RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: Ultrasound Guided Micro-Fragmented Adipose Transfer Graft for Partial Thickness Rotator Cuff Tears, Single-Blind Randomized Controlled Trial

PROTOCOL NO.: **N/A**

SPONSOR: Maryland Stem Cell Research Fund

INVESTIGATORS:

☐
John Ferrell III, MD
11200 Rockville Pike, Suite 230
Northern Bethesda, Maryland, 20852
United States

☐
Sean Mulvaney, MD
116 Defense Highway, Suite 203
Annapolis, Maryland, 21401
United States

STUDY-RELATED PHONE NUMBER(S):

240-301-9200
(786) 271-2157

Taking part in this research is voluntary. You may decide not to participate, or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you have any questions, concerns, or complaints or think this research has hurt you, talk to the research team at the phone number(s) listed in this document.

A person who takes part in a research study is called a research or study participant. In this consent form "you" always refers to the research participant.

CONSENT SUMMARY

You are being asked to participate in this research study because you have a partial thickness rotator cuff tear, and your doctor has recommended an intra-tendinous injection of the shoulder for the treatment of pain and function associated with the partial thickness rotator cuff tear. The Orthobiologics Research Initiative INC. and Maryland Stem Cell Research Fund are conducting a research study to examine the efficacy of micro fragmented adipose tissue, also known as MFAT, to treat partial thickness rotator cuff tears of the shoulder. The purpose of this consent form is to help you decide if you want to participate in the research study.

You should not join this research study until you have read all of the information contained in this consent form, and all of your questions have been answered.

Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn things to help patients in the future.
- The main goal of regular medical care is to help each patient.
- Your participation is voluntary; the decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.
- Parts of this study may involve standard medical care. Standard medical care is the treatment normally given to patients by a physician for a certain condition or illness.
- Other parts of this study may involve experimental (investigational) devices or procedures that are being tested for a certain condition or illness. An investigational device is one that has not been approved by the U.S. Food & Drug Administration (FDA).
- After reading the consent form and having a discussion with the research staff, you should know which parts of the study are experimental and which are standard medical care.
- Your medical records may become part of the research record. If that happens, your medical records may be looked at and/or copied by the sponsor of this study and health authorities or other groups associated with the study.
- Your medical insurance may be billed for any standard medical care you receive during the research study. If your insurance company is billed, they may obtain access to your research records. In certain cases, insurance companies may not pay for treatment that is part of a research study.

VOLUNTARY PARTICIPATION AND WITHDRAWAL
Your participation in this study is voluntary. You may decide not to participate, or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any reason, including:

- if it is advisable for your health and wellbeing
- if you do not consent to continue in the study after being told of changes in the research that may affect you
- if any device malfunction during the procedure takes place which terminates the treatment
- In cases where it is not feasible to reschedule the procedure, subjects will be deemed “early termination”.

If you leave the study before the planned final visit, you may be asked by the study doctor to have some tests or procedures done so that you leave the study safely.

PURPOSE OF THE STUDY
This research study is being done to examine the effect of an injection of MFAT versus corticosteroid injection for the treatment of pain and loss of function associated with your partial thickness rotator cuff tear. About 60 participants will take part in this research.

Adipose tissue, commonly known as fat, has many natural reparative characteristics that help to promote a healing environment throughout the body. Micro fragmented adipose tissue (MFAT) is obtained by extracting fat from the human body and processed using the Lipogems System. The Lipogems System is an adipose tissue technology that is used to harvest, concentrate, and transfer a patient’s own fat for the repair, reconstruction, and replacement of injured or damaged tissue.

MFAT is sometimes used for the treatment of pain in partial thickness rotator cuff tears of the shoulder in patients who have failed to respond well enough to conservative, non-pharmacologic therapy or simple analgesics (e.g., acetaminophen). MFAT is used to provide a viscous tissue scaffold and support to help the natural healing process by supporting the repair, replacement, and reconstruction of damaged or injured tissue in your shoulder. The process of using MFAT via the Lipogems System has not been cleared by the Food and Drug for efficacy but is considered safe for clinical use.

This study is a developmental/feasibility study to determine the clinical use of MFAT for partial thickness rotator cuff tears. We consider this a supplemental treatment option that is not intended to replace current treatments.

The FDA has not approved MFAT for treatment of partial thickness rotator cuff tears. The device kit used in this trial has 510k clearance from the FDA for use in clinical settings. The use of the MFAT via the Lipogems System in this study is investigational.

PROCEDURES AND STUDY DETAILS

Individuals participating in this study will be referred to as participants. If you agree to participate in this study and provide a signed consent form you will be asked to undergo a few initial evaluations to determine if you are eligible to be in the study, this period of evaluation is called the screening period. If it is determined that you are not eligible for participation, you will not lose any medical benefits, and your doctor will continue to treat you.

Once you sign a consent form you will enter screening. During your screening visit(s), you will complete the following assessments:

Screening Visit

Your consent must be obtained prior to completing any study-related assessments. During the screening visit, you will be evaluated for study eligibility based on the eligibility criteria outlined within the protocol. Assessments to be completed at screening include but are not limited to the following:

- Collection of demographics (age at consent, sex at birth, race, and ethnicity)
- Collection of complete medical and surgical history
- Work status
- Collection of concomitant medications
- Physical exam (which will include height, weight, and BMI)
- Urine pregnancy test for females of childbearing potentialCompletion of patient reported outcome measure surveys
- MRI imaging *(If you have not had one recently)*

If you are determined to be eligible for study enrollment, you will be scheduled for a treatment visit. During the treatment visit you will complete the following assessments:

Treatment Visit

- Re-confirmation of subject eligibility
- Work status
- Urine pregnancy test for females of childbearing potential
- Collection of any updates in concomitant medications
- Adverse event collection
- Physical exam and collection of vital signs
- Lipoaspirate and MFAT analysis (removal of fat from your abdomen, flank, or buttocks for evaluation)
- Randomization
- Treatment

Once reconfirmed as eligible, you will undergo a fat tissue harvesting procedure where about 3 tablespoons of fat is harvested from the abdomen, flanks, or buttocks. The collected fat is then gently cleaned and prepared into MFAT via the Lipogems System.

Once the MFAT is processed and injections are prepared, you will be randomized and receive treatment into the affected shoulder. Depending on which group you are assigned to, you will either receive a treatment of MFAT or corticosteroid injected into your affected shoulder. Participants will be randomized 2:1 to receive the investigational MFAT injection which means that twice as many participants will receive MFAT. This means that you have 2 chances out of 3 to receive the MFAT and one chance out of 3 to receive an injection of corticosteroid. If you are randomized to the treatment group you will receive 3mls of MFAT (about 2 teaspoons), and if you are randomized to the control group you will receive 3ml of corticosteroids diluted in normal saline (about 2 teaspoons).

Patients randomized into the MFAT group will receive injection of MFAT into the rotator cuff tear and sham (fake) injection of the subacromial bursa. MFAT group patients will not be able to see which injection they are given. Patients in the CSI group will receive sham (fake) injection into the rotator cuff tear and the CSI injection into the subacromial bursa. The patients in the CSI group will not be able to see which injection they are given.

Once you have received treatment you will be closely monitored and must meet the discharge from care criteria outlined below in order to be released from the treatment facility.

Discharge from Care Criteria*

Participant Status:
Patient alert and oriented to time, place, and person
Pain controlled by analgesics
No nausea/vomiting
Ambulating (walking) without dizziness

***NOTE: If you do not reach the above stated criteria within 4 hours of the completion of the treatment procedure, you will be admitted to the hospital.**

Use of pain medications:

- You must stop taking prescription pain or prescription anti-inflammatory medication for the duration of the study, with the exception of Tramadol during the 72 hours immediately post-injection. You must also abstain from all NSAIDS for 7 days pre-injection and 2 weeks post-injection.
- In addition, you must stop usage of all over-the-counter pain medication (e.g., Acetaminophen or NSAID), for 7 days prior to any follow-up visit, with the exception of one “baby aspirin” per day for cardiovascular therapy or prophylaxis.
- During the study, you can take the following pain medications:
    - Acetaminophen (up to 3,000mg/day)
    - Ibuprofen (up to 1,200mg/day)
    - Meloxicam (Tablets up to 15 mg/day)

Once cleared for release you will be instructed to refrain from high impact overhead activities, lifting, or carrying heavy objects overhead for **at least 4 weeks.** During your follow-up visits the investigator will confirm when you will be cleared to return to activities as normal. While not required, use of a sling for 3-5 days with transition to physical therapy is recommended.

After your treatment visit you will be monitored for 12 months, with follow-up visits at month 12 (and any unscheduled visits). During this visit you will complete the following assessments.

- Collection of any updates in concomitant medications
- Work status
- Physical exam and collection of vital signs
- Adverse event collection
- Completion of patient reported outcome measure surveys
- Repeat MRI of the affected and treated shoulder
- You will not know which group you are assigned to until the study is completed. All participants will be followed using patient reported outcome surveys and MRI imaging so that their outcomes can be monitored and recorded completely.

No matter which group you are randomized to, and even if you stop the study intervention early, we would like to keep track of your health for up to five years after your injection to look at the long-term effects of your participation on this study. We would do this by having someone from this center call you to see how you are doing at least once per year. This may also include requested for patient reported outcome surveys to be completed to quantify your results.

RISKS AND DISCOMFORTS

There are risks, discomforts, and inconveniences associated with any research study that deserve careful thought.

The possible clinical risks associated with MFAT treatment may include, but are not limited to:

- Damage to tissues (e.g., ligaments, meniscus, cartilage, tendons)
- Delayed healing of needle entry points (lipoaspirate and bursal injections)
- Hematoma (clotted blood)
- Catching, locking, or crepitation (crackling sound) of the shoulder joint
- Shoulder stiffness
- Effusion (fluid around the shoulder)
- Inflammation
- Calcification
- Persistent pain, deformity, and/or discomfort
- Ongoing tendon degradation process
- Fat embolism (fat particles released into the blood stream that can potentially block circulation causing decreased oxygen to the heart and/or lungs)

There are also general risks associated to the Lipoaspirate procedure, which are:

- Delayed wound healing at harvest site
- Abdominal cosmetic changes
- Hematoma (clotted blood)

- Seroma (fluid collection)
- Temporary or permanent loss of sensation at the lipoaspiration site

The possible, known risks associated with procedures for shoulder pain include but are not limited to:

Fever	Infection (deep or superficial or systemic)
Chills	Cellulitis (bacterial infection of the skin and tissues underneath the skin)
Apprehension	Tenderness
Infiltration at injection site	Lightheadedness
Nausea	Fainting
Vomiting	Scar tissue formation
Pain	Hematoma (clotted blood)
Redness	Seroma (fluid collection)
Edema	Hemorrhage (excessive bleeding)
Swelling	Blood loss requiring transfusions
Inflammation	Renal (kidney), urinary, or gastrointestinal complications
Itching/rash	Pulmonary embolism (blood clot in lungs)
Bruising	Deep vein thrombosis (DVT) (blood clot in deep vein, typically in the leg)
Hypersensitivity (immune system reaction)	Anesthesia-related complications
Weakness	Temporary or permanent neuropathies (nerve pain)
Spasms	Heart attack
Tightness at the surgical site	Stroke
Wound secretions/drainage	Death

It is important to note that there may also be additional side effects that are not known at this time.

The investigator shall discuss specific risks associated with pregnancy and breastfeeding with all participants who are being considered as study subjects prior to study participation. You will not be allowed to participate in the research if you are pregnant or breastfeeding. If you are a female who can become pregnant, a urine pregnancy test will be done to confirm that you are not pregnant prior to enrollment.

You must use contraception for a minimum of 3 months post procedure.

You must immediately inform the investigator if you or your partner becomes pregnant during the study.

Other Risks
Risks Specific to Women of Child-Bearing Potential:
Women who are pregnant or nursing a child or planning to get pregnant, may not take part in this study. Before entering the study, you and your study doctor must agree on the method of birth control you will use during the entire study. If you think that you have gotten pregnant during the study, you must tell your study doctor immediately. The risks to an embryo or fetus if you become pregnant are currently unknown.

You may be exposed to biohazardous materials during the procedure which may include your own blood, adipose (fat) tissue, or other body fluids. In all cases, the research staff will wear sterile personal protective equipment and prevent contamination of biospecimens collected during the

procedure. You will be draped in sterile procedure covers during the procedure to prevent transfer of biological materials onto unwanted portions of your body.

Risks associated with MRI:
Exposure to radiation can cause harm, such as burning or an increased risk of developing cancer. Most radiation procedures use very small amounts of radiation. The amount of radiation used over the course of this study is small. This is not expected to cause harm. These test amounts are not much different from exposures in usual daily life. However, the exposure risk to radiation is cumulative over a lifetime, and the total should be kept as low as possible.

NEW INFORMATION
If any new information about the Lipogems System or this research study that might change your decision to be in this study becomes known while you are participating in the study your doctor will inform you in a timely manner. You may be asked to sign a new consent form if this occurs.

POTENTIAL BENEFITS
The possible benefits associated with the use of the Lipogems System for you, or future patients, may include but is not limited to:

- Improvement of affected shoulder function
- Reduction in pain of the affected shoulder
- Improvement in quality of the rotator cuff tissue

Your shoulder pain and rotator cuff tear may improve while you are in this study; however, this cannot be guaranteed since this is an investigational study. Your condition may not get better or may get worse during this study. The results of this study may help people with rotator cuff tears in the future. If the symptoms associated with your shoulder pain become so severe you drop out of the study, an option to receive the MFAT injection may be considered.

COSTS
Orthobiologics Research Initiative INC. and Maryland Stem Cell Fund will provide the treatment free of charge during this study. Tests and procedures that are done only for the study will not be billed to you or your insurance company.

You or your insurance company may be billed for:

- Any other standard medical care given during this research study.

You may want to talk with your insurance company about its payment policy for standard medical care given during a research study. If your insurance company does not pay, you may be billed for those charges.

You might have unexpected expenses from being in this study. Ask your study doctor to discuss the costs that will or will not be covered by the sponsor. This discussion should include who will pay the costs of treating possible side effects.

COMPENSATION
There is no compensation available for participation in this study other than a free of charge treatment and a free of charge MRI.

TRAVEL
It is expected for patients to be within traveling distance from the clinical location that this procedure is performed at. This allows patients to utilize appropriate imaging studies, return for follow-up visits, and complete any other required component of the study.

ALTERNATIVE TREATMENT
You do not need to be in this study to receive treatment for your condition. If you decide not to enter this study, there are other choices available for your treatment. These include:

- exercise
- glucosamine and chondroitin supplement use
- corticosteroid injections
- arthroscopic surgical reconstruction of the rotator cuff

Ask the study doctor to discuss these alternatives with you.

Confidentiality
Information from this study will be given to the sponsor. “Sponsor” includes any persons or companies that are contracted by the sponsor to have access to the research information during and after the study.

The information will also be given to the FDA. It may be given to health authorities in other countries where the study Lipogems may be considered for approval. Medical records which identify you and the consent form signed by you will be looked at and/or copied for research or regulatory purposes by:

- the sponsor,
- the FDA,
- Department of Health and Human Services (DHHS) agencies,
- Health authorities in other countries, and
- Institutional Review Board (IRB)/Independent Ethics Committee (IEC)
- Maryland Stem Cell Research Fund (MSCRF)
- Orthobiologics Research Initiative INC.

Absolute confidentiality cannot be guaranteed because of the need to give information to these parties.

DATA COLLECTION AND DATA MANAGEMENT

Participation in this trial will include responding to short surveys asking about your shoulder. You will receive Patient Reported Outcome Measure (PROM) surveys that ask about how painful your shoulder is and how it works for daily activities. These PROMs will allow the research team to determine changes in your pain and function during and after the trial. Only the research team and safety monitoring officials will have access to this data during the trial.

All PROM scores will be collected by a data collection system (PatientIQ). PatientIQ is a cloud-based, secure data collection system used in many research trials, including those run by ORI in the past. You will receive requests to complete PROMs at baseline (before your treatment), and 1-, 3-, 6-, 9-, and 12-months after your treatment. All timepoints must be completed in order for the research team to evaluate your progress and the benefits of both treatments. Each survey will be sent by email invitation or SMS text message to the patient, or completed with a member of the research team if needed due to technological difficulties.

The data collected by PatientIQ may be shared with the following parties:

- the sponsor,
- the FDA,
- DHHS agencies,
- Health authorities in other countries, and
- IRB and IEC
- MSCRF
- Orthobiologics Research Initiative INC.

Additionally, data collected may be published or shared at academic conferences or in presentations. In all cases, patient information will be removed and de-identified to protect your identity. We cannot guarantee that your information will remain confidential.

STUDY RESULTS

The results of this research study may be presented at meetings or in publications. Any time that the results are presented, we will take measures to ensure that the data is presented in a manner that does not disclose your identity.

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.

The Sponsor will ensure that the information provided on this Web site does not ever include any information that can identify you.

COMPENSATION FOR INJURY
If you are injured or get sick as a result of being in this study, call the study doctor immediately. The study doctor will help you receive appropriate medical treatment. Your insurance will be billed for this treatment. If you do not have insurance, you will assume responsibility for any incurred costs. No other payment is routinely available from the study doctor or sponsor, and there is no plan to provide compensation for loss of wages, lost time from work, personal discomfort, or for injuries or problems related to your underlying medical condition(s).

SOURCE OF FUNDING FOR THE STUDY
The sponsors Maryland Stem Cell Research Fund and Orthobiologics Research Initiative are paying the investigator and the research staff for the conduct of this research study.

QUESTIONS
Contact the research team at the phone number(s) listed in this document for any of the following reasons:

- if you have any questions about your participation in this study,
- if you feel you have had a research-related injury or a reaction to the study drug, or
- if you have questions, concerns or complaints about the research.

Do not sign this consent form unless you have had a chance to ask questions and have gotten satisfactory answers.

If you agree to be in this study, you will receive a signed and dated copy of this consent form for your records.

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: JP Faber of the Institute of Regenerative and Cellular Medicine ICRM IRB at (786) 271-2157.

The Institutional Review Board/Independent Ethics Committee is a group of people who independently review research.

The IRB/IEC will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact the IRB/IEC if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

NON-COERCION
If you are an employee or relative of an employee of this research center, you are under no obligation to participate in this study. You may withdraw from the study at any time and for any reason, and your decision to participate in the study, or any decision on your part to withdraw, will not have any effect on your/your family member's performance appraisal or employment at this clinical research center. You may refuse to participate, or you may withdraw from the study at any time without penalty or anyone blaming you or your family member.

Informed Consent Form

STATEMENT OF CONSENT

I have read this consent form (or it has been read to me). All my questions about the study and my part in it have been answered to my satisfaction. I freely consent to be in this research study.

I authorize the release of my medical and research records for the purpose of this study.

I understand that by signing this consent form, I have not given up any of my legal rights.

Your signature below documents your consent to take part in this research:

Signature of Subject	Signature Date (DDMMMYYYY)
Printed Name of Subject	Signature Time (AM/PM)
Signature of Person Obtaining Consent	Signature Date (DDMMMYYYY)
Printed Name of Person Obtaining Consent	Signature Time (AM/PM)

Informed Consent Form