Title: Postoperative Pain Control After Periarticular Injection During Total Knee Arthroplasty

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Document date: 8/8/2015

Document Type: Study Protocol and Statistical Analysis Plan

Help

Study:Do Intraoperative Periarticular Injections Improve Postoperative Pain Control in Patients Receiving Duramorph? – A Prospective, Double-Blinded, Randomized Controlled Trial (HM20004125)

Principal Investigator:	Gregory Golladay	**IRB Coordinator:**	Susan Kimbrough
Editors:	Gregory Golladay Melanie Morgan Teresa Potter Jibanananda Satpathy	**IRB Panel:**	IRB Panel A
PI Department:	Orthopaedic Surgery	**Approved Review Type:**	Full Board
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VCU Office of Research and Innovation

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Print Close

ID: HM20004125 HM20004125 View: SF - Study Identification

Study Identification

1. * **Select the Principal Investigator:**
   Gregory Golladay

2. * **Study Title:**
   Do Intraoperative Periarticular Injections Improve Postoperative Pain Control in Patients Receiving Duramorph? – A Prospective, Double-Blinded, Randomized Controlled Trial

3. * **Is this a student or trainee project in which activities will be carried out by that individual under your supervision (for example, dissertation or degree-required projects):**
   - ○ Yes
   - ● No

4. * **Please select the primary department or center that this study is being conducted under:**
   Orthopaedic Surgery

[redacted]

7. * **Select one of the following that applies to the project (selection will branch to new pages):**
   Note: VCU IRB offers guidance for many types of studies, including secondary data analysis studies, internet research, registries, EFIC, HUD, and Emergency Use protocols.
   See *https://research.vcu.edu/human_research/guidance.htm*
   - ● **Research Project or Clinical Investigation [*most exempt, expedited, and full board research studies]**
   - ○ Exception from Informed Consent (EFIC) for Planned Emergency Research
   - ○ Humanitarian Use of Device for Treatment or Diagnosis
   - ○ Humanitarian Use of Device for Clinical Investigation
   - ○ Emergency Use of Investigational Drug, Biologic or Device
   - ○ Treatment Use (Expanded Access to Investigational Product for Treatment Use)
   - ○ Center or Institute Administrative Grant Review
   - ○ Request for Not Human Subject Research Determination (i.e. request a letter confirming that IRB review is not required)

Federal Regulations

1. * Is this a FDA regulated study?

FDA regulated research includes all clinical investigations involving a test article and a human subject(s) that has been submitted for approval to the FDA or may be submitted in the future.
Check Yes if
- the study involves an IND/IDE, abbreviated IDE, IND/IDE exemption, HUD, expanded access, or is otherwise subject to 21 CFR 56,
- the study involves a test article being administered or dispensed to subjects NOT according to a clinicians' medical judgment but rather, per the study protocol, OR
- the study does not involve a test article but intends to provide safety or efficacy data to the FDA.

(●) Yes ( ) No

2. * Indicate the FDA regulated product(s) this study involves:

- [x] Drug
- [ ] Medical Device
- [ ] Biologic
- [ ] Dietary Supplement
- [ ] Food/Food Additive
- [ ] Color Additive
- [ ] Electronic Products for Human Use (radiation producing)
- [ ] Other

[redacted]

[redacted]

HM20004125 Gregory Golladay
Do Intraoperative Periarticular Injections Improve Postoperative Pain Control in Patients Receiving Duramorph? A Prospective, Double Blinded, Randomized Controlled Trial

Background, Rationale and Goals

1. * **Describe the study's background and what is currently known from the scientific literature, including citations, or upload a citation list in document upload. Use lay language whenever possible.**

There has been an increased interest in attaining adequate pain control after total knee arthroplasty for multiple reasons. Inadequate postoperative pain control correlates with decreased range of motion, decreased time to attaining therapy goals, increased length of stay, and poorer patient satisfaction.

The American Academy of Orthopaedic Surgeons and others have identified that pain control is associated with patient satisfaction – something used by the Centers for Medicare & Medicaid Services as a surrogate for quality of care and an integral component of a pay-for-performance system. Additionally, the financial situation of the health care system has cultivated an environment where there is increased pressure to minimize hospitals stays while maximizing early patient reported and functional outcomes.

Perioperative pain management is an area that continues to evolve to meet the needs of a more demanding healthcare system. The ideal analgesic should provide robust pain control, limited side effects, and have minimal effects on early postoperative rehabilitation. Because no single intervention can provide these necessities by itself, surgeons and anesthesiologists have turned to a multimodal regimen that targets different parts of the nociceptive pathway.

The advent of multimodal perioperative pain management has yielded numerous combinations of analgesic interventions including continuous epidurals, indwelling peripheral nerve catheters, single-shot peripheral nerve blocks, intraarticular injections, and periarticular injections. While these methods of analgesia were introduced to reduce the reliance on opioid-based therapy, recent publications have demonstrated that perioperative pain control continues to be suboptimal.

There have been previous randomized trials evaluating the efficacy of local infiltration analgesia (LIA) as a component of a multimodal postoperative analesgsia protocol. Of these studies, four evaluated the efficacy of continuous infusion catheters. The remaining studies did not use intrathecal morphine as a component of the multimodal postoperative protocol. Although six of the seven trials demonstrated reduced pain scores and opioid consumption, incomplete bias and incomplete blinding could have affected the outcomes.

Three authors have previously sought to compare the effectiveness of intrathecal morphine with LIA. Essving et al found that the LIA group had less morphine consumption and lower pain scores at rest and on movement in the first 48 hours, were more likely to be able to
climb stairs at 24 and 48 hours, met discharge criteria earlier, had a shorter hospital stay, and had greater patient satisfaction. Unfortunately, this study was biased, as it did not control for the supplemental systemic analgesia. Tsukada et al found that those who received a periarticular injection had lower pain scores at rest, improved range of motion at 24 and 48 hours, and a lower incidence of postoperative nausea. Tammachote et al found no difference between the two methods with regard to postoperative pain level, analgesic drug consumption, blood loss in drain, and knee function.

Even though there are numerous studies evaluating the efficacy of LIA, many are confounded by the lack of systemic analgesic standardization. No study to date has sought to determine the combined efficacy of intrathecal analgesia and periarticular injections with a standardized multimodal analgesia plan. Our study is a prospective, double-blinded, randomized, controlled trial which compares short-term (48 hour) postoperative outcomes in patients receiving intrathecal morphine with and without a periarticular injection.

The standard of care currently (for these two surgeons) is to use the joint 'cocktail' for all patients. The intervention in this study is to ask patients to 'NOT' receive the injection so as to assess it's effectiveness after TKR. The concentrations of each drug are typical for the use in peri-articular injections (not into but around the joint) as evidenced by a literature search and professional interaction with others in
the field.

(see references in uploaded documents)

2. * **Describe the study hypothesis and/or research questions. Use lay language whenever possible.**
The study hypothesizes that those receiving intrathecal Duramorph and local periarticular injections will have reduced narcotic use when compared with intrathecal Duramorph alone at 48 hours postoperatively.

3. * **Describe the study's specific aims or goals. Use lay language whenever possible.**
The study will assess and compare postoperative pain control in patients receiving intrathecal morphine with and without local periarticular injections.

4. * **Describe the scientific benefit or importance of the knowledge to be gained:**

This will objectively evaluate the benefits and/or risks of periarticular injections with regard to analgesia in a multimodal postoperative pain management plan. If there is no benefit from the injection this can be removed from the general protocol for TKR.

5. * **Describe any potential for direct benefits to participants in this study:**
Improved perioperative pain control in those receiving the injection and reduced risk of adverse outcomes from the injection for those in the control group.There will be no direct benefit expected for those patients in the control or placebo group.

6. * **Describe any potential for direct social impact in this study . For example, any engagement with specific communities to respond to community-identified needs, or ways the study will strengthen the well-being of the specific communities if applicable:**

[redacted]

Study Population

1. * **Provide the maximum number of individuals that**

   1. May participate in any study interaction or intervention (including screening, consenting, and study activities)
   AND/OR
   2. You obtain any data/specimens about (regardless of identifiability)

   at VCU and at other sites under the VCU IRB's oversight. See the help text for additional guidance.
   200

2. **If this is a multi-Center Project, what is the maximum anticipated number of subjects across all sites?**
   NA

3. * **Provide justification for the sample size by explaining how you arrived at the expected number of participants and why this number is adequate for answering the research questions:**
   Power established from a previous pilot study. A previously-approved (institutional review board) pilot study was performed to identify the number of patients needed to obtain sufficient power. Using a reduction in pain score of 50%, alpha of 0.05 and a power of 90%; a sample size of 64 in each group is necessary. The pilot study found that the pain scores were essentially equal by approximately 24 hours, therefore power was calculated for comparison up to about 12 hours postoperatively.

   This is also referenced in the research methods section.

   The final sample size was determined by the above power analysis and increasing to 200 to account for screen failures.

4. * **List the study inclusion criteria:**
   Patients 18 years of age and older, scheduled to undergo a total knee arthroplasty, able to provide informed consent. patients must receive Duramorph intrathecally.

6. * **List the study exclusion criteria:**
   Under the age of 18, using 80 morphine equivalents of narcotic pain medication preoperatively, had a history of allergic reaction to any of the medications used in the study, had creatinine clearance of less than 60 mL/min, currently pregnant, a BMI > 40 and a weight < 75kg. Patients unable to consent in English may be included by using the VCU language services to translate the consent. This population has traditionally been very low in the population that is being offered the study though, so it isn't anticipated to be needed. Patients will not be included if they are allergic to any of the study medications: ropivacaine, clonidine, ketorolac, or epinephrine.

8. * **Will individuals with limited English proficiency be included in or excluded from this research?**
   - (●) **Included**
   - ( ) Excluded - safety concerns if participants are unable to communicate with the study team
   - ( ) Excluded - instruments/measures only validated in English
   - ( ) Excluded - no prospect of direct benefit to individual participants
   - ( ) Excluded - minimal risk study
   - ( ) Excluded - lack of budget/resources for translation and interpretation [provide an explanation in next question]
   - ( ) Excluded - other reason [provide an explanation in next question]

7. **Justify the inclusion and exclusion criteria if you are either targeting, or excluding, a particular segment of the population / community. Provide a description of the group/organization/community and provide a rationale.**

Study Procedures

1. * **Describe the study hypothesis and/or research questions. Use lay language whenever possible.**
The study hypothesizes that those receiving intrathecal Duramorph and local periarticular injections will have reduced narcotic use when compared with intrathecal Duramorph alone at 48 hours postoperatively.

2. * **Describe the study's specific aims or goals. Use lay language whenever possible.**
The study will assess and compare postoperative pain control in patients receiving intrathecal morphine with and without local periarticular injections.

3. * **Choose all types of recruitment materials that may be used and upload them below:**
   - [ ] E-mail invitations
   - [ ] Phone Solicitation scripts (i.e. cold calls or random-digit-dialing)
   - [ ] Flyers, Mailed Letters or Newspaper/TV/Radio Ads
   - [ ] TeleGRAM announcements
   - [ ] Website text
   - [ ] Study-specific web sites (provide the design and text)
   - [ ] Social Media
   - [ ] EPIC MyChart Patient Portal research study descriptions
   - [ ] Psychology Research Participant Pool (SONA) study descriptions
   - [ ] Scripts for announcements made to groups
   - [ ] Other recruitment material
   - [x] **No recruitment materials**

4. * **Describe the study procedures/methods for identifying and recruiting participants. Address the following three aspects of recruitment in your response.**

   1. ***Identification of potentially eligible participants or secondary data/specimens of interest.***
      - **What database(s) will be queried to identify secondary data/specimens**
      - **How potential participants' contact information will be obtained**

   2. ***Recruitment procedures to invite participation in the study (when applicable):***
      - **How each of the written or verbal recruitment materials and reminders (selected above) will be used**
      - **Who will contact or respond to potential participants**
      - **Locations where recruitment procedures will take place**
      - **The timing and frequency of recruitment attempts**

   3. **Eligibility screening prior to consent and how those activities will be carried out (when applicable)**

   See the help text for additional guidance.
   Patients will be recruited at either the NOW center (Short Pump), Stony Point Outpatient Clinic or the Ambulatory Care Center clinics. Patients will be informed of the study once he/she has elected to undergo a total knee arthroplasty and has signed a consent for that procedure. If interested in joining the study, they will be given an informed consent to review and sign. The study will only be offered to those patients that have already signed a consent for the knee arthroplasty procedure.

   The attending physicians who have made the decision that a TKR is medically necessary will determine if a patient is eligible.

   The Orthopedic department has multiple studies being done in patients undergoing a TKR. Some of the studies have priority over others. Once it has been determined which studies a patient is being offered, they will be given a consent and it will be reviewed by the current orthopedic fellow. In the interest of improving our subject recruitment, some patients may be called via telephone to discuss the study. (see attached script). The actual consent will be reviewed and signed prior to surgery in the perioperative area where the patient will also have the opportunity to ask any further questions.

   The fellow may also review the study to all eligible patients at their medical appointments (these occur approximately one month prior to surgery). As noted previously, they will be given this information in a private examination room and given time to ask questions and/or to take the ICF home and peruse it. Any questions can be directed to the fellow. This is all done once the decision has been made to perform a TKR.

5. * **Does this study have a separate protocol document (i.e. a multisite or sponsor's protocol) that contains a detailed description of the study's methodology?**
   - ( ) Yes
   - (•) **No**

6. * **Since a separate protocol document is not uploaded, describe the proposed research using language understandable to those IRB committee members whose expertise is not scientific. The description must include:**

   1. A statement explaining the study design
   2. A detailed description of all the procedures that will be followed to carry out the study, preferably in sequential order, and in sufficient detail that the study's methods could be replicated
   3. A description of all research measures/tests/interventions that will be used (if applicable)

   See the help text for additional guidance
   Enrollment:
   A previously-approved (institutional review board) pilot study was performed to identify the number of patients needed to obtain sufficient power. Using a reduction in pain score of 50%, alpha of 0.05 and a power of 90%; a sample size of 64 in each group is necessary. The pilot study found that the pain scores were essentially equal by approximately 24 hours, therefore power was calculated for comparison up to about 12 hours postoperatively. 128 patients (64 in each group) undergoing primary total knee arthroplasty by three fellowship-trained orthopedic adult reconstruction surgeons at a single institution will be enrolled into a prospective, double blind, randomized controlled trial.

   Patients will be excluded if they are under the age of 18, currently using 80 morphine equivalents of narcotic pain medication daily (pre-operatively), have a history of allergic reaction to any of the medications used in the study, are pregnant, have creatinine clearance of less than 60 mL/min, a BMI > 40 or an actual weight < 75kg.

   Randomization:
   Each patient will be randomized to one of two groups: intrathecal morphine with intraoperative periarticular injection using a "joint cocktail" (treatment group) and intrathecal morphine with a placebo injection (placebo group) for perioperative pain management. A randomization schedule created by the pharmacy prior to the study will be used to determine to which treatment group each patient will be assigned. The pharmacists will prepare either injection and transport to the OR during each patient's procedure. The treatment group will received an injection of 50 mL of 0.5% ropivacaine, 0.8 mL (0.1mg/mL) clonidine, 1 mL (30 mg/mL) ketorolac, 0.5 mL (1 mg/mL) epinephrine, and 47.7 mL 0.9% saline for a total volume of 100 mL. The patients in the placebo group will receive 100 mL of 0.9% saline.

   Preoperative Intervention:

The regional anesthesia team will perform a combined spinal/epidural using ropivicaine and Duramorph. Patients will also receive 200 mg of celecoxib, 300mg of gabapentin, 975 mg of oral acetaminophen, and a 1.5 mg scopolomine patch. Each patient will then receive weight-based dosing of a preoperative antibiotic (cefazolin for MRSA negative patients without a cephalosporin allergy, cefazolin and preoperative vancomycin for MRSA positive patients, and Clindamycin for those with an established cephalosporin allergy) and 1 gram of IV tranexamic acid (unless contraindicated) within one hour of incision

Intraoperative Intervention:
All knee arthroplasties will be performed by four surgeons via the medial peripatellar approach. Implants being used include the Depuy Sigma or Stryker Triathlon cruciate retaining total knee arthroplasty systems. 20 mL of the injection will be placed into the posteromedial capsule after the final bony cuts are completed. While the cement cures, 10 mL will be injected into the infra-patellar fat pad, 20 mL into the quadriceps tendon/medial arthrotomy, 10 mL into the MCL insertion/pes anserine soft tissue sleeve, 10 mL into the supra-patellar pouch, 10 mL into the lateral retinaculum, and 20 mL into the subcutaneous tissue.

Patients will be allowed to receive extra epidurals during the operative procedure itself. The duration of pain relief for these injections is very short-lived and does not last past when the epidural catheter is removed. Since this is done prior to leaving the post-recovery area, it is very unlikely that these extra epidurals would affect pain scores once the patient is on the nursing unit.

Screen failures will be those patients that receive any other dose of Duramorph than 0.2mg intrathecally, and those that do not receive intrathecal morphine (occasionally the projected anesthesia plan is changed at the time of surgery and the patient does not receive intrathecal morphine).

A volume of 100ml as injected into the peri-articular injection is usual. Currently this is what is being done as standard of care.

The data collection form will be completed by Terry Potter PharmD. This will be done retrospectively--after the patient has been discharged from the hospital post TKR. See data collection form for details.

As a standard of practice in the hospital currently, a patient is asked for his pain score (0 to 10) as well as whether that value is acceptable to him/her. Due to excessive variability in the previous responses this information will no longer be collected. The sole research measure will be the morphine equivalents for the 48 hour period postoperatively.

Postoperative medications:
All patients will receive perioperative antibiotics (cefazolin for MRSA negative patients without an cephalosporin allergy, cefazolin and preoperative Vancomycin for MRSA positive patients, and Clindamycin for those with an established cephalosporin allergy). Generally, Coumadin will be used for postoperative chemical venous thromboembolism (VTE) prophylaxis unless consult services recommended otherwise. Patient controlled anesthesia (PCA)'s will not be used, and patients will be placed on a regimen of IV Morphine or hydromorphone and oral oxycodone or hydromorphone postoperatively. Patients will be allowed to receive additional epidurals during the operative procedure as determined by the presiding anesthesiologists. These injections will be one time injections only.

Outcome Measures:
As per above, the VAS scale will not be used as a research measure due to excessive variability in pervious participants. The sole research measure will be the amount of morphine equivalents given in the 48 hour period postoperatively.
Secondary outcomes include patient's subjective rating of the pain as being acceptable (yes/no), UPAT score before and after physical therapy, length of ambulation during physical therapy, amount of narcotics required (milligram dosage in morphine equivalents), presence of immediate postoperative complications within the first 48 hours, and the quantity of anti-nausea medication required.

Statistical Analysis
T-tests will be used to assess the quantity of narcotics used during the 48 hour postoperative period, length of ambulation during physical therapy, the change in UPAT score pre/post physical therapy, and the quantity of anti-nausea medication required. Chi square tests will be used to assess the patient's pain score acceptability and the presence/absence of immediate postoperative complications.

7. * The IRB only reviews research activities, so indicate which of the study activities are:

- Being performed exclusively for research purposes (i.e. they would not otherwise be done apart from this study) VERSUS.
- Alterations of routine activities/procedures (e.g. the study is altering the timing, frequency, method, location, amount, etc.) VERSUS.
- Being done for other purposes and whose data/results will be used secondarily in the study (e.g. standard medical or psychological tests, routine education practices, quality improvement initiatives, etc.).
The study patients are being asked to possibly forego the joint cocktail in order to assess it's effects on pain control post-operatively-- from a primary TKA. If a patient declines to be in the study they will most likely get the joint cocktail as part of their surgery. The joint cocktail being used as standard of care is the same as the study with the exception of no clonidine. That medication has been removed fro the standard of care injection due to a shortage of the clonidine.

8. If applicable, describe alternatives (research or non-research) that are available to potential participants if they choose not to participate in this study:
They will receive our current regimen (which includes a periarticular injection with the same ingredients with exception of the clonidine which has been removed due to a medication shortage, as the study treatment) as a part of their postoperative multimodal pain management plan.

[redacted]

Project Details

1. * **Select all of the following types of interventions that apply to this study (selections will branch):**
   - [ ] Social/Behavioral Interventions or experimentation / Tasks / Environmental manipulations
   - [ ] Deception (misleading participants through false or incomplete information)
   - [x] **Drug(s) / Biologics / Supplement(s) / Other Compounds (investigational products or products whose administration is dictated by the study protocol and not per the physician's clinical judgment)**
   - [x] **Placebos**
   - [ ] Safety and/or effectiveness evaluation of Bio-Medical Device(s), including in-vitro diagnostic devices/assays, mobile medical apps, software functions, and HUDs used in clinical investigations
   - [ ] Washout Periods
   - [ ] Expanded Access - Treatment Use of an Investigational Product
   - [ ] Medical or Surgical Procedures (eg: physical exam, clinical procedures, scans, etc)
   - [ ] Specimen/biological sample collection
   - [ ] None of the Above

2. * **Describe the nature/content of the placebo and justify the use of placebo control.**
   Some surgeons still do NOT use periarticular injections routinely during total knee arthroplasty. Given that patients already receive multiple different interventions as a part of their postoperative pain management plan, the use of these injections may not have an additive value. In order to obtain objective data regarding the periarticular injections' impact on postoperative analgesia, we will need to exclude it from one group for a true comparison.

3. * **Select all of the following types of interactions that apply to this study (selections will branch):**
   - [ ] Surveys / Questionnaires /Written responses to questions (including data entry)
   - [ ] Active internet data collection (i.e. using the internet to interact or intervene directly with research participants)
   - [ ] Interviews / Focus Groups / Verbal responses to questions
   - [ ] Audio / Video recording or photographing participants
   - [ ] Observations
   - [ ] Passive internet data collection (i.e. passively observing online behavior)
   - [ ] Educational Settings/Assessments/Procedures
   - [x] **None of the Above**

4. * **Select all types of secondary information and/or specimens that apply to this study (selections will branch): See the help text for definitions.**
   - [x] **Individually identifiable Health Information (PHI or RHI)**
   - [x] **Secondary data/specimens NOT from a research registry or repository**
   - [ ] Information/specimens from a research registry or repository (Usage Protocol)
   - [ ] Information/specimens originally collected for a previous research study
   - [ ] Publicly available information/specimens
   - [ ] Government-generated or collected information that was or will be obtained for nonresearch activities [only applicable to research conducted by or on behalf of a Federal department or agency]
   - [ ] No secondary data/specimens will be used

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Bio-Medical Drug / Biologic / Supplement / Other Compound Details

1. * List all drugs and/or biologics:

	Drug	Manufacturer	Types	FDA Labeling	IND Holder	IND Number
View	ketorolac tromethamine (Toradol	Roche Bioscience	Other (Drug or Compound Not Listed Above)	No	Not Required	
View	Epinephrine	Multiple	FDA Approved and being used as approved	Yes	Not Required	
View	ropivacaine	various	FDA Approved and being used as approved	Yes	Not Required	
View	Clonidine	Multiple	Other (Drug or Compound Not Listed Above)	No	Not Required	

2. * Will the Investigational Drug Service (IDS) pharmacy be utilized:
Yes

[redacted]

Secondary Data/Specimen Details

1. * **Describe the source(s) and nature of the information/specimens being obtained. This response should:**

   a. Identify where the data/specimens will come from (e.g., another researcher's registry, pathology lab, commercial source, medical records, etc.); and
   b. List what types of specimens will be obtained (when applicable); and/or
   c. List all data elements that will be obtained (when applicable). A data collection form or other documentation may be uploaded and referenced here.
   the data being collected includes pain medicine administered for the first 48 hours after surgery. There is a data collection form uploaded in documents. Visual analogue scores are not being collected any longer due to poor reliability.

2. * **Describe whether any agreement exists between you and data/specimen provider that states you will never have access to the ability to identify the participants (i.e. access to identifiers or the code key) and that you will not attempt to re-identify individuals.**
   Each subject has a subject number that is being assigned by RedCap (the index number) used as a code. This number is used on the data collection form. Once all data is collected and entered into RedCap this form will be destroyed. Once all data is collected and analyzed all identifiers will be removed from RedCap.

   The patient identifiers are in redcap and will not be used in any way that would identify the patient by name. The data will be used in aggregate when reporting the results.

3. * **When the information/specimens were originally collected, did individuals provide consent for secondary research use of their data/specimens (i.e. consent to another research study or to a research registry)?**
   - ○ Yes
   - ● No

Contingency Plan

This page will be used by the IRB in the event that an institution-wide emergency situation arises that requires contingency plans.

A contingency plan describes the alternative procedures that a study would want to use in case of an emergency that prevented normal study activities from occurring. It is a form of adaptive protocol. It enables the VCU IRB to quickly approve alternative study activities along with criteria for when those activities would or would not be put into effect. For example, in 2020, some studies had a COVID-19 Contingency Protocol approved that described alternative remote procedures that they would switch to whenever the University restricted in-person research activities.

In all studies, investigators are strongly encouraged to plan prospectively and build flexibilities into their regular protocols (regardless of whether an emergency situation exists) as well as think about what they would do in an emergency situation. For example, windows for timed study visits, ranges instead of exact values, flexibilities in inclusion criteria, etc. Flexibility and adaptations that are built into the protocol will reduce the number of changes that have to be submitted to the IRB and should reduce the number of incidents of deviations and noncompliance by investigators.

Further instructions and smartform questions on this page will be released from the IRB in the event of such an institution-wide emergency situation.

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Consent Process

1. * List all consent groups:

	Group	Types	Waivers	Roles	Roles - Other	Electronic Signatures	Consent	Coercion	Decision	Re-Consent
View	Patients Undergoing Knee Arthroplasty	Signed Consent by Participant	No Waivers Requested	Principal Investigator Co/Sub-Investigator Research Coordinator			Consent (research) will be obtained after the patient has signed the consent for the knee arthroplasty. Once this is signed the patient will be approached by the surgeons or coordinators to offer this study. This will occur in a private office or examination room at Stony Point, ACC clinic, the NOW clinic or the perioperative area.		The time period to make a decision will be a matter of weeks to months. The study will be presented to patients once a decision has been made to undergo a TKR (consent has been signed). The time period between surgery decision and surgery is variable and patient specific--but there is adequate time to make a decision	N/A

[redacted]

Risks, Discomforts, Potential Harms and Monitoring

1. * **Describe the risks of each research procedure to participants or others. For each identified risk, provide an assessment of the anticipated seriousness and likelihood of the risk. Some examples of possible risks include but are not limited to:**
   - **Physical risks (e.g. bodily harms or discomforts, side effects, etc.)**
   - **Psychological risks (e.g. emotional, mental, or spiritual harms or discomforts, changes to thoughts, beliefs, or behaviors, etc.)**
   - **Research data risks (e.g. loss of confidentiality and privacy)**
   - **Social or legal risks (e.g. impacts on relationships or reputation, legal or criminal justice actions for self or others, etc.)**
   - **Financial risks (e.g. impacts on income, employability, or insurability, loss of services, etc.)**
   - **Other risks (e.g. unforeseeable risks of experimental procedures, risks related to particular study designs (randomization, washout, placebo, withholding care/services, deception), etc.)**

   See the help text for additional guidance.

   The risks to the participants include:
   For those receiving injections, potential adverse reactions as listed in the informed consent. These risks are extrapolated from FDA package labeling in which the route of administration is different from the current use (peri-articular versus IV, IM or epidural use). Adverse effects from this injection (it has been used for years by the orthopedic surgeons in this manner) anecdotally is minimal--generally the most common is temporary nerve palsy and this is very rare.

   For those NOT receiving injections, reduced postoperative pain control and the need for more narcotic pain medication postoperatively.

   There is no way to quantify the risks that we mention in the ICF since several of the drugs are being used off-label and there is no data on adverse effects except from the primary literature. Most studies that have used this type of pain control have reported no adverse effects (from the drugs). The risks noted in the ICF are extrapolated from the oral or IV use.

   We have provided a further review of the literature surrounding the use of the periarticular injections (uploaded documents)

2. * **Describe how each of the risks/harms/discomforts identified above will be minimized:**
   A full review of the patient's medical record, including allergies, will be performed to minimize allergic and other adverse drug reactions. The periarticular injection will be placed in a region away from nerves so as to prevent temporary or permanent weakness/numbness.

   In patients who do not receive the periarticular injection, they will continue to receive other important components of the perioperative multimodal analgesia protocol.

   Patients are monitored at least daily by medical staff after undergoing TKR. Nursing protocol monitors pain scores and pain acceptance rates on an hourly basis post-surgically. Any side effects will be noted during this monitoring process. As previously noted, the risks in this study are notably, potential pain by not receiving the peri-articular joint injection, since all patients who are NOT enrolled in the study will likely receive the injection.

3. * **Describe any potential risks or harms to a community or a specific population based on study findings (e.g. information that could be stigmatizing or derogatory):**
   None

4. **Where appropriate, discuss provisions for ensuring necessary medical, professional, or psychological intervention in the event of adverse events to the subjects:**
   If there is any adverse reaction to the injection this will be handled by the orthopedic physicians who are caring for the patient during their surgery.

6. * **Describe criteria for when the investigator would withdraw an individual participant from the study; such as safety or toxicity concerns, emotional distress, inability to comply with the protocol, etc.:**
   If there is a toxicity or adverse reaction concern, the patient will be withdrawn from data collection and treated appropriately according to current medical guidelines and standards.

   Any toxicity event or adverse effects will be managed with the use of fluids, and medications such as anti-emetics. Patient level of monitoring may be increased to allow for closer observation and treatment. Other treatment interventions will be managed with additional interventions as deemed necessary by the treating physicians.

8. * **Summarize any pre-specified criteria that would trigger the investigator/sponsor/monitoring committee to stop or change the study protocol due to safety concerns:**
   NA

   Data and Safety Monitoring
   Data and safety monitoring is a system for checking the study's data at regular intervals over the study period to identify and address issues that could affect the safety of research participants. This requirement is in accordance with 45 CFR 46.111.

   The purpose of data and safety monitoring plan is to set forth study team procedures for monitoring/addressing:
   - Participant safety (physical, psychological, etc.)
   - Data validity
   - Early stopping (termination) based upon changes in risks and benefits.

7. * **Indicate if this study will have a Data Safety Monitoring Board (DSMB) or a Data Safety Monitoring Plan (DSMP): [Required for all greater than minimal risk studies]**
   - [ ] DSMB
   - [x] **DSMP**
   - [ ] No DSMB/DSMP [Note: This response is not applicable for greater than minimal risk studies]

8. * **Describe your Data Safety Monitoring Plan for monitoring the study's data to ensure the safety of participants. This plan should include (but is not limited to) the following elements:**
   1. Who will monitor data
   2. What data and/or processes will be reviewed
   3. When and how frequently monitoring will occur
   4. What report/documentation will be submitted to the IRB at the time of continuing reviews

   See the help text for additional guidance.

   The primary objective is to assess and compare postoperative pain control in patients receiving intrathecal morphine with and without a local periarticular injection.

   Opiate requirements postoperatively (morphine equivalents) will be assessed.

   OVERSIGHT RESPONSIBILITIES
   Oversight of the trial is provided by the Principal Investigator (PI), Dr. Gregory Golladay and Dr. Jibanananda Satpathy.

MONITORING PROCEDURES
Dr. Golladay assures that informed consent is obtained prior to performing any research procedures, that all subjects meet eligibility criteria, and that the study is conducted according to the IRB-approved research plan.

Study data are accessible at all times for the PI and co-investigators to review. The PI and co-investigators review(s) study conduct including accrual, screen failures, protocol deviations on a quarterly basis. The PI and co-investigators review AEs individually in real-time and in aggregate on a quarterly basis. The PI and co-investigators review(s) serious adverse events (SAEs) in real-time. The PI ensures all protocol deviations, AEs, and SAEs are reported to the IRB according to the applicable regulatory requirements.

COLLECTION AND REPORTING OF SAEs AND AEs
For this study, the following standard AE definitions are used:
Adverse event: Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure.
Serious Adverse Event: Any AE that results in any of the following outcomes:
• Death
• Life-threatening
• Event requiring inpatient hospitalization or prolongation of existing hospitalization
• Persistent or significant disability/incapacity

AEs are graded according to the following scale:

Mild: An experience that is transient, & requires no special treatment or intervention. The experience does not generally interfere with usual daily activities. This includes transient laboratory test alterations.

Moderate: An experience that is alleviated with simple therapeutic treatments. The experience impacts usual daily activities. Includes laboratory test alterations indicating injury, but without long-term risk.
Severe: An experience that requires therapeutic intervention. The experience interrupts usual daily activities. If hospitalization (or prolongation of hospitalization) is required for treatment it becomes an SAE.

The study uses the following AE attribution scale

Not related: The AE is clearly not related to the study procedures (i.e., another cause of the event is most plausible and/or a clinically plausible temporal sequence is inconsistent with the onset of the event).

Possibly related: An event that follows a reasonable temporal sequence from the initiation of study procedures, but that could readily have been produced by a number of other factors.

Related: The AE is clearly related to the study procedures.

AEs are identified during hospital admission, when potential AEs are assessed through a review of the hospital chart on a daily basis and a physical examination of the subject.

SAEs and specific procedure-associated AEs are reported to the VCU Institutional Review Board (IRB) within 24 hours. In addition, all AEs are reported according to the VCU IRB AE reporting guidelines.

MANAGEMENT OF RISKS TO SUBJECTS
Expected AEs
Expected AEs (although risk is very low based on published research and 15 years of experience) associated with the drugs used in the periarticular injection includes:
1. Ropivacaine
a. Cardiotoxicity
b. Hepatotoxicity
c. Nausea
d. Hypotension
e. Vomiting
f. Bradycardia
g. Tinnitus
h. Dizziness
i. Dry mouth

2. Ketorolac
a. Platelet dysfunction
b. Renal toxicity
c. Gastrointestinal bleeding

3. Epinephrine
a. Hypertension
b. Tachycardia
c. Arrhythmias

4. Clonidine
a. Hypotension
b. Bradycardia
c. Pruritis
d. AV block
e. Sedation
f. Dizziness
g. Dry mouth

AE Management
Any AEs will be managed with the use of fluids, and medications such as anti-emetics. Patient level of monitoring may be increased to allow for closer observation and treatment. Other treatment interventions will be managed with additional interventions as deemed necessary by the treating physicians.

DATA ANALYSIS PLANS
There will be no interim analysis for safety, efficacy or both. Due to the low risk of this study—currently the surgeons involved in this study have used this multimodal periarticular injection for the last 15 years and have noted no adverse events that could be attributed to the injection—an interim analysis was deemed not necessary for safety. Additional considerations were the increased cost of more subjects when performing an interim analysis. Expected AEs will be assessed after each procedure and during the subsequent hospitalization and discussed at the quarterly research meetings (as noted above). Any unexpected AE will be reported to the VCU IRB within 24 hours as required by the VCU IRB. There are no planned stopping rules.

PLAN FOR DATA MANAGEMENT
Compliance of regulatory documents and study data accuracy and completeness will be maintained through an internal study team quality assurance process.
Confidentiality throughout the trial is maintained by all patient information being maintained in the Red Cap database which is only accessible by members of the study team. No paper documents are kept.

Privacy

Privacy refers to an individual's right to control how others view, record, or obtain information about them. When privacy is violated it can involve such things as

- Being asked personal questions in a public setting;
- Being publicly identified as having a particular characteristic or diagnosis;
- Being seen entering a place that might be stigmatizing;
- Being photographed, videotaped or observed without consent;
- Disclosure of personal information to unauthorized people

Privacy is not the same as confidentiality because privacy protections apply to people, and confidentiality protections apply to data. Confidentiality protections should be described on the Data Confidentiality page of this form, not here.

Instructions for this page:

Select all the applicable ways that the research team will protect participants' privacy throughout the course of the study. Not all will be applicable to every study.

To elaborate on any response, also click the "Other Protections" checkbox to provide further explanation in the last free-text question.

Read the entire page before filling out the form.

1. * **Protections when conducting one-on-one in-person interventions or interactions (for groups see Q2 below):**
   - [x] **Conducting study activities in locations that maximize privacy (limited people around, closing doors, drawing drapes around beds, monitoring voice volume, etc.)**
   - [x] **Verifying identity before discussing personal information.**
   - [x] **Asking the participant if they are comfortable answering questions in that location**
   - [x] **Asking the participant if they are comfortable with having other people present (if any)**
   - [ ] Moving away from other people when conducting activities in public spaces or offering a private space
   - [ ] Offering other options of ways to respond to sensitive questions (i.e. pointing, clicking, or writing) if uncomfortable verbally responding
   - [ ] Using generic signs on research rooms and spaces, particularly for research on stigmatizing or sensitive topics
   - [ ] Other protections not listed in this question – describe below
   - [ ] N/A – study has no in-person interventions or interactions with participants

2. * **Protections when conducting group interventions or interactions:**
   - [x] **Conducting study activities in locations that maximize privacy (limited people passing by, closing doors, monitoring voice volume, etc.)**
   - [x] **Moving to a more private area to answer questions or to discuss concerns**
   - [ ] Discussing privacy with the participants and the importance of not talking outside the group about what other people say during the group session
   - [ ] Allowing participants to use a pseudonym or limiting use of individuals' names during the group activity
   - [ ] Asking everyone in a public group setting (e.g. classrooms, workshops) to turn something in (blank or filled) so participants do not have to self-identify when turning in materials
   - [ ] Collecting paper forms in a closed box or envelope rather than passing to others or leaving in an open area
   - [ ] Limiting participant identifiers that would be visible on paper documents (i.e. using study IDs instead of direct identifiers)
   - [ ] Allowing people to distance themselves from other participants during group activities
   - [ ] Offering other options of ways to respond to sensitive questions (i.e. pointing, clicking, or writing instead of speaking)
   - [ ] Using generic signs on research rooms and spaces, particularly for research on stigmatizing or sensitive topics
   - [ ] Ensuring non-participating individuals are not captured on recordings or in photos
   - [ ] Other protections not listed in this question – describe below
   - [x] **N/A – study has no group interventions or interactions**

3. * **Protections when conducting remote interventions or interactions (e.g. phone, text, email, video-conference, tele-health, online, etc.):**
   - [x] **Conducting study activities in locations where study staff can maximize their own privacy (limited people around, closing doors, monitoring voice volume, etc.)**
   - [ ] Leaving/sending generic messages that avoid using study and participant identifiers, such as names, study titles, clinics, study topics, etc.
   - [ ] Obtaining permission prior to sending text messages
   - [ ] Advising the participant to move to a location where they are comfortable answering questions and will not be overheard
   - [ ] Advising online participants to complete the activity at a time and location where they will be comfortable answering questions
   - [ ] Ensuring non-participating individuals are not captured on recordings or in photos
   - [ ] Offering other options of ways to complete the activity (i.e. online, paper, phone) if more privacy is desired
   - [ ] Offering a way to save and return later to the online activity if privacy is compromised
   - [ ] Other protections not listed in this question – describe below
   - [ ] N/A – study has no remote interventions or interactions with participants

4. * **Protections when mailing study materials to/from participants:**
   - [ ] Obtaining permission to mail study materials
   - [ ] Confirming/verifying the accuracy of addresses before mailing items
   - [ ] Ensuring the participant is able to personally receive mailed materials and has a way to protect their own privacy if they do not want others to know they are receiving research communications (i.e. notifying participants of when to expect it)
   - [ ] Using return address labels and document headers that avoid study identifiers, such as study names, clinics, study topics, etc.

- [ ] Avoiding or limiting use of participant identifiers and health information on mailed documents (i.e. using study IDs instead of direct identifiers)
- [ ] Providing a return mailing address label or pre-addressed envelope to ensure returned items are sent to the correct address
- [ ] Communicating receipt of mail from participants and/or asking them to notify you when they mail it to ensure study documents are not lost in transfer
- [ ] Offering other options of ways to complete the activity (i.e. by phone or online) if desired
- [ ] Other protections not listed in this question – describe below
- [x] **N/A – not mailing any materials to/from participants**

6. * **Protections when analyzing or disseminating study data** *Applicable to all studies*:

- [x] **Working only in locations where the study team can ensure privacy (not working in close proximity to non-study personnel, closing doors, closing/putting away documents/files before leaving, etc.)**
- [x] **Securing physical materials only in locations that ensure privacy (access limited to authorized study personnel)**
- [x] **Only sharing data/specimens in accordance with the Sharing Plan outlined in this smartform**
- [ ] Obtaining explicit parental permission before disseminating or sharing recordings or photos of children
- [ ] Blurring/redacting/hiding faces and other identifiable features/marks (tattoos, scars, birthmarks, distinctive voice, etc.) in recordings or photos prior to disseminating or sharing
- [ ] Only publishing or presenting aggregate results or findings (i.e. no individual-level information)
- [ ] Taking additional steps to protect participant identities when publishing or presenting individual-level information, quotations, results, images – describe below
- [ ] Other protections not listed in this question – describe below

8. Describe any other way(s) that the research team will protect participants' privacy. ***See the help text for additional guidance.***

All patient interactions will be done in a private examination room or practitioner offices at the Stony Point Ambulatory Center, ACC clinics, NOW center (Short Pump) or the perisurgical areas. These offices are all private, with doors that close. No patient will be approached in the waiting area. No images will be taken.

Once data collection is complete, all data will be de-identified and there will be no risk to the patient. Prior to de-identification, all data will be housed on a password protected computer in a locked office at the VCU Medical Center (within RedCap).

All patients (whether receiving the active injection or the placebo) will have the injection prepared in the investigational pharmacy and delivered to the OR either the day prior to or the morning of the surgery. The labels on the syringes will not note the treatment group, thus keeping the blinding. This is the only research activity while the patient is hospitalized. After the surgical procedure, all activities will be standard post-op treatment. The research activity will occur later via chart review (mg of pain medicine)

Data Confidentiality and Storage

Confidentiality refers to the way private, identifiable information about a participant or defined community is maintained and shared. It describes how the study's research materials (data, specimens, records, etc.) are protected from unauthorized access.

Instructions for this page:
Select all the ways that the research team will keep the study materials and data confidential throughout the course of the study. Not all will be applicable to every study.
To elaborate on any response, also click the "Other Protections" checkbox to provide further explanation in the last free-text question.

Read the entire page before filling out the form.

1. * **Protections for paper research materials:**
   - [x] **Maintaining control of paper documents at all times, including when at an off-campus location**
   - [x] **Limiting or avoiding use of participant identifiers on paper documents (i.e. using study IDs instead of direct identifiers)**
   - [x] **Storing paper documents in a secure location accessible only to authorized study personnel**
   - [x] **Promptly transcribing, scanning, or abstracting data from paper into electronic platforms with destruction of the paper copy**
   - [x] **Proper destruction of paper records (and obtaining prior permission when required) in accordance with VCU Records Management policies**
   - [ ] Other protection not listed in this question – describe below
   - [ ] N/A – no paper research materials

2. * **Protections for research specimens:**
   - [ ] Maintaining control of specimens at all times, including when at an off-campus location
   - [ ] Storing specimens in a secure location accessible only to authorized study personnel
   - [ ] Labeling specimens with subject ID or other coded information instead of direct identifiers
   - [ ] Final destruction of specimens will be devoid of any identifiable information
   - [ ] Other protection not listed in this question – describe below
   - [x] **N/A – no research specimens**

3. * **Protections for electronic files/data - See https://ts.vcu.edu/about-us/information-security/data-management-system/**
   - [x] ***Required for all studies* Use VCU-approved methods of data storage, transmission, and transfer (see https://dms.vcu.edu)**
   - [x] **Remotely accessing VCU network storage to store data when at off-campus locations**
   - [ ] Ensuring unauthorized individuals who might share a device do not have access to study materials (e.g. individual logins, separate accounts)
   - [x] **Using VCU-approved data collection tools and apps (e.g. REDCap) and storing exported analysis files in VCU-approved storage locations (see https://dms.vcu.edu)**
   - [ ] When using non-VCU-approved electronic data collection tools, storage locations, data transfer platforms, and mobile apps (e.g. Dropbox, Box, Survey Monkey, Fitbits, novel apps):
     • consulting with VCU Information Security on proper data management (see https://ts.vcu.edu/askit/essential-computing/information-security/);
     • advising participants about the terms of use and privacy policies of those sites/apps;
     • limiting or avoiding use of identifiers; and
     • removing data promptly from the external location after transferring it to a VCU storage location
   - [ ] De-identifying the research data by replacing subjects' names with assigned subject IDs
   - [x] **Storing the study's linkage key in a password-protected and VCU-approved storage location (see https://dms.vcu.edu)**
   - [ ] When analyzing particularly sensitive information, using computers that are unconnected from the internet.
   - [x] **Proper destruction of electronic records (and obtaining prior permission when required) in accordance with VCU Records Management policies**
   - [ ] Other protection not listed in this question – describe below

4. * **Protections for computers and research devices/apps that are provided to participants for use in the study:**
   - [ ] Transferring data promptly from the device/app to a VCU storage location
   - [ ] Setting strong passwords on computers and research devices (when applicable)
   - [ ] When providing devices or mobile apps to children, informing parents about the settings and how to manage them (if applicable), internet access, and any other installed apps on the device
   - [ ] Other protection not listed in this question – describe below
   - [x] **N/A – no computers or devices/apps being provided for participant use**

6. * **Protections for email/online communications**
   - [ ] Only using VCU/VCU Health email addresses for study-related communications
   - [ ] Only using VCU/VCU Health–approved methods of teleconferencing or video conferencing (e.g. Zoom) (for studies involving HIPAA, contact VCU or VCU Health Information Security [as appropriate] about HIPAA-compliant systems)
   - [ ] Other protection not listed in this question – describe below
   - [x] **N/A – no email/online communications**

8. **Specify any other places where this study's paper and electronic research data and/or physical specimens will be stored and any other ways they will be secured from improper use and disclosure.**

   See the help text for additional guidance.
   Only those members listed in this IRB will have access to this information. Once all data is collected, it will be placed into a de-identified data base for review. Protected Health Information will be kept on a password-protected computer in a locked office at VCU Medical Center (within RedCap). If PHI requires transportation to another VCU site, it will be placed on an ecrypted transportation device (there should be no reason for this to occur).

7. * **If research data that contains any of the 18 HIPAA identifiers will be released to person(s) or group(s) outside of the VCU study team or the PI's department, identify the data recipient(s) along with their VCU department or other institutional or organizational affiliation(s).**
   None to be shared

8. * **Select all identifiers that will be collected as part of this study (including for recruitment, data gathering, data analysis, etc.), even if the data will eventually be anonymized:**
   - [x] **Names**

- [ ] Geographic Locators Below State Level
- [ ] Social Security Numbers
- [x] **Dates (year alone is not an identifier)**
- [ ] Ages over 89 (age under 89 is not an identifier)
- [ ] Phone Numbers
- [ ] Facsimile Numbers
- [ ] E-mail Addresses
- [x] **Medical Record Numbers**
- [ ] Device Identifiers
- [ ] Biometric Identifiers
- [ ] Web URLs
- [ ] IP Addresses
- [ ] Account Numbers
- [ ] Health Plan Numbers
- [ ] Full Face Photos or Comparable Images
- [ ] License/Certification Numbers
- [ ] Vehicle ID Numbers
- [ ] Other Unique Identifier
- [ ] No Identifiers
- [ ] Employee V#

8. * **If the study will code (i.e. de-identify) the research data by replacing subjects' names with assigned subject IDs, explain the following aspects of the coding process:**

- The process for how subject IDs will be generated/assigned (e.g. random, sequential)
- Whether there will be a key that links the subject ID with direct identifiers.

If a key will be created, describe
- The place where the key will be stored
- The role(s) of all individuals who will have access to the key
- When the key will be destroyed

See the help text for guidance.
There will be one key linking the patient name/MRN to their code listed on the data collection form. This will be a computer file which will be on a password protected computer in a locked office at VCU Medical Center. This key will be destroyed once data collection is complete. The coding key will be available to the orthopedic fellows and the data analyst (Terry Potter). Once the key is destroyed the data will be completely de-identified. This key and all data will be located in the VCU Red Cap database.

Data Retention

1. * **Select all of the ways that individually identifiable information obtained during pre-screening and/or screening will be handled for individuals who DO NOT qualify for the study:**
   - [x] **Immediately destroy the information and identifiers (no data collected)**
   - [ ] Immediately destroy the identifiers connected with the data (anonymization)
   - [ ] Store until the end of study & then destroy
   - [ ] Use as "screening failure" data by members of the study team
   - [ ] Provide to others outside of the research team (with the participant's permission)
   - [ ] Request permission from participant to maintain and use the identifiable information
   - [ ] Other
   - [ ] N/A - study does not require screening procedures

2. * **Will participants be able to withdraw their data (paper, electronic, or specimens) from the study (e.g. ask that it be destroyed or returned) if they no longer wish to participate? (FDA-regulated studies should select No - see help text)**
   - ( ) Yes
   - (•) **No**

3. * **What will happen to the research materials (e.g. data, specimens, documents, etc.) when the research has been completed?**
   - ( ) Stored indefinitely with identifiers removed
   - ( ) Stored indefinitely with identifiers attached
   - (•) **Destroyed at the end of study once the minimum time required for data retention has been met per VCU Data Retention Policy and/or sponsor retention requirements**
   - ( ) Destroyed when notified by sponsor but not less than the minimum time required for data retention per VCU Data Retention Policy
   - ( ) Other

HM20004125 Gregory Golladay
Do Intraoperative Periarticular Injections Improve Postoperative Pain Control in Patients Receiving Duramorph? A Prospective, Double Blinded, Randomized Controlled Trial

Sharing Plan

This page addresses times when investigators may be required to share information about participants or may desire to share their research information/specimens with the aim of advancing science. This page creates a plan for when and how information/specimens could be shared.

Try to anticipate all reasonably foreseeable sharing so that the consent document can also reflect that information. However, it is acceptable to amend this page later and explain either how re-consent of previously and currently enrolled participants will occur or why re-consent should not be required.

The IRB reviews this page against the consent document (if one exists) to demonstrate the ethical principle of Respect for Persons by confirming that plans for sharing do not go against what participants would understand about the use of their data/specimens.

The IRB also ensures there are adequate protections for the privacy of participants and the confidentiality of participants' data/specimens when data is shared with others.

1. * **Is it likely investigators could discover information about child/elder abuse or neglect that would require mandatory reporting by the investigators or staff?**

   The Code of Virginia requires that most medical personnel and all employees of institutions of higher education report suspected child/elder abuse or neglect.

   ○ Yes
   ● **No**

2. * **Is it likely investigators could discover a previously unknown reportable disease or condition that would require mandatory reporting by the investigators or staff (i.e., HIV , coronavirus, hepatitis, etc.)?**

   ○ Yes ○ No

3. * **Will the sponsor or investigator obtain a Certificate of Confidentiality for this study?**

   Certificates of Confidentiality (CoC) are issued by the National Institutes of Health (NIH), the FDA and CDC to protect identifiable research information from forced disclosure. All human subject research studies regardless of funding can qualify to receive a CoC. A CoC is automatically issued for research that was ongoing on December 13, 2016, or initiated after that date. For more information, see https://humansubjects.nih.gov/coc/

   ● **No - Will not obtain CoC for this study**
   ○ Yes - CoC has been obtained or issued automatically
   ○ Yes - CoC request is pending

4. * **Select the way(s) that information or biospecimens (including DNA) may be used by the VCU PI or VCU study team for other future research projects (i.e. analyses beyond/apart from the aims of this study)?**
   See help text for definitions.

   ☐ Will use directly identifiable information or specimens.

   ('Directly identifiable' means that identifiers like name, medical record number, social security number, etc. are included in/attached to the dataset/specimens. Maintaining identifiable data for future research is treated as a registry by the VCU IRB. The IRB must approve the new research use in an amendment to this study or as part of a new study before the project is initiated. You will be asked more questions about this on a later page)

   ☐ Will use de-identified or indirectly identifiable information or specimens.

   ('De-identified' means that a linkage/key code exists that links identifiers to data/specimens. When the researcher holds both the data and the key, the VCU IRB considers the subjects to be readily identifiable. Maintaining identifiable data for future research uses is treated by the IRB as a registry. The IRB must approve the new research use in an amendment to this study or as part of a new study before the project is initiated. You will be asked more questions about this on a later page)

   ☐ Will use anonymized information or specimens.

   ('Anonymized' means that 1) no linkage/key codes exist that link identifiers to data/specimens; and 2) subjects cannot be readily identified, i.e. no direct or indirect identifiers or identifiable combinations of variables. The VCU IRB considers uses of anonymized data/specimens to not be human subject research.)

   ☑ Will use aggregate results (summary-level results), not individual-level information or specimens.

   (The VCU IRB considers uses of aggregate data to not be human subject research because there are no individual subjects.)

   ☐ Will contribute to an existing registry or repository

   (You will be asked more questions about this on a later page.)

   ☐ Will not use information/specimens for purposes beyond this study.
   ☐ Not sure and will submit an amendment when known
   ☐ Other use(s) of individual-level information in a way not listed above

5. * **Select the way(s) the VCU PI/study team may share information or biospecimens (including DNA) with other researchers who are not on this study team (i.e. for analyses beyond/apart from the aims of this study).**
   See help text for definitions.

   ☐ Will share directly identifiable information or specimens with other researchers.

   ('Directly identifiable' means that identifiers like name, medical record number, social security number, etc. are included in/attached to the dataset/specimens. Maintaining identifiable data for future research uses is treated by the VCU IRB as a registry. The data recipient's use of identifiable data would require them to obtain IRB review. You will be asked more questions about this on a later page.)

Will share de-identified or indirectly identifiable information or specimens with other researchers.

('De-identified' means that a linkage/key code exists that links identifiers to data/specimens. The VCU researcher maintains the key but does not share it with any other researchers. The recipient's use of de-identified data/specimens may not be human subject research if there is documentation that the key will never be shared with the recipient, but they should check with their own IRB about review requirements. You will be asked more questions about this on a later page.)

Will share anonymized information or specimens with other researchers.

('Anonymized' means that 1) no linkage/key codes exist that link identifiers to data/specimens; and 2) subjects cannot be readily identified (i.e. no direct or indirect identifiers or identifiable combinations of variables). The VCU IRB considers uses of anonymized data/specimens by other researchers to not be human subject research, but the recipient should check with their own IRB about review requirements.)

Will only share aggregate results (summary-level results), not individual-level information or specimens.

(The VCU IRB considers uses of aggregate data to not be human subject research because there are no individual subjects. The data recipient should check with their own IRB about review requirements.)

- [ ] Will contribute to an existing registry or repository (You will be asked more questions about this on a later page.)
- [ ] Will submit data to an NIH genomic data repository (You will be asked more questions about this on a later page.)
- [x] **Will not share information/specimens with other researchers.**
- [ ] Not sure and will submit an amendment when known
- [ ] Other sharing of individual-level information with other researchers

6. * **The Principal Investigator certifies that after the study has been closed with the VCU IRB, the following conditions will be met whenever individual level research information and/or specimens are used or shared:**

- The identities of participants who are represented in the dataset/specimens will not be readily ascertainable or otherwise re-identifiable by the recipient;
- If a linkage/code key is created, it will be maintained at VCU and not shared with the recipient under any circumstances;
- The PI will have no knowledge that the remaining information could be used alone or in combination with any other information to identify the individuals represented in the data; and
- The PI agrees to abide by this sharing plan even after the study has been closed with the VCU IRB.

- (●) **Yes**
- ( ) No
- ( ) N/A - No sharing will occur

Pertinent Results and Incidental Findings

1. * **Is it likely investigators could discover a participant's previously unknown condition (e.g. pregnancy, disease, suicidal thoughts, wrong paternity, genetic results, or other findings that may be of importance to health or well-being) or if a participant is engaging in illegal or reportable activities:**

- ○ Yes
- ● **No**

Populations with Special Considerations

1. * **Check all participant groups that will be either**

   a) Specifically included in this study or

   b) Discernable in the research data/specimens.

   (Selections will branch)

- [ ] Children
- [ ] Emancipated minors
- [ ] Wards of the State
- [ ] Pregnant women or fetuses
- [ ] Neonates or Post-delivery Materials
- [ ] Prisoners
- [ ] Decisionally Impaired Adults
- [ ] VCU / VCUHS students or trainees
- [ ] VCU / VCU Health System employees
- [x] **Individuals with limited English proficiency**
- [ ] Active military personnel
- [ ] Student populations in K-12 educational settings or other learning environments
- [ ] Members of a federally recognized American Indian and Alaska Native tribe
- [ ] None of the Above

Limited English Proficiency

1. * **Describe how Non-English speaking or limited English proficiency participants will be able to communicate with the study staff at enrollment and throughout the study. Include the following information:**
   - *how the initial informed consent process will be handled*
   - *how the research team plans to interact with LEP participants throughout the conduct of the study*
   - *whether there will be a qualified interpreter or assistive translational devices available*
   - *whether the study consent document will be translated or a short form consent document will be used*
   - *the names of the individuals or professional groups who will provide oral interpretation or written translation services, and their qualifications*

   Non English speaking patients will be able to communicate with the study staff via translation services available at VCU health System language services. Since this is a 1-2 day study period, ongoing translation services will not be needed after the consent is signed. Nursing staff on the orthopedic unit will use the same translation services during the patient's stay after knee arthroplasty, but this is normal care and not part of the research.

   Since the expected number of patients with limited English proficiency is < 5% we will use the short form process to consent these patients.

2. * **Describe any additional risks or harms to the individual because of their limited English proficiency and how these will be minimized.**

   The additional risk or harm that could affect these patients is the lack of understanding of the study details. This will be fully minimized by using the appropriately credentialed translators from VCU Language services.

[redacted]

HM20004125 Gregory Golladay
Do Intraoperative Periarticular Injections Improve Postoperative Pain Control in Patients Receiving Duramorph? A Prospective, Double Blinded, Randomized Controlled Trial

Types of Sites

VCU Site Information

1. * **Select all VCU sites that will be utilized in this study:**
   - ☐ Children's Hospital of Richmond at VCU
   - ☐ Clinical Research Services Unit (CRSU)
   - ☐ Massey Cancer Center
   - ☐ VCU Health Community Memorial Hospital
   - ☐ VCU Health Tappahannock Hospital
   - ☑ **VCU Medical Center**
   - ☐ Other VCU Health Location
   - ☐ VCU Monroe Park Campus
   - ☐ VCU Qatar
   - ☑ **Other VCU Site**

Non-VCU Site Information

Non-VCU sites should be selected whenever any of the following situations apply:
a) Non-VCU sites that will be collaborating on a VCU-led study
b) Non-VCU sites that will be deferring to the VCU IRB for IRB review
c) Non-VCU sites where VCU investigators will be overseeing study interventions or interactions
d) Non-VCU sites/locations where VCU investigators will conduct study activities

2. * **Select any of the following non-VCU sites utilized in this study:**
   - ☐ McGuire VAMC
   - ☐ Foreign Sites
   - ☐ Other Non-VCU Sites
   - ☑ **No Non-VCU Sites**

3. * **Is this a multi-center study being led by VCU?**
   - ○ Yes ● **No**

[redacted]

HIPAA

In order for VCUHS to meet HIPAA regulations regarding accounting of disclosures, data retention, and data destruction requirements for PHI data obtained without patient authorization, members of the study team (including principal investigators) are directed to consult with VCU Informatics to obtain any VCUHS data. This does not include obtaining data for which the study team has patient authorization. [VCU Health System Authority and Affiliates Policy COMP-014]

For data requests, including preparatory to research and research with decedents, submit a request for the desired PHI, or for a consultation on alternate methods to obtain the data, at https://informatics.vcu.edu.

HIPAA Privacy Board Requirements

For guidance, see https://www.vcuhealth.org/our-story/who-we-are/compliance-services/compliance-services

1. * **Select the source of the individually identifiable Health Information. See help text for definitions.**
   - [x] **PHI associated with or derived from (i.e. obtained from or entered into) VCU Health medical records or VCU Dental Care records**
   - [ ] Research Health Information (RHI) created or received by a study and kept solely in study records (e.g. self reported or the result of research tests and not entered into health records)
   - [ ] PHI associated with or derived from (i.e. obtained from or entered into) a non-VCU HIPAA covered entity's health records

2. * **Summarize the types of health information that will be obtained or used in this research. Do not describe only the identifiers that you will collect or use during the study.**
   Patients will be identified at their preoperative office visits with their surgeon. There will be no searching of the information system to find suitable patients; these patients are all being seen as part of their treatment/consultation for knee arthroplasty.

   We will use patient's names, medical record numbers, and the dates of the operative procedures to identify those who have consented to be randomized as well as to review the required information in their electronic medical record. Only those points of interest will be included in the post hospitalization chart review. A master list will be kept on a password-protected computer in a locked office at the VCU Medical Center system.

3. * **Describe the source(s) of the protected health information (e.g. informatics or which clinical databases):**
   The VCU Medical Center electronic medical record.

4. * **Does the PI certify that this study's access to and use of the protected health information is limited to the minimum amount necessary to be able to effectively conduct the research?**
   - (●) **Yes**
   - ( ) No

5. * **Select all pathways this research will employ to use or access PHI (selections will branch):**
   - [ ] De-identified Data (none of the 18 identifiers are recorded or associated with the research data)
   - [ ] Limited Data Set
   - [ ] Waiver of Authorization
   - [ ] Partial Waiver of Authorization (temporary waiver for recruitment purposes and/or waiver of some elements of Authorization)
   - [x] **Signed Authorization Combined with Consent Form**
   - [ ] Signed Authorization as Stand-Alone Form

Bio-Medical Project Drugs

1. * **Drug:**
ketorolac tromethamine (Toradol

2. * **Manufacturer:**
Roche Bioscience

3. * **Select all types that apply:**

- [ ] FDA Approved and being used as approved
- [ ] Marketed Drug/Biologic Exempt from IND
- [ ] Investigational Drug/Biologic/Supplement used as drug
- [ ] Supplement
- [ ] Over the Counter Medication
- [x] **Other (Drug or Compound Not Listed Above)**

4. * **Will the doses of drug administered and the dosing schedule match FDA approved labeling:** ***(If not, include all doses and dosing schedules in the Methods)***

- ○ Yes
- ● **No**
- ○ Not Applicable

5. * **Select who holds the Investigational New Drug (IND) application for the drug/biologic:**

- ○ External to VCU Sponsor or Investigator
- ○ VCU Sponsor-Investigator
- ○ VCU Sponsor who is not the Investigator
- ● **Not Required**

6. **Indicate the drug's IND number, if applicable. If the drug qualifies for IND exemption, enter "IND Exempt":**

Bio-Medical Project Drugs

1. * **Drug:**
   Epinephrine

2. * **Manufacturer:**
   Multiple

3. * **Select all types that apply:**

- [x] **FDA Approved and being used as approved**
- [ ] Marketed Drug/Biologic Exempt from IND
- [ ] Investigational Drug/Biologic/Supplement used as drug
- [ ] Supplement
- [ ] Over the Counter Medication
- [ ] Other (Drug or Compound Not Listed Above)

4. * **Will the doses of drug administered and the dosing schedule match FDA approved labeling:** ***(If not, include all doses and dosing schedules in the Methods)***

- (●) **Yes**
- ( ) No
- ( ) Not Applicable

5. * **Select who holds the Investigational New Drug (IND) application for the drug/biologic:**

- ( ) External to VCU Sponsor or Investigator
- ( ) VCU Sponsor-Investigator
- ( ) VCU Sponsor who is not the Investigator
- (●) **Not Required**

6. **Indicate the drug's IND number, if applicable. If the drug qualifies for IND exemption, enter "IND Exempt":**

Bio-Medical Project Drugs

1. * **Drug:**
ropivacaine

2. * **Manufacturer:**
various

3. * **Select all types that apply:**

- [x] **FDA Approved and being used as approved**
- [ ] Marketed Drug/Biologic Exempt from IND
- [ ] Investigational Drug/Biologic/Supplement used as drug
- [ ] Supplement
- [ ] Over the Counter Medication
- [ ] Other (Drug or Compound Not Listed Above)

4. * **Will the doses of drug administered and the dosing schedule match FDA approved labeling:** ***(If not, include all doses and dosing schedules in the Methods)***

- (●) **Yes**
- ( ) No
- ( ) Not Applicable

5. * **Select who holds the Investigational New Drug (IND) application for the drug/biologic:**

- ( ) External to VCU Sponsor or Investigator
- ( ) VCU Sponsor-Investigator
- ( ) VCU Sponsor who is not the Investigator
- (●) **Not Required**

6. **Indicate the drug's IND number, if applicable. If the drug qualifies for IND exemption, enter "IND Exempt":**

Bio-Medical Project Drugs

1. * **Drug:**
   Clonidine

2. * **Manufacturer:**
   Multiple

3. * **Select all types that apply:**

- [ ] FDA Approved and being used as approved
- [ ] Marketed Drug/Biologic Exempt from IND
- [ ] Investigational Drug/Biologic/Supplement used as drug
- [ ] Supplement
- [ ] Over the Counter Medication
- [x] **Other (Drug or Compound Not Listed Above)**

4. * **Will the doses of drug administered and the dosing schedule match FDA approved labeling:** ***(If not, include all doses and dosing schedules in the Methods)***

- ○ Yes
- ● **No**
- ○ Not Applicable

5. * **Select who holds the Investigational New Drug (IND) application for the drug/biologic:**

- ○ External to VCU Sponsor or Investigator
- ○ VCU Sponsor-Investigator
- ○ VCU Sponsor who is not the Investigator
- ● **Not Required**

6. **Indicate the drug's IND number, if applicable. If the drug qualifies for IND exemption, enter "IND Exempt":**

Consent Groups

1. * **Enter a descriptive name for this consent / assent group:**
Patients Undergoing Knee Arthroplasty

2. * **Select all that apply to this consent / assent group:**

	Name
☑	**Signed Consent by Participant**
☐	Signed Parent/Guardian Permission or Legally Authorized Representative Consent
☐	Signed Assent by Child or Decisionally Impaired Adult
☐	Verbal Assent by Child or Decisionally Impaired Adult
☐	Short Form Consent (limited applicability)
☐	None of the Above (select waiver below)

3. * **Select all electronic signature platforms that apply to this consent / assent group:**
- ☐ Not using electronic signature platforms
- ☐ DocuSign Part 11 (FDA regulated studies)
- ☐ DocuSign (standard platform for non-FDA regulated studies)
- ☐ REDCap e-Consent
- ☐ Other electronic signature platform

4. **If Other is selected, explain:**

5. * **Select any waivers that apply to this consent / assent group:**

☑	**No Waivers Requested**
☐	Waiver of All Consent or Some Elements in Consent Form
☐	Waiver of Parental Permission or Legally Authorized Representative Consent
☐	Waiver of All Assent by Child or Decisionally Impaired Adult
☐	Waiver of Signature on Consent/Permission Forms (waiver of documentation of consent)
☐	Exception from Informed Consent (for emergency research only)

6. * **Select all study team role(s) that will obtain consent / assent from this group:**

☑	**Principal Investigator**
☑	**Co/Sub-Investigator**
☐	Medical or Psychological Responsible Investigator
☐	Lead Student/Trainee Investigator (leading their own project)
☑	**Research Coordinator**
☐	Research Nurse
☐	Consultant
☐	Research Assistant
☐	Pharmacist
☐	Statistician
☐	Regulatory Coordinator
☐	Trainee/Student(working on project)
☐	Other
☐	N/A: Requesting Waiver of Consent

7. * **Describe the consent procedures used for this group. Address each point below:**

- **When and where consent will occur**
- **What will be covered during the consent discussion**
- **How the consent discussion will occur (e.g. in-person, phone, video conference)**
- **How you will reconfirm consent on an ongoing basis, if applicable**

Consent (research) will be obtained after the patient has signed the consent for the knee arthroplasty. Once this is signed the patient will be approached by the surgeons or coordinators to offer this study. This will occur in a private office or examination room at Stony Point, ACC clinic, the NOW clinic or the perioperative area.

8. **Select the processes for minimizing any potential perception of undue influence to participate, particularly when there is a pre-existing relationship between the participant and the researcher (e.g. treatment provider/patient; instructor/student; supervisor/employee, etc.):**

- [ ] Having a 3rd person (family/friends, another study team member, etc.) present during the consent / assent discussion
- [ ] Having an independent advocate (e.g. advocate for decisionally impaired adults, wards) present during the consent / assent discussion
- [ ] Removing physical symbols of authority like white coats or police badges
- [ ] Sitting down beside the participant instead of standing over them
- [ ] If obtaining consent / assent in a clinical setting, letting patients sit instead of lie down (if they are able to)
- [ ] Moving to a more neutral location like a conference room
- [ ] Obtaining consent / assent after other services/interactions have been completed (e.g. after school or the clinic visit)
- [ ] Having a mandatory wait period for the participant to go home and think before they sign consent /assent
- [ ] Sharing the consent / assent discussion between two people (i.e. a clinician might be the best person to explain study procedures and risks, but then they could step out and let a research assistant finish the consent process)
- [ ] Other protection(s) not listed here – describe below
- [ ] N/A: Requesting Waiver of Consent

8. * **Describe the other ways the study team will minimize any potential perception of undue influence to participate:**
   No coercion will occur; patients will be told that if they do not agree to participate, they will get the standard of care joint injection.

10. * **How much time will participants be given to make a decision:**
    The time period to make a decision will be a matter of weeks to months. The study will be presented to patients once a decision has been made to undergo a TKR (consent has been signed) . The time period between surgery decision and surgery is variable and patient specific--but there is adequate time to make a decision

11. **If applicable, describe the procedures for consenting children upon entering adulthood or participants who are no longer decisionally impaired:**
    N/A