment of knee osteoarthritis: A systematic review and meta-analysis. Medicine, 101(8), e28838. https://doi.org/10.1097/MD.0000000000028838
2. Mayoral, O., Salvat, I., Martín, M. T., Martín, S., Santiago, J., Cotarelo, J., & Rodríguez, C. (2013). Efficacy of Myofascial Trigger Point Dry Needling in the Prevention of Pain after Total Knee Arthroplasty: A Randomized, Double-Blinded, Placebo-Controlled Trial. Evidence-Based Complementary and Alternative Medicine, 2013, 1–8. **https://doi.org/10.1155/2013/694941**
3. "The Opioid Epidemic in the United States." SHADAC. Last modified May 15, 2024. Accessed July 21, 2024. **https://www.shadac.org/opioid-epidemic-united-states**.
4. Trasolini, Nicholas A., Braden M. McKnight, and Lawrence D. Dorr. "The Opioid Crisis and the Orthopedic Surgeon." The Journal of Arthroplasty 33, no. 11 (November 2018).
5. Ma, Yan-Tao, et al. "Dry Needling on Latent and Active Myofascial Trigger Points versus Oral Diclofenac in Patients with Knee Osteoarthritis: A Randomized Controlled Trial." BMC Musculoskeletal Disorders, vol. 24, no. 1, Jan. 2023, p. 36. DOI.org (Crossref), **https://doi.org/10.1186/s12891-022-06116-9**.
6. R Core Team (2022). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL **https://www.R-project.org/**.
7. Cohen, J. (1988). Statistical power analysis for the behavioral sciences (2nd ed.). Hillsdale,NJ: Lawrence Erlbaum. R Core Team (2022). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

20.2 Abbreviations and Acronyms:

mL – milliliter

PACU – Post-anesthesia Care Unit
POD – post-operative day
TKA – Total knee arthroplasty