Department of Orthopaedic Surgery
University of Southern California Keck School of Medicine
1200 N. State Street, GNH 3900
Los Angeles, CA 90033

Study Title: Ability of Oral Steroid (Oxandrolone) to Halt Fatty Infiltration and Aid Rotator Cuff Healing: A Double-Blind, Randomized Clinical Trial

Principal Investigator: George F. Hatch III, MD

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

You have been asked to participate as a subject in a medical experiment. Before you decide whether you want to participate in the experimental procedure, you have a right to the following information:

CALIFORNIA LAW REQUIRES THAT YOU MUST BE INFORMED ABOUT:

1. The nature and purpose of the study.
2. The procedures in the study and any drug or device to be used.
3. Discomforts and risks reasonably to be expected from the study.
4. Benefits reasonably to be expected from the study.
5. Alternative procedures, drugs, or devices that might be helpful and their risks and benefits.
6. Availability of medical treatment should complications occur.
7. The opportunity to ask questions about the study or the procedure.
8. The ability to withdraw from the study at any time and discontinue participation without affecting your future care at this institution.
9. Be given a copy of the signed and dated written consent form for the study.
10. The opportunity to consent freely to the study without the use of coercion.

I have carefully read the information contained above and I understand fully my rights as a potential subject in this study.

Date: _____ Time: _____

Signature: _____
(Research Participant)

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INFORMED CONSENT

TITLE: Ability of Oral Steroid (Oxandrolone) to Halt Fatty Infiltration and Aid Rotator Cuff Healing: A Double-Blind, Randomized Clinical Trial

PRINCIPAL INVESTIGATOR: George F. Hatch III, MD

DEPARTMENT: Orthopaedic Surgery

24-HOUR TELEPHONE NUMBER: 1-800-USC-CARE

We invite you to take part in a research study. Please take as much time as you need to read the consent form. You may want to discuss it with your family, friends, or your personal doctor. You may find some of the language difficult to understand. If so, please ask questions. If you decide to participate, you will be asked to sign this form. There is no cost to you for taking part in this study.

WHY IS THIS STUDY BEING DONE?

This study is about healing after a rotator cuff tear repair procedure. We hope to learn if a biologic medication: Oxandrolone, a synthetic derivative of the human hormone Testosterone (the principal male sex hormone and an anabolic steroid) is effective in aiding in the healing process and restoring muscle mass. Oxandrolone is approved by the U. S. Food and Drug Administration (FDA) for malnutrition associated with severe trauma or burns. In this study the use of oxandrolone is experimental.

You are invited as a possible participant because you are between 40 and 75 years of age have had a rotator cuff tear requiring surgery for repair. All participants will be at the University of Southern California (USC).

WHAT IS INVOLVED IN THE STUDY?

This study consists of several parts. Before you begin any of the study activities, you will be asked to sign this Informed Consent Form.

If you decide to take part, this is what will happen:

Upon enrollment in the study your clinic visit will go forward as planned. All pertinent records related to your surgery and clinic visit will be saved in a coded and password-protected database for the purposes of our study. In addition, data recorded at standard of care follow-up visits will be collected from your medical record.

You will visit the Clinical Exercise Research Center (CERC; CHP Building) at USC Health Sciences Campus 7 times during a 2 year study period:

- Prior to surgery at your pre-operative visit
- At 2 weeks, 6 weeks, 12 weeks, 24 weeks, 1 year, and 2 years after surgery

You will also undergo Magnetic Resonance Imaging (MRI) scans without contrast at 12 weeks, 1 year, and 2 years after surgery.

Your physical therapy will be performed at the USC Physical Therapy Associates clinic on the Health Sciences Campus under their supervision or at another center under the supervision of a licensed physical therapist designated by your surgeon. This will be the same rehabilitation program that would be recommended for you to complete whether or not you decide to take part in this study.

You will be randomly assigned to one of two groups (test group or placebo group) by a method similar to flipping a coin. Both groups will receive the same standard-of-care structured rehabilitation after surgery but only one of those groups will receive Oxandrolone. You have a 50% chance of being placed in the group that will receive the study medication, which will be taken 12mg twice a day for males and 6mg twice a day for females for a total of 12 weeks.

If you are not randomized to receive Oxandrolone, you will be placed in the placebo group and will receive a placebo medication, which will look similar to Oxandrolone, but without any active ingredients. The pharmacy will provide all study medications.

You, the research team, and your surgeon will not know which medication you are receiving. In an emergency, the principal investigator can find out which medication you received.

Study Timeline:
You will be tested on multiple occasions. Information will be collected at your visit before surgery, the day of surgery, and at 2 weeks, 6 weeks, 12 weeks, 24 weeks, 1 year, and 2 years after surgery. Surgery will be performed by your Orthopaedic surgeon. Physical therapy will follow a pre-defined protocol with a licensed physical therapist. Physical function testing and questionnaires will take place at USC or CERC. MRI scans will be performed at USC.

The following timeline provides the dates involved in the study and what will be done on those days. You will also be responsible for attending physical therapy outside of this study.

Schedule of Events

Event	**Pre-Procedure**	**Procedure Day**	**Post-Operative Week**					
			2	**6**	**12**	**24**	**52**	**104**
Informed Consent	x							
Demographics	x							
Confirm Inclusion/Exclusion Criteria	x	x						
Medical History	x	x						
Physical Examination – Range of Motion	x	x	x	x	x	x	x	x
Vital Signs	x	x	x	x	x	x	x	x

Randomization		x						
MRI	x				x		x	x
Body Composition	x		x	x	x	x	x	x
Questionnaires (ASES, VAS, PASS)	x	x	x	x	x	x	x	x
Shoulder Strength - Hand Dynamometer	x	x	x	x	x	x	x	x
Testosterone level and Oxandrolone level	x		x			x		
Lab Draw (Liver Enzymes)	x		x			x	x	x

Blood Draw
Blood will be collected to monitor any adverse effects on your health and to assess study drug levels.

Body Composition Testing by Bioelectrical Impedance
The Biospace InBody 530 device measure body composition as you stand on a scale-like device while grasping two handles; one in each hand. The device works by sending a very low-voltage electric signal through your body to determine water content, body fat percentage, and lean (muscle) mass. The voltage is so low that you cannot feel it. This test takes about two minutes.

Physical Function Tests
Before surgery, on the day of surgery, and at 2 weeks, 6 weeks, 12 weeks, 24 weeks, 1 year, and 2 years after surgery tests of maximal muscle strength of your shoulder will be performed with a handheld dynamometer, a device used to measure strength.

Questionnaires
You will be asked to complete the American Shoulder and Elbow Surgeons Shoulder Score (ASES), Visual Analog Scale (VAS) for pain, and Patient Acceptable Symptom State (PASS) questionnaires in order to help gauge outcome.

Orthopaedic Surgery
Surgery will be performed by your Orthopaedic surgeon.

Physical Therapy
Rehabilitation will follow a standard guideline under the supervision of a licensed physical therapist and your doctor.

Pregnancy and Breast Feeding
The drug used in this study is unsafe for unborn babies. Women who are pregnant or nursing a child may not take part in this study. If you are breastfeeding and do not want to stop, you may not take part in this study. If you are a woman who could become pregnant, you must have a pregnancy test to make sure you are not pregnant before entering the study.

Additionally, you and your doctor must agree on the method of birth control you will use during the entire study and 6 weeks after completing treatment with Oxandrolone. Medically acceptable contraceptives include hormonal contraceptives (birth control pills, patches, implants, rings, or injections), barrier methods (such as a condom or diaphragm) used with a spermicide, an intrauterine device (IUD), or surgical sterilization (hysterectomy or tubal ligation for women, vasectomy for men).

If you think that you have gotten pregnant during this study, contact your doctor immediately. If you are pregnant, you will be removed from the study.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

MRI without contrast

MRI is a painless procedure that only requires that you lie quietly on a padded table that gently glides you into the magnet. While the scanner is performing your scan, you will hear some humming and thumping sounds which are normal. If you are prone to claustrophobia (fear of enclosed spaces) you should notify the technologist. Because of the magnetic field and radio frequencies, people with a heart pacemaker, brain aneurysm clips, and some implanted metallic or electrical devices should not have an MRI. It is important that you inform the technologist if you have any of these metallic appliances.

Oxandrolone

Although this study involves a relatively short course of Oxandrolone, it may still have unwanted effects on your body.

IMPORTANT WARNING:

Medications similar to oxandrolone may have caused damage to the liver or spleen (a small organ just below the ribs) and tumors in the liver. Tell your doctor if you drink or have ever drunk large amounts of alcohol or used street drugs and if you have or have ever had liver disease. Tell your doctor and pharmacist if you are taking any of the following medications or herbal products: acetaminophen (Tylenol, others), cholesterol lowering medications (statins), comfrey tea, iron products, isoniazid (INH, Nydrazid), kava, methotrexate (Rheumatrex), niacin (nicotinic acid), or rifampin (Rifadin, Rimactane).

If you experience any of the following symptoms, call your doctor immediately: upset stomach; extreme tiredness; unusual bruising or bleeding; lack of energy; loss of appetite; pain in the upper right part of the stomach; yellowing of the skin or eyes; flu-like symptoms; pale, cool, or clammy skin; extreme thirst; fast but weak pulse; vomiting; or fast shallow breathing.

Oxandrolone may increase the amount of low density lipoprotein (LDL; 'bad cholesterol') and decrease the amount of high density lipoprotein (HDL; 'good cholesterol') in your blood. This may increase your risk of developing heart disease. Tell your doctor if you or anyone in your family has or has ever had high cholesterol, heart disease, a heart attack, chest pain, or a stroke. Also tell your doctor if you smoke or have ever smoked and if you have high blood pressure or diabetes.

Keep all appointments with your doctor and the laboratory. Your doctor will order certain tests to check your body's response to oxandrolone. Oxandrolone may damage the liver or increase LDL without causing symptoms. It is important to have regular laboratory tests to be sure that the liver is working properly and that LDL has not increased.

Talk to your doctor about the risks of taking oxandrolone.

Oxandrolone may cause side effects. Tell your doctor if any of these symptoms are severe or do not go away:

- difficulty falling asleep or staying asleep
- depression
- nervousness or unusual excitement
- changes in sex drive or ability
- constipation

Some side effects can be serious. The following symptoms are uncommon, but if you experience any of them or those listed in the IMPORTANT WARNING section, call your doctor immediately. Some of these side effects may never go away if they are not treated immediately:

- swelling of the arms, hands, feet, ankles or lower legs
- new or worsening acne
- deepening of voice, increase in facial hair, baldness, and changes in genital structures in women
- abnormal menstrual periods
- enlarged penis or erections that come too often or do not go away
- pain, swelling, or decreased size of testes
- enlarged breasts
- frequent, difficult, or painful urination
- bone pain
- slowed heartbeat
- pain on your side (between your stomach and back)
- confusion
- extreme thirst

- muscle twitches or weakness
- tingling in arms or legs
- weakness or heaviness in legs
- changes in skin color

Oxandrolone may decrease fertility in men. Talk to your doctor if your partner plans to become pregnant while you are taking oxandrolone.

Tell the physician or get medical help right away if you have any of the following symptoms that may be related to a very bad side effect:

- Signs of an allergic reaction, like rash; hives; itching; red, swollen, blistered, or peeling skin with or without fever; wheezing; tightness in the chest or throat; trouble breathing or talking; unusual hoarseness; or swelling of the mouth, face, lips, tongue, or throat.
- Erections (hard penis) that happen often or last a long time.
- Pimples (acne).
- Not able to pass urine or change in how much urine is passed.
- Muscle weakness.
- Very nervous and excitable.
- Any unexplained bruising or bleeding.
- Shortness of breath, a big weight gain, or swelling in the arms or legs.

Tell the physician or get medical help if any of these side effects or any other side effects bother you or do not go away:

- Nervous and excitable.
- Not able to sleep.
- Change in sex ability.

<u>BIA devices</u>
There are no known side effects of bioelectrical impedance.

<u>Physical Function Testing and Range of Motion</u>
These tests may be uncomfortable to perform.

<u>Rehabilitation</u>
These steps will be supervised by your physical therapist but may feel difficult or uncomfortable.

<u>Blood Draws</u>
There is a risk of temporary discomfort from the needle stick, bruising, bleeding, and soreness at the blood draw site. Rarely, and infection or fainting can occur.

<u>Questionnaires</u>
Some of the questions may make you feel uneasy or embarrassed. You can choose to

skip or stop answering any questions that make you uncomfortable.

Breach of Confidentiality
There is a small risk that people who are not connected with this study will learn your identity or your personal information.

WILL YOUR INFORMATION BE KEPT PRIVATE?
We will keep your records for this study confidential as far as permitted by law. However, if we are required to do so by law, we will disclose confidential information about you. The University of Southern California's Institutional Review Board (IRB) may review your records. The IRB is a research review board that is made up of professionals and community members who review and monitor research studies to protect the rights and welfare of research participants. We may publish the information from this study in journals or present it at meetings. If we do, we will not use your name.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by US 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.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS STUDY?
You may not receive any direct benefit from taking part in this study. Your participation in this study may contribute to the development of optimal treatment for rotator cuff tears and evaluate the potential use of Oxandrolone as an adjunct therapy in surgical recovery.

WHAT OTHER OPTIONS ARE THERE?
An alternative would be not to take part in this study, and continue with your current care.

WHAT ARE THE COSTS?
The medication will be provided free of charge while you are participating in this study.

Some tests and procedures are done only because of the research. The study will pay for tests and procedures that are done only because you are in this study. The medication will be provided free of charge while you are participating in this study.

Some tests and procedures are done for your routine health care, and you would receive them even if you were not participating in this study. You and/or your health plan/insurance will be billed for the tests and procedures you need for routine health care while you are in this study. You will be billed in the same way as if you were not in a study. You will be responsible for any co-payments and deductibles required by your insurance. Some health plans/insurance companies will not pay these costs for people taking part in studies. Check with your health plan/insurance company to find out what

the will pay for.

If you have any questions about which tests or procedures will be billed to you and/or your health plan/insurance, ask the study doctor.

WHAT HAPPENS IF YOU GET INJURED OR NEED EMERGENCY CARE?

It is important that you tell the study doctor, George Hatch III, MD, if you feel that you have been injured because of taking part in this study. You can tell the physician in person or call at (323) 442-5860.

If you think you have been hurt by taking part in this study, tell the study doctor immediately. If you require treatment because you were injured from participating in this study, treatment will be provided. You and/or your health plan/insurance will be billed for this treatment. The study sponsor will not pay for this treatment.

There are no plans to offer any type of payment for injury. However, by signing this form you have not given up any of your legal rights.

WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?

During the study, we may learn new things about the risks or benefits of being in the study. If we do, we will share this information with you. You are free to change your mind about being in the study based on this information.

WHAT ARE YOUR RIGHTS AS A PARTICIPANT, AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE?

Your participation in this study is voluntary. Your decision whether or not to take part will not affect your current or future care at this institution. You are not giving up any legal claims or rights. If you do decide to take part in this study, you are free to change your mind and stop being in the study at any time. If the withdrawal must be gradual for safety reasons, the investigator will tell you.

CAN YOU BE REMOVED FROM THE STUDY?

You may be removed from this study without your consent for any of the following reasons; 1) you do not follow the investigator's instructions; 2) at the discretion of the investigator; 3) you injury gets worse; 4) the investigator closes the study. If this happens, the investigator will discuss other options with you.

WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

You may contact George F. Hatch, III M.D. at (323) 442-5860 with any questions, concerns, or complaints about the research or your participation in this study. If you feel you have been hurt by taking part in this study, please contact George F. Hatch, III M.D. at (323) 442-5860. If you have questions, concerns, or complaints about the research and are unable to contact the research team, contact the Institutional Review Board (IRB) Office at 323-223-2340 between the hours of 8:00 AM and 4:00 PM, Monday to

Friday. (Fax: 323-224-8389 or email at irb@usc.edu).

If you have any questions about your rights as a research participant, or want to talk to someone independent of the research team, you may contact the Institutional Review Board Office at the numbers above or write to the Health Sciences Institutional Review Board at LAC+USC Medical Center, General Hospital Suite 4700, 1200 North State Street, Los Angeles, CA 90033.

You will get a copy of this consent form.

AGREEMENT:

I have read (or someone has read to me) the information provided above. I have been given a chance to ask questions. All my questions have been answered. By signing this form, I am agreeing to take part in this study.

Name of Research Participant	Signature	Date Signed (and Time)

Name of Witness	Signature	Date Signed

I have personally explained the research to the research participant and answered all questions. I believe that he/she understands the information described in this informed consent and freely consents to participate.

Name of Person Obtaining Informed Consent	Signature	Date Signed (and Time)