Augmentation of ACL Reconstruction with Bone Marrow Stem Cells and Amnion Collagen Matrix Wrap

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RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE OF PROJECT: **Augmentation of ACL Reconstruction with Bone Marrow Stem Cells and Amnion Collagen Matrix Wrap: A Blinded Randomized Controlled Trial**

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RESEARCH SITE(S): Andrews Research and Education Foundation and Baptist Physicians Group

SPONSOR: Arthrex

INVESTIGATOR CONTACT INFORMATION:

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INTRODUCTION:

In order to decide whether you wish to participate in this research study, you should understand why the study is being done, how the study will be run, the types of study procedures involved, your time commitments, and the possible risks and/or benefits to make an informed decision. This process is known as "informed consent."

This written consent form provides detailed information about the research study. This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. Before you decide to take part in this study, you may want to think about it more, or discuss it with family or friends. You can take a copy of this form home with you before making your decision. Your participation in this study is voluntary. You should not join this research study until all of your questions are answered to your satisfaction.

If you wish to participate in this research study, you will be asked to sign this consent form. You will be asked to sign before any study procedures are done. You will be given a copy of this consent form to keep for your records.

PURPOSE OF THE RESEARCH STUDY:

You are being asked to participate in research being conducted by the Andrews Research and Education Foundation (AREF) and Baptist Physicians Group. The purpose of this study is to evaluate the use of wrapping an anterior cruciate ligament (ACL) graft with a collagen matrix tissue wrap and injecting bone marrow aspirate concentrate which contains stem cells, obtained from you, under the wrapping and into the graft.

SELECTION OF SUBJECTS:

The study involves 20 patients undergoing ACL reconstruction with patellar (knee cap) tendon autografts and 20 patients with hamstring autografts for a total of 40 patients. If you are between the ages of 18 and 45 years old and are scheduled to have ACL reconstruction with autologous grafts from either the patellar tendon or hamstring tendon you can be in the study. If you have a prior surgical procedure or significant prior injuries to the same knee as the knee that will be undergoing ACL reconstruction you cannot be in the study. If you have difficulty obtaining internet access or do not have an active e-mail address you cannot be in the study. If you are unable to complete MRI examinations, during which you will have to lie still in an enclosed space, due to claustrophobia or anxiety you cannot be in the study.

RESEARCH PROCEDURES:

If you meet the above criteria, you will have the study explained in detail and you will have to give your written consent to be in the study. If you are randomized into the collagen wrap stem cell group

during the normal ACL reconstruction surgery, bone marrow aspirate will be obtained either through a hole in the end of your femur (upper leg bone) or your iliac crest (hip bone). The bone marrow aspirate will be processed to concentrate the stem cells. Stem cells will then be injected underneath the wrap surrounding the autologous graft (patellar or hamstring tendon) and into the graft. Any remaining stem cells from you will be destroyed. If you are randomized to the control group, you will undergo standard ACL reconstruction surgery.

Blinding: Since the study records how you are feeling and progressing as part of its measurements, the intention of the study is to not let you know whether you received a collagen wrap with stem cell ACL reconstruction or a standard ACL reconstruction because that knowledge may influence your answers. For this purpose, if you are randomized to the standard ACL reconstruction group, in addition to standard ACL reconstruction surgery, a bandage and dressing will be placed along your hip bone in order to keep you unaware to which group you were randomized until the end of the study. At the end of the study, it will be revealed to you into which group you were enrolled.

As part of the study, photographs will be taken of the inside of your knee joint to document the delivery of the bone marrow aspirate concentrate which contains stem cells under the collagen matrix and into the graft. You will be enrolled in the Surgical Outcome System, an online program that uses questionnaires to track how you feel and your ability to do activity. You will have to answer these questionnaires pre-surgery, and then post-surgery at 2 weeks, 6 weeks, 3 months, 6 months, 1 year and 2 years.

You will also need to complete all normal pre-operative, operative and post-operative protocols for the ACL procedure. You will also need to perform the standard post-operative rehabilitation exercise program under the direction of a physical therapist

As part of the study, at 3, 6, 9 months and one-year post-surgery you will undergo a magnetic resonance imaging (MRI) so that the structure of the surgical graft and your knee in general can be examined.

After the 12-month MRI, you will be offered the opportunity to undergo a needle biopsy of the surgical graft arthroscopy performed under local anesthesia so that the cellular structure of the graft can be examined. This is an additional part of the study and you can participate in the study without having the biopsy of the surgical graft.

RISKS AND DISCOMFORTS:

If you are randomized to the collagen wrap stem cell group, we will be harvesting the stem cells from inside your femur or iliac crest (hip bone) while you are asleep during surgery. There will also be a small needle insertion hole in your femur or iliac crest (hip bone) for the bone marrow stem cell collection, which will be about the same size as an IV insertion. This may have some minor pain or

swelling and there is a very minor risk of infection. If cells are harvested from your iliac crest, there will be a small 5mm incision, which is about ¼ of an inch. Potential risks and side effects of the use of bone marrow stem cell injections include pain and swelling. We have been using bone marrow stem cell injections into the knee for the treatment of knee arthritis and to augment ACL reconstruction surgery and have not found an increase in pain and swelling in these patients. Collagen wrap has been safely used by doctors to treat foot wounds, decrease scarring in spine surgery, and promote healing in eye-surgery. Although it has been inserted safely into joints in animal studies, it has not been studied as a wrap for ACL surgery in humans. Potential but undocumented risks in this application could include pain, swelling, infection, or an immune response. These risks are small as it is believed that collagen wrap decreases the risk of infection and an immune response in spine surgery and eye-surgery.

If you choose to have a needle biopsy of the surgical graft arthroscopy at the 12-month point, the risks include minor puncture site pain and infection as well as the risk of pain and/or an allergic reaction to numbing medicine, lidocaine.

There is a small risk of the disclosure of your protected health information, which will be minimized where possible including removing all identifiable information from data collection sheets and storing study information in secure locations as described in more detail below.

ALTERNATIVES:

You do not have to participate in this study and can choose to have the recommended ACL reconstruction surgery performed without the collagen wrap or harvest of the stem cells.

BENEFITS:

If you are selected to receive the collagen matrix tissue wrap and injecting bone marrow aspirate concentrate which contains stem cells procedure there is no charge to you and you may experience accelerated graft healing. You will also receive the follow-up MRI scans at no cost to you. Your answering the questionnaires with the Surgical Outcome System also allows your physician the opportunity to remotely monitor your surgical health progress and outcomes. Due to your participation in the study, future patients may benefit from the information obtained from the study.

CONFIDENTIALITY:

All patient protected health information and other confidential information is protected by state and federal law, unless you allow it to be disclosed. Your individual responses will not be reported, only the results of all participants as a group. During the course of this study, your information will be identified by a letter-number combination. Any new information that might develop during the course of the project will be provided to you if that information might affect your willingness to

participate in the project. Pictures of you will be taken only if you sign below where it states: "I am willing to have photographs taken of the inside of my knee for use in presentations or publications."

All information and data collected during this research will be recorded on the appropriate forms and stored in a locked room in the AREF research facility. In addition, all subject data forms, including summary information and spreadsheets, will be scanned and stored in a secure password protected folder on a laptop that only the study investigators will have access to, and will be permanently deleted following publication of any and all manuscripts written as a result of this research. Records related to this study will be retained in a secure location for as long as required by applicable law, but no less than a period of 3 years after the completion of the study. At this time, all records will be properly destroyed.

HIPAA and PROTECTED HEALTH INFORMATION:

We know that information about you and your health is private. We are dedicated to protecting the privacy of that information. Because of this promise, we must get your written authorization (permission) before we may use or disclose your protected health information, also called "PHI," or share it with others for research purposes.

You can decide to sign or not to sign this authorization section. However, if you choose not to sign this authorization, you will not be able to take part in the research study. Whatever choice you make, about this research study will not have an effect on your access to medical care.

The United States government has issued a privacy rule to protect the privacy rights of patients ("Privacy Rule"). This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your health information. This section describes your rights and explains how your health information will be used and disclosed for this study.

During this study, the researchers will need to use personal health information about you. Your personal health information is health information about you that could be used to identify you because it includes information, such as your name, address, telephone number, photograph, date of birth, social security number, new and existing medical records, or the types, dates, and results of various tests and procedures. This may include information in your medical record and information created or collected during the study. By signing this consent, you are agreeing to allow the research personnel to use your personal health information to carry out this study.

By signing this document, you also allow the research staff to disclose your personal health information to outside entities who may be directly involved in completing the study project. The study data that the researchers send to these entities will not include your name, address, or social security number, but instead, will be designated with a code number. However, your medical records can be reviewed or copied at the study site by regulatory authorities or other oversight bodies,

including the Baptist Hospital Institutional Review Board. The purpose of these reviews is to make sure the study is being conducted properly and that the data is being collected correctly, or for other purposes allowed by law.

Your personal health information may no longer be protected by the Privacy Rule once it is disclosed, your personal health information will be kept as confidential as possible under the law; however, absolute confidentiality cannot be guaranteed.

If you cancel this authorization, the researchers will no longer use or disclose your personal health information under the authorization for this study, unless it is needed to preserve the scientific integrity of the study. Information obtained before you cancel this authorization may still be used by the researchers.

COST AND COMPENSATION:

There will be no cost to you for participating and you will not receive any money for participating in this research. In the unlikely event of an emergency, the AREF will provide basic first aid medical treatment. However, if you were to require additional medical care as a result of participating in this study, you would need to contact your personal physician at your own expense.

The Investigators, the employers of the Investigators, and the Research Site does not have programs for compensating subjects for injury or complications related to human subjects' research. Any treatment will be at your expense.

VOLUNTARY PARTICIPATION/WITHDRAWAL:

Taking part in this study is voluntary. Your medical treatment, costs of treatment and eligibility for benefits will not be affected if you decide not to sign this Consent Form or participate in the study. In the event new information becomes available that may affect your willingness to participate in this study, this information will be given to you so that you can make an informed decision about whether or not to continue your participation.

QUESTIONS:

It is your right, as a research participant, to ask questions at any time regarding the procedures involved and any aspects of this study including the potential benefits or risks. For any questions you may have for the researcher, you may contact them at (850) 916-8702.

If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research, you may contact the Baptist Hospital Institutional Review Board* at (850) 469-2227. The IRB will not be able to answer some types of questions, such as questions about appointment times.

*The IRB is a group of individuals who independently review research

STATEMENT OF CONSENT TO PARTICIPATE IN THIS RESEARCH STUDY:
By signing this consent form I agree to and acknowledge the following statements:

I agree to participate as a subject in this study and for my protected health information to be released as described in this consent.
I understand that my participation is completely voluntary, and that I may withdraw at any time without prejudice by sending a written request to the researcher at the Sports Medicine Research Lab, Andrews Research and Education Foundation, 1020 Gulf Breeze Pkwy, Gulf Breeze, FL 32561.
I have read and understand the above information and have been given the opportunity to discuss it and ask questions.
I understand that this authorization does not have an expiration date.
I have received a copy of this authorization form for my records.
I have been informed that I may contact the investigators by phone at (850) 916-8702 in order to answer any questions that I may have at any time during my participation.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

_____
Printed Name of Person Conducting Informed Consent Discussion

_____ _____
Signature of Person Conducting Informed Consent Discussion Date

_____
Printed Name Supervising Investigator

_____ _____
Signature of Supervising Investigator Date

PHOTOGRAPH CONSENT:
Please indicate your preference below with regard to photographs to be taken of you during your participation:

_____ I am willing to have photographs taken of the inside of my knee for use in presentations and/or publications.

_____ _____
Signature of Participant Date