Tranexamic Acid Has No Effect on Post-operative Hemarthrosis or Pain Control Following ACL Reconstruction Using Bone Patella Tendon Bone Autograft: A Double-Blinded Randomized Control Trial

NCT03631355

October 12, 2020

Reducing Hemarthrosis in Anterior Cruciate Ligament Reconstruction with BTB Autograft by the Administration of Intravenous Tranexamic Acid: A Double-Blind Randomized Control Study

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Protocol Number: 18-00538

Version Date: February 26, 2020

I. PURPOSE OF THE STUDY AND BACKGROUND

Purpose

The purpose of the proposed study is to evaluate the effects of administering intravenous tranexamic acid (TXA) to patients undergoing anterior cruciate ligament (ACL) reconstruction with bone-patellar tendon-bone autograft to minimize hemarthrosis within the knee joint and post operative pain.

Rationale

The anterior cruciate ligament (ACL) is the most common ligament injured in the knee, with as many as 246,000 tears occurring per year in the United States[7] Disruption of the ACL commonly occurs with a pivot-shift mechanism during athletic activity. Rupture of the ACL leads to anterior translation of the tibia with an associated impaction of the posterolateral tibial plateau against the midportion of the lateral femoral condyle. Upon impact, the articular cartilage overlying the bone marrow edema lesion is exposed to significant loads, potentially causing irreversible local injury and the release of pro-inflammatory, catabolic cytokines and chemokines into the joint space.[10, 14, 17] This acute phase of injury is characterized clinically by pain, an effusion and associated decreased knee range of motion.

ACL reconstruction is typically recommended in the young, active patient population in an effort to stabilize the knee and restore normal function. Bone-patellar tendon-bone autograft has shown to have the most successful outcomes. Several complications of both procedures include postoperative bleeding and swelling of the knee joint. There are two sources of bleeding after an ACL reconstruction including an intra-articular site and the donor site (extra-articular)[16]. Both sites can experience bleeding postoperatively leading to hemarthrosis and additional pain, which can prolong the recovery process. One technique utilized to reduce perioperative bleeding is the use of a tourniquet. Currently, other techniques are being tested to reduce perioperative bleeding. As a result, tranexamic acid (TXA) has been proposed as a solution to decrease these postoperative complications.

TXA is a synthetic anti-fibrinolytic agent that competitively inhibits the activation of plasminogen to plasmin by blocking tissue plasminogen activator and at higher concentrations directly inhibits plasmin[4, 9]. Plasmin, an enzyme that degrades fibrin clots, fibrinogen, procoagulant factors V and VIII[4]. Inhibition of plasmin decreases proteolytic action thus leading to clot formation and stabilization[4]. TXA is indicated in patients with hemophilia for short-term use (two to eight days) to reduce or prevent hemorrhage and reduce the need for replacement therapy during and following tooth extraction[13]. Administering TXA during the surgery will reduce the amount of plasmin in the system decreasing blood loss within and after the surgery. One gram of intravenous tranexamic acid (TXA) will be administrated before tourniquet inflation and before closure of the incision, as 1 g has been shown to be a safe amount with minimal side effects[16].TXA has already been shown to decrease perioperative bleeding in total knee arthroplasty and total hip arthroplasty, without increasing the risk of deep vein thrombosis[1, 2, 6, 8, 11, 15, 18].

This study is not being conducted under an IND number and will be conducted under IND exemption. This investigation is not intended to be reported to the FDA in support of a new

indication for use nor support any other significant change in the labeling or advertising for the drug. The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product. The route of administration (IV) and dosage of 1 g has been shown to be safe and effective[13, 16]. The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50; and The investigation is conducted in compliance with the requirements of 312.7.

We hypothesize that administration of TXA will reduce perioperative bleeding in BTB ACL reconstruction procedure with minimal side effects as compared to controls (no TXA). As a result, swelling and postoperative pain will decrease thus improving postoperative outcomes. By comparing two cohorts receiving the same procedure and administering TXA to one cohort, we can determine if the TXA affects perioperative bleeding and if decreasing perioperative bleeding will decrease postoperative pain and swelling.

Study Design

This will be a single-center, double-blinded randomized controlled study. The study is comparing blood loss and postoperative pain and swelling in two cohorts: patients undergoing BTB ACL reconstruction who receive TXA during surgery and patients who do not receive TXA. The intravenous tranexamic acid will be administered before surgery begins and after the tourniquet is released at the conclusion of the surgery. Blood loss will be measured via measuring the amount of blood in the drain at the conclusion of the surgery. Patients will be asked on postoperative day 1, 2 and 7 to rate their pain according to the VAS scale. Patients will have their knee swelling measured immediately postoperatively and at their one-week follow up visit. The swelling ratio is defined as the postoperative mean circumference of upper pole of patella and lower pole of patella divided by the preoperative values.[9]

Primary Objective

The primary objective of the study is to determine if there are any differences in blood loss between patients undergoing BTB anterior cruciate ligament reconstruction who receive TXA compared to patients who do not receive it.

Secondary Objective

Secondary objective of the study is to determine is there is a difference in post operative pain and swelling between patients undergoing BTB anterior cruciate ligament reconstruction who receive TXA and patients who do not receive it.

II. CHARACTERISTICS OF THE RESEARCH POPULATION

Number of Subjects

We will aim to enroll a total of 110 subjects (55 per cohort) as determined by the priori sample size calculator.

Gender of Subjects

Men and women will be included in this study.

Age of Subjects
Subjects included study will be aged 18-60 years, inclusive.

Racial and Ethnic Origin
There are no enrollment restrictions based on race or ethnic origin.

Inclusion Criteria
Patients will be screened for eligibility using the following criteria. All study subjects must meet the following inclusion criteria:

- Patients undergoing a BTB anterior cruciate ligament reconstruction
- Patients ages 18-60, inclusive
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Exclusion Criteria
Patients meeting the following criteria will be excluded from participation in this study:

- Legally incompetent or mentally impaired (e.g., minors, Alzheimer's subjects, dementia, etc.)
- Younger than 18 years of age
- Older than 60 years of age
- Any patient considered a vulnerable subject: pregnant women or fetuses, children, cognitively impaired adults, prisoners
- history of coagulation abnormalities and thromboembolic disease or current abnormal coagulation test values
- history of stroke or acute coronary syndromes within 3 months before surgery
- Preoperative (chronic) anticoagulation therapy
- Abnormal coagulation profile
- Renal failure (serum creatinine > 250 μmol/L [2.83 mg/dL]) or liver cirrhosis
- Sickle cell disease
- ACL reconstruction by a method other than BTB
- Patients with a history of hypersensitivity to Percocet and/or TXA

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Vulnerable Subjects
We do not intend to enroll vulnerable subjects.

Subject withdrawal criteria.
Patients are free to withdraw at any time from the study before or after surgery.
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III. METHODS AND PROCEDURES

Methods and Procedures
Patients indicated and scheduled for a BTB ACL reconstruction will be identified from faculty surgeon case logs at the NYU Langone Health, Langone Orthopedic Hospital Sports Medicine Division. After informed consent is obtained, a chart review of patients' medications and past

medical histories will be performed based on their electronic medical records to identify any current pain medications or exclusion criteria. In order to maintain the blind, the resident assisting the surgeon will randomize the patient to one of two cohorts using REDCap. Both the resident and surgeon are members of the study team.

- Cohort 1: 1 gram of intravenous tranexamic acid (TXA) before tourniquet inflation and 1 gram of IV TXA before closure of the incision
- Cohort 2: Will not receive TXA.

The resident physician and anesthesiologist will not be blinded to the study, however the surgeon and study team members will remain blinded. Before the surgery begins, the resident will prepare the patient and the TXA will be administered (if assigned) before the tourniquet is placed, at which point the surgeon will be called into the room. The administration of TXA will not prolong the surgery and will not add any additional risks of prolonged anesthesia The surgeon will exit the surgery before closure at which point, the TXA will be administered (if assigned) and the resident physician will close the incision.

Immediate post-operative management will not be affected by this study. All patients will receive a standardized regimen of aspirin for DVT prophylaxis and Percocet for pain management, which is standard of care post-operative treatment.

Information to be recorded pre-operatively includes age, sex, height, weight, BMI, and American Society of Anesthesiology (ASA) classification. Intra-operative information will also be recorded, including operative time, and estimated blood loss. During the surgery, a suction device is utilized to remove excess blood from the surgical site and sucked into the suction drain and placed into a measuring cup. We will measure the perioperative blood loss by looking at the measuring cup and seeing how much blood is inside. The objective is to have the average blood loss of the cohort receiving TXA less than the cohort not receiving TXA. Knee swelling postoperatively will be measured using the swelling ratio. The swelling ratio is defined as the circumference of the operative limb divided by the circumference of the contralateral limb. Pain severity scores at rest will be assessed by use of a visual analog scale (VAS; 0 = no pain, 10 = worst pain imaginable) at 0.5, 1, 1.5, 2, 4, 6, 24, and 48 hours as well as 7 days after surgery. Percocet consumption will be recorded at 24 hours, 1 day, 2 days and 7 days after surgery. Incidence of TXA-related side effects (nausea/vomiting, itching, anxiety, increased thirst, rapid heartbeat) in the first 24 hours will be noted. Time to discharge from the post-anesthesia care unit (PACU) and time to discharge from the hospital will be recorded. Patients will be in the study a duration of two weeks, until their post-operative follow up visit.

Data Analysis and Statistical Plan

Statistical analysis will be performed using chi-squared and/or fisher's exact testing depending on size for binary variables. An a priori power analysis was conducted to estimate the minimum sample size needed to achieve 83% power (1 – b) at the .05 significance level which was calculated to be 50 patients. Therefore, we added 10 patients to account for potential exclusions, totaling 110 patients. Variables used in the power calculation were taken from the literature including an assumed effect size of 0.5 and standard deviation (SD) of 2. This large sample size will provide enough information to truly determine a difference between cohorts. This sample size and statistical analysis was used in similar studies looking at the effects of TXA in ACL

reconstruction[5, 12].

Continuous variables will be compared with paired t-tests if the data is approximately normally distributed. If the data is not normally distributed, Mann-Whitney tests will be used. All protected health information will be removed prior to statistical analysis. We will use patient subjective pain, perioperative blood loss and knee swelling data as statistical endpoints. Subjective pain will be measured with the VAS (visual analogue scale), perioperative blood loss will be measured looking at blood loss from the suction drain after surgery. We are looking for a statistically significant difference in perioperative blood loss between the two cohorts. The swelling ratio is defined as the postoperative mean circumference of upper pole of patella and lower pole of patella divided by the preoperative values according to our previous study[9]. The endpoints must be statistically significant between the two cohorts to show TXA is effective.

Data and Safety Monitoring Plan

Data monitoring will be done by Dr. Jovan Popovic, the anesthesiologist, and Dr. Alaia, the principal investigator will oversee the conduct of the study. They will review the following accumulated data quarterly.

They will monitor whether or not:

1. Collection and storage of patient data was performed in a sensitive and secure manner, as defined in the informed consent form and protocol, ensuring information is stored on REDCap.
2. All study activities were conducted with primary emphasis on patient care and wellbeing, ensuring the patients are not in discomfort and have an abnormally high VAS following the surgery.
3. If there were any adverse events, and if so were addressed appropriately and per protocol
4. The risk/benefit to patients has remained the same throughout the course of the study.

The study will be stopped if there are unexpected severe AE's in more than one patient. Adverse events will be defined as negative reactions to the intravenous TXA during or after surgery, including seizures, vision problems. We will submit summaries of data and safety monitoring annually.

Data Storage and Confidentiality

Data recorded from this study will be organized in REDCap. Participant medical information will only be available to the principal investigator and research staff as necessary for data analysis. All patient health information will be de-identified and assigned a code. Information linking participants' names, social security numbers and medical record numbers will be stored in a secure location separate from the medical information. No data will be shared to anyone outside of the study team.

Adverse Event Reporting

Information about any breach of confidentiality will be documented in the electronic data collection system and/or on the paper CRFs, as appropriate. It will be the responsibility of the Principal Investigator to report any Serious Adverse Event (SAE) that occurs during the course

of the prospective data collection to the Institutional Review Board (IRB) within the timeframe specified by NYU SoM.

IV. RISK/BENEFIT ASSESSMENT

Risk

This study involves risk of medication side effects as well as a breech of confidentiality. Intravenous TXA can cause the following side effects:

- Anxiety
- blurred vision
- changes in vision
- chest pain
- confusion
- cough
- dizziness or lightheadedness
- fainting
- fast heartbeat
- greatly increased or decreased frequency of urination or amount of urine
- increased thirst
- loss of appetite
- nausea or vomiting
- numbness of the hands
- pain, redness, or swelling in the arm or leg
- sudden shortness of breath or troubled breathing

Rare side effects include:

- Convulsions or seizures
- Orthostatic hypotension
- sweating
- trouble seeing
- unusual tiredness or weakness.

Protection against Risks

Patients will be screened for any contraindication to aspirin or Percocet use.

The patients will stay in the recovery unit a minimum of 3 hours after surgery as the mean duration of the effect of TXA is 3 hours and be monitored by the recovery unit nurses[3, 12]. Patients will be instructed to call the principal investigator and visit the emergency department if there is are any symptoms of calf swelling or chest pain within the first seven days following surgery.

Additionally, all patients will be de-identified and given a code. Information linking the patient codes to the participants' names and medical record numbers will be stored in a secure location separate from the medical information. Access to the information linking the linkage codes with participant identifiers shall be restricted.

Potential Benefits to the Subjects

Patients may experience less pain post-operatively, and may require less narcotics use, which has a steeper side-effect profile. However, these benefits cannot be guaranteed.

Additionally, it is the hope of the research team that results of this study will benefit future patients and their physicians by providing more information regarding the use of acetaminophen after surgery. This will allow for a more open and informed dialogue, and possibly a change standard of care treatment.

V. INVESTIGATOR'S QUALIFICATIONS AND EXPERIENCE

The CV, medical license, and human subjects' tutorial completion report are attached for all investigators who are participating in this study. All research personnel have medical research experience and are qualified to participate in this quality study. Most importantly, staff have been properly educated and certified with CITI training to conduct research in a matter that will maintain full patient confidentiality. The research coordinator for this study is trained in GCP principles and practices and will be responsible for compliance with GCP guidelines for all study investigators and research assistants.

VI. SUBJECT IDENTIFICATION, RECRUITMENT AND CONSENT/ASSENT

Method of Subject Identification and Recruitment

Appropriate patients, who meet all of the inclusion criteria and none of the exclusion criteria, who require a BTB ACL reconstruction, will be identified from the clinical offices of the investigator surgeons.

Process of Consent

Written consent will be obtained from subjects who are eligible candidates for BTB ACL reconstruction based upon their medical condition (as determined by their physician). The consent process will take place during the office visit when it is determined necessary to perform the procedure—at which time the investigator has determined subject's voluntary participation has been upheld. Subjects will be informed about the study and the intended purpose. They will be given the opportunity to ask questions and receive thorough explanations. They will be made aware of the possible risks and anticipated benefits. They will also be informed of alternative procedures. Subjects will then be given another opportunity to ask questions and agree or disagree to consent.

Subject Capacity

All subjects enrolled in this study will have capacity to provide informed consent.

Consent Forms

Written consent will be obtained from the patient.

Documentation of Consent

Signed consent forms will be kept in a binder and stored in a locked file cabinet.

Costs to the Subject

Subjects will not incur any additional financial costs as a participant in this study.

Payment for Participation

No payments/reimbursements will be provided to subjects for their participation in this study.

VII. References

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NYU Langone MEDICAL CENTER

Research Subject Informed Consent Form

Title of Study: **Reducing Hemarthrosis in Anterior Cruciate Ligament Reconstruction with BTB Autograft by the Administration of Intravenous Tranexamic Acid: A Double-Blind Randomized Control Study**
Study Number: S18-00538

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1. About volunteering for this research study

You are being invited to take part in a research study. Your participation is voluntary which means you can choose whether or not you want to take part in this study.

People who agree to take part in research studies are called “subjects” or “research subjects”. These words are used throughout this consent form. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. You may also decide to discuss this study and this form with your family, friends, or doctor. If you have any questions about the study or about this form, please ask us. If you decide to take part in this study, you must sign this form. We will give you a copy of this form signed by you for you to keep.

2. What is the purpose of this study?

The purpose of this study is to see if giving intravenous (IV, through a vein) tranexamic acid (TXA) to patients undergoing anterior cruciate ligament (ACL) reconstruction results in decreased bleeding in the joint and decreased post-operative pain and swelling when compared to patients who undergo ACL reconstruction without TXA.

During ACL reconstruction, bleeding occurs inside the joint and from the site where the tendon is taken for the repair. This can prolong the recovery process as pain and swelling occur after surgery. TXA helps blood to form clots by blocking the function of plasmin (a protein) that prevents clot formation. The US Food and Drug Administration (FDA) approved the use of TXA to stop excessive bleeding in people with hemophilia (an inherited condition affecting the body’s ability to form blood clots) undergoing tooth extraction. In this study, TXA is considered an investigational drug because it is not FDA-approved for reducing bleeding associated with ACL reconstruction.

You are being asked to participate in this study because you are going to have ACL reconstruction surgery on your knee.

3. How long will I be in the study? How many other people will be in the study?

You will be part of the study for 1 week, until your post op follow up visit. We expect to enroll approximately 110 subjects in this research study.

4. What will I be asked to do in the study?

If you decide to participate in this study, you will be asked to sign this consent form prior to any research activities taking place. We will then review your chart for your demographics (age, sex, etc.), height and weight, body mass index (BMI), and medications and past medical history to confirm your eligibility to participate.

If you are eligible to participate in the study, you will be randomized (assigned by chance, like flipping a coin) either to the group receiving TXA or the group not receiving TXA. You and your surgeon will not know which group you will be assigned to. If you receive TXA, you will be getting 1 gram through an IV before the surgery starts and 1 gram after the surgery is complete. Regardless of which group you are assigned to, you will continue your standard care as planned, which includes taking aspirin and Percocet to prevent clotting complications and to reduce post-operative pain. The duration of your surgery and time under anesthesia will not be affected (i.e. prolonged) if you receive TXA.

We will collect information about your surgery such as how long it takes the surgeon to complete the operation and how much blood is lost.

After your surgery, we will measure how much your knee has swelled. We will monitor you for TXA side effects over the next 24 hours. We will collect the time you are discharged from the post anesthesia care unit (PACU) as well as the time you are discharged from the hospital.

You will be asked to report pain, side effects, and the amount of Percocet you need to take to control your pain.

The pain scale we will be using is the visual analogue scale (VAS), a scale consisting of a drawn line from 0 to 10 – you will be asked to mark where you believe your pain is (0 = no pain and 10 = the worst pain). These scores will be recorded at 30 minutes and 1, 2, and 4, 24, 48, hours and 1 week after surgery.

You will also report whether you used any Percocet and, if so, the amount of Percocet taken at 24 hours, 1 day, 2 days, and 7 days after your surgery.

5. What are the possible risks or discomforts?

The following are risks and discomforts that you may experience during your participation in this research study:

Side effects of intravenous tranexamic acid (TXA) (<5% or fewer than 5 out of 100 people) **may include:**

- anxiety
- blurred vision
- changes in vision

- chest pain
- confusion
- cough
- dizziness or lightheadedness
- fainting
- fast heartbeat
- greatly increased or decreased frequency of urination or amount of urine
- increased thirst
- loss of appetite
- nausea or vomiting
- numbness of the hands
- pain, redness, or swelling in the arm or leg
- sudden shortness of breath or troubled breathing

Rare, but serious side effects of IV tranexamic acid (TXA) may include (< 1% or fewer than 1 out of 100 people)

- convulsions or seizures

Other rare, but serious side effects of IV tranexamic acid (TXA) may include (< 0.5% or fewer than 5 out of 1,000 people)

- dizziness, faintness, or lightheadedness when getting up suddenly from a lying or sitting position
- sweating
- trouble seeing
- unusual tiredness or weakness.

Your doctor will go over the side effects of the standard care medications before and after the surgery.

Potential Loss of Confidentiality: While every effort will be made to keep your information confidential, there is the potential risk of loss of confidentiality. In order to minimize this risk, any information that can identify you will be removed and replaced with a unique study ID that only the study coordinator/investigators will know.

In addition, this research may involve risks that are currently unforeseeable.

If any physical or psychological discomfort is experienced, or you no longer want to participate in the study, you can withdraw at any point and it will not affect the ongoing care you receive.

6. Can I be in the study if I am pregnant or breastfeeding?

Because taking part in this study may harm an embryo, fetus, or breastfeeding baby, you should not become pregnant, breastfeed a baby, or father a child while participating in this study. Risks to the patient include increase in blood sugar and reduced ability to fight infection. Risks to the fetus include hormonal imbalance. Other risks may not yet be known.

If you are currently pregnant, you will not be able participate in the study. You should not become pregnant while you are participating in this study. If you are able to become pregnant, you will be required to use a medically accepted method of birth control while you participate in the study: These methods include:

- Hormonal methods like birth control pills, patches, vaginal rings or implants,

- Barrier methods such as condoms or a diaphragm used with spermicide (a foam, cream or gel that kills sperm),
- Intrauterine device (IUD),
- Abstinence (no sex).

If you become or you think you have become pregnant during the study, you must tell the principal investigator right away and must tell your obstetrician or other health care provider caring for you during your pregnancy that you took part in this study. If you become pregnant, you will have to stop taking part in the study for safety reasons. The principal investigator may ask you to provide information about the outcome of your pregnancy and the health of your baby.

7. What if new information becomes available?

During the course of this study we may find more information that could be important to you. This includes information that might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

8. What are the possible benefits of the study?

If you are randomly assigned to the group who receives the study drug, you may experience less pain and swelling post-operatively and may require less post-operative pain medication, such as Percocet. However, these benefits cannot be guaranteed. It is hoped that the knowledge gained from this study will be of benefit to others in the future.

9. What other choices do I have if I do not participate?

You do not have to participate in this study to receive ongoing care for your condition.

10. Will I be paid for being in this study?

You will not be paid for your participation in this study**.**

11. Will I have to pay for anything?

You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study, or if your insurance agrees in advance to pay. If you have health insurance, the cost of these services will be billed to your insurance company. If your insurance does not cover these costs or you do not have insurance, these costs will be your responsibility. The cost of the study drug will be provided free of charge.

12. What happens if I am injured from being in the study?

For medical emergencies contact 911. If you think you have been injured as a result of taking part in this research study, tell the principal investigator as soon as possible. The principal investigator's name and phone number are listed at the top of page 1 of this consent form.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the NYU School of Medicine or Medical Center to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

13. When is the study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped or your participation ended at any time by your physician without your consent because:

- The principal investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The principal investigator or other body responsible for monitoring the safety of the study has decided to stop the study.

If you decide to participate, you are free to leave the study at any time. Leaving the study will not interfere with your future care, payment for your health care or your eligibility for health care benefits.

14. How will you protect my confidentiality?

Your medical information is protected health information, or “PHI”, and is protected by federal and state laws, such as the Health Insurance Portability and Accountability Act, or HIPAA. This includes information in your research record as well as information in your medical record at NYU Langone Health. In compliance with NYU Langone Health policies and procedures and with HIPAA, only those individuals with a job purpose can access this information.

Medical information created by this research study may become part of your medical record. We may include your research information in your medical record for several reasons, including for the billing of services provided in connection with the study, to securely document any medical services you receive, and so that other members of the NYU Langone Health community who may treat you have access to important information about your health.

You have a right to access information in your medical record. In some cases, when necessary to protect the integrity of the research, you will not be allowed to see or copy certain information relating to the study while the study is in progress, but you will have the right to see and copy the information once the study is over in accordance with NYU Langone Health policies and applicable law.

15. HIPAA Authorization

As noted in the Confidentiality section above, federal law requires us, and our affiliated researchers, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions. We are asking for your permission (authorization) to use and share your health information with others in connection with this study- in other words, for purposes of this research, including conducting and overseeing the study.

Your treatment outside of this study, payment for your health care, and your health care benefits will not be affected even if you do not authorize the use and disclosure of your information for this study.

What information may be used or shared with others in connection with this study?

All information in your research record for this study may be used and shared with those individuals listed in this section. Additionally, information in your medical record that the research team believes may be important to the study may be accessed by those listed here. This includes, for example, results from your physical examinations, x-ray images, laboratory tests, procedures, questionnaires, and diaries.

Who may use and share information in connection with this study?
The following individuals may use, share, or receive your information for this research study:

- The Principal Investigator, study coordinators, other members of the research team, and personnel responsible for the support or oversight of the study.
- The study sponsor: Department of Orthopaedic Surgery
- Governmental agencies responsible for research oversight (e.g., the Food and Drug Administration or FDA).
- Health care providers who provide services to you in connection with this study, and laboratories or other individuals who analyze your health information in connection with this study.

Your information may be re-disclosed or used for other purposes if the person who receives your information is not required by law to protect the privacy of the information.

What if I do not want to give permission to use and share my information for this study?
Signing this form is voluntary. You do not have to give us permission to use and share your information, but if you do not, you will not be able to participate in this study.

Can I change my mind and withdraw permission to use or share my information?
Yes, you may withdraw or take back your permission to use and share your health information at any time for this research study. If you withdraw your permission, we will not be able to take back information that has already been used or shared with others. To withdraw your permission, send a written notice to the principal investigator for the study noted at the top of page 1 of this form. If you withdraw your permission, you will not be able to stay in this study.

How long may my information be used or shared?
Your permission to use or share your personal health information for this study will never expire unless you withdraw it.

16. Optional permission for future use

NYULMC would also like to store, use, and share your health information from this study in research databases or registries for future research conducted by NYULMC or its research partners. To give this additional permission, check the box below and write your initials where indicated. You may still participate in this study even if you do not give us this additional permission.

NYULMC will continue to protect the confidentiality and privacy of this information as required by law and our institutional polices. If you give this additional permission, you will continue to have the rights described in this form. You have the right to take back this additional permission at any time.

☐ Checking this box indicates my permission to store, use, and share my health information from this study in research databases or registries for future research conducted by NYULMC or its research partners.

_____
Subject Initials

17. The Institutional Review Board (IRB) and how it protects you

The IRB reviews all human research studies – including this study. The IRB follows Federal Government rules and guidelines designed to protect the rights and welfare of the people taking part in the research studies. The IRB also reviews research to make sure the risks for all studies are as small as possible.

The NYU IRB Office number is (212) 263-4110. The NYU School of Medicine's IRB is made up of doctors, nurses, non-scientists, and people from the community.

18. Who can I call with questions, or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on top of the page 1 of this consent form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Institutional Review Board (IRB) at (212) 263-4110.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

When you sign this form, you are agreeing to take part in this research study as described to you. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer.

Name of Subject (Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date