

Sciatic Peripheral Nerve Blockade for Pain Control Following Hamstring Autograft Harvest in Adolescents: A Comparison of Two Techniques

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ABSTRACT

Anterior cruciate ligament reconstruction utilizing a hamstring autograft is a surgical technique that has gained popularity among orthopedic surgeons caring for adolescent patients. While utilization of a hamstring autograft is a revered technique, harvest of the hamstring yields significant pain. Sciatic peripheral nerve blockade has proven to reliably provide analgesia at the hamstring donor site. Single-injection sciatic peripheral nerve blockade is considered a basic and effective technique, making its use following anterior cruciate ligament reconstruction standard practice in many institutions. The duration of action of single-injection sciatic peripheral nerve blockade may fail to outlast the pain arising from the hamstring donor site, prompting some clinicians to employ continuous sciatic peripheral nerve blockade via an indwelling catheter. A lack of comparative effectiveness studies exists in the literature regarding the duration of action of peripheral nerve blockade necessary to adequately provide pain control following hamstring autograft harvest, resulting in disagreement among clinicians as to best pain control practices. Proponents of continuous sciatic peripheral nerve blockade assert that while more costly, the extended duration of analgesia afforded by this technique improves pain control postoperatively and decreases the use of other pain medications. Advocates of single-injection sciatic peripheral nerve blockade cite concerns associated with continuous sciatic peripheral nerve blockade known to be detrimental to rehabilitation, such as decreased active knee flexion and increased risk of falls. The purpose of this research is to compare the effect of single-injection sciatic PNB to continuous sciatic PNB on 1) postoperative pain control as measured by self-reported pain scores, pain medication use, and unplanned hospital admission due to poor pain control, 2) active knee flexion, and 3) patient satisfaction with pain control following ACL reconstruction with a hamstring autograft. The findings of this study have the potential to guide informed clinical reasoning and decision making regarding sciatic peripheral nerve blockade techniques following hamstring autograft harvest in adolescents undergoing anterior cruciate ligament reconstruction.

I. BACKGROUND AND SIGNIFICANCE

Anterior cruciate ligament (ACL) injury is the most prevalent injury treated in orthopedic sports medicine. The incidence of ACL injuries continues to increase with approximately 250,000 now occurring annually in the United States (Gagnier, Morgenstern, & Chess, 2012). As such, ACL reconstruction has become a common surgical procedure and is frequently performed on an outpatient basis. ACL reconstruction has historically been avoided in skeletally immature patients due to concerns of injuring the immature physes, resulting in growth deformities. Adolescents with ACL injuries were typically treated conservatively, with many orthopedic surgeons relying on non-surgical techniques, such as bracing and activity restrictions, for treatment. Advances in surgical techniques, however, now allow ACL reconstruction to be performed safely and effectively in skeletally immature patients. Subsequently, the incidence of ACL reconstruction in the adolescent population has increased approximately 300 percent in the last two decades.

Currently the mean age of ACL reconstruction is 18 years indicating half of the number of patients undergoing ACL reconstruction are adolescents (Silvers & Mandelbaum, 2007). Given the decreasing age of patients now undergoing this surgical procedure, orthopedic surgeons are charged with ensuring optimal ACL longevity following reconstruction.

Several options exist for replacement of the damaged ligament during ACL reconstruction in adolescents, yet the use of a hamstring autograft has emerged as the technique of choice due to the overall decreased morbidity and proven long-term stability when compared to other ligament reconstruction options (Mehta, Mandala, Foster, & Petsche, 2010; Pallis, Svoboda, Cameron, & Owens 2012). As such, there has been a marked increase in the use of hamstring autografts for reconstruction of the injured ACL in adolescents due to the favorable long-term outcome profile of this surgical technique when compared to other available graft reconstruction options. The growing trend to use a hamstring autograft for ligament reconstruction is a departure from the technique typically employed in the adult population, where use of an allograft tendon, or transplant tendon from another individual, has been the predominant technique employed. The use of hamstring autograft creates new concerns for surgeons and anesthesiologists alike, as this technique is known to lead to significant pain at the hamstring donor site during the postoperative period. The significance of the pain secondary to hamstring autograft harvest remains undetermined beyond the initial 24 hours postoperatively, however, as it has yet to be fully investigated (Bushnell, Sakryd, & Noonan, 2010). The harvesting of a hamstring autograft, however, yields significant postoperative pain for which no consensus exists among clinicians as to how to best treat.

Sciatic peripheral nerve blockade (PNB) has proven to abate hamstring donor site pain in a reliable fashion while avoiding undesirable opioid-related side

effects (Bushnell, Sakryd, & Noonan, 2010). The efficacy of sciatic PNB can be attributed to the origin of pain following hamstring autograft harvest, graft fixation, or both, which lies in the sciatic nerve distribution (Frost, Grossfeld, Kirkley, Litchfield, Fowler, & Amendola, 2000). Controversy remains as to whether single-injection or continuous sciatic PNB is most appropriate following ACL reconstruction with a hamstring autograft. Single-injection sciatic PNB is a regional anesthetic technique employed to anesthetize the sciatic nerve with a single dose of local anesthetic. This technique offers pain control for a limited amount of time based on the volume and concentration of local anesthetic used. Continuous sciatic PNB entails placing a continuous perineural infusion (CPI) catheter so that local anesthetic may be released slowly but continuously adjacent to the sciatic nerve (perineural) for several days postoperatively. While both techniques of sciatic PNB alleviate pain in the immediate postoperative period, only continuous PNB has the ability to reliably provide analgesia on subsequent postoperative days.

No consensus exists regarding the duration of sciatic PNB necessary to effectively provide pain control following ACL reconstruction with a hamstring autograft. The disagreement among clinicians as to best practices of pain control following ACL reconstruction with a hamstring autograft is largely due to the lack of evidence comparing single-injection and continuous sciatic PNB following hamstring autograft harvest. Mismanagement of pain can be detrimental, resulting in negative physiological, psychological, and economic consequences (Agin & Glass, 2005). Failure to address pain may lead to future impairment in functioning as well as heighten anxiety and fear, which in turn may further increase the perception of pain (Matthews, 2011). Continued mismanagement of pain results in increased suffering and misery that can ultimately impact one's lifestyle and personality (Beales, Holt, Keen & Mellor, 1983). In addition, unaddressed pain can cause great disruption to families caring for patients. From an economic perspective, the mismanagement of pain can lead to slower rates of recovery, resulting in increased healthcare-related costs and time away from school and work (Twycross, 2002).

There is evidence that sciatic PNB, regardless of technique, significantly reduces pain when compared to intravenous opioids during the initial 24-hour postoperative period following knee surgery (Wegener, van Ooij, van Dijk, Hollmann, Preckel, & Stevens, 2011). As such, single-injection sciatic PNB, which can last up to 24 hours, should provide adequate analgesia precluding the need for oral narcotic or nonsteroidal anti-inflammatory medications following ACL reconstruction with a hamstring autograft. It remains unknown, however, if any benefit is gained during the initial 72-hour postoperative period from extending analgesia for the hamstring donor site via continuous sciatic PNB. While continuous sciatic PNB with a CPI catheter extends the duration of analgesia, it also extends the duration of anesthesia potentially leading to a decrease in motor function and subsequently active knee flexion. The sciatic nerve innervates the hamstrings, which are responsible for knee flexion (Distad &

Weiss, 2013). The decrease in active knee flexion may impede the ability of the patient to begin rehabilitation on the first postoperative day. This is an important consideration because early rehabilitation, which includes contraction of the quadriceps and hamstring muscles as well as weight bearing exercises with the aid of crutches, leads to faster recovery of long-term range of motion and a lower incidence of knee laxity following ACL reconstruction when compared to delayed rehabilitation (Shaw, Williams, & Chipchase, 2005; Pinczewski et al., 2007). Determining the duration of sciatic PNB required to effectively control pain following ACL reconstruction with a hamstring autograft, without impeding active knee movement, will help define best practice going forward.

II. RESEARCH QUESTION

This study aims to answer the following research question: Does the duration of sciatic PNB impact the ability to effectively provide postoperative pain control following ACL reconstruction with a hamstring autograft in the adolescent population?

III. PURPOSE OF THE STUDY

The purpose of this research is to compare the effect of single-injection sciatic PNB to continuous sciatic PNB on 1) postoperative pain control as measured by self-reported pain scores, pain medication use, and unplanned hospital admission due to poor pain control, 2) active knee flexion, and 3) patient satisfaction with pain control following ACL reconstruction with a hamstring autograft. The results of this research have the potential to positively impact pain control for the adolescent population undergoing this surgical procedure and foster responsible utilization of limited resources.

SPECIFIC AIM 1. The first aim of the study is to explore the impact of sciatic PNB technique on hamstring donor site pain control postoperatively.

H1.a. The extended duration of analgesia offered by continuous sciatic PNB decreases pain scores during the initial 72 hours following hamstring autograft harvest when compared to single-injection sciatic PNB.

H1.b. The extended duration of analgesia offered by continuous sciatic PNB decreases oral pain medication use during the initial 72 hours following hamstring autograft harvest when compared to single-injection sciatic PNB.

H1.c. The extended duration of analgesia offered by continuous sciatic PNB decreases the incidence of unplanned admission due to poor pain control during the initial 72 hours following hamstring autograft harvest when compared to single-injection sciatic PNB.

SPECIFIC AIM 2. The second aim of the study is to explore the impact of sciatic PNB technique on active knee flexion postoperatively.

H2. The extended duration of analgesia offered by continuous sciatic PNB does not delay active knee flexion during the initial 72 hours following hamstring autograft harvest when compared to single-injection sciatic PNB.

SPECIFIC AIM 3. The third aim of the study is to explore the impact of sciatic PNB technique on patient satisfaction with postoperative pain control.

H3.1. The extended duration of analgesia offered by continuous sciatic PNB improves patient satisfaction during the initial 72 hours following hamstring autograft harvest when compared to single-injection sciatic PNB.

IV. PREVIOUS CLINICAL EXPERIENCE

Concurrent Research Studies: The Department of Anesthesiology is not currently conducting another protocol with this patient population.

By the Investigator: This investigator currently is conducting research regarding the efficacy of regional anesthetic techniques at Cincinnati Children's Hospital Medical Center (CCHMC). Recruitment for an IRB-approved study comparing the efficacy of ultrasound-guided transversus abdominis plane blockade with surgeon performed ilioinguinal/iliohypogastric blockade following unilateral inguinal herniorrhaphy is on-going.

By Other Investigators: Sciatic PNB has been reported to most reliably decrease hamstring donor site pain, however, there remains no consensus as to the duration of action required to effectively control donor site pain throughout the postoperative period (Tran, Ganley, Wells, Ganesh, Minger, & Cucchiaro, 2005; Bushnell, Sakryd, & Noonan, 2010).

To date, there has only been one study reported in the literature comparing single-injection and continuous sciatic PNB. Continuous sciatic PNB was reported to offer significant advantages in pain control for adults only during the initial 24 hours following knee surgery (Wegener, van Ooij, van Dijk, Hollmann, Preckel, & Stevens 2011). It should be noted, however, this study does not refer to ACL reconstruction, rather the study population is comprised of patients undergoing total knee replacement making it challenging to appropriately translate and apply the clinical knowledge gained from that study to other clinical scenarios.

V. STUDY DESIGN

This study employs an experimental posttest-only design with repeated follow-up, with the gate control theory of pain serving as the theoretical foundation. An experimental posttest-only design with repeated follow-up is appropriate for this study, as the outcome is not relevant until after the intervention is complete. This

study is a randomized prospective observational study to compare the effect of single-injection sciatic PNB to continuous sciatic PNB on postoperative pain control, active knee flexion, and patient satisfaction with pain control following ACL reconstruction with a hamstring autograft.

A. Study Protocol:

The intervention in this study will be one of two techniques for sciatic PNB: single-injection PNB or continuous sciatic PNB with a CPI catheter. The PNB protocol will be assigned by computer-generated randomization. All study participants will receive standard care, including standard anesthetic care as recommended by the American Society of Anesthesiologists and the American Association of Nurse Anesthetists, and the surgical procedures will be in accordance with those set forth by the American College of Surgeons. Anesthetic management will be left to the discretion of the clinical team providing anesthesia care, which includes, but is not limited to, the amount of inhalation anesthetic and intravenous opioids each study participant receives throughout the intraoperative portion of the study.

All sciatic PNB will be performed following the induction of general anesthesia, but prior to the end of anesthesia. For patients randomized to the single-injection sciatic PNB group, ultrasound will be utilized to identify the sciatic nerve in the sub-gluteal region. Once the sciatic nerve is identified, 1 mL/kg (to a maximum volume of 20 mLs) of 0.2% ropivacaine without epinephrine will be injected into the perineural space surrounding the sciatic nerve.

For patients randomized to the continuous sciatic PNB group, ultrasound will be utilized to assist the anesthesia team with placing the catheter tip adjacent to the sciatic nerve in the sub-gluteal region in preparation for continuous infusion of local anesthetic postoperatively. Once proper placement of the sciatic CPI catheter is verified, 1 mL/kg (to a maximum volume of 20 mLs) of 0.2% ropivacaine without epinephrine will be administered incrementally over two minutes. An infusion of 0.125% ropivacaine will be started at the end of surgery at a rate of 3-4 mL/hr (based on patient weight) for 48 hours postoperatively. While assessments will be made through 72 hours postoperatively, CPI catheters will only remain in-situ for 48 hours, as the incidence of infection increases should an indwelling CPI catheter remain greater than 48 hours (Jeng, Torrillo, & Rosenblatt, 2010).

Following sciatic PNB, continuous femoral PNB will be performed. Patients in both study groups will receive continuous femoral PNB with a CPI catheter to provide analgesia to the anterior aspect of the knee, as this is an accepted standard of practice following ACL reconstruction. Ultrasound will be utilized to assist the anesthesia team with placing the catheter tip adjacent to the femoral nerve in the inguinal region in preparation for continuous infusion of

local anesthetic postoperatively. Once proper placement of the femoral CPI catheter is verified, 1 mL/kg (to a maximum volume of 20 mLs) of 0.2% ropivacaine without epinephrine will be administered incrementally over two minutes. An infusion of 0.125% ropivacaine will be started at the end of surgery at a rate of 6-8 mL/hr (based on patient weight) for 48 hours postoperatively.

The recommended dosing range of ropivacaine is 0.2-0.4 mg/kg/hr (Chelly, 2009). Therefore, patients weighing 60 kg or more will receive infusions of 0.125% ropivacaine at a rate of 8 mL/hr via the femoral CPI catheters and a 0.125% ropivacaine at a rate of 4 mL/hr via the sciatic CPI catheter (as applicable). Patients weighing less than 60 kg will receive an infusion of 0.125% ropivacaine at 6 mL/hr via the femoral CPI catheter and 3 mL/hr via the sciatic CPI catheter (as applicable). These parameters ensure that the total local anesthetic dose remains within the recommended dosing guidelines should a patient be randomized to receive both continuous femoral PNB and continuous sciatic PNB. In addition, establishing weight based infusion rates allows for the study group receiving one CPI catheter and the group receiving two CPI catheters to be as similar as possible thereby improving the ability to compare the outcomes of each study group.

Patients will not be blinded as to what study group they have been randomized to participate in. Blinding of subjects can be beneficial in studies because it minimizes the introduction of biases stemming from awareness. Blinding is not always possible, however. For example, in this study it would be challenging to blind subjects to the sciatic nerve block treatment group, as one group will have an indwelling sciatic CPI catheter and the other will not. One means of blinding study participants would be to insert sciatic CPI catheters in all patients and infuse local anesthetic in one group and a placebo in the other group, however, the costs and potential risks, such as opportunity for infection, potential tissue damage and potential for abscess formation secondary to infusion of a placebo, makes blinding of study participants prohibitive.

1. Sciatic Peripheral Nerve Blockade Description:

Under ultrasound-guidance, the sciatic nerve can readily be identified in the posterior thigh. The nerve appears hyperechoic and can be traced distally to the popliteal fossa, where it divides into the tibial and common peroneal nerves. Local anesthesia is injected under real-time visualization following a negative aspiration. If a single-injection block is done, local anesthesia is deposited adjacent to the sciatic nerve within the fascial plane, but not within the epineurium. Should a CPI catheter be placed, the CPI catheter will be placed under ultra-sound guidance, with the tip of the catheter being placed immediately adjacent to the sciatic nerve, after the local anesthesia has been deposited.

Peripheral Nerve Blockade Related Risks: While the general risks for peripheral nerve blockade apply to femoral and sciatic nerve blockade, the site of injection for these blocks is considered relatively low risk. The risks of the drug in the current study are no different than would be expected when the drug is used in any other local infusion. As with any local anesthetic drug, high doses or unintentional intravascular injection may lead to high plasma levels and related myocardial depression, decreased cardiac output, heart block, hypotension, bradycardia, ventricular arrhythmias, including ventricular tachycardia and ventricular fibrillation, and possibly cardiac arrest.

Risks related to the drug utilized in the current study ropivacaine are characteristic of those associated with other amide-type local anesthetic drugs, which include:

- Urticaria
- Pruritus
- Erythema
- Angioneurotic edema
- Tachycardia
- Sneezing
- Nausea
- Vomiting
- Elevated temperature
- Possibly anaphylactoid symptomology

Additionally, there is a low risk of mild discomfort or inconvenience to the subject, as they will receive regional blockade of some nature. Additionally, unforeseen risks may include, but are not limited to:

- Needle trauma
- Intraneural injection
- Intravascular injection
- Local anesthetic toxicity
- Hematoma
- Infection
- Poor/failed block

Finally, risks related to the use of a CPI catheter are rare, but include:

- Infection
- Infusion pump malfunction
- Local anesthetic toxicity
- Skin irritation or allergic reaction secondary to dressing material
- Unintentional CPI catheter dislodgement

- Fluid (local anesthetic) leakage at the CPI catheter insertion site
- Falls secondary to motor blockade

2. Risk Benefit Analysis:

Benefits: Subjects in this research study are unlikely to gain any personal benefit on the day of the study from their participation as the decisions of the clinical team caring for the patients will be guided by the randomized study protocol. The knowledge gained may be of benefit in the management of future adolescent patients who require ACL reconstruction. The ability to effectively provide pain control will lead to more efficient utilization of healthcare resources.

Study Related Risks: The risks associated with this study are minimal and are related to PNB. Both techniques of sciatic PNB included in this study are accepted techniques in clinical practice. All risks related to sciatic PNB are incidental, that is, associated with PNB, not the study itself as this is an observational study.

Risks/Benefit Analysis: It is the opinion of the principal investigator (PI) that this study is classified as “minimal risk but without direct benefit to participants”.

B. Subject Population:

A subject may be INCLUDED in this study if:

1. The subject is male or female;
2. The subject is of any racial or ethnic group;
3. The subject is age 10 years to 18 years (inclusive);
4. The subject is scheduled for the following:
Unilateral ACL reconstruction with a hamstring autograft under general anesthesia on an outpatient basis, and not being performed in conjunction with any other surgical procedures;
5. The subject is American Society of Anesthesiologists (ASA) patient classification I-II;
6. The subject or legally authorized representative has consented to femoral and sciatic peripheral nerve blockade for the procedure and the consent for peripheral nerve blockade has been obtained by a clinician (MD, DO, CRNA or APRN) authorized to obtain consent;
7. The subject’s legally authorized representative has given written informed consent to participate in the study and when appropriate, the subject has given assent or consent to participate.

A subject will be EXCLUDED from this study if:

1. Additional surgical procedures are being performed concurrently;
2. The subject is ASA classification > II;
3. The subject has pre-existing allergies to amide local anesthetics;

4. The subject is scheduled for overnight hospital admission;
5. The subject has any other condition, which in the opinion of the principal investigator, would not be suitable for participation in the study, including but not limited to coagulopathy, preexisting central or peripheral nervous systems disorders, and local infection or sores at the anticipated site of needle insertion;
6. Unsuccessful PNB or CPI catheter placement occurs during the study.

In addition, patients undergoing ACL reconstruction under the care of Dr. Charles Mehlman at CCHMC will be recruited for comparative analysis. Currently, Dr. Mehlman is the only Orthopedic Surgeon at CCHMC who does not allow his patients to receive peripheral nerve blockade following ACL reconstruction with hamstring autograft. Following his patients for 72 hours postoperatively with the same data collection tool used for the other patients enrolled in this study would provide a benchmark for comparison. There would be interventions for his patients, as their participation is purely observational in nature.

C. Selection and Recruitment of Participants:

The PI will work closely with the research coordinator and the co-investigators to screen and identify appropriate subjects listed on the daily operating room schedule at the Liberty Campus of CCHMC according to the inclusion and exclusion criteria defined in the study protocol. Once a potential subject is identified, either the PI or the research coordinator will discuss the purpose and procedures of the study with the patient and his or her guardian(s). Hospital-approved interpreters will be utilized for non-English speaking patients and/or guardian(s). Participants and their guardians will be informed of the voluntary nature of participation and the ability to drop out of the study at any time without negative consequences. If the guardian(s) express interest in participating in the study, they will be asked to read the written informed consent. When appropriate, assent or consent to participate will be obtained from the patient. Written assent will be obtained from the patient if the patient is ≥ 11 years of age and is able to provide written assent, which represents standard policy with regards to age of assent at CCHMC.

To allow for the broadest application of clinical outcomes, enrolled subjects will vary in their physical characteristics to the greatest extent possible given the inclusion and exclusion criteria.

1. Preparation:

Following identification of a potential subject, the patient and/or his/her parent(s)/guardian(s) may be called prior to scheduled surgery to initiate the informed consent process and to determine family interest in participation. If the patient and/or guardian(s) express interest during the phone call and the patient qualifies for the study, the family will be approached in Same Day Surgery by one of the study team members to

complete the informed consent process. Once all questions have been answered and the informed consent signed, the patient will be enrolled in the study at which time the subject will be assigned a study identification number. Written assent will be obtained if the child is ≥ 11 years of age and is able to provide written assent.

2. Vulnerable Populations:

Children from 10 years to 18 years of age (inclusive) will be recruited for this study after obtaining written informed consent from their parents and assent when appropriate (age >11 years).

D. Sample Size Determination:

Power analysis was performed to estimate an adequate sample size to support statistical conclusion validity and so that correct inferences can be made about the relationships between study variables. The standardized effect size was calculated to equal 0.5. Assuming an alpha of 0.05, power of 0.80 and a standardized effect size of 0.5, 64 patients will be required for each treatment group based on anticipated difference in patient reported pain scores due to sciatic PNB technique. Projected sample sizes were increased approximately ten percent from 64 per group to total of 70 subjects per group in an effort to account for patient attrition and lost data, therefore, a total of 140 patients will be enrolled in the study. Additionally, if the loss in patients is unequal between groups, yielding a significant disparity between study group composition, additional subjects may be added to account for this unequal loss.

Despite the presence of multiple confounding variables, the calculated sample size is sufficient to determine if a significant difference in outcomes measures exists secondary to sciatic PNB technique. Additionally, the sample size does not need to be altered based on the equation: $N > 50 + 8k$, where N is the number of cases and k is the number of predictors (Warner, 2013). In this study there is only one predictor, sciatic PNB technique, which is anticipated to impact outcomes following ACL reconstruction.

E. Randomization:

A computer generated randomization scheme will be used to assign 70 patients to each treatment group. The randomization will be done using the maximum allowable percent deviation method. This algorithm conducts a search to find a randomization list for which all percent deviations are less than or equal to the maximum allowable percent deviation of 10%. The randomization scheme will be sent to the PI who will then prepare and maintain a log of subject assignments. The PI will notify the participating surgeon and anesthesia team of the treatment (single-injection or continuous sciatic PNB) that is to be given to the next consented patient. The research coordinator will remain blinded to the assigned treatment plan until data collection has been completed.

F. Components of Cincinnati Children's Hospital Medical Center to be Utilized for this Study:

Subjects undergoing unilateral ACL reconstruction with a hamstring autograft on an outpatient basis at the Liberty Campus of CCHMC will be recruited from the OR schedule.

G: Data Collection:

Participants will be in the research study for approximately 4 days; the day of surgery and for follow-up phone calls once a day for the first three days after surgery. A minimum of three phone calls may be made after the patient is discharged. Once enrolled in the study, a unique study identification number will be assigned to each study participant. Assigning a unique patient identifier to each study participant allows any data gathered pertaining to them to be attached to this number rather than any patient identifiers, further ensuring that a breach in confidentiality does not occur (Polit & Beck, 2012). After obtaining written consent from the guardian(s), the medical record of the patient will be reviewed for further inclusion and exclusion criteria.

All data gathered will be used specifically for research purposes. Data collected preoperatively will include age, gender, BMI, ASA physical status, previous surgical history, self-reported tolerance of pain, self-reported level of activity since time of ACL injury, and the name of the orthopedic surgeon scheduled to perform ACL reconstruction. In addition, several questions regarding the patient's anxiety level will be asked to determine whether or not the patient has a history of anxiety that may impact pain and/or satisfaction scores postoperatively (see Appendix A). This data will be collected from the patient's medical record during the preoperative phase and directly from the patient and/or guardian(s) when appropriate. Data on study group assignment, analgesic requirement, the length of surgery, length of pneumatic tourniquet inflation time, pneumatic tourniquet inflation pressure, and systolic blood pressure at time of pneumatic tourniquet inflation will be gathered during the intraoperative phase.

In an effort to discern the impact of sciatic PNB technique on the outcome measures, data on self-reported pain scores, doses of oral pain medications, unplanned admission to the hospital due to poor pain control, and patient satisfaction will be gathered while the patient remains in the post anesthesia care unit (PACU). Data collection will then continue for 72 hours postoperatively following discharge from the PACU. Patients will document data measures on supplied data collection instruments (see Appendix B).

The patient or their guardian will record pain scores once every 6 hours for 72 hours postoperatively. In addition, the patient or their guardian will note the

date and time their leg was no longer numb behind their knee. The orthopedic surgeon performing the ACL reconstruction or a member of his orthopedic team will prescribe all postoperative oral pain medication. The oral pain medication typically prescribed is either Percocet or Vicodin. Vicodin, a schedule 3 controlled substance, is approximately half as potent as Percocet, which is a schedule 2 controlled substance. The patient will record the time and dose of all oral pain medication taken during the 72 hours postoperative period. The patient or their guardian will also record data regarding pain associated with active knee flexion once every 12 hours for 72 hours postoperatively. In addition, the patient or their guardian will record satisfaction with pain control once every 12 hours for 72 hours postoperatively.

The research coordinator may collect all data recorded by the patient and/or their guardian via telephone interview. Data will be collected using the same data collection tool given to the study participants to avoid instrumentation and maintain interrater reliability. Untoward events, such as unplanned hospital admission, CPI catheter dislodgement, or local anesthetic toxicity, will also be noted should they occur. This information will be collected from the patient or guardian once every 24 hours by the research coordinator during the 72-hour postoperative period; the postoperative period begins at the time of discharge from the PACU.

1. Survey(s) and Questionnaire(s):

Patients and their guardian will be given data collection instruments to complete postoperatively at the time of enrollment to facilitate recall when conveying information to the study staff during telephone conversations. The data collection instruments will be available in different languages and utilized for non-English speaking patients and/or guardians. The patient and their guardian(s) will receive training regarding the data collection tool both during the time of enrollment and again prior to discharge from the hospital. At the time of enrollment, essential phone numbers, including home phone and cell phone numbers, will be collected. Should the patient and/or guardian lose the data collection sheet, additional copies can be emailed to them upon request. Hospital-approved interpreters will be utilized for non-English speaking patients and/or guardian(s).

The goal of the data collection tool is to promote accurate data recording, limit the likelihood of missing information, and to promote efficient and accurate data entry into REDCap™. Prior to the start of study enrollment, the data collection tool will be piloted in an effort to reduce error in the measurement process. Five volunteers undergoing ACL reconstruction with a hamstring autograft at the

Liberty Campus of CCHMC will be sought out to trial the data collection tool. Refinement of the data collection tool will center on reliability and validity of the tool. Focusing on stability, internal consistency, and interrater reliability during the pilot of the tool will allow for estimates of the tool's reliability. Stability, or test-retest reliability, is determined by administering the tool two different times to the same individuals and determining the correlation between the two sets of scores (Kimberlin & Winterstein, 2008). Cronbach's alpha, which is a function of the average intercorrelations of items and the number of items in the scale, is the most widely used method for estimating internal consistency (Kimberlin & Winterstein, 2008). Interrater reliability requires completely independent ratings of the same event by more than one individual (Kimberlin & Winterstein, 2008). Tests of the tool's validity will focus on construct validity, content validity, and criterion-related validity. Evaluation of construct validity requires an examination of the relationship between the outcome measures being evaluated and variables related to the construct being measured by the instrument (Kimberlin & Winterstein, 2008). As there is no statistical test to determine whether a measure adequately represents a construct, content validity typically relies upon the judgment of experts in the field (Kimberlin & Winterstein, 2008). Assessment of criterion-related validity will focus on the tool's ability to accurately predict how well the scores of a given measure correlate with the scores of the other measures of the same construct. Revisions will be made to the data collection tool as necessary prior to the start of the study.

H. Period of Time Estimated to Complete the Study:

Each enrollment will take variable time to complete depending on the length of the surgical procedure and amount of time required in the recovery room. Following enrollment, data is collected for 72 hours postoperatively. The entire study will take approximately 2 years to enroll and complete.

VI. DATA STORAGE AND STATISTICAL ANALYSIS

A. Data Storage:

Data confidentiality will be maintained by data being stored in a password protected computer and hard copies of subject information stored in a locked office. All data is collected from the study participant will be entered into REDCap™ (Park City, Utah) by the research coordinator. REDCap™ is a secure web application for building and managing databases securely that was specifically designed to support clinical and translational research

(Harris, Taylor, Thielke, Payne, Gonzalez, & Conde, 2009). Confidentiality of the data will be maintained through the use of a password-protected computer and any hard copies of subject information stored in a locked office accessible only to members of the Department of Anesthesia.

The study records will be made available for review only to the Institutional Review Board and the Food and Drug Administration (FDA) per CCHMC policy. The FDA is a branch of the federal government that establishes regulations and guidelines for clinical research to protect participants from unreasonable risks. Furthermore, the FDA ensures consumers have reliable information and that medical treatments are not only safe, but effective as well. The subjects' names or any other identifiers will not be used in published information relating to this study and will be treated as confidential per the Health Insurance Portability and Accountability ACT (HIPAA) of 1996. Per the HIPAA Privacy Rule, prior to dissemination of results, all health information will be deemed individually unidentifiable by employing the approved Safe Harbor method of de-identification that entails the removal of 18 types of identifiers.

B. Primary Endpoint Analysis:

The hypothesis that the extended duration of analgesia offered by continuous sciatic PNB decreases pain scores during the initial 72 hours following hamstring autograft harvest when compared to single-injection sciatic PNB will be tested with two separate tests. Both Pearson's correlation and the Wilcoxon Mann Whitney test will be utilized to test his hypothesis, as controversy surrounds the analysis of Likert scale data. It has been argued that only nonparametric statistics should be used on Likert scale data, as the intervals between the scale values may not be equal (Jamison, 2004). Taking this into consideration, the pain scores recorded for each patient will be totaled and an average pain score will be calculated for each study participant. This will allow the data to be measured on a continuous scale, thereby meeting the criteria of Pearson's correlation. Pearson's correlation is a parametric test that measures the degree and direction of linear relationship between two variables (Gravetter & Wallnau, 2000). The Wilcoxon Mann Whitney test will also be used to analyze pain scores recorded at each 12-hour period to determine if there is a difference in outcomes related to the duration of analgesia provided by sciatic PNB technique. This test is appropriate when there is one IV with two independent groups and the DV is ordinal in nature. The Wilcoxon Mann Whitney test is a nonparametric test of the null hypothesis that two populations are the same against an alternative hypothesis. This test uses the relative position of the data in a rank ordering, rather than the actual values. Using both parametric and nonparametric tests will increase confidence when drawing conclusions should both tests lead to the same results.

The hypothesis that the extended duration of analgesia offered by continuous sciatic PNB decreases oral pain medication use during the initial 72 hours following hamstring autograft harvest when compared to single-injection sciatic PNB will be tested with the Independent Samples *t*-Test. The Independent Samples *t*-Test is appropriate when there is one IV with two independent groups and the DV is continuous in nature (Field, 2009). The Independent Samples *t*-Test is used to compare differences between separate groups when there are two experimental groups (single-injection sciatic PNB and continuous sciatic PNB) and different study participants have been used in each group (Field, 2009).

The hypothesis that the extended duration of analgesia offered by continuous sciatic PNB decreases the incidence of unplanned admission due to poor pain control during the initial 72 hours following hamstring autograft harvest when compared to single-injection sciatic PNB will be tested with the Chi-square test. The Chi-square test is used to determine if there is a relationship between two categorical variables (Field, 2009). As the data for this DV are categorical, the focus during analysis is placed on frequencies rather than means. The Chi-square test can be used to determine if there is a significant difference between the expected frequencies and observed frequencies in one or more categories (Field, 2009).

The hypothesis that the extended duration of analgesia offered by continuous sciatic PNB does not delay active knee flexion during the initial 72 hours following hamstring autograft harvest when compared to single-injection sciatic PNB will be tested using the Wilcoxon Mann Whitney test. The hypothesis that the extended duration of analgesia offered by continuous sciatic PNB improves patient satisfaction during the initial 72 hours following hamstring autograft harvest when compared to single-injection sciatic PNB will also be tested using the Wilcoxon Mann Whitney test. The Wilcoxon Mann Whitney test is appropriate to test both these hypotheses, as this test is designed to evaluate the difference between two treatments (single-injection sciatic PNB and continuous sciatic PNB) using data from an independent measures study (Gravetter & Wallnau, 2000). During analyses, testing may be altered based on the recommendations of the statistician to better analyze the collected data. Intention-to-treat analysis will not be employed, as this may skew results and it is often difficult to obtain outcome data for study participants who have dropped out of the study (Polit & Beck, 2012).

Prior to any analyses, the distribution of the demographic variables will be compared between the two treatment groups. All statistical tests will be two-sided with a significance level of $\alpha=0.05$ and will be conducted using SAS[®] software, (Version 9.2, Cary, NC). Following the enrollment of the initial 30 subjects (with 15 in each study group), an interim analysis utilizing the statistical tests later described will be performed to determine if statistically

significant differences exist between the outcome measures of each sciatic PNB technique. Performing an interim analysis limits the number of patients exposed to study procedures. If statistically significant differences exist such that one of the two sciatic PNB techniques clearly produces superior patient outcomes, the study will be stopped. However, should the outcomes measures of each sciatic PNB technique be found to be equivalent and without statistically significant differences enrollment will continue.

VII. DATA SAFETY AND MONITORING

Adverse events will be collected until data collection is complete. Adverse events will be recorded on the case report forms. Details will include an explanation of the event, seriousness, anticipation, treatment, resolution and relatedness to the study treatment. All study-related adverse events will be followed through to completion

A. Adverse Event Definitions:

The definitions for adverse event, adverse device effect, serious adverse event, serious adverse device effect, and unanticipated adverse device effect are provided below (ANSI/AAMI/ISO 14155-2:2003, 21 CFR 812.3(s)).

Adverse Event: an adverse event is any untoward medical occurrence in a subject, which need not be related to the treatment under investigation.

Adverse Peripheral Nerve Blockade Blockade Effect: an adverse peripheral nerve blockade effect is any untoward or unintended response to regional blockade, which may result from insufficiencies in the deployment of the ultrasound machine, or from provider error.

Serious Adverse Event: a serious adverse event is an adverse event that results in death, inpatient hospitalization, severe or permanent disability, a life threatening illness or injury, fetal distress, fetal death, a congenital abnormality, a birth defect, or medical or surgical intervention to prevent permanent impairment to body or structure.

Serious Adverse Peripheral Nerve Blockade Effect: a serious adverse peripheral nerve blockade effect is an adverse regional blockade effect that results in death, inpatient hospitalization, and severe or permanent disability or is life threatening.

Unanticipated Peripheral Nerve Blockade Effect: any serious adverse effect on health or safety or any life threatening problem or death caused by, or associated with, peripheral nerve blockade if the effect, problem, or death was not previously identified in nature, severity or degree of incidence in the

investigational plan, or application (including a supplementary plan or application) or any other unanticipated serious problem associated with peripheral nerve blockade that related to the rights, safety or welfare of subjects. Refer to the Peripheral Nerve Blockade Risk Analysis and Risk Assessment section for details on anticipated adverse regional blockade effects.

B. Adverse Event Reporting:

All serious adverse events will be reported to the IRB per IRB reporting requirements. These reports may include, but will not be limited to: date of onset; brief description of the events; their treatment; whether they resulted in death, inpatient hospitalization, severe or permanent disability or were life threatening; their relationship to the study device; and resolution. All unanticipated adverse device effects will be reported to the IRB.

C. Data Safety Monitoring Plan:

In an effort to ensure patient safety throughout the course of this study, a Data Safety Monitoring Plan has been established. The Data Safety Monitoring Committee shall convene at predetermined intervals to assess the progress of the study for potential patient-related adverse events. Such events include, but are not limited to: infection at the CPI catheter insertion site, infusion pump malfunction, local anesthetic toxicity, skin irritation or allergic reaction secondary to CPI catheter dressings, and falls secondary to motor blockade. Should 2 or more study-related adverse events occur, the study will be suspended immediately pending review of the study and results to date by the Data Safety Monitoring Committee. In addition, should any unforeseen study-related adverse event not previously reported in the literature occur, the study will be stopped for review by the Data Safety Monitoring Committee. Should the study be stopped at any point, enrollment will not resume until the Data Safety Monitoring Committee has determined that it is safe to resume the study. In addition, at any point during the course of the study should the Data Safety Monitoring Committee determine that it is not in the best interest of adolescent patients undergoing ACL with a hamstring autograft to continue the study, the study will be stopped.

D. Data Safety Monitoring Committee:

The Data Safety Monitoring Committee will meet to review the results of the study to date following the enrollment of the 30 participants, 60 participants, and 90 participants. In addition, the Data Safety Committee shall convene if 2 or more study-related adverse events occur related to this study. The Data Safety Monitoring Committee shall be comprised of 2 members of the Department of Anesthesia credentialed by CCHMC to perform peripheral nerve blockade but who are not part of this study (Dr. Vidya Chidambaran and Dr. Nancy Samol), a statistician, and a patient advocate. The patient advocate will be the parent of a patient who has previously undergone ACL reconstruction at the Liberty Campus of CCHMC.

VIII. PRIVACY AND CONFIDENTIALITY

All subjects screened and enrolled in this study will be identified only by their initials and/or assigned study number only. Data confidentiality will be maintained by data being stored in a password protected computer and hard copies of subject information stored in a locked office. All information collected will be treated as confidential, as provided by law. The study records will be made available for review only to the Institutional Review Board (IRB) and the Food and Drug Administration (FDA). The subjects' names or any identifier will not be used in published information relating to this study.

IX. FUNDING

This is a CCHMC investigator initiated study that has received financial support from the AANA Foundation.

X. COST AND PAYMENT FOR PARTICIPATION

The patient's insurance company will be charged for all PNB and associated equipment utilized in this observational study. This is not a departure from standard practice of care, as PNB is routinely employed for postoperative pain control following ACL reconstruction with a hamstring autograft in the adolescent population.

Patients undergoing surgery with Dr. Mehlman will not receive any charges related to PNB as they will not receive PNB per his discretion.

The patient's insurance company may be charged for continuing medical care and/or hospitalization including tests and treatments of any side effects of the study treatment that may occur. In the event that the insurance does not cover all costs, patients may incur additional costs because of treatment side effects.

A \$20.00 gift card will be distributed as incentive to all participants who enroll in this study. The gift card will be mailed upon completion of the data collection process during the three days following surgery.

XI. THIS STUDY IS AFFILIATED WITH ANOTHER IRB-APPROVED STUDY

We are collaborating research efforts with IRB Protocol 2008-0514 in order to determine if type of anesthesia (specifically type of sciatic nerve block) may have any effect on outcomes after ACL-Reconstruction. Therefore subjects that have

previously been enrolled in study 2008-0514, and have also been enrolled in this current project will be shared amongst the study staff to merge the data and investigate the effect of type of sciatic nerve block on outcomes after ACLR. For this retrospective analysis, we are requesting a waiver of documentation. Prospectively, subjects that are enrolled in the sciatic nerve block study will also be recruited for the ACL Outcomes study and those subjects that consent for participation in both will be shared amongst the studies.

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Appendix A
Preoperative Data Collection Instrument

PATIENT STUDY ID NUMBER: _____

Age (in years) on day of recruitment: _____

Gender (circle one): Male Female

BMI: _____

ASA physical status (circle one): I II

Previous surgery: Yes No

If yes, what surgery? _____

Self-reported preoperative pain score (0 = no pain, 10 = worst pain): _____

Self-reported tolerance of pain (circle one):

0 = Low tolerance of pain

1 = Moderate tolerance of pain

2 = High tolerance of pain

Self-reported level of activity since the time of ACL injury (circle one):

0 = Not active at all

1 = Not active

2 = Partially active

3 = Active

4 = Highly active

What is your level of anxiety today (0 = no anxiety, 10 = worst anxiety): _____

- Are you normally anxious (yes/no)? _____
- Do you take any prescriptive medications for anxiety (yes/no)? _____
- Are you currently, or have you in the past, seen a healthcare professional for treatment of your anxiety (yes/no)? _____

Parikh

Appendix B

Post-Discharge Data Collection Instrument

PAIN CONTROL:

Keep track of your pain score and location of pain:

Pain score: 0 = no pain, 10 = worst pain			
Pain location: F = front of knee, B = back of knee, X = both front & back			
6 hours		42 hours	
12 hours		48 hours	
18 hours		54 hours	
24 hours		60 hours	
30 hours		66 hours	
36 hours		72 hours	

Date and time the leg was no longer numb behind the knee: _____

Pain medicine prescribed (circle one): Vicodin Percocet Other: _____

Write down every time pain medication is taken:

[illegible]

ACTIVE KNEE MOVEMENT:

Rate the ability to bend the knee that was operated on:

Knee Movement	12 hours	24 hours	36 hours	48 hours	60 hours	72 hours
0 = Able to bend with no pain						
1 = Able to bend, but with pain						
2 = Too much pain to bend						

SATISFACTION:

Rate your overall satisfaction score with pain management:

Satisfaction Score	12 hours	24 hours	36 hours	48 hours	60 hours	72 hours
0 = Not satisfied at all						
1 = Not satisfied						
2 = Partially satisfied						
3 = Satisfied						
4 = Highly satisfied						

From your perspective, have you encountered any unexpected postoperative experiences?
