#3567 - Does Single Injection Adductor Canal Block Improve Postoperative Analgesia in Patients Receiving Periarticular Local Anesthesia Injections for Total Knee Arthroplasty?

Protocol Information

Review Type	Status	Approval Date	Continuing Review Date
Expedited	**Approved**	**Jul 19, 2024**	--

Expiration Date	Initial Approval Date	Initial Review Type
Jul 18, 2025	**Aug 25, 2023**	**Full Board**

Feedback

Approval Comment

The IRB Approval Letter can be downloaded in the Attachments section of the protocol.

Protocol Renewal Form

Renewal Information

Protocol Type

Are you submitting a renewal for an IRB, sIRB, or hSCRO protocol?

IRB (UCI is the IRB of Record)

IRB Renewal Instructions

Timing of Submission

Exempt and Expedited IRB protocols must submit a short version of the renewal every three (3) years unless determined otherwise by the IRB. Investigators should plan ahead and submit 60 days prior to the study's expiration date.

Full Committee IRB protocols must submit a renewal at least annually (not more than 365 days). Investigators should plan ahead to meet required continuing review dates. For full committee review protocols, please submit 90 days prior to the expiration date to guard against a lapse in IRB approval.

Amendments at the Time of Renewal

Please refrain from making major changes during the renewal as this could result in a lapse of IRB approval.

Protocol Closure

To close out an approved protocol at the time of renewal, the transaction must be submitted as Request Close. If this option was not initially selected and closure is required, please Abandon the draft and start again. For more information, visit Post-Review Responsibilities and select the Protocol Renewal Tab.

Renewal Screener

Does any of the following apply to the currently approved protocol:

- **research involves Greater than Minimal Risk (Full Committee)**
- **research is subject to Food and Drug Administration (FDA) regulations**
  - **Involves a drug**
  - **A clinical investigation of a medical device**
- **research is funded/supported by the Department of Justice (DOJ)**
- **current approval period is 1 year or less**

Yes (Continuing Renewal Required)

Protocol Expiration

Protocol Expiration

Has approval for this protocol expired or will it expire within 3 weeks?

No

Confirmation of Protocol

Study Team

Review the Study Team Section and consider whether anyone should be removed at this time via an Amendment.

RP Heat Map

Are RP tracked outside the approved protocol, in accordance with the RP Heat Map?

Yes, RP are tracked on a Study Team Log or other comparable log

Financial Interests

Review the Study Team section and specify below if there have been any changes in the study team's related financial disclosable interests.

See Conflict of Interest Oversight Committee (COIOC) for more details.

No, there have been no changes to the study's teams related disclosable financial interests

Relying Non-UCI Entity (as applicable)

When UCI is the IRB of Record for a non-UCI entity (i.e., site or independent investigator), review the sIRB section and remove any non-UCI entities (site or independent investigator) that are no longer *engaged* in research via an Amendment.

Clinicaltrials.gov Status

ClinicalTrials.gov Registration

Does this research meet the definition of a clinical trial that requires adherence to Clinicaltrials.gov (CT.gov)?

Yes

Confirm the accuracy of ClinicalTrials.gov section in the IRB protocol (select one):

Please review the ClinicalTrials.gov section in the IRB protocol to verify that the information is still accurate.

If any revisions are required, please submit an amendment to request a 'Change in Clinicaltrials.gov' and update the the protocol accordingly.

As lead researcher, I confirm that the CT.gov information is accurate as indicated in the protocol

Specify who is responsible for registering, maintaining, and updating the CT.gov record:

UCI Investigator

Confirm the accuracy of the information on the ClinicalTrials.gov Protocol Registration and Results System (PRS):

IMPORTANT! Per federal requirements (42 CFR 11.64(a)(1)(ii)), clinical trial registration information on PRS must be updated not less than once every 12 months.

Please review the information on PRS to verify that the following fields are accurate and up to date:

- **Study Status:**
  - **Record Verification Date: Not less than every 12 months, enter the date on which the responsible party last verified the clinical study information on PRS, even if no additional or updated information was submitted.**
  - **Overall Recruitment Status: 30 calendar days after a change in overall recruitment status, enter the status for the clinical study as a whole, based upon the status of the individual sites. If at least one facility in a multi-site clinical study has a status of "Recruiting," then the overall status for the study must be "Recruiting."**
  - **Primary Completion Date: 30 calendar days after the clinical trial reaches its actual primary completion date, enter the date that the final participant was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical study concluded according to the pre-specified protocol or was terminated. In the case of clinical studies with more than one primary outcome measure with different completion dates, this term refers to the date on which data collection is completed for all of the primary outcomes. IMPORTANT! This date cannot be in the past, please revise the date as necessary.**
  - **Study Completion Date: 30 calendar days after the clinical trial reaches its actual study completion date, enter the date the final participant was examined or received an intervention for purposes of final collection of data for the primary and secondary outcome measures and adverse events (for example, last participant's last visit), whether the clinical study concluded according to the pre-specified protocol or was terminated. IMPORTANT! This date cannot be in the past, please revise the date as necessary.**
- **Oversight:**
  - **Human Subjects Review Board Status: 30 calendar days after a change in status, ensure the status of IRB approval information is accurate.**
- **Contacts, Locations, and Investigator Information: 30 calendar days after a change, ensure the information is accurate.**

As leader researcher, I confirm that the clinical trial information (listed above) on PRS is accurate and up to date.

Enrollment Status

Accruals

Please mark the option that represents the current status of subject enrollments:
Enrollment and research procedures complete - only access to identifiable data / data analysis ongoing

Subject Enrollments

Please confirm the total number of subjects (i.e. individuals, specimens, records) approved by the UCI IRB in the Subject Populations section.

Indicate the number of new subjects enrolled since last IRB review:
0

Indicate the total number of subjects (including the number in the previous question) enrolled since initial UCI IRB approval:
88

Did the total number of subjects enrolled to date exceeds the total number approved by the IRB?
No

Indicate the total number of subjects enrolled per group since initial IRB approval:

Man (total):
35

Woman (total):
52

Nonbinary (total):
0

Not Collected (total):
0

Adults (total):
88

Minor (total):
0

Multi-Center Studies: If known, indicate the total number of subjects enrolled at ALL sites to date:
n/a

Subject Withdrawals

Early Termination(s)

Did the Lead Researcher or a Co-Researcher remove any subject(s) from the study?
No

Voluntary Withdrawal(s)

Did any subject(s) voluntarily withdraw from the study?
No

Reportable Events

Reportable Events

Have there been any problems that required prompt reporting to the UCI IRB?

No problems that require reporting

Complaints

Have there been any complaints from UCI participants or others that required reporting to the UCI IRB?

No

Progress Report

UCI Progress

Please provide a detailed description of the progress of the study, including a brief summary of any interim findings or trends, and plans for the next approval period:

Recruitment is complete and data analysis is waiting. The original PI on the study left the university making this an 'orphaned' study for a while, hence the delay in analysis. We have a summer research volunteer who is working on it now.

Relying Entity Progress (as applicable)

If UCI is the IRB of Record for a non-UCI entity, provide a progress report for each relying entity (e.g., number of participants enrolled at the sub-site; data analysis performed, if any, etc):
n/a

Sponsor Multi-Center Progress (as applicable):

Is a multicenter progress report / newsletter is available from the Sponsor?
Not Applicable

Internal and External Audits

Internal Audit(s)

Have any internal (UCI/UCI Health) audits occurred since last IRB review?
No

External Audit(s)

Have any external (FDA/OHRP/Sponsor) audits occurred since last IRB review?
No

Risk and Safety Assessments

Relevant Recent Literature

During the past year has there been anything in relevant literature that the IRB should consider when reviewing this application for continuing approval?

No

Current Risk/Benefit Assessment

Has there been a change in risk/benefit?

Take into account the information gathered during the past year such as interim results, reportable events/problems, changes in scientific knowledge, and/or relevant regulatory actions regarding study-wide safety and/or efficacy (e.g., product recall). This assessment should be sufficiently detailed to assist the IRB in determining whether continuation of IRB approval is appropriate.

No

Data Safety Monitoring Board (DSMB)

Has there been any new DSMB findings relating to subject safety?

Not applicable

Investigator's Brochure (IB)

For FDA regulated drug studies, enter the current version number and date of the Investigator's Brochure in the Supplemental Documents section.

End of renewal form!

IMPORTANT! Go to the next section to complete the amendment form.

Protocol Amendment Form

Amendment Instructions

Specify the type of submission:
RENEWAL: This is a renewal that does not require changes to the approved protocol

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End of amendment form!

Project Details

Project Title (100 words max):
Does Single Injection Adductor Canal Block Improve Postoperative Analgesia in Patients Receiving Periarticular Local Anesthesia Injections for Total Knee Arthroplasty?

Lead Researcher/Investigator:

Joseph Brian Rinehart

Lead Unit (i.e., Department, Organized Lead Unit, Center or Institute):

IR-7450 - ANESTHESIOLOGY & PERIOPERATIVE CARE (Lead Unit)

Kuali Research (KR) follows the KFS Organizational Unit Hierarchy.

- **Select the lead unit with 3 asterisks (***)**
- **UCSB hSCRO Researchers: Select ***UC Santa Barbara (UCSB)*****

ATTENTION! For new submissions, Department Chair (DC) or Organized Lead Unit Director (OLUD) sign-off in KRP is required before final committee approval will be granted. For more information, visit the listserv.

Submission Screener

Submission Type:

IMPORTANT! Be sure to select the correct 'Submission Type'. When 'Submission Type' is changed, the contents of the form will be cleared and replaced with a set of new questions specific to the submission type.

Institutional Review Board (IRB) Review

Lead Researcher's primary school/department/program is:

Biomedical (Health Sciences)

Select the level of review for this protocol:

Greater than Minimal Risk (Full Committee)

Is this expanded access, humanitarian use device, or right to try?

Not applicable

Specify who initiated/authored the project:
Investigator

Is this study an extension of a UCI IRB approved study (e.g., resubmission of ongoing exempt research; open label extension) or is it otherwise related to a UCI IRB approved study?
Yes

If yes, provide the protocol number for the UCI IRB approved protocol (enter multiple protocol numbers if appropriate):
IRB20141217 aka HS#2014-1217

Supplemental Documents

Does this study include a Sponsor's Master Protocol (MP) or detailed project proposal?
No

Project Funding

Select the funding source(s) (check all that apply):
Department or campus funds (includes department support, unrestricted funds, start-up funds, personal funds, campus program awards, etc.)

Clinical Trials

Is the research a *clinical investigation*?

A *clinical investigation* is any experiment that involves a *test article* and one or more *human subjects*, and that meets any one of the following:

- **Any administration of approved drugs for research purposes that is not according to their approved indications, route of administration, population, or dose**
- **Any activity that evaluates the safety or effectiveness of a medical device**
- **Any activity the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit**

An individual becomes a *human subject* for FDA purposes if their data or specimens are used as the recipient of the test article or control. For example, when retrospective data are used as the control, the individuals become human subjects. Likewise, when an individual's blood sample is used to test an assay, the individual becomes a human subject.

Yes

Clinicaltrials.gov

Registration on ClinicalTrials.gov may be required if one (or more) of the following is true:

- **Study meets the definition of an Applicable Clinical Trial (ACT) (ACT Checklist)**
- **Study is NIH funded and meets the NIH definition of a clinical trial**
- **Study is DoD funded and registration is required by your specific program**
- **Study meets the International Committee of Medical Journal Editors (ICMJE) definition of a clinical trial**
- **Study includes reimbursement of Medicare claims**

Does this research meet the definition of a clinical trial that requires adherence to Clinicaltrials.gov (CT.gov)?

Yes

Specify the rationale for CT.gov registration (check all that apply):

Applicable clinical trial

Provide the CT.gov registration NCT # (Enter 8-digit sequence of numbers only):

02276495

ATTENTION!

School of Medicine (SOM) Researchers: All clinical trials must be performed under the auspices of an Organized Lead Unit (OLU).

Alpha Stem Cell Clinic (ASCC)
Center for Clinical Research (CCR)
Chao Family Comprehensive Cancer Center (CFCCC)
Institute for Memory Impairments and Neurological Disorders (MIND)

Go to Project Details -> Lead Unit and verify the appropriate OLU for the trial.

Scientific/Scholarly Review

Investigator-authored research involving greater than minimal risk to subjects (full board review) requires scientific/scholarly merit prior to IRB review - with few exceptions.

The following options identify the scientific merit process for the proposed research and the order of IRB review. Researchers should work with their Departments and the applicable committee (e.g., PRMC) to coordinate the review of their projects, as necessary.

The proposed research qualifies as greater than minimal risk, investigator-initiated biodmedical research.

REQUIRED! Review from the Biostatistics, Epidemiology and Research Design (BERD) unit of the Institute for Clinical and Translational Science (ICTS) is required. The UCI IRB staff will coordinate the review in conjunction with the expertise of the BERD.

Please click on the following link to arrange a consultation with one of the ICTS BERD Statisticians: ICTS BERD Statisticians - Consultations.

Is the research cancer-related?

No

Other UCI Committee Reviews

Research involving human subjects sometimes requires the approval or authorization of Other Reviews Required by UCI (e.g., School of Medicine Review Committees).

Additional Review by the following Committees *may* be required prior to IRB review:

- **Human Stem Cell Oversight (hSRCO) Committee**
- **Institutional Biosafety Committee (IBC)**
- **Radiation Safety Committee (RSC)**

For a list of all ancillary committees, their requirements and how they relate to the IRB review process, refer to the Other UCI Required Reviews Chart.

Potentially Hazardous Materials

Specify if any of the following hazardous materials are used for research-related purposes (i.e., not for standard of care) (check all the apply):

Not Applicable

Study Team

- **Lead Researcher (LR): The LR must meet LR Eligibility requirements or have a Faculty Sponsor (FS) listed who is eligible.**
- **Co-Researcher (CR): CRs are key personnel for conducting the research study. These individuals work closely with the LR to design, conduct, and/or report on the research.**
- **Research Personnel (RP): Review the RP Heat Map to determine whether they should be listed below.**
- **Administrative Contact (AC): Add ACs in the Permissions tab. Do NOT list below.**
- **Non-UCI researchers: Address non-UCI researchers in the Single IRB Reliance (sIRB) section. Do NOT list below.**

Researcher:

Joseph Brian Rinehart

Email:

jrinehar@uci.edu

Financial Interest:

hSCRO RESEARCHERS:

IMPORTANT! Please mark "No" for this question. COI does NOT apply to hSCRO research.

IRB RESEARCHERS:

To promote the objectivity of the research, all researchers are required to disclose their related disclosable financial interests, per the IRB COI Policy. If you have any questions about the COI process in general, contact the COI team.

Each member of the study team for this protocol must be asked the following question to comply:

"Do you, your spouse/registered domestic partner, and dependent children have any disclosable financial interests* (i) that would reasonably appear to be affected by this research study; or (ii) in entities whose financial interests would reasonably appear to be affected by this research study?"

No

Training:

hSCRO RESEARCHERS:

IMPORTANT! Please ignore the training column. It is only relevant for IRB researchers. hSCRO researchers are NOT required to take CITI training courses.

IRB RESEARCHERS:

IMPORTANT! Incomplete or expired CITI training will delay IRB approval. For more information, visit HRP Training and Education.

All study team members must complete the following Collaborative Institutional Training Initiative (CITI) trainings:

- **Human Subjects Research Protections and**
- **Good Clinical Practice, as applicable**

Joseph Rinehart has no training courses on file.

Degree:
MD

Position/Title:
Vice Chair of Research

IR-7450 - ANESTHESIOLOGY & PERIOPERATIVE CARE (Lead Unit)

Affiliation:
UCI Faculty

Researcher Role:
Lead Researcher

Permissions:
Full Access

Duties:
Oversight of Research
Access/Analyze Identifiable Information
Research Procedures (specify below)

Specify which research procedures:
Data analysis and manuscript writing

Specify relevant training and experience for the referenced duties/responsibilities:
Dr. Rinehart is a board-certified UCI Health anesthesiologist. He serves as the Vice Chair of Research for the department of Anesthesiology and chairs IRB E committee. He has extensive clinical research experience including funded research and countless publications.

Researcher:

Paulette M Mensah

Email:

pmensah@uci.edu

Financial Interest:

hSCRO RESEARCHERS:

IMPORTANT! Please mark "No" for this question. COI does NOT apply to hSCRO research.

IRB RESEARCHERS:

To promote the objectivity of the research, all researchers are required to disclose their related disclosable financial interests, per the IRB COI Policy. If you have any questions about the COI process in general, contact the COI team.

Each member of the study team for this protocol must be asked the following question to comply:

"Do you, your spouse/registered domestic partner, and dependent children have any disclosable financial interests* (i) that would reasonably appear to be affected by this research study; or (ii) in entities whose financial interests would reasonably appear to be affected by this research study?"

No

Training:

hSCRO RESEARCHERS:

IMPORTANT! Please ignore the training column. It is only relevant for IRB researchers. hSCRO researchers are NOT required to take CITI training courses.

IRB RESEARCHERS:

IMPORTANT! Incomplete or expired CITI training will delay IRB approval. For more information, visit HRP Training and Education.

All study team members must complete the following Collaborative Institutional Training Initiative (CITI) trainings:

- **Human Subjects Research Protections and**
- **Good Clinical Practice, as applicable**

Paulette Mensah has no training courses on file.

Degree:
BA

Position/Title:
Clinical Research Supervisor

IR-7450 - ANESTHESIOLOGY & PERIOPERATIVE CARE (Lead Unit)

Affiliation:
UCI Staff

Researcher Role:
Co-Researcher

Permissions:
Full Access

Duties:

Access/Analyze Identifiable Information
Research Procedures (specify below)

Specify which research procedures:

Data Analysis, manuscript writing, and research related coordination.

Specify relevant training and experience for the referenced duties/responsibilities:

Ms. Mensah has led the clinical OR and pain team research activities within the department for the last 6 year an has 11 years of research experience. She manages the department's research volunteer program and all IRB-approved, funded, and unfunded research activities. She will be assisting the lead PI with day-to-day research operations.

Researcher:

Michael Ma

Email:

mma3@uci.edu

Financial Interest:

hSCRO RESEARCHERS:

IMPORTANT! Please mark "No" for this question. COI does NOT apply to hSCRO research.

IRB RESEARCHERS:

To promote the objectivity of the research, all researchers are required to disclose their related disclosable financial interests, per the IRB COI Policy. If you have any questions about the COI process in general, contact the COI team.

Each member of the study team for this protocol must be asked the following question to comply:

"Do you, your spouse/registered domestic partner, and dependent children have any disclosable financial interests* (i) that would reasonably appear to be affected by this research study; or (ii) in entities whose financial interests would reasonably appear to be affected by this research study?"

No

Training:

hSCRO RESEARCHERS:

IMPORTANT! Please ignore the training column. It is only relevant for IRB researchers. hSCRO researchers are NOT required to take CITI training courses.

IRB RESEARCHERS:

IMPORTANT! Incomplete or expired CITI training will delay IRB approval. For more information, visit HRP Training and Education.

All study team members must complete the following Collaborative Institutional Training Initiative (CITI) trainings:

- **Human Subjects Research Protections and**
- **Good Clinical Practice, as applicable**

Michael Ma has no training courses on file.

Degree:
BS

Position/Title:
Anesthesia Research Volunteer

IR-7450 - ANESTHESIOLOGY & PERIOPERATIVE CARE (Lead Unit)

Affiliation:
UCI Other

Specify other UCI affiliation:
Former department staff returning as non-UCI medical student

Researcher Role:
Co-Researcher

Permissions:
Full Access

Duties:
Access/Analyze Identifiable Information
Research Procedures (specify below)

Specify which research procedures:
Data analysis and manuscript writing

Specify relevant training and experience for the referenced duties/responsibilities:

Mr. Ma is a former primary CRC on this project and member of the anesthesia research team for over 5 years. He will be returning to assist the completion of this study as a non-UCI medical student research volunteer .He comes with extensive knowledge of the study activities and original data collection activities. This expertise will be critical to finalizing data analysis, writing the manuscript, and closing out the study.

Are RP tracked outside the approved protocol, in accordance with the RP Heat Map?

Yes, RP are tracked on a Study Team Log or other comparable log

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sIRB Screener

At UCI, a single IRB (sIRB) will be required for the following types of non-exempt cooperative (multisite) research carried out within the United States:

1. **New studies approved on or after January 20, 2020 supported by an agency that has signed on to the Common Rule. For a full list of HHS Departments and Agencies that follow the Common Rule, please click here.**
2. **Research supported by NIH. Click here for the official notice from NIH: NOT-OD-16-094. There are some exceptions. For more about the NIH exceptions and additional information on the single IRB requirement for NIH supported research (in effect since January 25, 2018) click here.**

Are UCI researchers engaged in human subjects research activities (e.g., interact with subjects; have access to identifiable information) at a non-UCI location?

No

Are non-UCI researchers engaged in human subjects research activities (e.g., interact with subjects; have access to identifiable information)?

No

Non-Technical Summary

Provide a non-technical summary of the project that can be understood by non-scientists (250 words max):

REOPENING HS#2014-1217 TO FINALIZE DATA ANALYSIS AND COMPLETE MANUSCRIPT WRITING. Original non-technical summary below: Total knee arthroplasty (TKA), also known as total knee replacement, has been associated with a significant pain burden in the postoperative period. Methods to manage pain associated with this operation have in the past included injecting pain medication into the epidural space of the spinal cord, around a peripheral nerve, around the space surrounding the joint, or a combination of pain management techniques. In recent years, the femoral nerve block (injection of pain medication around the peripheral nerve, specifically the femoral nerve) has been proposed as an effective way to manage pain while sparing many of the undesirable side effects of narcotic pain medications. Traditional techniques of the femoral nerve block involve the injection of pain medication around the peripheral nerve at the level of the groin area. A nerve block at this point in the path of the femoral nerve affects all of the musculature of the front part of the thigh as well as the nerves responsible for sensation to the majority of the knee joint. The femoral nerve block performed at the level of the groin provides an excellent level of pain relief at the knee joint, but is also associated with weakness of the quadriceps muscle. The resultant quadriceps weakness can both slow the physical therapy process and be a risk factor for post-operative falls. Participation in physical therapy is a critical component of the rehabilitation process and is started as soon as tolerated by the patient. The ideal pain management technique would provide the same degree of pain relief as the femoral nerve block while preserving the strength in the front part of the thigh muscles. One suggested technique to achieve both of these goals is the injection of a large volume dilute local pain medication mixture around the joint during surgery. This has been used as a substitute to provide pain relief around the joint while maintaining strength in the quadriceps muscle and the ability to participate in physical therapy. This technique however, does not last long since the medication disperses away from the joint space. A variation of the femoral nerve block in the lower thigh, within a space called the adductor canal, has been demonstrated to provide

equivalent amounts of pain relief as a proximal femoral nerve block along with preservation of motor function to the quadriceps muscle. What is not as well-established is whether the combination of injecting pain medication directly around the joint space in the knee along with a single injection of pain medication in the adductor canal in the lower thigh can improve pain scores and extend the duration of pain relief provided compared to only an injection around the joint space.

Background & Purpose of Research

Describe the purpose, specific aims or objectives and specify the hypotheses or research questions to be studied:

The purpose of the proposed research is to determine the effect of a single injection adductor canal block (ACB) on pain scores within 24 hours post total knee arthroplasty (TKA). This study will compare three groups of patients: those who receive the ACB and local periarticular infiltration, those who receive placebo ACB and local periarticular injection, and those who receive the ACB and placebo periarticular injection.

The present study is a three-arm randomized clinical trial of:

- **A**. Local periarticular infiltration (injection of dilute local anesthetic) + Placebo ACB (nerve block performed with normal saline)
- **B**. Local periarticular infiltration (injection of dilute local anesthetic) + ACB (nerve block procedure performed with local anesthetic)
- **C**. ACB (nerve block performed with local anesthetic)

The primary objective being to compare the efficacy of all groups (**A**), (**B**) and (**C**) with each other with respect to 24 hr. post operative pain. The arm (A) was included to address the efficacy of local infiltration only in comparison with groups (B) and (C). Comparison of group (B) vs. (C) is also of primary interest of the study.

The current "standard of care" has not been established for Total Knee Arthroplasty. Nationwide there are large variations in postoperative pain management methods for total knee arthroplasty including lumbar epidural, intrathecal opioids, femoral nerve block with and without sciatic nerve block, local infiltration, local wound catheters, and adductor canal blocks. All three arms are well within acceptable standard practice for postoperative pain management for this population1.

The objective will be to answer the following research questions:

- Does the addition of an adductor canal block to a periarticular injection improve postoperative pain scores in TKA patients at specific time intervals?
- Does the addition of an adductor canal block to periarticular injection decrease opioid use in TKA patients?
- Is there a difference in maximum pain scores and/or opioid consumption between those receiving adductor canal blocks only versus those receiving local infiltration analgesia.

Subject Population(s)

Targeted subject populations/data sources (check that apply):

Adults

Subjects who are unable to communicate in English

Eligibility Criteria

1. **Specify the Inclusion/Exclusion Criteria.**
2. **Provide a breakdown per subject cohort, as applicable (e.g., adults vs parents vs children).**
3. **IMPORTANT! If utilizing UCI Health Enterprise Data & Analytics services, include specific timeframes for each eligibility factor, as applicable.**
    a. **Example:**
    - **Birth sex: female**
    - **Age: >= 18 years old as of 2020-01-01**
    - **The result of the most recent SARS-CoV-2 test (of any type), performed between 2020-01-01 and 2020-12-31, was positive**
    - **With any sub-classification of type 2 diabetes (E11*) diagnosed at any date prior to 2020-01-01**
    - **Did NOT have an ED visit between 2020-01-01 and 2020-12-31**

Category/Group Eligibility
Adults Receiving Total Knee Arthroplasty (TKA)

Inclusion Criteria
• Males and Females age 18+ years old having total knee arthroplasty(TKA) at UCI Medical Center
• American Society of Anesthesiologists physical status I to III

Exclusion Criteria
• Allergy to local anesthetics
• Pregnancy
• Nursing Mothers
• Children<18 years of age
• Opioid tolerant patients (defined as greater than 30mg Morphine equivalent consumed daily)
• BMI greater than 40

Is eligibility based on age, gender, pregnancy/childbearing potential, social/ethnic group, or language spoken (e.g., English Speakers only)?
Yes

1. **Identify each special population that is excluded from the study.**
2. **Provide the rationale for excluding each population.**

Example: ***Eligibility Group: Age 70+, Rationale: Disease that affects the elderly***

Age

- Patients who are younger than 18 years of age are physiologically different compared to the general population and hence, their data will create unnecessary skew when we perform statistical tests.

Pregnancy/Childbearing Potential

- This research does not directly benefit the pregnant woman and/or fetus, and biomedical knowledge can be obtained using subjects whoare not pregnant. Therefore, per federal regulations, pregnant womenwill be excluded from the present study.

Pre-Screening without Consent

Under the revised Common Rule, an IRB may approve a proposal for the investigator to obtain information or biospecimens to screen, recruit, or determine eligibility of prospective subjects for a research study without informed consent. In other words, the revised Common Rule removes the pre-2018 Common Rule requirement for an IRB to approve a waiver of informed consent for these types of activities. This change harmonizes with FDA.

[Refer to 45 CFR 46.116(g) of the revised Common Rule.]

Will the study team obtain information or biospecimens to screen, recruit, or determine eligibility of prospective subjects?

Yes

Pre-Screening Activities (check all that apply):

Study team will obtain patient information directly from medical records

Medical Records

Specify Medical Record Source (check all that apply):
Study team will access their own UCI patients' records and abstract data directly from those records

Data Points

Provide a complete list of ALL data points, variables, and/or information that will be collected/recorded (i.e. data abstraction form) for pre-screening/recruitment purposes:
Attached

If the list of variables will be attached as a separate document [i.e. case report form (CRF; eCRF)], enter "See Attached" above and check the confirmation box below.
The list of variables is attached as a separate document

IMPORTANT! Under a partial waiver of HIPAA authorization, only the minimum necessary information should be accessed for pre-screening/recruitment activities (i.e., determining eligibility and contacting the subject). The information should not be further accessed, used, or disclosed above and beyond pre-screening/recruitment activities until a signed consent form (and signed HIPAA authorization, as applicable) is obtained.

Explain why pre-screening/recruitment activities could not be done without access to the information listed above:
The medical records will be screened by the research team to identify the potential candidate(s) for inclusion/exclusion criteria. Inclusion/exclusion include data points such as BMI that can only be accessed through the study. If these activities are not completed, study activities could not happen.

Recruitment Methods

IMPORTANT!

- **Recruitment materials must adhere to UCI Recruitment Guidelines.**
- **Various templates are available here: IRB Forms → Recruitment Templates.**
- **Please submit all applicable recruitment materials or a Recruitment Material Master Template (Exempt/Expedited only).**
- **For more information, visit this HRP Webpage.**

Indicate all methods that will be used to recruit subjects for this study:

Recruitment Method:

Other recruitment methods

Specify 'Other' recruitment methods:

Study team members will approach their own patients, students, employees for participation in the study. UCI study team members will screen UCIMC medical records to determine subject eligibility and approach patients directly about study participation

Recruitment Method:

Clinicaltrials.gov

REQUIRED! The ClinicalTrials.gov statement must be in all applicable consent documents.

HIPAA Authorization

Does this study involve the creation, access, use, or disclosure of medical records; or does the study involve observations of clinical interactions [i.e., Protected Health Information (PHI)]?

Yes

Identify the Health Insurance Portability and Accountability Act (HIPAA) Authorization process (check all that apply):

Partial waiver of HIPAA authorization requested for screening/recruitment purposes only. Signed authorization obtained prior to further access to PHI.
Signed HIPAA authorization obtained

Waiver of HIPAA Authorization

The Health Insurance Portability and Accountability Act (HIPAA) and the California Confidentiality of Medical Information Act (CMIA) address medical confidentiality and access to medical information for research studies that use, create, or disclose health care related data and records, termed "personal health information."

- **HIPAA Authorization Waivers: The HIPAA Privacy Standard [45 CFR 164.512(h)(i)(2)(ii)] requires that certain criteria be met in order to grant a waiver of individual authorization for research uses of Personal (Protected) Health Information.**

For more information, visit: Protected Health Information.

Partial Waiver of HIPAA

A Partial Waiver of HIPAA Authorization is Requested.

Does the use or disclosure of personal health information involve more than minimal risk?

No

Would the granting of the waiver adversely affect privacy rights and welfare of the individuals whose records will be used or disclosed?

No

Explain (justify) the above answer:

TIP! Consider the following:

- **Are there are other federal, state, or local laws that provide rights to potential subjects to require informed consent**
- **How will the study team prevent adverse affects to subjects' privacy rights and ensure their welfare**

All research personnel are aware of and been trained in UCI/HIPAA policies and practices. Info collected during this time will only be used for pre-screening and a subject will sign a HIPAA Authorization prior to further use of their PHI.

Could the research practicably* be conducted without a waiver of HIPAA authorization?

IMPORTANT! *Practicably means capable of being done; it should not be determined by considerations of convenience, cost, or speed.

No

Explain why research could not be done if authorization was required:

TIP! Consider the following:

- **Demonstrate that it is impracticable to perform the research, and not just impracticable to obtain consent.**
- **Would scientific validity be compromised through bias, have an impact on study power, etc. if consent was required**
- **Would there be ethical concerns or increased risk/harm to subjects if consent were required**
- **Are there pragmatic limitations that make it impossible for the study team to consent subjects such as insufficient time, an inability to identify subjects, an inability for staff to consent the number of subjects needed, etc**

The study team will need access to medical records to properly identify and pre-screen subjects for the trial.

Could the research practicably* be conducted without access to, use or disclosure of the personal identifiers listed in the PHI question?

IMPORTANT! *Practicably means capable of being done; it should not be determined by considerations of convenience, cost, or speed.

No

Explain why research could not be done without access to, use or disclosure of PHI:

The study team will access PHI for screening and tracking purposes.

Are the privacy risks reasonable relative to the anticipated benefits of the research?

Yes

Describe the risk/benefit analysis performed to explain the answer above:

The study team is aware of and trained in UCI/HIPAA policies and practices. All PHI collected prior to obtain consent will only be used for the purpose of pre-screening subjects.

Describe the plan to destroy the personal identifiers at the earliest opportunity, or provide a health or research justification for retaining the identifiers:

PHI will be destroyed per UCI/FDA trial policies and practices.

Describe the plan to protect the personal identifiers from improper use and disclosure (i.e., describe data security methods):

Only study team members will be allowed access to the collected PHI. All information will be kept on secure UCI encrypted networks or in locked cabinets within the Anesthesia Research office.

Provide assurance that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of PHI would be permitted.

As the Lead Researcher, I assure all of the above

Informed Consent Process

Identify the methods of Informed Consent or assent process as applicable for each participant population (check all that apply):

No informed consent (no direct contact)

Non-English Speakers

What type of consent process will be used for Non-English Speaking Participants?

The English version of the consent materials will be translated for non-English speaking participants or their LAR once IRB approval is granted. An interpreter will be involved in the consenting process.

Indicate how non-English speaking subjects or their LAR will be consented in their language and who will be responsible for interpreting and facilitating the informed consent discussion for the non-English speaking subjects:

The study team has 24-hour access to a translation service with sufficient medical expertise to discuss the research in this study

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Waiver or Alteration of Consent

Select the option for the Waiver or Alteration of the Consent:

OPTION A (*Most Common*): General Waiver or Alteration of the Consent

45 CFR 46.116(f)

Does the research involve more than Minimal Risk? [45 CFR 46.116(f)(3)(i)]

No

Could the research practicably* be carried out without the waiver or alteration? [45 CFR 46.116(f)(3)(ii)]

No

Explain why research could not be done if consent was required:

Alternatively, if appropriate, type "Same as HIPAA waiver".

Original data was obtained with approved consent documents. Study team only intends to analyze this data. It would be extremely difficult to obtain reconsents for the nearly 90 subjects enrolled.

If the research involves using identifiable private information or identifiable biospecimens, could the research practicably be carried out without using such information or biospecimens in an identifiable format? [45 CFR 46.116(f)(3)(iii)]

No

Explain why the research could not be done without using information or biospecimens in an identifiable format:

Original data was obtained with approved consent documents. Study team only intends to analyze this data

Will the waiver or alteration adversely affect the rights and welfare of the subjects? [45 CFR 46.116(f)(3)(iv)]

TIP! Consider the following:

- **Are there are other federal, state, or local laws that provide rights to potential subjects to require informed consent**
- **How will the study team prevent adverse affects to subjects' privacy rights and ensure their welfare**

No

Provide the rationale on why the waiver or alteration will NOT adversely affect the rights and welfare of the subjects:

Alternatively, if appropriate, type "Same as HIPAA waiver".

Original data was obtained with approved consent documents. Study team only intends to analyze this data

Whenever appropriate, will the subjects be provided with additional pertinent information after participation?

N/A: No additional information will be provided to subjects

Sample Size

IMPORTANT! **Researchers access will be limited to the sample size numbers provided below. Should researchers need access beyond these numbers, an amendment must be approved by the IRB.**

TIP! **UCI has multiple tools that allow researchers to perform cohort identification analyses for their research with de-identified patient data from the UCI Health Enterprise Data Warehouse.**

- **Cohort Discovery Tool (CDT) - Powered by i2b2**
- **TriNetX - Email ori@uci.edu to request an account**
- **Slicer Dicer for EPIC**

For more information, please contact Health Enterprise Data & Analytics.

Provide sample size numbers in the table below:

Pre-Screen Number:

- **Estimate/anticipate the number of individual-level information needed to screen, recruit, or determine eligibility of prospective subjects. This number should reflect an estimate based on the anticipated rate of screen failure and/or rate of enrollment.**
- **IMPORTANT! Do not access any identifiable information/record prior to securing IRB approval.**

Maximum Number:

- **Estimate/anticipate the number of individuals to be consented. Include withdrawals and screen failures.**
- **For research with no subject consent (i.e. medical record review), estimate/anticipate the number of individual-level information and/or biospecimens to be accessed/analyzed.**

Expected / Target Number:

- **Specify the target number of individuals needed to complete the study.**
- **For research with no subject contact (i.e. medical record review), specify the minimum necessary number of individual-level records and/or biospecimens needed to address the research question.**

Category/Group:
Adults Receiving Total Knee Arthroplasty (TKA)

Age Range:
18 and over

Pre-Screen Number:
125

Maximum Number:
90

Expected / Target Number:
63

Pre-screen Number Determination:

Explain how the pre-screen number was determined (e.g., cohort discovery, anticipated rate of enrollment):
Anticipated rate of enrollment

Sample Size Determination:

1. **Explain how the target sample size was determined (e.g., power analysis; precision estimation).**
    a. **Power analysis should (at least) match the primary outcome/endpoint.**
2. **Provide justification of the effect size for the primary outcome based on preliminary data, current knowledge/ literature and/or cost consideration.**
    a. **If appropriate, provide justification for any significant difference between the max and expected numbers listed above.**
3. **If appropriate, provide sample size justification for secondary outcomes.**

Power analysis/Sample size determination: A power analysis was performed using a 2-sided 2-sample t-test with a significance level of 0.017 to encounter for 3 pairwise comparisons to be performed for the primary outcome. From our clinical data, we observed an average max pain score value of 6.1 +/- 1.9 for arm (a), and we expect the max pain score will be 4.1 for arm (c) and 2.1 for arm (b). We calculated that 21 patients in each group (total of 63) will provide the study an 82% power to detect a difference of 2 in average max pain score between the treatment groups, and a 96% power to detect a difference of 2.5.

Will this study take place only at UCI (i.e., does NOT involve other non-UCI sites)?

Yes

Project Locations

Check all sites where UCI investigator(s) will conduct research activities (e.g., recruitment, informed consent, and research procedures including accessing identifiable, private information about participants):

UCI Health Facilities or Sites (e.g. hospital, clinics, etc.)

Indicate where the research will be performed (check all the apply):

United States

Study Design & Statistics

Include an explanation of the study design (e.g., randomized placebo-controlled, cross-over, cross-sectional, longitudinal, etc.) and, if appropriate, describe stratification/ randomization/blinding scheme:

The present study is a three-arm randomized clinical trial of:
A. Local periarticular infiltration (injection of dilute local anesthetic) + Placebo ACB (nerve block performed with normal saline)
B. Local periarticular infiltration (injection of dilute local anesthetic) + ACB (nerve block procedure performed with local anesthetic)
C. ACB (nerve block performed with local anesthetic)

On the day of surgery (with informed consent), the patient will be randomized via sealed envelope into (A), (B), or (C).
(A) ACB control (20 ml saline injection) + Local infiltration (anesthetic as required by standard of care),
(B) ACB study (20ml 0.5% Ropivacaine) + Local infiltration
(C) ACB study (20 ml 0.5% Ropivacaine).

Is this a study for which a statistical analysis plan is appropriate (e.g. quantitative study design)?

Yes

Describe the statistical methods for the stated specific aims and hypotheses. The analysis plans should match the stated study specific aims and hypotheses:

The comparison of group means among the 3 treatment groups with regards to maximum average pain score within 24 hours postoperative (primary outcome).
The research hypothesis is that the average maximum pain scores within 24 hours postoperative will be significantly lower in both ACB treatment groups comparing to the ACB controls.

Provide precise definitions of the study endpoints and criteria for evaluation; if the primary outcomes are derived from several measurements (i.e., composite variables) or if endpoints are based composite variables, then describe precisely how the composite variables are derived:

Predictors
Variable(s) of interest:
Primary outcome: Average maximum pain scores within 24 hours postoperative.
Secondary Outcomes:

1. 24 Hour post-surgical opioid use
2. PACU opioid use
3. Average daily opioid use during hospitalization
4. Length of stay
5. Average NRS pain score
6. Physical therapy achievements

Covariates/Cofounders
The most common confounders in the study of postoperative pain management include:

1. preexisting pain
2. preoperative anxiety level
3. age

Describe the statistical method(s) that will be used to analyze the primary outcome(s) or endpoints:

Statistical Analysis: The primary analysis will be a 2-sample t-test comparing the difference in average max pain score within 24 hours between each pair (3 pairs) of the 3 treatment groups. The significance level is set at 0.017 for each test. Secondary analysis will utilize analysis of covariance (ANCOVA) to evaluate the treatment difference while adjusting for the effect of covariates.

If appropriate describe secondary or post hoc analyses of primary outcome(s) or other exploratory analysis and if necessary, provide a breakdown of the methods used per outcome or endpoint:

For secondary outcomes, ANCOVA will be applied and *post hoc* pairwise comparisons will be performed if a significant group difference was observed and multiple comparison adjustment will be performed. If the data is found to be violated with parametric assumption, appropriate non-parametric method will be applied.

Safety Monitoring Plan

UCI IRB requires that all clinical investigations involving greater than minimal risk to subjects develop a data and safety monitoring plan to assure the safety and welfare of the research subject/patient.

This is aligned with with NIH requirements and with federal regulations that require that IRBs assure that the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects/patients.

For clinical protocols involving a test article, it is common to have an independent Data Safety Monitoring Board (DSMB).

Please read the applicable HRP webpage for further guidance.

Does this protocol require a Safety Monitoring Plan?

Yes

- **Feel free to cut and paste into this section from the following sources, as applicable:**
  - **For NIH-sponsored clinical trials, the Data Safety Monitoring Plan (DSMP) should be part of the grant application.**
  - **For industry sponsor-initiated clinical trials, a FDA-approved DSMP should be part of the Master Protocol or the Data Safety Monitoring Committee/Board Charter.**
  - **For protocols conducted at the Institute for Clinical and Translational Science (ICTS) or Cancer Center (PRMC), the DSMP information approved by one of these committees should be inserted into this section**

- **REQUIRED! Submit the following documents, as applicable in the Attachments section:**
  - **Signed DSMB recommendation forms from independent DSMB.**
  - **The finalized DSMB charter must be submitted before enrollment begins.**

Provide details of those individuals who will be responsible for the safety oversight of your protocol, including the relevant experience/expertise of each individual (for UCI investigator initiated studies conducted only at UCI, provide the names and titles as well):

The board will be comprised of the Department of Anesthesiology and Perioperative Care Research Council. The council is composed of researchers, educators, and administration that oversee all aspects of research of the department. One of the duties of the council is to ensure the safety of all research being conducted with the department. The Members are the following: Dr.Scott Engwall, Chair of the Department of Anesthesiology & Perioperative Care; Dr. Cameron Ricks, Associate Clinical Professor and Director of the Medical Education Simulation Center; Dr. Kei Togashi, Associate Clinical Professor; and Dr. Sean Ostlund, Assistant Professor and Director of the Ostlund Research Lab.

Indicate how frequently accumulated protocol data will be reviewed and evaluated for participant safety, protocol conduct and progress, and, when appropriate, efficacy:

The committee meets in-person or via Zoom on a quarterly basis. They also communicate on a regular basis with research updates.

Describe the events that would trigger an unscheduled review. Also include stopping guidelines and un-blinding rules if applicable:

Events such as protocol deviations, adverse events and major changes to the approved study protocol would trigger an unscheduled review.

List who will be *locally* monitoring and collecting information on adverse events and/or unanticipated problems (e.g., UCI Lead Researcher, Research Coordinator, etc.).

Include the name, title and experience of the individual(s) and further describe each individual's role in the oversight of subject/patient participating in the protocol.

Aside from the lead researcher, Paulette Mensah, who is a senior CRC and the Clinical Research Supervisor, will be locally monitoring and collecting information on adverse events and/or unanticipated problems.

Describe the plan for annual reporting of the participants' safety, and the protocol's conduct, progress, and efficacy, when appropriate:

The PI will submit a CPA to the IRB for annual reporting of study progress, participants' safety and enrollment status.

Project Procedures

Research Procedures (check all that apply):

Clinical Investigation involving an Investigational Drug or Biological Product (including the on or off label use of an FDA approved drug)
Secondary use of Identifiable Private Information (i.e., Medical/Student Records)

Clinical Phase of Study

Indicate the phase(s) of the study, if applicable:

Phase IV

Provide a detailed chronological description of the procedures:

REOPENING HS#2014-1217 TO FINALIZE DATA ANALYSIS AND COMPLETE MANUSCRIPT WRITING. Original study procedures below:

Subjects will be recruited at the time of their preoperative clearance visit. Eligible patients are those that present for TKA and meet inclusion criteria. Subjects will be consented during their preoperative visit within the Center for Perioperative Care. If they have not made a decision by the end of the visit they will be approached on the day of surgery as well. On the day of surgery the patient will be randomized via sealed envelope into either the:

1. ACB control (20 ml saline injection) + Local infiltration (anesthetic as required by standard of care),
2. ACB study (20ml 0.5% Ropivacaine) + Local infiltration
3. ACB study (20 ml 0.5% Ropivacaine).

The following individuals are blinded to the treatment types:
1. Anesthesiologist performing the nerve block
2. Postoperative nurse

A member of the acute pain service will perform the nerve block in the preoperative holding area. The perioperative joint surgical home pathway will not be altered and the patient will proceed to the operating room as per pathway protocol. A postoperative nurse will assess pain scores. The subjects will attend standard of care physical therapy sessions where their physical therapists will record the subjects' physical therapy achievements onto their medical record, which will then be accessed by authorized research personnel for data collection.

Specify the total duration of a subject's participation in the study and clearly outline the duration of participation for each study visit and sub-study, as applicable:

1 day (day of surgery) : Verification or obtain informed consent, randomization, obtain block

List all data collection tools (e.g., measures, questionnaires, observational tool) below; include citations for standardized/ validated measure(s):

Attached

Are all data collection tools standardized or validated?

Yes

UCI Health Clinical Services

Will this study require clinical items/ services from UC Irvine Health?

No

Use of Identifiable Information

Source of Information

Indicate the types/sources of identifiable private information (check all that apply):

UCI Health Medical Records

Medical Records

IMPORTANT! Access to UCI health data is facilitated through data stewards identified by the Health Data Governance Committee (HDGC).

Specify how UCI-Health medical records will be obtained:

Study team will obtain information directly from UCI Health medical records

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Data Points

Specify the date-range of the data used for the project (e.g. January 2002 to January 2020):

Initial eAPP approval (September 2014) through expiration date of last approved IRB (July 2021).

Provide a complete list of ALL data points, variables, and/or information that will be collected (i.e. data abstraction form):

Randomization: A. ACB control (20 ml saline injection) + Local infiltration (anesthetic as required by standard of care), B. ACB study (20ml 0.5% Ropivacaine) + Local infiltration C. ACB study (20 ml 0.5% Ropivacaine). The following individuals are blinded to the treatment types: 1. Anesthesiologist performing the nerve block 2. Postoperative nurse A member of the acute pain service will perform the nerve block in the preoperative holding area. The perioperative joint surgical home pathway will not be altered and the patient will proceed to the operating room as per pathway protocol. A postoperative nurse will assess pain scores. The subjects will attend standard of care physical therapy sessions where their physical therapists will record the subjects' physical therapy achievements onto their medical record, which will then be accessed by authorized research personnel for data collection. Variable(s) of interest: 1. Primary outcome: Average maximum pain score within 24 hours postoperative. 2. Secondary Outcomes: a. 24 Hour post-surgical opioid use b. PACU opioid use c. Average daily opioid use during hospitalization d. Length of stay e. Average NRS pain score f. Physical therapy achievements Covariates/Cofounders The most common confounders in the study of postoperative pain management include: 1. preexisting pain 2. preoperative anxiety level 3. age

If the list of variables will be attached as a separate document [i.e. case report form (CRF; eCRF)], enter "See Attached" above and check the confirmation box below.

The list of variables is attached

Investigational Drug or Biologic

- **Upload the Investigator Brochure (IB) or Package Insert in the Attachments section to identify the agent(s) to be used in this clinical investigation. Be sure the uploaded items contain the following:**
  - **Product Description**
  - **Clinical Pharmacology**
  - **Dosage and Guidelines for Administration (Optional)**
  - **Dosage and administration in this investigation (if different from approved)**
  - **Toxicity and Known Side Effects**
  - **Precautions and Contraindications**

- **IMPORTANT! Documentation of a FDA Investigational New Drug (IND) Application for the use of an investigational agent (drug/biologic) must be provided to the IRB for review and before IRB approval may be granted.**

- **Please read the HRPP webpage for information about the use of drugs in clinical investigations.**

Generic Name:
Ketorolac

Trade Name/Biologic:
Toradol

Product Manufacturer:
Allergan

Does the product meet the FDA definition of a *drug*?
Yes

Identify the regulatory status of the product to be used in this study:
The product is approved by the FDA and will be used according to the FDA label

You may reference the section title and page number(s) of the Investigator Brochure or Package Insert rather than pasting or transcribing the relevant information in the following agent information questions.

REQUIRED! Submit the Investigator Brochure or Package Insert in the Attachments section.

Specify the product description:

Ketorolac (Toradol) is a non-steroidal anti-inflammatory drug used as an analgesic for short-term management of moderate to severe pain.

Specify the clinical pharmacology:

Ketorolac tromethamine is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits analgesic activity in animal models. The mechanism of action of ketorolac, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition. The biological activity of ketorolac tromethamine is associated with the S-form. Ketorolac tromethamine possesses no sedative or anxiolytic properties. Ketorolac tromethamine is a racemic mixture of [-]S- and [+]R-enantiomeric forms, with the S-form having analgesic activity.

Specify the indications for use:

Ketorolac is used for short-term management (up to 5 days) of moderately severe acute pain that otherwise would require narcotics. It most often is used after surgery.

Specify the dosage and guidelines for administration (Optional):

Treatment should be started with ketorolac injection. Tablets are used only if treatment is continued after patients begin to eat and drink. The total duration of therapy should not exceed 5 days because of the potential for gastrointestinal bleeding and other side effects. The recommended adult intravenous single dose is 15 to 60 mg. Multiple intravenous doses of 15 or 30 mg every 6 hours, not to exceed 60 or 120 mg a day, also may be used. Following intravenous therapy, the recommended dose is one or two tablets initially followed by 1 tablet every 4-6 hours, not to exceed 40 mg daily. The smaller dose is used for patients with poor kidney function or those older than 65 years.

Specify the dosage and administration in this investigation (if different from approved):

N/A

Specify the toxicity and known side effects:

Common side effects from ketorolac include rash, ringing in the ears, headaches, dizziness, drowsiness, abdominal pain, nausea, diarrhea, constipation, heartburn, and fluid retention. NSAIDs reduce the ability of blood to clot and therefore increase bleeding after an injury. Ketorolac may cause ulcers and bleeding in the stomach and intestines, particularly with use for more than five days.

Specify the precautions and contraindications:

Do not take if allergic to aspirin or other nonsteroidal anti-inflammatory drugs-NSAIDs (such as ibuprofen, naproxen, celecoxib); or if you have any other allergies. tell your doctor or pharmacist your medical history, especially of: asthma (including a history of worsening breathing after taking aspirin or other NSAIDs), bleeding or clotting problems, blood disorders (such as anemia), heart disease (such as previous heart attack), high blood pressure, liver disease, growths in the nose (nasal polyps), throat/stomach/intestinal problems (such as bleeding, heartburn, ulcers), stroke, swelling of the ankles/feet/hands. This medication may infrequently make you more sensitive to the sun. Avoid prolonged sun exposure, tanning booths, and sunlamps. Use a sunscreen and wear protective clothing when outdoors. Older adults may be more sensitive to the effects of the drug, especially bleeding in the stomach/ intestines or kidney problems. Using high doses for a long time may increase this risk. Before using this medication, women of childbearing age should talk with their doctor(s) about the benefits and risks (such as miscarriage). Tell your doctor if you are pregnant or if you plan to become pregnant.

Describe how the investigational agent will be prepared, controlled and who will be responsible for management of the agent:

UCI Health IDS Pharmacy

IMPORTANT! All investigational product (IP) utilized at UCI Health must be under the control of UCI Health Investigational Drug Services (IDS) Pharmacy. This includes storage, control, and distribution of IP.

Generic Name:

Ropivacaine

Trade Name/Biologic:

Naropin

Product Manufacturer:

AstraZeneca

Does the product meet the FDA definition of a *drug*?

Yes

Identify the regulatory status of the product to be used in this study:

The product is approved by the FDA and will be used according to the FDA label

You may reference the section title and page number(s) of the Investigator Brochure or Package Insert rather than pasting or transcribing the relevant information in the following agent information questions.

REQUIRED! Submit the Investigator Brochure or Package Insert in the Attachments section.

Specify the product description:

Naropin (ropivacaine) is used as a long-acting local anesthetic for surgical anesthesia and acute pain management.

Specify the clinical pharmacology:

: Ropivacaine is a member of the amino amide class of local anesthetics and is supplied as the pure S-(-)-enantiomer. Local anesthetics block the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, by slowing the propagation of the nerve impulse, and by reducing the rate of rise of the action potential. In general, the progression of anesthesia is related to the diameter, myelination, and conduction velocity of affected nerve fibers. Clinically, the order of loss of nerve function is as follows: (1) pain, (2) temperature, (3) touch, (4) proprioception, and (5) skeletal muscle tone.

Specify the indications for use:
surgical anesthesia, epidural block for surgery, major nerve block, local infiltration, acute pain management, and epidural continuous infusion or intermittent bolus (postoperative or labor).

Specify the dosage and guidelines for administration (Optional):
20 ml 0.5% Ropivacaine

Specify the dosage and administration in this investigation (if different from approved):
N/A

Specify the toxicity and known side effects:
Dizziness, nausea, or vomiting may occur.

Specify the precautions and contraindications:
: Naropin is contraindicated in patients with a known hypersensitivity to ropivacaine or to any local anesthetic agent of the amide type.

Describe how the investigational agent will be prepared, controlled and who will be responsible for management of the agent:
UCI Health IDS Pharmacy

IMPORTANT! All investigational product (IP) utilized at UCI Health must be under the control of UCI Health Investigational Drug Services (IDS) Pharmacy. This includes storage, control, and distribution of IP.

Return of Results

Will Individual results be shared with subjects?

No

Will overall study results will be shared with subjects?

The overall study results will be listed on Clinicaltrials.gov

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Risk Assessment

Risks and Discomforts

1. Describe and assess any reasonably foreseeable risks and discomforts associated with each procedure for each subject population — physical, psychological, social, legal or other.

2. If this study will involve the collection of identifiable private information, even temporarily, for which the disclosure of the data outside of the research could reasonably place the subjects at risk, include the risk of a potential breach of confidentiality.

A bullet point list is recommended.

RISK ASSESMENT

a) The main intervention of this study is a peripheral nerve block. The most common complication of nerve blocks are:

1. Vascular injury or hematoma: Inadvertent puncture of adjacent vascular structures can lead to perineural hematoma and is more likely to occur in patients who are anticoagulated. The majority of vascular punctures resolve with direct pressure to the block injection site.
2. Infection. Infection risk for single shot peripheral nerve block is negligible.
3. Nerve injury. Neurologic injuries after single shot peripheral nerve blocks are uncommon with rates reported on the order of 1 in 10,000 blocks to 0.9 in 1000 blocks.
4. Allergic reaction to local anesthetic. Uncertain incidence.
5. Intravascular injection. Inadvertent intravascular injection of local anesthetic may lead to local anesthetic toxicity depending upon the volume injected or injection into an adjacent vessel.

b) There is a chance of breach of confidentiality. There will be a unique code assigned to each participating patient and only necessary information for pain assessment will be obtained. Only the lead investigator and approved UCIMC study team members will have access to identifiable information for organization purposes only. All data will be de-identified before any statistical tests and/or publications.

The potential benefits of receiving the nerve block are improved pain control and ambulation during the first 24 hours following surgery.

EXPEDITED/FULL COMMITTEE ONLY: Include an assessment of their expected frequency (e.g., common – 65%, less common – 40%, unlikely – 5%, rare - <1%) and the seriousness (mild, moderate, severe).

Discuss what steps have been taken and/or will be taken to prevent and minimize any risks/potential discomforts to subjects:

The steps taken to prevent and minimize any risks/potential discomforts to eligible subjects in all experimental groups include routine monitoring applied before, during, and after the administration of the nerve block. Ultrasound guidance will be utilized for the adductor canal block, aiding in the avoidance of critical structures such as blood vessels. The nerve block technique will be standardized and limited to the three listed co-researching anesthesiologists with expertise in performing the nerve block. All participating patients in each of the experimental groups of the present study will be randomized to receive at least one intervention to reduce pain in the postoperative period. All patients will be either given sedation or be under anesthesia when the interventions are performed as this is the standard of care protocol when performing a peripheral nerve block. Throughout the study, a periodic review of the data will be performed to assess whether or not there any large changes in postoperative pain scores and to evaluate if a protocol revision is required.

Screening records will be destroyed for patients that are not enrolled and subject identifiable data will be protected for the subjects enrolled in the study.

Confidentiality Certificates

Specify whether a confidentiality certificate been issued for the study:

No

Potential Benefits

Is there the prospect of a direct benefit anticipated for subjects?

Yes

Describe the potential benefits subjects may expect to receive from participation in this study:

The potential benefits of receiving the nerve block are improved pain control and ambulation during the first 24 hours following surgery.

Specify the expected potential societal/scientific benefit(s) of this study:

Potential societal/scientific benefits from the present study would include improved pain control and ambulation during the first 24 hours following surgery for total knee arthroplasty (TKA) patients.

Alternatives to Participation

Describe the alternatives to participation in the study available to prospective subjects. Include routine (standard of care) options as well as other experimental options, as applicable (check all that apply):

No alternatives exist. The only alternative to study participation is not to participate in the study

Participant Compensation

Compensation is when participants are paid for their time & efforts in research.

- Compensation should be offered on a prorated basis when the research involves multiple sessions.
- For additional information about researcher's/department's responsibilities and current Accounting procedures, see **UCI Policy Sec. 701-03**.

For more information see: Compensation Info.

Are participants compensated?

No

Participant Costs

Will subjects or their insurers be charged for study procedures?

No

Reimbursement

Will subjects be reimbursed for out-of-pocket expenses?

No

Confidentiality of Research Data

CA Information Protection Act

Are University of California / UC Irvine records (e.g., medical, student, employment, etc.) disclosed to the research team?

CA Civil Code §1798 – California Information Protection Act (CIPA)

§1798.3 (c) The term *disclose* means to disclose, release, transfer, disseminate, or otherwise communicate all or any part of any record orally, in writing, or by electronic or any other means to any person or entity.

No

Participant Identifiers

Will any subject/patient identifiers be collected or retained for data analysis, recruitment, consenting and/or compensation?

Yes

Indicate the subject/patient identifiers that will be collected or retained for data analysis, recruitment, consenting and/or compensation (check all that apply):

All elements of dates that are directly related to an individual: birth date, admission date, discharge date, death date, and all ages over 89

Medical record numbers

Names

Coding Identifiers

Will a code be used to link subject/patient identifiers with the information and/or biospecimens?

A code will be used. Subject/Patient identifiers will be kept separately from the information and/or biospecimens. The code key will be destroyed at the earliest opportunity, consistent with the conduct of this research

Presentation/Publication

Specify whether subject/patient identifiers will be disclosed in presentations and/or publications:

Subject/Patient identifiers will not be disclosed

Identifier Retention

Specify how long all subject/patient identifiers will be retained. This includes identifiers stored in paper format, stored electronically as well as video recordings, audio recordings, photographs, etc.:

Destroyed after publication/presentation or end of protocol

Info/Biospecimen Storage

Indicate how information and/or biospecimens (including signed consent forms) will be stored (check all that apply):
Information will be maintained electronically. Information will be password protected and maintained in an encrypted format
Information will be maintained in hard copy. Information will be stored in a locked area that is not accessible to non-study team members
Information will be maintained on an UCI enterprise cloud platform

Encrypted Format

Specify where the information will be maintained electronically:
Maintained on UCI encrypted servers

Hard Copy

Specify where the information will be maintained in hard copy:
Physical consents and/or hardcopy documents with identifi ableinformation are locked in cabinets within the research offi ces whichrequire badge access to enter.

Enterprise Cloud Platform

For enterprise cloud storage, select the location that adheres to the UCI Protection Level required for the research information:
Google Drive
Microsoft OneDrive

Info/Biospecimen Transport

Will subject identifiers be transported or maintained on portable devices (e.g., laptop, smartphone, external hard drive, etc.)?

IMPORTANT! Only the "minimum data necessary" should be stored on portable devices or transported as doing so makes it susceptible to loss or theft.

- **If there is a necessity to use a portable device, the research files must be encrypted, and subject identifiers transferred to a secure system as soon as possible.**
- **If transporting data/biospecimens the method of transport must be secure.**

No

Info/Biospecimen Retention

Indicate how long research information/biospecimens will be retained:

In accordance with UCOP policy, information/biospecimens will be retained for 10 years after the end of the calendar year in which the research is completed, unless otherwise specified in the award agreement

Info/Biospecimen Sharing

The research team, authorized UCI personnel, the study sponsor (as applicable) and regulatory entities such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP), may have access to participants' study records to protect their safety and welfare.

Sharing Within Scope of Project

Will research materials (information/ biospecimens) be shared with collaborators (i.e., researchers not covered under the UCI project), for purposes within the scope of the current project?

No

Sharing Outside Scope of Project

Will information and/or biospecimens be shared, used again, or stored for undefined future research purposes beyond the scope of the current protocol?

No

Attachments

For UCI IRB templates, visit IRB Forms.

ATTENTION! If requisite documentation is not attached, the submission will be returned as incomplete.

Maximum file size is 30MB

EXPIRATION NOTICE FOR HS# 2014-1217.PDF

Attachment Type

Other

File Comments
Expiration of original IRB (pre KRP transition)

File Name

Status (HRP Use Only)

Agenda (HRP Use Only)

DATA ABSTRACTION.DOCX

Attachment Type
Other

File Comments
Data Abstraction Sheet

File Name

Status (HRP Use Only)

Agenda (HRP Use Only)

TIMELINE V3.DOCX

Attachment Type
Case Report Form (CRF, eCRF)

File Comments
CRF

File Name

Status (HRP Use Only)

Agenda (HRP Use Only)

2014-1217_CONSENT_06-22-18.PDF

Attachment Type
Consent Form

File Comments
Previously approved ICF - this is a reopening for data analysis (not needed)

File Name

Status (HRP Use Only)

Agenda (HRP Use Only)

2014-1217_HIPAA_AUTHORIZATION_UCI (1).DOCX

Attachment Type
HIPAA Research Authorization Form

File Comments
Previously approved HIPAA - this is a reopening for data analysis (not needed)

File Name

Status (HRP Use Only)

Agenda (HRP Use Only)

UCI-HIPAA-AUTHORIZATION_NEW.DOCX

Attachment Type
HIPAA Research Authorization Form

File Comments
Updated HIPAA - this is a reopening for data analysis (not needed)

File Name

Status (HRP Use Only)

Agenda (HRP Use Only)

RECRUITMENT.DOCX

Attachment Type
Recruitment Material

File Comments
Placeholder

File Name

Status (HRP Use Only)

Agenda (HRP Use Only)

3567 RENEWAL APPROVAL LETTER 07-19-24.PDF

Attachment Type
UCI IRB Approval Letter

File Comments

File Name

Status (HRP Use Only)
Approved

Agenda (HRP Use Only)

Lead Researcher Certification

Investigator's Assurance

As Lead Researcher, I have ultimate responsibility for the performance of this study, the protection of the rights and welfare of the human subjects, and strict adherence by all co-investigators and research personnel to all Institutional Review Board (IRB) requirements, federal regulations, and state statutes for research involving human subjects.

I hereby assure the following:

1. The information provided in this application is accurate to the best of my knowledge.
2. The information provided in this application has been discussed and shared with my Department Chair. Any requests for changes based on this discussion are included in this application upon submission or will be initiated by the research team either during the IRB review process or via an amendment.
3. All named individuals on this project have read and understand the procedures outlined in the protocol and their role on the study.
4. All named individuals on this project have completed the required Educational research tutorials and have been made aware of the "Common Rule" (45 CFR Part 46), applicable Food and Drug Administration (FDA) regulations (21 CFR Parts 50, 56, 312 and 812), have read the Belmont Report, and UCI's Federalwide Assurance (FWA) that are available on the Human Research Protections Program (HRP) website.
5. All experiments and procedures involving human subjects will be performed under my supervision or that of another qualified professional listed on this protocol.
6. Any responses submitted on my behalf by named individuals on this project I have prospectively agreed to.
7. I understand that, if the study described in this IRB application is supported by a federal award or used as a basis for a proposal for funding, it is my responsibility to ensure that the description of human subjects activities in the proposal/award is identical in principle to that contained in this application. I will submit modifications and/or changes to the IRB as necessary to assure the proposal/award and application are identical in principle.

I and all co-investigators and research personnel agree to comply with all applicable requirements for the protection of human subjects in research including, but not limited to, the following:

1. Obtaining the legally effective informed consent of all human subjects or their legally authorized representatives (unless waived) and using only the currently approved, stamped consent form (if applicable).
2. Per federal regulations, once a human research study has received IRB approval, any subsequent changes to the study must be reviewed and approved by the IRB prior to implementation except when necessary to avoid an immediate, apparent hazard to a subject. See Reporting of Unanticipated Problems.
3. Reporting any unanticipated problems involving risk to subjects or others, including protocol violations per UCI IRB policy. In addition, HIPAA privacy violations must be PROMPTLY disclosed to the UCI Privacy Officer. There are time requirements for

reporting these breaches of confidentiality, which, if not met, may result in monetary damages to the researcher and the institution.

4. Responding appropriately to subjects' complaints or requests for information about the study; and reporting to the IRB any subject complaints that are not resolvable by the study team.
5. Promptly providing the IRB with any information requested relative to the project.
6. Assuring the appropriate administration and control of investigational test articles (i.e., investigational drugs, biologics or devices) by a qualified investigator or other appropriate individual or entity (e.g., UCI Health pharmacy), and assuring use and maintenance of an Investigational Drug/Biologic Accountability Log or Device Accountability Log.
7. Registering applicable clinical trials with clinicaltrials.gov. For more information about this topic, visit the ClinicalTrials.gov web page or the HRP webpage. The consequences of not meeting the registration and reporting requirements include monetary damages to the researcher and the institution.
8. Obtaining continuing review prior to study expiration (I understand if I fail to apply for continuing review, approval for the study will automatically expire, and all human research activities must cease until IRB approval is obtained).
9. Promptly and completely complying with an IRB decision to suspend or terminate its approval for some or all research activities.
10. Submitting to a routine review of human subject research records. The Compliance & Privacy Office at UCI Health performs ongoing routine reviews of open biomedical research protocols, in an effort to ensure in part that human subject research activities are conducted in accordance with regulations, laws and institutional policies regarding the protection of human subjects. In addition, the HRP unit of the Office of Research has developed the Education Quality and Improvement Program (EQUIP). Through EQUIP, HRP staff conduct periodic quality improvement monitoring and educational outreach.
11. For clinical trials initially approved by the IRB on or after January 21, 2019, posting one (1) IRB-approved clinical trial consent form at a publicly available federal website. The consent form must be posted after recruitment closes, and no later than 60 days after the last study visit. For additional guidance, refer to the OHRP FAQs on Informed Consent.
12. Filing a final report with UCI HRP at the conclusion of this project.

As the Lead Researcher, I assure all of the above

Investigators' Disclosure of Financial Interest

In order to inform research subjects of circumstances that may affect their decision to participate in this study, all researchers are required to disclose their financial interests with outside institutions.

The Lead Researcher of the protocol must ask the following question of all study team members:

"Do you, your spouse/registered domestic partner, and dependent children together have any disclosable financial interests (i) that would reasonably appear to be affected by the research; or (ii) in entities whose financial interests would reasonably appear to be affected by the research?"

A member of the study team who answers in the affirmative will be contacted by the Conflict of Interest Oversight Committee (COIOC) to obtain additional information regarding their specific financial interest(s).

IMPORTANT! If there has been a change in the financial disclosures of the LR or the study team, please also request a 'Change in Financial Interests'.

As Lead Researcher, I certify that the disclosures for all study team members are accurate

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Need Help?

Submission Delay

There is a time delay (up to 1 minute) after selecting "submit". During this time the system performs a validation check to ensure requiste prompts have been addressed.

Please do not refresh or close the page. The transaction will eventually go through.

Kuali is currently working to resolve the performance issues our customers are experiencing. Thank you for your patience and your partnership.

Contact the Office of Research

For KRP technical questions or issues:

- **Visit the KRP User Guide**
- **Contact Electronic Research Administration (ERA)**

For IRB questions and regulatory or institutional guidance:

- **Visit Human Research Protections (HRP)**
- **Contact the HRP staff**

Administrative Details Form

Project Status

Committee:
IRB A

Project Status:
Approved

Date of Action/Determination:
07-19-2024

Amendment Status:

Date of Amendment Action/Determination:

ERA Transcription Date:

Not applicable for new studies submitted after September 07, 2021

Pre-2018 Common Rule:

Not applicable for studies initially approved after January 21, 2019

Date of Transition:

Not applicable for studies initially approved after January 21, 2019