Protocol Title: A Prospective Randomized Trial of Biologic Augmentation with Mesenchymal Stem Cells in patients Undergoing Arthroscopic Rotator Cuff Repair

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RUSH

CONSENT/AUTHORIZATION FOR PARTICIPATION IN A RESEARCH STUDY

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Sponsor(s): Department of Orthopedic Surgery
Rush University Medical Center

Name of Participant: _____

Key Information:

You are being invited to participate in a research study. Research studies answer important questions that might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

Taking part in this research study is voluntary. You do not have to participate in this study and may choose to leave the study at any time. If you decide not to participate in this study or leave the study at a later time, your health care, benefits, or relationship with Rush University Medical Center will not change or be affected.

The purpose of this study is to compare how well patients do after having surgery (arthroscopic rotator cuff repair) if they receive injections of bone marrow versus not receiving injections of bone marrow. The bone marrow that is aspirated, or removed from your body with a needle, is processed by an U.S. Food and Drug Administration (FDA) approved centrifuge system (device used to separate out substances in a liquid).

During surgery, bone marrow can be taken from your body and then processed in a machine to isolate components associated with natural healing of the body. These components of the bone marrow are then injected into your shoulder injury to see if this may help the body repair itself more quickly.

If you agree to participate in this study, your participation may last up to five years from the time

you are enrolled in the study and you will be asked to complete four study visits that will be scheduled on the days of your regular clinic visits at 7-10 days, 1 month, 6 months, and 12 months.

Participants in this study will still undergo routine care as if they were not participants in the study. This includes arthroscopic shoulder surgery (rotator cuff repair), and physical examination at follow-up office visits.

As a subject in this study, during your already planned shoulder surgery, bone marrow may or may not be aspirated (removed with a needle) from your hip, leg or arm bone and re-injected into your injured shoulder. You have an equal chance of being assigned to the group that does or does not receive bone marrow aspirate injection. Being a subject in the study does not guarantee that you will or will not receive this injection. All subjects will have a small incision (cut) on their hip, knee or shoulder whether or not they receive bone marrow. This is necessary to prevent subjects from knowing which group they are in until after the study which could affect the study results.

As part of the study, regardless of whether or not you received the bone marrow aspirate injection, you will be asked to fill out questionnaires that provide information about your shoulder pain, function and overall health before your surgery, at each follow-up visit, and annually for 5 years. You will also undergo an additional MRI one year after surgery for the doctor to evaluate how your shoulder has healed. These additional steps (questionnaires and follow-up MRI) are part of the research study and not part of routine care.

There are risks to you for participating in this study. In this study there are risks associated with conventional arthroscopic rotator cuff repair. The injection of the bone marrow into the shoulder area can cause: bleeding, peripheral nerve injury, muscle weakness, and infection, pain, redness or swelling at the injection site.

The area of the body where the bone marrow is harvested (taken from) may feel sore for a few days. Harvest recipients can usually return to normal routine activities within a couple of days, but it may take weeks before you feel fully recovered. There is a risk of infection related to the bone marrow harvest, but this is typically very low. In addition, there is also a risk of loss of confidentiality if someone other than the investigators obtains your medical information or your identity. For a detailed description of risks you should know about, please see the "What are the risks and discomforts of participating in this study?" section of this consent form.

You may not directly benefit from taking part in this study. Patients who receive bone marrow aspirate injections may experience better healing of their shoulder than patients who do not. The only alternative to participating in this study is not to participate.

<u>Detailed Information</u>: Please review the rest of this document for details about the above topics and additional information you should know before making a decision about whether or not you will participate in this study.

<u>Why are you being invited to participate in this study?</u>
You are being asked to participate in this study because you will be having arthroscopic rotator cuff repair.

How many participants will take part in this study?
Approximately 130 participants are expected to take part in this study at Rush University Medical Center.

What are the activities you will be doing if you participate in this study?
Participants in this study will still undergo routine care as if they were not participants in the study. This includes arthroscopic shoulder surgery (rotator cuff repair), and physical examination at follow-up office visits.

As a subject in this study, during your already planned shoulder surgery, bone marrow may or may not be aspirated (removed with a needle) from your hip, leg or arm bone and reinjected into your injured shoulder. You have an equal chance of being assigned to the group that does or does not receive bone marrow aspirate injection. Being a subject in the study does not guarantee that you will or will not receive this injection. All subjects will have a small incision (cut) on their hip, knee or shoulder whether or not they receive bone marrow. This is necessary to prevent subjects from knowing which group they are in until after the study which could affect the study results.

As part of the study, regardless of whether or not you received the bone marrow aspirate injection, you will be asked to fill out questionnaires that provide information about your shoulder pain, function and overall health before your surgery, at each follow-up visit, and annually for 5 years. You will also undergo an additional MRI one year after surgery for the doctor to evaluate how your shoulder has healed. These additional steps (questionnaires and follow-up MRI) are part of the research study and not part of routine care.

What are the risks and discomforts of participating in this study?

There are risks to you for participating in this study. The risks associated with participation in this study include risks associated with conventional arthroscopic rotator cuff repair.

You will receive a pre-operative x-ray as part of your routine shoulder evaluation, which exposes you to radiation. All persons have a risk up to several percent, depending on age, of developing a cancer (or second cancer) over their lifetime, even if they receive no medical radiation at all. In most cases, your cancer risk after receiving medical radiation is so slightly increased from your natural cancer risk with no medical radiation that the difference is hard to measure.

The injection of the bone marrow into the shoulder area can cause: bleeding, peripheral nerve injury, muscle weakness, and infection, pain, redness or swelling at the injection site.

The area of the body where the bone marrow is harvested (taken from) may feel sore for a few days. Harvest recipients can usually return to normal routine activities within a couple of days, but it may take weeks before you feel fully recovered. There is a risk of infection related to the bone marrow harvest, but this is typically very low.

Questionnaires: Some of the questions on the quality-of-life questionnaires ask the subject to consider areas of their life which, they may not commonly think about. There are no physical

risks from completing the questionnaires, but the questions could cause concern or possibly emotional distress.

Other risks of arthroscopic rotator cuff repair include bleeding, infection, injury to nerves or vessels, stiffness, failure of repair, and persistent (long-term) pain or not obtaining full function of the shoulder. None of these risks are specifically increased if you participate in the study.

There is also a minimal risk of loss of confidentiality of your medical information. Rush University Medical Center and the study staff will take every precaution to ensure that your data is kept secure in encrypted databases and in locked rooms only accessible to study staff.

What are the reproductive risks of participating in this study?

Women

Pregnant women will not be included in this study. All women of childbearing age in the study will be required to use an acceptable form of birth control during study participation. You are responsible for using an effective birth control method such as birth control pills, barrier method (such as condoms or diaphragms), intrauterine device (IUD), hormone implants or surgical sterility while you are taking part in this study. Once you have completed treatment, you may discontinue use of birth control after the completion of the study. If you become pregnant, you must notify the stud doctor immediately. The risks to the embryo of fetus if you become pregnant are currently unknown.

What if there is new information that may affect your decision to participate in this study?
During this study, you will be told about important findings (either good or bad), such as changes in the risks or benefits of participation in the study or new choices to participation that might cause you to change your mind about being in the study. If new information is shared with you, you may be asked to sign a revised consent form in order to continue participating in this study.

Will you receive your individual results from the study?
Generally, activities performed for research purposes are not meant to provide clinical information. We may learn things about you from this study which could be important to your health or treatment. However, we will not share these results with you because this is a randomized research trial and your assignment to either the treatment or control group is known only to the research staff.

Can you leave or be removed from this study?
You have the right to leave a study at any time without penalty. For your safety, however, you should consider the study doctor's advice about how to leave this study. If you leave this study before the final study visit, the study doctor may ask you to complete the final steps.

The researchers and Sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interests;
- You do not follow the instructions;

- The study is cancelled for any reason.

What about confidentiality of your medical information?

This authorization is voluntary. Rush University Medical Center and its affiliates ("Rush") will not withhold or refuse your treatment, payment, enrollment, or eligibility for benefits if you do not sign this authorization. You do not have to sign this authorization, but that means that you cannot be in the study or receive study-related treatment.

By signing this document, you voluntarily authorize (give permission to) Dr. Cole, his study team and other Rush personnel involved with the conduct and review of this study (which may include off-site personnel) to use or disclose (release) health information that identifies you for the study described in this document.

During the study, Dr. Cole and his study team will collect Protected Health Information (PHI) about you for the purposes of this research. PHI is your health information that includes your medical history and new information obtained as a result of this study. Some of this information will come from your medical record. The health information that Rush may use or disclose for this research includes:

- Medical history
- Physical exam information
- Surgical history
- Laboratory test results

Dr. Cole and his study team may share your health information and the results of your study-related procedures and tests with people outside of Rush who assist with the conduct and review of this study. The persons who receive your health information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, but only if permitted by the laws governing them. Your health information described above may be used or disclosed to:

- To the Researchers
- The study Sponsor, Rush Department of Orthopedic Surgery
- Monitoring agencies such as the Food and Drug Administration (FDA), the National Institutes of Health and the Rush Institutional Review Board (IRB).

While you participate in the study you will have access to your medical record, but Dr. Cole is not required to release to you study information that is not part of your medical record. Rush is required by law to protect your health information, and study records that identify you will be kept confidential. The results of study tests/procedures performed as part of this study may become part of your medical record. Any study information in your medical record will be kept indefinitely. Your identity will not be revealed on any report, publication, or at scientific meetings.

You have a right to inspect and copy the information to be disclosed with this authorization and you may obtain a copy of the information by contacting the office listed below.

If you no longer want to be in the study and do not want your future health information to be used, you may change your mind and revoke (take back) this authorization at any time by writing to Dr. Cole at 1611 W. Harrison St, Chicago, IL 60612. If the authorization is revoked, you will

no longer be allowed to participate in the study and previously authorized individuals/entities may still use or disclose health information that they have already obtained about you as necessary to maintain the integrity or reliability of the current study.

This authorization is valid for the entirety of this research study. It will expire upon completion of the study or if you revoke (take back) the authorization.

If you withdraw from this study, the data already collected from you may not be removed from the study records. The study doctor and/or study team may ask you whether they can continue to collect follow-up data on you. If follow-up information will be requested, you will be asked to sign a separate consent form before this information can be collected.

Records of participation in this study will be maintained and kept confidential as required by law.

The Rush Institutional Review Board (IRB) will have access to your files as they pertain to this research study. The IRB is a special committee that reviews new and ongoing human research studies to check that the rules and regulations are followed regarding the protection of the rights and welfare of human participants.

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. This research study can be found by searching for the following Clinical Trial Registry Number (NCT#): 02484950.

What are the costs to participate in this study?

All costs that are part of your usual medical care will be charged to you or your insurance company. You should check with your insurance company before you enroll in this research study. The cost of the follow-up MRI will not be charged to you or to your insurance company and will be paid for by the sponsor.

Will you be paid for your participation in this study?

No monetary compensation will be given to you if you participate.

Your participation in this research study may contribute to the development of commercial products from which the Department of Orthopedics or others may derive economic benefit. You will have no rights to any products, patents or discoveries arising from this research, and you will receive no economic benefit.

What if you are injured as a result of your participation in this study?

If you get ill or injured from being in the study, Rush University Medical Center will help you get medical treatment. You should let the study doctor know right away that you are ill injured. If you believe you have become ill or injured from this study, you should contact Dr. Cole at telephone number 312-432-2817.

You should let any health care provider who treats you know that you are in this study. If you do

seek medical treatment, please take a copy of this document with you because it may help the doctors where you seek treatment to treat you. It will also provide the doctors where you seek treatment with information they may need if they want to contact your study doctor.

You or your health insurance plan will be billed. No money has been set aside to pay the costs of this treatment. Health insurance plans may or may not cover costs of research-related injury or illness. You should check with your insurance company before deciding to participate in this research study. The study staff will assist you in obtaining pre-authorization from your insurance company. Costs not covered by insurance could be substantial.

Rush University Medical Center has no program for financial compensation or other forms of compensation for injuries which, you may incur as a result of participation in this study. By signing this form, you are not giving up any legal rights to seek compensation of injury.

What other information should you know about?
Investigator Financial Disclosure

This research study is supported by a product manufactured by Arthrex, Inc. Dr. Cole (the investigator on the study) receives extra money from Arthrex, Inc. for activities that are not a part of the study. The activities are for consulting, license or royalty and receiving funds for other research projects. It was determined by a conflict committee that the relationship was considered unlikely to affect your safety and/or the scientific quality of the study. This decision was given to the IRB for its review and approval of the study. If you would like more information, please contact Dr. Cole, 312-432-2817.

Who can you contact for more information about this study?
Questions are encouraged. If you have further questions about this study, you may call Carla Edwards, PhD at 312-563-5735 or email her at Carla_edwards@rush.edu.

Who can you contact if you have concerns about your rights as a study participant?
Questions about the rights of research participants may be addressed to the Rush University Medical Center Office of Research Affairs at 1-800-876-0772.

What are your rights as a study participant?
Taking part in this study is voluntary. If you choose not to participate in this study or to leave the study at any time, your health care, benefits or relationship at Rush University Medical Center will not change or be affected. If you choose to leave this study and you do not want any of your information to be used, you must inform Dr. Cole writing at the address on the first page. Dr. Cole may still use your information that was collected prior to your written notice.

SIGNATURE BY THE PARTICIPANT
information given or someone has read it to you. You have had the opportunity to ask questions, which have been answered satisfactorily to you by the study staff. You do not waive any of your legal rights by signing this consent/authorization form. You will be given a signed copy of this document.

Name of Participant	Signature of Participant	Date of Signature

SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:
I attest that all the elements of informed consent described in this consent document have been discussed fully in non-technical terms with the participant. I further attest that all questions asked by the participant were answered to the best of my knowledge.

Signature of Individual Obtaining Consent	Date of Signature

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