

**North Shore-Long Island Jewish Health System
Campus: Lenox Hill Hospital
Consent for Participation in a Research Study**

**Effect of intraoperative application of autologous PRP on post operative morbidity in
ACL reconstruction using autologous bone patellar tendon bone graft harvest**

Principal Investigator: Stephen J. Nicholas

Sponsor: Arthrex

Introduction:

You are being asked to volunteer as a subject in a research study. **Taking part in research is completely voluntary.** This consent form provides you with the information you will need in order to consider whether you would like to participate in this study.

The investigator of this study will explain the purpose of the study, including how the study will be carried out and what you will be expected to do. The investigator will also explain the possible risks, possible benefits and alternatives of being in the study. You should ask the investigator any questions you have about any of these things before you decide whether you wish to take part in the study. If you decide to participate in this study, you will be asked to sign and date this consent form to indicate that you agree to participate. This process is called informed consent.

You are invited to participate in a research study. Research is a way of gaining new knowledge. A person who participates in a research study is called a “subject” rather than a patient.

Why is this research study being done?

The purpose of this research study is to investigate whether or not platelet rich plasma (PRP) may help to improve healing and decrease post operative pain in patients undergoing anterior cruciate ligament (ACL) reconstructive surgery using their own patellar tendon grafts. PRP is a form of treatment that uses the patients own blood sample to enhance healing. Nearly 200,000 ACL surgeries using the patients own patellar tendon for reconstructions are performed annually, however, many of these patients suffer from postoperative pain located at the site of the patellar tendon graft.

You are being asked to participate in this study because your injury and subsequent surgical treatment using your own patellar tendon as graft represents the patient type we believe stands to benefit from improved outcomes with the use of PRP.

Why is this research?

This is a research study because the application of PRP to patellar tendon graft harvest sites is being compared to the standard procedure of patellar tendon graft harvest without the application of PRP. The

researchers are interested in learning whether or not the application of PRP to the graft donor site leads to an improvement in post-operative outcome measures of healing and pain.

How many people will take part in this study?

This research study hopes to enroll 50 patients. All of the patients enrolled in this study will be operated on at this site (SurgiCare of Manhattan).

How long will you be in this study?

The entire study duration is 24 months. As an enrolled participant, you should expect to be seen at 2 weeks post-op and then at 1, 3, 6, 12, 18 and 24months for a total number of 7 visits. A table has been included below listing the activities, imaging, and time commitment that each visit will require from you over the course of the entire study.

Post Operative Visit #	Weeks After Surgery	Time	Imaging	Physical Exam	Patient Questionnaire
1	2	20min	None	✓	✓
2	4	20min	None	✓	✓
3	12	35min	XR's	✓	✓
4	24	50min	MRI	✓	✓
5	48	20min	None	✓	✓
6	72	20min	None	✓	✓
7	96	20min	None	✓	✓

If you choose to take part in this study, the study procedures will last for 1 hour, and you will be followed for another 24 months. You will be asked to attend a total of 7 office follow up visits. We have listed above the approximate time commitment that each visit will require. The first two follow up visits and the final three follow up visits will each require approximately 15 minutes. Ten of those minutes will be dedicated to you filling out some standardized questionnaires. The five additional minutes will be dedicated towards a brief physical examination that will be performed by one of your doctors, followed by a second brief physical examination that will be performed by one of the researchers. There are two post office visits that will require a slightly larger time investment on your part. This is the 12 and 24 week post op office visits. The 12 week visit will require a total of 35 minutes during which time x-rays of your knee will be taken. During the 24 week visit, an MRI of your knee will be obtained, and the total office visit will be approximately 50 minutes.

What will happen in this research study?

If you choose to enroll in this study, the following is a brief time-line with descriptions of the procedures that will take place.

After signing consent for your standard of care ACL reconstructive surgery, you will be asked to sign consent to enroll as a participant in this research study. You will be subjected to the following interventions that are not normally a part of ACL reconstruction:

- ❖ This study will be “randomized” in order to achieve the best possible study results that will reflect only outcomes related to the PRP and not any bias on the part of those enrolling you in the study or performing the surgery. You will be randomly selected to receive one of two possible treatments: ACL reconstruction with PRP applied to the graft harvest site or ACL reconstruction alone, without any PRP. By randomizing you in this way, it ensures that you will be assigned to a group by chance (like flipping a coin). You will have an equal chance of being in either group.
- ❖ This study will be “double blinded” to order to achieve the best possible study results that will reflect only outcomes related to the PRP and not any bias on the part of those evaluating the study results. This means that neither you nor the investigators directly involved in the study procedures will be allowed to know whether or not you received any PRP or not during your surgery until the study is complete. The study is done this way because knowing whether you are in a group can change the results of the study. We will not tell you which group you are in since the research study staff will not know your group either. However, we can quickly find out which group you are in if we ever need to know for your safety.
- If you are randomized into the treatment arm of the study (selected to receive the PRP), a sample of blood totaling 10cc (less than one tablespoon) will be drawn by the anesthesiologist at the beginning of the procedure. This will occur in the operating room, after you have been anesthetized or “put to sleep.” This blood will be drawn using the IV line which will have been previously placed by the anesthesiologist at the start of the case as part of standard practice for this surgery. This means that you will not be subjected to any additional needle sticks nor will you be caused any additional discomfort from the blood draw by participating in this study.
- If you are randomized into the control arm of the study (not selected to receive the PRP), you will not undergo a blood draw nor will you receive any treatment with the PRP. Neither you nor the investigators will know if you had a blood draw or received PRP. Therefore, the remaining study procedures will be the same for all individuals in the study.

By agreeing to enroll in the study you are agreeing to be seen at seven post operative visits over the course of 24 months.

- At the beginning of each of your follow up visits, you will be asked to fill out brief questionnaires. These questionnaires will require approximately 10 minutes of your time to fill out. These questionnaires will ask you about the characteristic, severity, and location of any postoperative pain you may experience. They will also ask you to judge your function level after the surgery and compare that to your function levels prior to your injury. After your doctor gives you a physical, the study investigator will also perform a short physical that should take approximately 5 minutes.
- At your 3 and 6 month follow up visits, imaging studies will be done in addition to your physical and questionnaires. Details regarding these imaging procedures are included below:

- X-Ray imaging of the Knee: At your 3 month follow-up, 3 X-rays of your knee will be taken on location in the office of Dr. Nicholas. These x-rays are taken as part of standard of care for all patients that undergo ACL reconstruction, and not only those that choose to participate in this study. These x-rays will require an additional 15 minutes of your time during that visit.
- Magnetic Resonance Imaging of the Knee: At your 6 month follow-up, an MRI of your knee will be obtained on location in Dr Nicholas' office. This will be used to assess the effect, if any, that the PRP may have on the healing of the donor site. This MRI exam is unique to this study and would not be normally done as part of standard of care for your surgery. This imaging will require an additional 30 minutes of your time during that visit.

Drugs and Devices used in this study:

- The process of PRP preparation and administration will be as follows: Prior to the start of every surgery, the anesthesiologist will obtain an intravenous (IV) line to administer anesthesia for your surgery. Those patients randomized to undergo treatment with PRP will have approximately 1 tablespoon worth of blood withdrawn. This will only be done on those patients who were enrolled in the study and randomized to the treatment group (group assigned to receive PRP).
- Briefly, the blood sample is put through a series of filtering cycles by spinning it in a device called a centrifuge. This process helps to concentrate the PRP or platelet rich plasma, which is a portion of your blood that contains the chemicals we are studying. After this has been prepared, we will apply it to your surgical wound at the end of the surgery.
- The application of the PRP will be done at the very end of the surgery by a fellow or resident participating in the case, but not a study investigator. This will ensure that neither you nor any member of the research group will know whether you received PRP or not. The PRP sample that has been prepared will be placed into the portion of your patella bone that was used to harvest the graft (donor site). A small portion of the patellar tendon known as para-tenon will be used to hold the PRP sample in place (Para-tenon is a special name given to the tissue that surrounds the patellar tendon and provides nutrients and blood supply). It is standard procedure to sew the para-tenon back over the graft harvest site at the end of an ACL reconstruction. If randomized to receive the PRP, the only thing we will be doing differently is laying the PRP sample down on the patellar bone before we close the para-tenon.
- Since PRP is created from your own blood without the addition of any added chemicals or biochemical modification, it does not require FDA approval for its use. The machines that are used to spin the blood samples and help to create PRP are approved and regulated by the FDA. Our study will be performed using an "Arthrex" centrifuge to prepare our samples. This device has gained full FDA approval. More information on this can be found at:

<http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicalApprovalsbyYear/ucm172950.htm>

What are the risks and discomforts of this research study? What could go wrong?

Since this study is randomized, your group may receive less effective treatment or have more side effects than the other group. The potential risks and discomforts that you might experience while on this study are outlined below.

Platelet Rich Plasma:

Since PRP is a formulation created entirely from your own blood, the complications and risks are extremely low. The anesthesiologist who prepares the blood is highly skilled and will carefully sterilize the skin prior to obtaining the sample.

Another side effect that is common is an initial increase in pain and inflammation at the site where the PRP is injected. This occurs because the platelets and blood sample contain natural chemicals that stimulate the immune system. This type of complication is short lived and when it does occur, is treated effectively with pain medication and anti-inflammatory medications, such as Ibuprofen.

Please inform the investigator if you have a bleeding disorder or are on a medication known to thin the blood such as Coumadin or Lovenox. These participants have a higher risk of bleeding when compared with normal bleeding characteristics.

Blood-Drawing:

There are no major risks of having your blood drawn in this study. You will be fully anesthetized (in a clinically induced sleep) while the blood is drawn, which therefore eliminates the pain of the injection. In addition, the blood will be drawn through the IV that is already being placed as part of your scheduled surgery. Therefore, you will not experience any additional bruising or discomfort as a result of participating in this study.

Magnetic Resonance Imaging (MRI):

Since MRI machines use magnets and radio waves to take images of the body, you are not subjected to any radiation. However, you might experience discomfort with having to lie on a narrow enclosed couch for 15 minutes as the machine takes the images. In addition, the machine produces loud tapping noises that might cause you some discomfort. Earplugs will be provided to you to help reduce the noise. Also, some people with claustrophobia (fear of closed spaces) may find the MRI scanner too confining.

It is very important that you tell the researcher about any metal objects, devices or implants that are in or on your body before you enter the scanner room. All metal objects must be removed before entering the magnet room. The MRI may cause any metal in or on your body to move. In some cases, having those devices may mean that you should not have an MRI scan.

If the scan reveals a condition that could affect your health, you will be referred for the proper follow-up care to your primary care physician or another specialist.

X-rays:

As a result of the x-ray imaging, you will be exposed to radiation during the 3 month follow-up session. Since having x-rays is part of standard of care for post ACL reconstruction surgery, you will not be exposed to any additional radiation by participating in this study. While we cannot be sure any dose of radiation is completely safe, the amount you will be exposed to in this study is not known to cause health problems.

Surveys:

There are no risks associated with completing the survey. However, you might feel discomfort from completing the survey as a result of the questions being asked.

Breach of Confidentiality:

Although it is unlikely, there is a small risk that there can be a breach of confidentiality if patient information is disclosed to unauthorized individuals. All measures to ensure patient confidentiality will be employed. Data will be de-identified and entered into a password-protected computer only accessible to investigators on this study.

Unknown Side Effects:

As with any new procedure or treatment, there might be side effects that are unknown at this time. You will be closely watched for side effects. You should report any unusual events to the study staff.

Risks to Women of Childbearing Potential and Pregnant Women

We do not know the effects of PRP on fertility or a fetus. For this reason, if you believe you are pregnant or have a chance of becoming pregnant, you should not take part in this study. A urine pregnancy test will be performed prior to the start of study procedures. If you are pregnant, you will not be allowed to be in the study. If you become pregnant during the study, please notify the investigator immediately. The investigator might have to withdraw you from the study and closely monitor you through your entire pregnancy.

The side effects of this experimental procedure on newborns are also not known; therefore, if you are currently breastfeeding you cannot be in this study.

What are the benefits of this research study?

If you are randomized to receive PRP in this study, you may directly benefit by having decreased healing time and decreased post operative pain. This may allow you to return to pre-injury activity levels faster than individuals that have the standard of care autologous bone patellar tendon bone reconstruction of their ACL. In addition, this study may provide knowledge on the benefits of PRP in graft site healing and patient satisfaction following ACL reconstruction. This information can then be used to change the standard treatment for patients requiring this surgery in the future.

If you do not want to take part in this research study, what are your other choices?

If you do not join this study, you have other choices for treatment. Talk to your doctor about your choices.

Possible choices may include:

- Application of PRP to the graft harvest site without participation in the study;
- Standard treatment – ACL reconstruction with autograft bone patellar tendon bone;
- No surgical treatment, including physical therapy and plyometric training; or
- Comfort care.

Are there any costs for being in this research study?

This research study is funded partially “Arthrex.” The remainder of the costs associated with this study will be incurred by Dr Stephen Nicholas at NY Orthopedics and the Nicholas Institute of Sports Medicine and Athletic Trauma.” You will not have any added costs from being in this study. All study related visits, procedures and medications will be given to you at no cost. Neither you nor your insurance company will be billed for your participation in this research.

The portion of the study that involves the preparation of the PRP is the portion of the study that will be funded partially by “Arthrex” as they have donated their centrifuge and other equipment (syringes) needed to prepare the PRP.

What are your rights as a research participant?

Your participation in this project is voluntary. The quality of your medical care will be the same, whether you join, refuse to join, or decide to leave the study.

If you do not join the study you will not be penalized or lose benefits to which you are entitled. If you join the study you may withdraw at any time without prejudice to your future care at the North Shore-LIJ Health System. Follow-up examinations may be needed to assure your well-being.

Could you be taken off the study before it is over?

It is also possible that your participation in this study may end without your consent. This decision may be made by a researcher, study sponsor or the Institutional Review Board (IRB- the committee that oversees research at this institution).

Reasons for withdrawal may include:

- Failure to follow instructions,
- Failure to show up for study visits,
- It is not in your best interest to continue on this study, or
- The study is stopped.

If you withdraw from this study or if you are withdrawn from the study, any data (or samples) already collected will continue to be used. However, no new data will be collected.

What happens if new information is learned?

You will be told of any new findings that may change your decision to continue to participate. Your consent to continue to take part in this study may be obtained again.

What happens if I am hurt or injured from participating in this study?

If you are hurt from being in the study, you will receive medical care and treatment as needed from the North Shore-Long Island Jewish Health System. However, you will be responsible for the costs of such medical treatment, directly or through your medical insurance or other forms of medical coverage. No money will be given to you.

What will happen with the information we collect as part of this research study?

Any study information about you will be kept private and will only be given out with your permission. If the results of this study are published, your name will not be used. Your research records will be private to the extent allowed by law. In order to make sure the research is done properly, the Institutional Review Board (IRB - the committee that oversees research at this institution) may need access to information about your participation in this study.

What information will be collected and used for this study?

If you agree to be in this study, we will collect health information that identifies you. We may collect the results of tests, questionnaires and interviews. We may also collect information from your medical record. We will only collect information that is needed for the research. This information has been described in this consent form. If you sign this consent form, you are giving us permission to collect, use and share your health information. This permission is called authorization.

Who else will see your information?

Study records that identify you will be kept private. You will not be identified in study records or publications disclosed outside the North Shore-Long Island Jewish Health System.

The following reviewers may access your study and medical records to make sure that this study is being done properly:

- Federal and state government oversight agencies (FDA)
- The North Shore-LIJ Health System Institutional Review Board (IRB - the committee that reviews research at this institution)

We will do our best to protect the privacy of your records but it is possible that once information is shared with people listed on this form, it could be released to others.

In the future, we may publish results of this study in scientific journals, and we may present it at scientific meetings. If we do, we will not identify you.

If the researchers learn about potential serious harm to you or someone else or other public health concerns, it will be shared with the appropriate authorities.

Will you be able to access your records?

If your research records are used for decisions related to your clinical care, then you have the right to review this information and request changes. This is limited to information about your treatment, and does not include information related to procedures or tests that are for research purposes only. You may access this information only after the study analysis is complete. You have the right to know who has

and who will see your records. To request this information, or for any questions related to your health information, you may contact the Research Privacy Officer at 516-562-2018.

How long will your health information be kept?

There is no limit on the length of time we will keep your information for this research because it may be analyzed for many years. You are allowing access to this information indefinitely. If you change your mind about participating in this study, we will keep any information collected about you. However, we will not collect any new information on you.

Can you change your mind?

If you change your mind about being in the study, you may withdraw at any time. If you want us to stop collecting your health information, you need to send a letter to the researcher at the following address:

Dr. Stephen Nicholas
Lenox Hill Hospital
130 East 77th Street
New York, NY. 10075

Your letter needs to say that you have changed your mind and do not want the researcher to collect and share your health information. You may also need to leave the research study if we cannot collect any more health information. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it

Does the investigator of this study receive money if you take part?

Funding for this research study is provided by Arthrex, NY Orthopedics and The Nicholas Institute of Sports Medicine and Athletic Trauma (NISMAT).

Arthrex is an industry sponsor. They are the creators of the equipment used to process blood samples and create the PRP. They have sponsored the study in as much as they have donated the costs for use of all equipment related to obtaining the PRP.

The remainder of the funding is internal. Internal sources for funding this research include NY Orthopedics and NISMAT. Both will fund the additional costs associated with data collection, MRIs, and follow up physical examinations.

Dr Stephen Nicholas is an investigator for this study. He is interested in both your healthcare and the conduct of this research. You do not have to take part in a research study conducted by your doctor.

Who can answer your questions about this study?

If you have any questions about the study, you may call Brian Walters, M.D. at (212) 737-3301. If you have questions about side effects or injury caused by research you should call Brian Walters M.D. at (212) 737-3301. If you need emergency care, dial 911 or go to the nearest Emergency Room. If you have questions about your rights as a research participant, or concerns about being in the study, you may contact the Office of the Institutional Review Board (the committee that oversees research at this institution) at (516) 562-3101. A signed copy of this consent form will be given to you.

Summation/Signature:

I have read the above description of the research study. I have been informed of the risks and benefits involved and all my questions have been answered to my satisfaction. Furthermore, I have been assured that a member of the research team will answer any future questions that may arise. I voluntarily agree to participate in this study and know that I can withdraw this consent to participate at any time without penalty. By signing this form, I have not waived any of the legal rights that I would otherwise have.

Signature of Subject

Date

Printed Name of Subject

Signature of Witness

Date

Printed Name of Witness

Investigator's Statement:

In addition to advising the above subject of other forms of treatment and therapy which are appropriate, I have offered an opportunity for further explanation of the risks and discomforts which are, or may be associated with this study and to answer any further questions relating to it.

Signature of Investigator

Date

Printed Name of Investigator