Official Title: Continuous Vs Single Shot Adductor Canal Block After ACL Reconstruction – A Randomized Study

NCT: NCT04101682

Document Date: August 11, 2020

Northwell Health

RESEARCH PROTOCOL

Protocol Title:	Continuous Vs Single Shot Adductor Canal Block After ACL Reconstruction – A Randomized Study
Principal Investigator:	Randy Cohn
Primary Contact Name:	Nicholas Frane
Primary Contact Phone:	7634395741
Primary Contact E-mail:	nfrane@northwell.edu
Date Revised:	8/11/2020
IRB Number:	18-0811

Guidelines for Preparing a Research Protocol

Instructions:

- You do not need to complete this document if you are submitting an *Application for Exemption* or *Application for a Chart Review*.
- Do not use this template if:
  - Your study involves an FDA regulated product. In this case, use the *Clinical Trial Protocol Template.*
  - Your study has a protocol from a sponsor or cooperative group. In this case, use the *Protocol Plus*.
  - Your study is a registry or repository for data and/or samples, In this case, use *Protocol Template – Registry Studies.* .
- If a section of this protocol is not applicable, please indicate such.
- Do not delete any of the text contained within this document.
- Please make sure to keep an electronic copy of this document. You will need to use it, if you make modifications in the future.
- Start by entering study information into the table above, according to these rules:
  - Protocol Title: Include the full protocol title as listed on the application.
  - Investigator: include the principal investigator's name as listed on the application form
  - Date Revised: Indicate the date at which the protocol was last revised
  - IRB Number: Indicate the assigned IRB number, when known. At initial submission, this row will be left blank.
- Once the table information in entered, proceed to page 2 and complete the rest of the form.

↓ Continue to next page to begin entering information about this study ↓

1. PREVIOUS STUDY HISTORY

Has this study ever been reviewed and rejected/disapproved by another IRB prior to submission to this IRB?

No ☐ Yes – if yes, please explain:

2. BRIEF SUMMARY OF RESEARCH

- *The summary should be written in **language intelligible to a moderately educated, non-scientific layperson**.*
- *It should contain a clear statement of the rationale and hypothesis of your study, a concise description of the methodology, with an emphasis on what will happen to the subjects, and a discussion of the results.*
- *This section should be ½ page*

We will be randomizing patients to either receive an adductor canal block in the operating room postoperatively as single shot of 20-30cc bupivacaine or to have a catheter inserted into the adductor canal which will be attached up to a continuous infusion pump of bupivacaine that will have a set flow rate over the next couple days. Our hypothesis is that patients will have better pain control, sleep, and decreased opioid consumption with the use of a continuous infusion pump

3. INTRODUCTION/BACKGROUND MATERIAL/PRELIMINARY STUDIES AND SIGNIFICANCE

- *Describe and provide the results of previous work by yourself or others, including animal studies, laboratory studies, pilot studies, pre-clinical and/or clinical studies involving the compound or device to be studied.*
- *Include information as to why you are conducting the study and how the study differs from what has been previously researched, including what the knowledge gaps are.*
- *Describe the importance of the knowledge expected to result*

ACL reconstruction is a common procedure performed ranging an estimated 60,000 to 175,000 times a year in the United states (6). Many factors can contribute to clinical outcome with ACL reconstruction, most notably with pain and rehabilitation. Numerous tactics are employed to help alleviate postoperative pain, ranging from simple conservative management such as ice and elevation, to oral and IV narcotics. Current trends in management aim to reduce the use of narcotics and to investigate various alternative modalities for achieving analgesia without compromising clinical outcomes. One way of achieving this is with use of peripheral nerve blocks. Administered by an anesthesiologist or certified nurse anesthetist, analgesia is delivered to a peripheral nerve using ultrasound guidance and in some incidences a catheter is then placed overlying the nerve sheath. This

catheter is then connected to a device with a reservoir that administers local anesthetic at a set rate that can be locked or manipulated by the user, which gives the theoretical advantage of continuous analgesia of the operative site.

Historically, other methods were used to combat post-operative pain. Buchko et al looked at intra-articular analgesia after arthroscopic ACL reconstruction and found an increased rate of chondrolysis, which was similar to other studies that looked at its use in the shoulder joint (11). Use of peripheral nerve blockade is not new practice and has been described throughout the literature. Manickam et al showed 100% success rate and full blockade after twenty minutes with use of the adductor canal block (12). The safety and efficacy of the Continuous Peripheral Nerve Block (CPNB) has been thoroughly investigated. Carvhalo et al found that the addition of a peripheral catheter added only 10 minutes to procedural time versus single shot peripheral nerve block (14). In a group of 35 trauma patients it was found that despite continuous peripheral nerve infusion, serum levels of Ropivicaine were well below toxic levels (15). A review article by Nicolotti et al found that the incidence of positive cultures of placed catheters varied widely from 6%-57%, but the actual incidence of positive cultures resulting in clinical infection was 0%-3.2% (13). The large discrepancy between the two values was found to be likely due to inadequate skin preparation and improper technique with removal.

Some studies have shown the efficacy of CPNB use and concluded with positive results. A multicenter prospective study of use of CPNBs found high quality postoperative pain reduction along with low rates of neurologic or infectious complications (1) and according to Enneking et al. CPNBs have been shown to improve patient satisfaction and improve rehabilitation compared to IV narcotics after orthopedic surgery for both upper and lower extremity (3). A more recent study prospectively looked at CPNB vs placebo (Normal Saline) performed in the upper extremity and found that there was a statistically significant reduction in pain, opioid use, sleep disturbances and increase in patient satisfaction scores (4). A large meta analysis by Richman et al looked at the efficacy of CPNBs and found statistically significant reduction in opioid use, pain up to 72 hours postoperative and decrease in episodes of nausea and vomiting (5) with use versus opioid analgesia.

In the lower extremity two main methods of block are employed, femoral nerve block (FNB) or adductor canal block (ACB). The use of FNB in ACL reconstruction, as shown by Mulroy et al, was found to have superior efficacy in pain control and reduction in opioid consumption when testing single shot FNB vs sham (9). One complication of FNB is quadricep muscle weakness, which Jaeger et al. demonstrated as a 49% reduction from baseline while ACB reduced strength 8% from baseline (10). Kwofie at al found that with ACB vs FNB that there was a statistically significant preservation in balance and strength in ACB compared to FNB (8). These studies show the advantages of ACB to anesthetize surgical sites without compromising quadriceps strength and balance. Abdallah et al showed that using ACB versus FNB reduced quadriceps weakness with similar functional outcomes and pain reduction in ACL reconstruction (7). The superiority of

continuous catheter delivery over single injection in regards to pain and reduction and opioid use have not been shown in the literature. To our knowledge there are no randomized controlled trials that compare single injection versus CPNB in the adductor canal following ACL reconstruction. In this study we look to compare these two methods of analgesia after ACL reconstruction examining the effects on pain control, opioid use, and satisfaction scores.

4. OBJECTIVE(S)/SPECIFIC AIMS AND HYPOTHESES

- *A concise statement of the goal(s) of the current study.*
- *The rationale for and specific objectives of the study.*
- *The goals and the hypothesis to be tested should be stated.*

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		
To Compare the efficacy of two different modes of administration of peripheral nerve block for postoperative pain control after primary ACL reconstruction.	Pain control as measured by a visual analogue scale (0-10) on post operative day 1,2,3,4,7, and at first follow up visit (Day 14).	Our study seeks to better clarify the effectiveness of two postoperative pain control methods after ACL reconstruction. Visual analogue scale is commonly used to assess pain in postoperative patients. This is an easy way to assess patients pain in a quick and easy to understand method.
Secondary		
To compare the daily opioid consumption in patients post operatively after ACL Reconstruction.	This will be measured as daily consumption of oxycodone (morphine equivalents) on post operative day 1,2,3,4,7, and 14.	A secondary objective of our study would be to examine pain control objectively by opioid consumption each day. This is a secondary measure of the efficacy of pain control. The hope is that with better pain control via peripheral nerve block patients would be less reliant on opioid pain medication.
To determine the effectiveness of pain control and quality of sleep.	We will measure this by asking if they had a disturbance in their sleep or trouble getting to sleep through email surveys.	Our study wants to look at how pain control and sleep quality are correlated and to analyze if better pain control also allowed patients to have better postoperative sleep habits.

General Well Being	Short Form - 12 Survey given preoperatively and at 14 days post operatively.	This assessment test is to classify changes in general health and wellbeing, physical, and mental health.
Knee Assessment Score	International Knee Documentation Committee Subjective Knee Form (IKDC) to be given preoperatively and at 14 days post operatively.	Designed to assess patients with a variety of knee disorders.

5. RESOURCES AVAILABLE TO CONDUCT THE HUMAN RESEARCH

- *Explain the feasibility of meeting recruitment goals of this project and demonstrate a potential for recruiting the required number of suitable subjects within the agreed recruitment period*
    - *How many potential subjects do you have access to?*
- *Describe your process to ensure that all persons assisting with the trial are adequately informed about the protocol and their trial related duties and functions*

We will be recruiting patients from multiple surgeons who perform ACL reconstructions in an attempt to get a higher number of patients. Our recruitment is estimated to last 9-12 months to get an adequate number of patients. In the event that we are still in need we can extend the trial a few months in order to capture the adequate number of participants. All the involved providers and staff will be given the same instructions which are standardized to ensure that each facility and staff follow the same protocol. In addition, there will be a resident investigator or co investigator at each site to oversee the project.

6. RECRUITMENT METHODS

- *Describe the source of potential subjects*
- *Describe the methods that will be used to identify potential subjects*
- *Describe any materials that will be used to recruit subjects. A copy of any advertisements (flyers, radio scripts, etc.) should be submitted along with the protocol.*
- *If monetary compensation is to be offered, this should be indicated in the protocol*

We will include multiple different sites to increase our enrolment participants. All patients will be recruited in the outpatient setting after being diagnosed with an

ACL tear and deciding to have operative reconstruction with one of the participating surgeons. At that point, the patients will be recruited for the study. There will be no active recruiting outside of the surgeon's patient population that requires surgical reconstruction of their ACL.

In regards to retention, the patients will agree to the time points to participate in the email surveys from REDCAP. The surveys have automatic reminders every 2 hours in addition the study co-investigators will receive notifications and can contact the patient's if they do not complete the surveys at the agreed time. The patients will have a postoperative visit 10-14 days after the indicated surgery with the attending physician. The patient will also be contacted via telephone on post-operative day 1, 2, 3, 4 and 7 to assess for adverse events.

7. ELIGIBILITY CRITERIA

- *Describe the characteristics of the subject population, including their anticipated number, age, ranges, sex, ethnic background, and health status. Identify the criteria for inclusion or exclusion of any subpopulation.*
- *Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, children, prisoners or other institutionalized individuals, or others who are likely to be vulnerable. You cannot include these populations in your research, unless you indicate such in the protocol*
- *Similarly, detail exclusionary criteria: age limits, special populations (minors, pregnant women, decisionally impaired), use of concomitant medications, subjects with other diseases, severity of illness, etc.*

INCLUSION CRITERIA - In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Provision of signed and dated informed consent form
2. Stated willingness to comply with all study procedures and availability for the duration of the study
3. Male or female, aged >16 years old
4. In good general health as evidenced by medical history and deemed medically healthy enough to tolerate surgery by the patient's primary care physician
5. MRI with evidence of ACL tear, and wanting to have an ACL reconstruction surgery
6. Ability to take oral medication and be willing to adhere to the study intervention, including telephone calls and access to email.
7. Have a working telephone and electronic device with ability to access email that allows them for daily communication to complete the electronic correspondence.

EXCLUSION CRITERIA - An individual who meets any of the following criteria will be excluded from participation in this study:

1. Current daily opioid requirement exceeding the equivalent of 15mg morphine
2. Daily prescription of corticosteroid, tricyclic antidepressant, gabapentin, or tramadol
3. Carrying the diagnosis of chronic pain syndrome, uncontrolled anxiety, history of schizophrenia or related psychiatric disorders
4. History of alcohol or drug abuse/addiction
5. History of preexisting nerve damage in the surgical extremity
6. Knee surgery (same knee) in the previous 12 weeks
7. Anticipated knee surgery in the other knee planned in the ensuing 6 months
8. Diabetic patients with blood sugar values exceeding 250 mg/dl in the previous month
9. BMI >40Kg/m2
10. Pregnancy, which will be determined by a serum or urine HCG test on the day of surgery.
11. Incarceration
12. Inability to communicate with staff, including being unreachable by telephone and/or e-mail.
13. Revision ACL reconstruction
14. Patient reconsideration after initial agreement.
15. Non-English speaking subjects

8. NUMBER OF SUBJECTS

- *Indicate the total number of subjects to be accrued locally. If applicable, distinguish between the number of subjects who are expected to be pre-screened, enrolled (consent obtained), randomized and complete the research procedures.*
- *If your study includes different cohorts, include the total number of subjects in each cohort.*
- *If this is multisite study, include total number of subjects across all sites.*

We will enroll 78 patients in the event that we lose some to follow up or if patients decide to unenroll in the study. We don't foresee many patients being lost to follow up because all patients will be enrolled only until their first follow up visit. The historic rate of patient's not following up with the surgeons after ACL reconstruction is almost 0.

9. STUDY TIMELINES

- *Describe the duration of an individuals participation in the study*
- *Describe the duration anticipated to enroll all study subjects*
- *The estimated date of study completion*

Study Duration - 1 Year
Each Individual's Participation –up to 14 days, depending on the date of initial follow up visit after the procedure. After that, the patients will follow up with their respective surgeons at time points determined by the surgeon for routine follow up.

10. ENDPOINTS

- *Describe the primary and secondary study endpoints*
- *Describe any primary or secondary safety endpoints*

A participant is considered to have completed the study if he or she has completed all phases of the study including the last visit or the last scheduled procedure. The end of the study is defined as completion of the last visit or procedure which we defined as the initial follow up visit in the office and the final survey will be sent out 14 days after the indicated surgery.

11. RESEARCH PROCEDURES

- *Include a detailed description of all procedures to be performed on the research subject and the schedule for each procedure.*
- *Include any screening procedures for eligibility and/or baseline diagnostic tests*
- *Include procedures being performed to monitor subjects for safety or minimize risks*
- *Include information about drug washout periods*
- *If drugs or biologics are being administered provide information on dosing and route of administration*
- *Clearly indicate which procedures are only being conducted for research purposes.*
- *If any specimens will be used for this research, explain whether they are being collected specifically for research purposes.*
- *Describe any source records that will be used to collect data about subjects*
- *Indicate the data to be collected, including long term follow-up*

Screening evaluation will occur during the preoperative visit prior to surgery which generally occurs within 28 days prior to surgery. No separate screening is indicated in this study.

Patients will be asked to participate in the study if they are having ACL Reconstruction surgery with one of the orthopedic surgeons who is participating in the study. They will be informed and consented in the office or in the preoperative holding area prior to surgery.
Patients undergo ACL reconstruction at either Plainview, Franklin, Huntington, Long Island Jewish, or North Shore University Hospital.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an adverse event (AE). However,

if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

We will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit/call, we will inquire about the occurrence of AE/SAEs since the last visit/survey/call. Events will be followed for outcome information until resolution or stabilization.

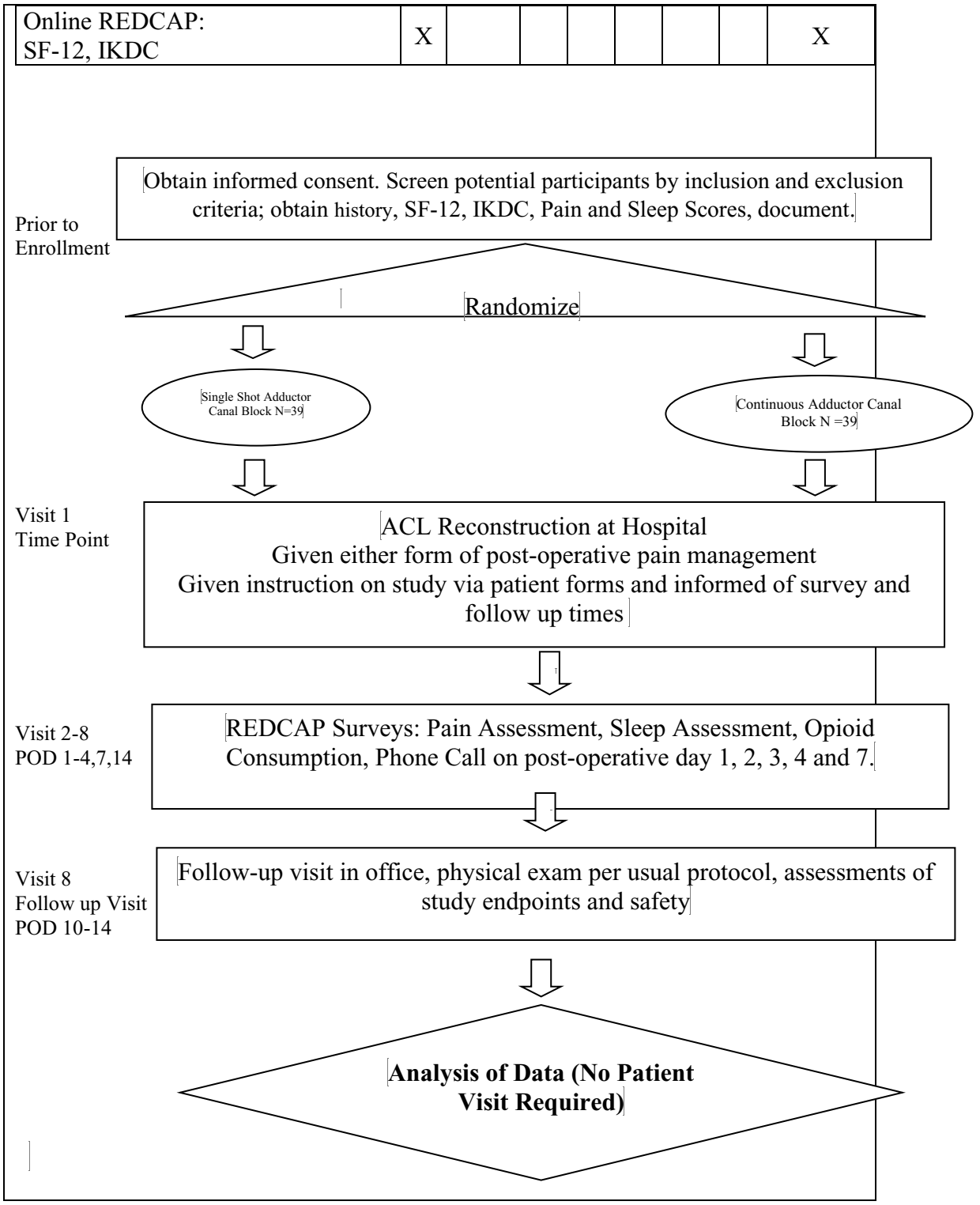
Study procedures and evaluations

- All patients who are enrolled in this study will have been evaluated and determined to be a candidate for ACL reconstruction surgery. The indications for surgery, determination of need for surgery and physical examination determining this need are independent from the interventions and outcomes being assessed by this study.
- **Efficacy Assessment plan-** All patients will be sent surveys through REDCAP, which is a secure patient secure electronic data capture software on postoperative days 1,2,3,4, 7 and 14. A nd be assessed in person at the post-operative visit which usually falls between post op day 10-14 depending on weekend and convenience. They will be surveyed for primary and secondary outcomes . Primary outcome will be assessed using visual analog scale 0-10. Secondary outcomes; Opiate consumption, Sleep quality, disturbances in sleep, global health assessment through the SF-12, and knee function through IKDC pre operatively and POD 14. The patient will also be contacted via telephone on post-operative day 1, 2, 3, 4 and 7 to assess for adverse events.
- Screening evaluation will occur during the preoperative visit prior to surgery which generally occurs within 28 days prior to surgery. No separate screening is indicated in this study.
- Procedure for administering study intervention and follow-up procedures. The participant will be seen in the preoperative holding suite prior to surgery to ensure that the patient is still willing to undergo randomization for the study. The patient will then undergo randomization by a computer-based software and the anesthesiologist will be informed of the plan. The participant will undergo anesthesia at the discretion of the anesthesiologist per routine given the participant's clinical baseline. The participant will undergo ACL reconstruction based on the standard of care treatment. Following surgery but prior to leaving the operating room the anesthesiologist will place the adductor canal block and the catheter based on the participant's randomization under ultrasound guidance to ensure proper placement of the block. The participant will then undergo routine

post-operative care in the recovery suite with routine recovery room vital checks. For participants who are randomized to the continuous pump group, the pump will be assembled and filled by pharmacy and attached to the previously placed catheter while the participant is in the recovery room. Once the participants are awake and alert in the recovery room, a study investigator will review the study specifics again, including the surveys with written information on the questions that will be asked. They will also be given written instructions on how to use the continuous pumps and how to remove it. If the patient is uncomfortable removing it themselves, they can come to the office to have it removed. For participants who received a continuous pump the investigator will go over the function of the pump, troubleshooting, and how to remove the pump at home. All participants will be discharged home from the recovery room after they have met the routine discharge criteria following existing standard of care recovery room protocols. The patient will also be contacted via telephone on post-operative day 1, 2, 3, 4 and 7 to assess for adverse events.

- All data will be recorded in an encrypted database which is HIPPA and IRB compliant. All participant information will be labeled with a participant study identification number with no identifiable information documented.

Procedures	**In Office visit/schedule**	**Study Day 1, Day of Operation**	**Study Day 2 (POD 1)**	**Study Day 3 (POD 2)**	**Study Day 4 (POD 3)**	**Study Day 5 (POD 4)**	**Study Day 8 (POD 7)**	**Final Study Day, in office visit (POD 10-14)**
Informed consent	X							
Demographics	X							
Medical history	X							
Randomization	X							
Administer study intervention		X						
Physical exam (including height and weight)	X	X						X
Preoperative Workup per standard protocol	X							
Pregnancy test [b]		X						
Adverse event review and evaluation	X		X	X	X	X	X	
MRI/Imaging assessment	X							
Online RedCAP Surveys (VAS, sleep disturbance, Opioid Consumption	X	X	X	X	X	X	X	X



12. STATISTICAL ANALYSIS

- *Describe how your data will be used to test the hypotheses.*
- *State clearly what variables will be tested and what statistical tests will be used.*

- *Include sample size calculations.*
- *If this is a pilot study, state which variables will be examined for hypothesis generation in later studies.*

Blinding:
Due to the nature of the intervention (bolus block, continuous infusion pump), it is not possible to blind the physicians or patients.

Consent:
Consent will be obtained during the preoperative visit, prior to surgery.

Randomization:
Subjects will be randomly assigned in a 1:1 ratio to either bolus block or continuous catheter. The randomization will be stratified by hospital (Plainview, Franklin, Huntington, Long Island Jewish, or North Shore University Hospital.

The Biostatistics Unit will develop a randomization procedure using a permuted block design within the Biostatistics Randomization Management System (BRMS).

Additional details of the procedure, including required record keeping, will be further developed upon approval of this protocol. The Biostatistics Unit has extensive experience in implementing and in producing detailed documentation for such procedures.

Intention to Treat (ITT):
All analyses will be carried out according to the ITT principle. The ITT population will be all subjects randomized, regardless of what treatment they actually received. All patients will be analyzed in the group to which they were randomized.

Statistical Considerations:
Specific Aims:
To compare the efficacy of two postoperative pain control methods (bolus block, continuous catheter) in patients undergoing ACL reconstruction.

Primary Outcome
Outcomes measured on post-operative days 0, 1,2,3,4,7, and at the post-operative follow-up visit. (Outcomes for days 0, 1,2,3,4, and 7 will be obtained via email and electronic surveys . Outcomes for the post-operative follow-up visit will be measured during the postoperative visit which takes place between days 10 and 14. This will be referred to as "Day 10").

- Pain Control

- Maximum pain will be measured on a scale of 0 to 10, where 0 represents no pain and 10 represents the worst possible pain. Patients will report the maximum pain felt in the 24 hours
- Current pain will be measured on a scale of 0 to 10, where 0 represents no pain and 10 represents the worst possible pain.
- Daily opioid consumption (expressed as morphine equivalents).

Secondary Outcomes

Outcomes measured on post-operative days 1,2,3,4,7, and at the post-operative follow-up visit.

- Quality of Sleep
  - Trouble falling asleep due to pain (yes,no)
  - Wake due to pain (yes,no)

Outcomes measured at post-operative follow-up visit

- Satisfaction with surgery, on a scale of 0 to 10, where 0 represents extremely dissatisfied and 10 extremely satisfied
- Adverse events: Adverse events will be assessed at each visit. At the end of the study, each subject will be categorized as having had one or more adverse events, or not having had any adverse events.
- Serious Adverse events: Serious adverse events will be assessed at each visit and via telephone on post-operative day 1, 2, 3, 4 and 7. At the end of the study each subject will be categorized as having had one or more serious adverse events, or not having had any serious adverse events.

Statistical Methods:

Primary Outcomes:

For each outcome, repeated measures analysis of variance (RMANOVA), where post-operative pain control method (bolus block, continuous catheter) is the between subjects effect and post-operative day is the within subjects effect will be used to examine the association between pain control method and that outcome. Site (stratification variable) will be included as a covariate in each model. The interaction of post-operative control method and day will be included in the model. If the interaction is significant, then pairwise comparisons of pain control method at each day will be carried out within the RMANOVA model. If the usual assumptions required for the ANOVA model are not met, then a suitable transformation, or an appropriate non-parametric method will be used.

Secondary Outcomes:

For binary outcomes measured on days 1,2,3,4,7 and 10:

For each outcome, a generalized linear mixed model (GLMM) for binary clustered (i.e., hierarchical) data will be used to examine the association between pain control method and that outcome. GLMM will be used to account for the hierarchical structure of the data, (namely, multiple days within a subject). Site (stratification variable) will be included as a covariate in each model.

For binary outcomes measured on day 10 only:

For each outcome, logistic regression will be used to examine the association between pain control method and that outcome. Site (stratification variable) will be included as a covariate in each model.

For satisfaction with surgery:
Analysis of variance (ANOVA) will be used to examine the association between pain control method and satisfaction with surgery. Site will be included as a covariate in the model. If the usual assumptions required for the ANOVA model are not met, then a suitable transformation, or an appropriate non-parametric method will be used.

Sample Size Justification:
In a published study of 85 patients undergoing arthroscopic shoulder surgery, patients were randomly assigned to catheter (43 patients) or single-shot block (42 patients) for postoperative analgesia. Median pain with movement on day 3, measured on a visual analog pain scale, 6 in the single-shot group and 4 in the catheter group. As there is limited information available regarding postoperative pain levels following ACL reconstruction, we will assume that the difference in pain levels between bolus block and continuous catheter will be similar (i.e. continuous catheter will be 2 points lower than bolus block). The standard deviation will be estimated as 2.5. This estimate was obtained by dividing the range (10-0) by 4.

The proposed analysis will examine pain levels over multiple days during the postoperative period. If a significant interaction between treatment and day is found, it will be of interest to determine which days differ. Although this comparison will be carried out within the ANOVA model, the 2 sided two sample t-test will be used for purposes of calculating the required sample size. A sample size of 39 subjects per group will yield 80% power to detect a 2 point difference between the two groups on any single day using a two sided two-sample t-test at the 0.01 significance level. The reason for applying this "Bonferroni-type" adjustment is that pairwise comparisons will be carried out for 6 different days, and with this number of statistical tests, it is more likely to find a significant difference at the nominal 5% level when one does not actually exist. Based on our experience, most, if not all patients return for the postoperative visit, and therefore, no adjustment for drop-out has been made. Therefore, the proposed sample size will be 78 subjects (39 for each treatment group).

13. SPECIMEN BANKING

- *If specimens will be banked for future research, describe where the specimens will be stored, how long they will be stored, how they will be accessed and who will have access to the specimens*
- *List the information that will be stored with each specimen, including how specimens are labeled/coded*
- *Describe the procedures to release the specimens, including: the process to request release, approvals required for release, who can obtain the specimens, and the information to be provided with the specimens.*

n/a

14. DATA MANAGEMENT AND CONFIDENTIALITY

- *Describe the data and specimens to be sent out or received. As applicable, describe:*
  - *What information will be included in that data or associated with the specimens?*
  - *Where and how data and specimens will be stored?*
  - *How long the data will be stored?*
  - *Who will have access to the data?*
  - *Who is responsible for receipt or transmission of data and specimens?*
- *Describe the steps that will be taken to secure the data during storage, use and transmission.*

There will be no data in regard to specimens in this study. All recorded data with respect to the questions listed above will be recorded onto a data sheet on the Northwell REDCap software to ensure patient confidentiality and encryption. Only investigators and co investigators will have access to the REDCap file which will be secured by password. Once the data has been analyzed the patient specific information will be deleted.

15. DATA AND SAFETY MONITORING PLAN

A specific data and safety monitoring plan is only required for greater than minimal risk research. For guidance on creating this plan, please see the Guidance Document *on the HRPP website.*

Part I – this part should be completed for all studies that require a DSMP.
Part II – This part should be completed when your study needs a Data and Safety Monitoring Board or Committee (DSMB/C) as part of your Data and Safety Monitoring Plan.

Part I: Elements of the Data and Safety Monitoring Plan

- *Indicate who will perform the data and safety monitoring for this study.*
- *Justify your choice of monitor, in terms of assessed risk to the research subject's health and well being. In studies where the monitor is independent of the study staff, indicate the individual's credentials, relationship to the PI, and rationale for selection*
- *List the specific items that will be monitored for safety (e.g. adverse events, protocol compliance, etc)*
- *Indicate the frequency at which accumulated safety and data information (items listed in # above) will be reviewed by the monitor (s) or the DSMB/C.*
- *Where applicable, describe rules which will guide interruption or alteration of the study design.*
- *Where applicable, indicate dose selection procedures that will be used to minimize toxicity.*
- *Should a temporary or permanent suspension of your study occur, in addition to the IRB, indicate to whom will you report the occurrence.*

DSMP form is attached

Part II: Data and Safety Monitoring Board or Committee

- *When appropriate, attach a description of the DSMB.*
- *Provide the number of members and area of professional expertise.*
- *Provide confirmation that the members of the board are all independent of the study.*

n/a

16. WITHDRAWAL OF SUBJECTS

- *Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent*
- *Describe procedures for orderly termination*
- *Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection.*

Participants may withdraw voluntarily from the study at any given time with no reason as is outlined in the informed consent for participation in the study. Any participant who withdraws from a study arm will still be contacted for follow-up assessments as outlined within this protocol unless the participant elects to forgo follow-up contact with the study assessors. This will include the surveys for outcome assessment, phone calls made on the subsequent postoperative days and the office visit following surgery. Discontinuation from the continuous administration of local anesthetic prior to completion of the medications' dosing will not be deemed a withdrawal from the study but rather a discontinuation of treatment and the participant will continue to be followed up with for assessment of study outcomes with notation of the discontinuation of treatment within the database and the reason for discontinuation documented.

All participants who discontinue intervention will be followed in order to assess for potential adverse events, serious adverse events and any unanticipated problems pertaining to the use or administration of the study medications.
Adverse events include but are not limited to block failure, allergy to local anesthetic, persistent pain at injection/catheter site, local skin irritation at catheter site, pump/device failure.
Should a participant experience any of the serious adverse events listed in the next section, this participant will immediately be halted from their study intervention. These patients will be recommended to seek immediate care for assessment of their serious adverse event to best ensure patient safety. Should a patient experience an adverse event or unanticipated event, the study investigator who is contacted will determine if the participant's event meets criteria for discontinuation of treatment.

ADVERSE EFFECTS OF TREATMENT

Risks associated with single shot adductor canal block

1. Peripheral Nerve Injury
    a. This is a rare complication that is usually transient and goes away with time. The estimated incidence is .5% for any nerve irritation after the procedure. The risk of injury to the nerve that is permanent in 1/10,000. These are very rare in part due to the implementation and success of ultrasound use for guidance of the needle and/or catheter during nerve blockade. This allows the anesthesiologist direct visualization to differentiate between perineural, intraneural, and interfascicular.
    b. These injuries will be monitored with a physical examination after the procedure once the patient has woken from anesthesia. Any deficits beyond what is expected by the nerve blockade will be followed at post-operative visit in the office to evaluate for resolution of transient symptoms. In the event of a peripheral nerve injury there is no intervention that can change the outcome of the block that has been delivered. If symptoms fail to progressively improve, neurological consultation should be sought in 3-4 weeks. Incomplete lesions with evidence of moderate or severe deficit are an indication for early neurological consultation and consideration of neurophysiologic testing (nerve conduction studies and electromyography).
2. Local Anesthetic System Toxicity
    a. Ranges from mild symptoms of metallic taste, agitation, and circumoral numbness to more severe findings such as seizure, respiratory arrest, cardiac arrhythmias.
    b. Manifestations of local anesthetic toxicity typically appear 1 to 5 minutes after the injection, but onset may range from 30 seconds to as long as 60 minutes. These symptoms will be monitored for and usually happen because of accidental injection into the vascular system. This is exceedingly rare with the advent of ultrasound

guidance and direct visualization of the injection. During the procedure the patients are attached to full monitors which will monitor blood pressure, cardiac rhythm, oxygen saturation. Any noticeable severe findings are treated with supportive care with propofol, lipid infusions which can reverse the effects from the local anesthesia.

c. Lipid infusion protocol as recommended by the ASEA practice advisory on local anesthetic systemic toxicity is as follows:
    i. 1.5 ml kg21 bolus of 20% lipid emulsion Infusion at 0.25 ml kg21 per min for at least 10 min after return of circulatory stability Consider giving a second bolus and increasing infusion to 0.50 ml kg21 if circulatory stability not attained Upper limit of lipid emulsion recommended is 10 ml kg21 over the first 30 min.
d. In addition, the patients will be on a monitor in the post anesthesia recovery unit until they are deemed stable and ready for discharge. Any abnormalities will be noted by the nurse taking care of the patient who would inform the anesthesiologist and surgeon. This is standard protocol at our institution when any regional blocks are given for post-operative patients.
e. The patients will be given a hand out and instructed to watch for signs or symptoms such as chest pain, rapid heart beating, difficulty breathing, or seizure like activity. If any of these symptoms are present, they would normally be observed immediately after the block is performed or while the patient is still being monitored, however after discharge they will still be informed to watch for symptoms in the event of a delayed response. They will be instructed to call the study PI or safety officer and likely be sent to the emergency room for evaluation.

3. Local Infection
    a. For single shot adductor canal blocks the risk of infection is very low. To minimize this risk the site is prepped in sterile fashion with either chlorhexidine or iodine scrub. The injecting physician washes hands and uses sterile gloves and instruments for the course of this procedure.
    b. Perioperative antibiotics will also be given which is standard protocol for ACL reconstruction regardless of catheter insertion or not.
    c. In the event that the patient notices any skin irritation, redness, foul smell, or drainage form the site of the injection, they will be advised to first call the safety officer, PI, or other co-investigator to describe their symptoms. The patients will also watch for fevers or chills. If infection is suspected they will be sent to the emergency room or surgeons office for evaluation and further testing. They may be started on a course of oral antibiotics if an infection is concerning after evaluation.

Risks associated with continuous peripheral nerve catheter placement:

1. Both anesthetists and surgeons recognize the benefits of peripheral nerve catheters (PNCs). The continuous infusion of local anesthetic near a peripheral nerve or plexus produces fewer systemic side-effects than i.v. opioids, increases postoperative patient satisfaction, and can allow for faster functional recovery of the operated limb.
2. Block Failure
    a. Occasionally, there are instances when the catheter is passed easily but the nerve block fails to provide adequate anesthesia or analgesia.
    b. This is rare with the use of ultrasound guidance and localization of the continuous catheter.
    c. In the event of a block failure or inadequate placement that is not providing the patient any relief, the catheter will be removed either by the patient or post operatively depending on when it is discovered.
    d. The practicing anesthesiologist will discuss with the patient the option of either trying a second time to place the catheter successfully in the post anesthesia recovery area or discontinuing the block altogether.
3. Accidental Catheter Migration/Removal
    a. The incidence of accidental catheter removal is reported in the literature at about 1%. The use of sterile adhesive tagaderm dressing has been implemented to firmly secure the catheter to the skin to avoid migration or fall out. The dressing is checked to be secure after it has been applied.
    b. In the event that the catheter is accidently removed or dislodged during the course of the study, it should be removed and there will be no further intervention once the patient has been discharged home. The patient can place a Band-Aid over the catheter site and notify the coinvestigator or PI.
4. Localized Infection
    a. Localized inflammation is infrequent (0–10%), and local infection (0–3%), abscess formation (0–0.9%), and sepsis occur even more rarely.
    b. Transparent dressings are used to reduce the number of dressing changes while appropriately monitoring the site for signs of inflammation
    c. Since the continuous catheter remains in for 48-72 hours, it does pose a theoretical increased risk of infection compared to a single shot adductor canal block although this has not been proven in the literature. To minimize this risk the site is prepped in sterile fashion with either chlorhexidine or iodine scrub. The injecting physician washes hands and uses sterile gloves and instruments for the course of this procedure.

d. Perioperative antibiotics will also be given which is standard protocol for ACL reconstruction regardless of catheter insertion or not.
e. In the event that the patient notices any skin irritation, redness, foul smell, or drainage form the site of the injection, they will be advised to first call the safety officer, PI, or other co-investigator to describe their symptoms. The patients will also watch for fevers or chills. If infection is suspected they will be sent to the emergency room or surgeons office for evaluation and further testing. They may be started on a course of oral antibiotics if an infection is concerning after evaluation

5. Local Anesthetic System Toxicity
    a. The patients with a continuous catheter will be receiving a fixed rate of flow of local anesthetic to the nerve site for 48-72 hours. This does put them at a theoretical risk for toxicity while they are at home with the catheter in even though the dosage is well below the threshold for systemic toxicity. They will be educated on the following signs and symptoms similar to the single shot patients.
    b. Ranges from mild symptoms of metallic taste, agitation, and circumoral numbness to more severe findings such as seizure, respiratory arrest, cardiac arrhythmias.
    c. Manifestations of local anesthetic toxicity typically appear 1 to 5 minutes after the injection, but onset may range from 30 seconds to as long as 60 minutes. These symptoms will be monitored for and usually happen because of accidental injection into the vascular system. This is exceedingly rare with the advent of ultrasound guidance and direct visualization of the injection. During the procedure the patients are attached to full monitors which will monitor blood pressure, cardiac rhythm, oxygen saturation. Any noticeable severe findings are treated with supportive care with propofol, lipid infusions which can reverse the effects from the local anesthesia.
    d. Lipid infusion protocol as recommended by the ASEA practice advisory on local anesthetic systemic toxicity is as follows:
        i. 1.5 ml kg21 bolus of 20% lipid emulsion Infusion at 0.25 ml kg21 per min for at least 10 min after return of circulatory stability Consider giving a second bolus and increasing infusion to 0.50 ml kg21 if circulatory stability not attained Upper limit of lipid emulsion recommended is 10 ml kg21 over the first 30 min.
    e. In addition, the patients will be on a monitor in the post anesthesia recovery unit until they are deemed stable and ready for discharge. Any abnormalities will be noted by the nurse taking care of the patient who would inform the anesthesiologist

and surgeon. This is standard protocol at our institution when any regional blocks are given for post-operative patients.

f. The patients will be given a hand out and instructed to watch for signs or symptoms such as chest pain, rapid heart beating, difficulty breathing, or seizure like activity. If any of these symptoms are present, they would normally be observed immediately after the block is performed or while the patient is still being monitored, however after discharge they will still be informed to watch for symptoms in the event of a delayed response. They will be instructed to call the study PI or safety officer and likely be sent to the emergency room for evaluation.

Unanticipated events will be assessed on a case by case basis and the study investigators will determine if the patient should be halted/discontinued and whether or not they should seek immediate care.

Any participant who is discontinued from treatment will continue to be assessed following the previously stated follow-up procedure.

The data to be collected at the time of study intervention discontinuation will include the following:

- All data pertaining to the patient's enrollment in the study including which arm of the study they were randomized to, whether or not they received the treatment to which they were randomized, all outcome data that was recorded up to the time of discontinuation and any stated reason for discontinuation will be documented.
- Should a participant experience a known complication of the medication this will be recorded as an adverse event, serious adverse event, or unanticipated event as noted above.
- The participants will continue to be followed according the protocol and their outcome data will continue to be obtained as is possible given the situation.
- A case report form page will be produced for any participant who discontinues treatment or withdraws, this will include the date and any specific reasons for discontinuation/withdrawal from the study.

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue or withdraw a participant from the study for the following reasons:

- Serious adverse event
- Pregnancy
- Significant study intervention non-compliance

- If any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant. Adverse events or unanticipated events will be assessed on a case by case basis and discontinued as noted in the section above.
- If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.
- An investigator will discontinue/withdraw a patient from study participation if they are not deemed contactable, this will be defined as inability to contact after 3 separate attempts are made at least 2 hours apart across two days.

The reason for participant discontinuation or withdrawal from the study will be recorded on the Case Report Form (CRF) as noted in the section above. Subjects who sign the informed consent form and are randomized but do not receive the study intervention they are randomized to will be followed in the study as if they have obtained their intervention this deviation from protocol will be documented for post-hoc analysis reasons. Subjects who sign the informed consent form, and are randomized and receive the study intervention, and subsequently withdraw, or are withdrawn or discontinued from the study, maintained in the group to which they are randomized for assessment documentation with notation made as to their withdrawal to assist in the post-hoc analysis.

Study participants who are randomized to the continuous infusion cohort will be provided with information about the pumps themselves and troubleshooting advice. They will also be provided with contact information for the investigators should they run into issues. The troubleshooting of the device will be done as noted in the above section and need for discontinuation of the therapy will be assessed as noted above with safety concerns as the primary reason for discontinuation.

A participant will be considered lost to follow-up if he or she fails to respond to study surveys followed for more than one day of follow up, misses the phone calls, or misses the post-operative office visit planned for postoperative day 10-14 and is unable to be contacted by the study site staff.

The following actions must be taken if a participant fails to respond to study surveys or return to the clinic for a required study visit:

- The investigators will attempt to contact the participant and reschedule the missed visit planned for Post-op days 10-14 and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant

(where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts will be documented in the participant's medical record or study file. After 3 attempted phone calls spanning two postoperative days the patient will be deemed lost to follow-up.

- Should a participant be unreachable for one day of the study follow-up this will not be deemed a loss to follow-up, however this occurrence will be documented in the data and accounted for in the analysis phase of the study.

Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

17. RISKS TO SUBJECTS

- *Describe any potential risks and discomforts to the subject (physical, psychological, social, legal, or other) and assess their likelihood and seriousness and whether side effects are reversible. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects.*
- *Include risks to others , like sexual partners (if appropriate)*
- *Discuss why the risks to subjects are reasonable in relation to the anticipated benefits and in relation to the importance of the knowledge that may reasonably be expected to results*
- *Describe the procedures for protecting against or minimizing any potential risks, including risks to confidentiality, and assess their likely effectiveness.*

Risks associated with single shot adductor canal block

4. Peripheral Nerve Injury
    a. This is a rare complication that is usually transient and goes away with time. The estimated incidence is .5% for any nerve irritation after the procedure. The risk of injury to the nerve that is permanent in 1/10,000. These are very rare in part due to the implementation and success of ultrasound use for guidance of the needle and/or catheter during nerve blockade. This allows the anesthesiologist direct visualization to differentiate between perineural, intraneural, and interfascicular.
    b. These injuries will be monitored with a physical examination after the procedure once the patient has woken from anesthesia. Any deficits beyond what is expected by the nerve blockade will be followed at post-operative visit in the office to evaluate for resolution of transient symptoms. In the event of a peripheral nerve injury there is no intervention that can change the outcome of the block that has been delivered. If symptoms fail to progressively improve, neurological consultation should be sought in 3-4 weeks. Incomplete lesions with evidence of moderate or severe deficit are an indication for early neurological consultation and consideration of neurophysiologic testing (nerve conduction studies and electromyography).

5. Local Anesthetic System Toxicity
    a. Ranges from mild symptoms of metallic taste, agitation, and circumoral numbness to more severe findings such as seizure, respiratory arrest, cardiac arrhythmias.
    b. Manifestations of local anesthetic toxicity typically appear 1 to 5 minutes after the injection, but onset may range from 30 seconds to as long as 60 minutes. These symptoms will be monitored for and usually happen because of accidental injection into the vascular system. This is exceedingly rare with the advent of ultrasound guidance and direct visualization of the injection. During the procedure the patients are attached to full monitors which will monitor blood pressure, cardiac rhythm, oxygen saturation. Any noticeable severe findings are treated with supportive care with propofol, lipid infusions which can reverse the effects from the local anesthesia.
    c. Lipid infusion protocol as recommended by the ASEA practice advisory on local anesthetic systemic toxicity is as follows:
        i. 1.5 ml kg21 bolus of 20% lipid emulsion Infusion at 0.25 ml kg21 per min for at least 10 min after return of circulatory stability Consider giving a second bolus and increasing infusion to 0.50 ml kg21 if circulatory stability not attained Upper limit of lipid emulsion recommended is 10 ml kg21 over the first 30 min.
    d. In addition, the patients will be on a monitor in the post anesthesia recovery unit until they are deemed stable and ready for discharge. Any abnormalities will be noted by the nurse taking care of the patient who would inform the anesthesiologist and surgeon. This is standard protocol at our institution when any regional blocks are given for post-operative patients.
    e. The patients will be given a hand out and instructed to watch for signs or symptoms such as chest pain, rapid heart beating, difficulty breathing, or seizure like activity. If any of these symptoms are present, they would normally be observed immediately after the block is performed or while the patient is still being monitored, however after discharge they will still be informed to watch for symptoms in the event of a delayed response. They will be instructed to call the study PI or safety officer and likely be sent to the emergency room for evaluation.
6. Local Infection
    a. For single shot adductor canal blocks the risk of infection is very low. To minimize this risk the site is prepped in sterile fashion with either chlorhexidine or iodine scrub. The injecting physician washes hands and uses sterile gloves and instruments for the course of this procedure.

b. Perioperative antibiotics will also be given which is standard protocol for ACL reconstruction regardless of catheter insertion or not.
c. In the event that the patient notices any skin irritation, redness, foul smell, or drainage form the site of the injection, they will be advised to first call the safety officer, PI, or other co-investigator to describe their symptoms. The patients will also watch for fevers or chills. If infection is suspected they will be sent to the emergency room or surgeons office for evaluation and further testing. They may be started on a course of oral antibiotics if an infection is concerning after evaluation.

Risks associated with continuous peripheral nerve catheter placement:

6. Both anesthetists and surgeons recognize the benefits of peripheral nerve catheters (PNCs). The continuous infusion of local anesthetic near a peripheral nerve or plexus produces fewer systemic side-effects than i.v. opioids, increases postoperative patient satisfaction, and can allow for faster functional recovery of the operated limb.
7. Block Failure
    a. Occasionally, there are instances when the catheter is passed easily but the nerve block fails to provide adequate anesthesia or analgesia.
    b. This is rare with the use of ultrasound guidance and localization of the continuous catheter.
    c. In the event of a block failure or inadequate placement that is not providing the patient any relief, the catheter will be removed either by the patient or post operatively depending on when it is discovered.
    d. The practicing anesthesiologist will discuss with the patient the option of either trying a second time to place the catheter successfully in the post anesthesia recovery area or discontinuing the block altogether.
8. Accidental Catheter Migration/Removal
    a. The incidence of accidental catheter removal is reported in the literature at about 1%. The use of sterile adhesive tagaderm dressing has been implemented to firmly secure the catheter to the skin to avoid migration or fall out. The dressing is checked to be secure after it has been applied.
    b. In the event that the catheter is accidently removed or dislodged during the course of the study, it should be removed and there will be no further intervention once the patient has been discharged home. The patient can place a Band-Aid over the catheter site and notify the coinvestigator or PI.
9. Localized Infection

a. Localized inflammation is infrequent (0–10%), and local infection (0–3%), abscess formation (0–0.9%), and sepsis occur even more rarely.
b. Transparent dressings are used to reduce the number of dressing changes while appropriately monitoring the site for signs of inflammation
c. Since the continuous catheter remains in for 48-72 hours, it does pose a theoretical increased risk of infection compared to a single shot adductor canal block although this has not been proven in the literature. To minimize this risk the site is prepped in sterile fashion with either chlorhexidine or iodine scrub. The injecting physician washes hands and uses sterile gloves and instruments for the course of this procedure.
d. Perioperative antibiotics will also be given which is standard protocol for ACL reconstruction regardless of catheter insertion or not.
e. In the event that the patient notices any skin irritation, redness, foul smell, or drainage form the site of the injection, they will be advised to first call the safety officer, PI, or other co-investigator to describe their symptoms. The patients will also watch for fevers or chills. If infection is suspected they will be sent to the emergency room or surgeons office for evaluation and further testing. They may be started on a course of oral antibiotics if an infection is concerning after evaluation

10. Local Anesthetic System Toxicity
    a. The patients with a continuous catheter will be receiving a fixed rate of flow of local anesthetic to the nerve site for 48-72 hours. This does put them at a theoretical risk for toxicity while they are at home with the catheter in even though the dosage is well below the threshold for systemic toxicity. They will be educated on the following signs and symptoms similar to the single shot patients.
    b. Ranges from mild symptoms of metallic taste, agitation, and circumoral numbness to more severe findings such as seizure, respiratory arrest, cardiac arrhythmias.
    c. Manifestations of local anesthetic toxicity typically appear 1 to 5 minutes after the injection, but onset may range from 30 seconds to as long as 60 minutes. These symptoms will be monitored for and usually happen because of accidental injection into the vascular system. This is exceedingly rare with the advent of ultrasound guidance and direct visualization of the injection. During the procedure the patients are attached to full monitors which will monitor blood pressure, cardiac rhythm, oxygen saturation. Any noticeable severe findings are treated with supportive care with propofol, lipid infusions which can reverse the effects from the local anesthesia.

d. Lipid infusion protocol as recommended by the ASEA practice advisory on local anesthetic systemic toxicity is as follows:
    i. 1.5 ml kg21 bolus of 20% lipid emulsion Infusion at 0.25 ml kg21 per min for at least 10 min after return of circulatory stability Consider giving a second bolus and increasing infusion to 0.50 ml kg21 if circulatory stability not attained Upper limit of lipid emulsion recommended is 10 ml kg21 over the first 30 min.
e. In addition, the patients will be on a monitor in the post anesthesia recovery unit until they are deemed stable and ready for discharge. Any abnormalities will be noted by the nurse taking care of the patient who would inform the anesthesiologist and surgeon. This is standard protocol at our institution when any regional blocks are given for post-operative patients.
f. The patients will be given a hand out and instructed to watch for signs or symptoms such as chest pain, rapid heart beating, difficulty breathing, or seizure like activity. If any of these symptoms are present, they would normally be observed immediately after the block is performed or while the patient is still being monitored, however after discharge they will still be informed to watch for symptoms in the event of a delayed response. They will be instructed to call the study PI or safety officer and likely be sent to the emergency room for evaluation.

Unanticipated events will be assessed on a case by case basis and the study investigators will determine if the patient should be halted/discontinued and whether or not they should seek immediate care.

Since identifiers are being recorded, there is also risk of loss of confidentiality of the patients

18. RESEARCH RELATED HARM/INJURY

- *Describe the availability of medical or psychological resources that subjects might need as a result of anticipated problems that may be known to be associated with the research.*
- *If the research is greater than minimal risk, explain any medical treatments that are available if research-related injury occurs, who will provide it, what will be provided, and who will pay for it.*

Adverse events and planned interventions prior to discontinuation

- Failure of catheter placement despite successful administration of single site injection- any participant who was randomized to receive a continuous

pump, but the catheter was unable to be placed will be discontinued from the continuous pump protocol, however these patient's will continue to be followed according to the above stated protocol and their outcomes assessed in an intent-to treat manner based on their initial randomization.

- Continuous Block failure- if patient perceives no benefit from block but pump appears to be functioning patient will be requested to continue the pumps use until the medication dosing is completed, a perceived block failure will be documented.
- Allergy to local anesthetic- if a patient reports a systemic allergic response including but not limited to shortness of breath, diffuse rash, or angioedema the patient will be recommended to discontinue the intervention and seek emergency care. If the patient reports a local confined rash or skin irritation around the catheter site with no systemic symptoms the patient will be recommended to take a dose of Benadryl and apply a warm compress, if symptoms resolve the patient will remain in the study if there is no resolution the patient will be told to discontinue the medication administration and seek care for further evaluation.
- Persistent pain at catheter site- the patient will be advised to place a cold or warm compress at the catheter site and adjust the adhesive bandage if necessary if these interventions do not alleviate the participants pain within 12 hours the patient will be advised to discontinue the intervention.

Pump/device failure- if the participant reports that the pump does not appear to be functioning properly the investigator who was contacted will assist the participant with troubleshooting the pump over the phone. If the investigator deems that the pump does not appear to be functioning after two independent attempts at troubleshooting/restarting the participant will be advised to discontinue the intervention at that time.

19. POTENTIAL BENEFIT TO SUBJECTS

- *Explain what benefits might be derived from participation in the study, noting in particular the benefit over standard treatment (e.g. a once-a-day administration instead of four times a day, an oral formulation over an IV administration).*
- *Also state if there are no known benefits to subjects, but detail the value of knowledge to be gained*

The idea is to evaluate the differences between 2 standard methods

1. To Compare the efficacy of two different modes of administration of peripheral nerve block for postoperative pain control after primary ACL reconstruction.
2. To compare the daily opioid consumption in patients, post operatively after ACL Reconstruction.
3. To determine the effectiveness of pain control and quality of sleep.
4. To compare patient satisfaction with their surgery based on method of pain control.

This will give us valuable information regarding our hypothesis that patients will have better pain control, satisfaction, sleep, and decreased opioid consumption with the use of a continuous infusion pump

20. PROVISIONS TO PROTECT PRIVACY INTERESTS OF SUBJECTS

- *Describe the methods used to identify potential research subjects, obtain consent and gather information about subjects to ensure that their privacy is not invaded.*
- *In addition consider privacy protections that may be needed due to communications with subjects (such as phone messages or mail).*

a. *All of the patient's information that will be collected for the study will be uploaded to Northwell's secure REDCAP data collections system. Password access and encryption will help ensure that all patient information will be kept private. Strict recording processes and careful handling of data will be used to ensure there is no breach of data that has been recorded. After the study information has been recorded and the study is complete this information will be deleted. These measures will help maintain patient privacy.*

b. *Information that will be gathered from the surveys will be done by one of the coinvestigators that has been listed. The data variables that are recorded will be directly entered to Northwell REDCAP which is protected by user name and password. All of the co investigators will be in direct contact with the subjects and there won't be any intermediate passing off of the information to be recorded which decreases the handling of patient specific information and results.*

c. *Regarding identifying potential research subjects: The senior orthopedic surgery attendings participating in the study have been informed to contact us when they have a potential subject who is planning to have an ACL reconstruction when they have been seen in the office. There will be no marketing or recruiting used outside of patients that are undergoing this procedure with the orthopedic surgeon.*

Informed consent will be obtained in a private area to ensure the subjects' privacy is protected.
We have informed consent as attached, we will use encrypted data collection, Northwell REDCap, including the answers to surveys and phone calls, to protect their information.

21. COSTS TO SUBJECTS

- *Describe any foreseeable costs that subjects may incur through participation in the research*
- *Indicate whether research procedures will be billed to insurance or paid for by the research study.*

No additional costs will be given to patients more than what they would be paying for their ACL reconstruction and perioperative pain management which are current routine procedures being done at all institutions.

22. PAYMENT TO SUBJECTS

- *Describe the amount of payment to subjects, in what form payment will be received and the timing of the payments.*

n/a

23. CONSENT PROCESS

If obtaining consent for this study, describe:

- *Who will be obtaining consent*
- *Where consent will be obtained*
- *Any waiting period available between informing the prospective participant and obtaining consent*
- *Steps that will be taken to assure the participants' understanding*
- *Any tools that will be utilized during the consent process*
- *Information about how the consent will be documented in writing. If using a standard consent form, indicate such.*
- *Procedures for maintaining informed consent.*

The informed consent will be attached ● Who will be obtaining consent ○ Consent will be obtained by the Principal Investigator or one of the individuals that have been approved by the IRB to obtain consent. ● Where consent will be obtained ○ Consent will be obtained in the Ambulatory Surgery unit prior to surgery or at the preoperative visit in the office by one of the IRB approved consenting investigators. Patients will be given the information on the study and it will be reviewed with them prior to obtaining consent. ● Any waiting period available between informing the prospective participant and obtaining consent: The orthopedic surgeon can

inform the patients of the study at the pre-operative office visit to give them time to think about it before obtaining consent in the ambulatory surgery unit. This will allow patients a period of time to think about the pros and cons of participating in this research study which will be determined on the day of surgery preoperatively.

- Steps that will be taken to assure the participants' understanding
  - We have attached patient handouts in our protocol and IRB form to give patients a full understanding of the study plans, interventions, risks and benefits of each.
  - In addition, we will go over this information with the patient in person to confirm that they understand the goals of the study and the potential benefit to the patient.
- Any tools that will be utilized during the consent process
  - Informed consent documentation
- Information about how the consent will be documented in writing. If using a standard consent form, indicate such.
  - We will be using a standard consent form which we have designed and included in our IRB submission.
- Procedures for maintaining informed consent.

Signed informed consent forms will be maintained in a secure office with limited access.

In the state of NY, any participants under the age of 18 are considered children. If your study involves children, additional information should be provided to describe:

- *How parental permission will be obtained*
- *From how many parents will parental permission be obtained*
- *Whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. The process used to determine these individual's authority to consent for the child should be provided*
- *Whether or not assent will be obtained from the child*
- *How will assent be documented*
- *Whether child subjects may be expected to attain legal age to consent to the procedures for research prior to the completion of their participation in the research. If so, describe the process that will be used to obtain their legal consent to continue participation in the study. Indicate what will occur if consent is not obtained from the now-adult subjects.*

-We will not be using subjects under the age of 16
-For age groups 16-18, we will provide all the information to the patient and the parents regarding the study, and obtain additional minor assent from the patient, and permission from 1 parent.
-Permission will not be obtained from individuals other than parents
-Assent form attached, for ages 16-18; will be used for documentation

If the subject becomes 18 before completion of participation in the study, we will reconsent the subject with an adult consent form

If the study involves cognitively impaired adults, additional information should be provided to describe:

- *The process to determine whether an individual is capable of consent*
- *Indicate who will make this assessment*
- *The plan should indicate that documentation of the determination and assessment will be placed in the medical record, when applicable, in addition to the research record.*
- *If permission of a legally authorized representative will be obtained,*
  - *list the individuals from who permission will be obtained in order of priority*
  - *Describe the process for assent of subjects; indicate whether assent will be required of all, some or none of the subjects. If some, which subjects will be required to assent and which will not.*
  - *If assent will not be obtained from some or all subjects, provide an explanation as to why not*
  - *Describe whether assent will be documented and the process to document assent*
  - *Indicate if the subject could regain capacity and at what point you would obtain their consent for continued participation in the study*

We will not be involving cognitively impaired adults in this study.

If the study will enroll non-English speaking subjects:

- *Indicate what language(s) other than English are understood by prospective subjects or representatives*
- *Indicate whether or not consent forms will be translated into a language other than English*
- *Describe the process to ensure that the oral and written information provided to those subjects will be in that language*
- *If non-English speaking subjects will be excluded, provide a justification for doing so*

Non-English-speaking subjects will be excluded due to lack of translated documentation, and the inability of each resident to translate the questions over the phone

24. WAIVER OR ALTERATION OF THE CONSENT PROCESS ☐ N/A

Complete this section if you are seeking an alteration or complete waiver of the consent process.

- *Describe the possible risks of harm to the subjects involved in this study and explain why the study involves no more than minimal risk to the subject:*
- *Explain why the waiver/ alteration will not adversely affect the rights and welfare of subjects*
- *Explain why it is impracticable to conduct this research if informed consent is required*
- *Explain why it is not possible to conduct this research without using the information or biospecimens in an identifiable form*
- *If appropriate, explain how the subjects will be provided with additional pertinent information after participation. If not appropriate to do so, explain why.*

n/a

Complete this section if you are obtaining informed consent but you are requesting a waiver of the documentation of consent (i.e., verbal consent will be obtained). *To proceed with a waiver based on these criteria, each subject must be asked whether they wish to have documentation linking them to this study.* ***Only complete subsection 1 OR subsection 2.***

SUBSECTION 1

- *Explain how the only record linking the subject to the research would be the consent document.*
- *Explain how the principal risk of this study would be the potential harm resulting from a breach in the confidentiality*
- *Indicate whether or not subjects will be provided with a written statement regarding the research.*

n/a

SUBSECTION 2

- *Describe the possible risks of harm to the subjects involved in this study and explain why the study involves no more than minimal risk.*
- *Confirm that the research only involves procedure for which consent is not normally required outside the research context.*
- *Indicate whether or not subjects will be provided with a written statement regarding the research.*

n/a

.

25. WAIVER OF HIPAA AUTHORIZATION ☐ N/A

Complete this section if you seek to obtain a full waiver of HIPAA authorization to use and/or disclose protected health information.

- *Describe the risks to privacy involved in this study and explain why the study involves no more than minimal risk to privacy:*
- *Describe your plan to protect identifiers from improper use or disclosure and to destroy them at the earliest time.*
- *Indicate why it is not possible to seek subjects' authorization for use or disclosure of PHI.*
- *Indicate why it is not possible to conduct this research without use or disclosure of the PHI.*
- *Indicate if PHI will be disclosed outside NSLIJ Health System, and if so, to whom. Note: PHI disclosed outside NSLIJ Health System, without HIPAA authorization needs to be tracked. Please see guidance at www.nslij.com/irb for information about tracking disclosures.*

n/a

Complete this section if you seek to obtain a partial waiver of the patient's authorization for screening/recruitment purposes *(i.e., the researcher does not have access to patient records as s/he is not part of the covered entity)*

Note: Information collected through a partial waiver for recruitment cannot be shared or disclosed to any other person or entity.

- *Describe how data will be collected and used:*
- *Indicate why you need the PHI (e.g.PHI is required to determine eligibility, identifiers are necessary to contact the individual to discuss participation, other)*
- *Indicate why the research cannot practicably be conducted without the partial waiver (e.g. no access to medical records or contact information of the targeted population, no treating clinician to assist in recruitment of the study population, other)*

n/a

26. VULNERABLE POPULATIONS:

Indicate whether you will include any of these vulnerable populations. If indicated, submit the appropriate appendix to the IRB for review:

- [X] *Children or viable neonate*
- [ ] *Cognitively impaired*
- [ ] *Pregnant Women, Fetuses or neonates of uncertain viability or nonviable*
- [ ] *Prisoners*
- [ ] *NSLIJ Employees, residents, fellows, etc*
- [ ] *poor/uninsured*
- [ ] *Students*
- [ ] *Minorities*
- [ ] *Elderly*
- [ ] *Healthy Controls*

If any of these populations are included in the study, describe additional safeguards that will be used to protect their rights and welfare.

Vulnerable population - Children age 16-18
We will obtain permission from 1 parent and assent from the patient after providing them all the necessary information to go forward with the study

27. MULTI-SITE HUMAN RESEARCH (COORDINATING CENTER)

If this is a multi-site study where you are the lead investigator, describe the management of information (e.g. results, new information, unanticipated problems involving risks to subjects or others, or protocol modifications) among sites to protect subjects.

n/a

28. REFERENCES/BIBIOGRAPHY

Provide a reasonable list of references directly related to the study. Any diagrams for new medical devices or brief reprints from journals might also prove useful.

1. *Capdevila X, Pirat P, Bringuier S, et al. Continuous peripheral nerve blocks in hospital wards after orthopedic surgery: a multicenter prospective analysis of the quality of postoperative analgesia and complications in 1,416 patients. Anesthesiology. 2005;103(5):1035–45.*
2. *Salviz EA, Xu D, Frulla A, Kwofie K, Shastri U, Chen J, Shariat AN, Littwin S, Lin E, Choi J, Hobeika P, Hadzic A; Continuous Interscalene Block in Patients Having Outpatient Rotator Cuff Repair Surgery: A Prospective Randomized Trial; Anesthesia & Analgesia; Vol 117(6), December 2013, p 1485–1492*
3. *Enneking FK, Wedel, DJ; The art and science of peripheral nerve blocks; Anesth Analg 2000;90:1–2.*
4. *Mariano ER, Afra R, Loland VJ, Sandhu NS, Bellars, RH, Bishop ML, Cheng GS, Choy LP, Maldonado RC, IIfeld BM; Continuous Interscalene Brachial Plexus Block via an Ultrasound-Guided Posterior Approach: A Randomized, Triple-Masked,Placebo-Controlled Study; Anesth Analg. 2009 May ; 108(5): 1688–1694. doi:10.1213/ane.0b013e318199dc86*
5. *Richman JM, Liu SS, Courpas G, Wong R, Rowlingson AJ, Mcgready J, Cohen SR, Wu CL; Does Continuous Peripheral Nerve Block Provide Superior Pain Control to Opioids? A Meta-Analysis; Anesth Analg 2006;102:248–57.*

6. *Buller LT, Best MJ, Baraga MG, Kaplan LD; Trends in Anterior Cruciate Ligament Reconstruction in the United States; Orthop J Sports Med; 2014 Dec 26;3(1):2325967114563664. doi: 10.1177/2325967114563664*
7. *Abdallah, FW, Whelan DB, CHan VW, Prasad GA, Endersby RV; Adductor Canal Block Provides Noninferior Analgesia and Superior Quadriceps Strength Compared with Femoral Nerve Block in Anterior Cruciate Ligament Reconstruction; Anesthesiology 5 2016, Vol.124, 1053-1064. doi:10.1097/ALN.0000000000001045.*
8. *Kwofie MK, Shastri UD, Gadsen JC, Sinha SK, Abrams JH, Xu D, Salviz EA; The effects of ultrasound-guided adductor canal block versus femoral nerve block on quadriceps strength and fall risk: a blinded, randomized trial of volunteers; Reg Anesth Pain Med 2013; 38:321-325.*
9. *Mulroy MF, Larkin KL, Batra MS, Hodgson PS, Owens BD; Femoral Nerve Block With 0.25% or 0.5% Bupivacaine Improves Postoperative Analgesia Following Outpatient Arthroscopic Anterior Cruciate Ligament Repair; Regional Anesthesia and Pain Medicine, Vol 26, No 1 (January–February), 2001: pp 24–29.*
10. *Jaeger P, Nielsen Z JK, Henningsen MH, Hilsted KL, Mathiesen O, Dahl, JB; Adductor Canal Block versus Femoral Nerve Block and Quadriceps Strength: A Randomized,*