Consent Form for Clinical Trials Study Title: "Lumbar Spine Muscle Degeneration Inhibits Rehabilitation-Induced Muscle Recovery
NCT: 03442374

University of California, San Diego
Consent to Act as a Research Subject

"Measurement of human spine muscle gene expression during open and minimally invasive spinal surgery"

Surgery and Exercise Group

Dr. R. Todd Allen, M.D., Ph.D. and associates are conducting a research study to find out more about the muscles in your neck and back before and after surgery. A total of approximately 140 participants will be enrolled at UCSD. Subjects will be enrolled into three groups. Of the 140 subjects, 80 subjects will be enrolled in the 'surgery and exercise' group, 40 subjects will be enrolled in the 'surgery and exercise' group, and 20 subjects will be enrolled in the 'non-surgical' group. The purpose of this study is to gather information about back muscles before and after surgery in order to help better understand what happens to skeletal muscles after spinal surgery and to study the effect of exercise on muscle structure and strength. This may assist in developing ways to minimize muscle damage during surgery, and determining the benefit of exercise, if any. You are being asked to participate in this study because you are a patient in a spine clinic, can tolerate a bout of exercise, and have been indicated for a spinal surgery for the first time or a revision surgery that allows us to look closely at your muscles during the scheduled operation. Research procedures may involve bouts of exercise, collection of information about back muscles through data collection, MRI (magnetic resonance imaging), laser diffraction (we will use light to measure the length of proteins in your muscle) and a muscle biopsy (removal and examination of muscle tissue) from people who will have back surgery. The laser used in this study has not been approved by the Food and Drug Administration (FDA) specifically for this use. It is considered an experimental device because it is being used explicitly for research purposes and its use is not part of your treatment. However, it is of such a low intensity (4.2mW) that it will not cause tissue injury.

Study Procedures
If you choose to participate in this study, the following will happen to you:

Data Collection:
Data about your demographics (age, sex, weight, height), medical history, surgical history, previous x-rays, MRIs, CTs etc. may be collected for research purposes. No information that could personally identify you will be maintained in our research records. You will be assigned a unique study identifier and this will be used to label your research records. This part will be done by the study team and will not require any time commitment from you. If you are from a non-UCSD institution, you may be asked to provide a HIPAA release form so that we may contact your clinic and request this information.

Pre-Operative Research MRI:

After signing the consent form, you may be contacted by a member of the research staff to schedule a Research MRI prior to your surgery. A MRI is a medical imaging technique that is used to image internal structures of the body, and is usually performed prior to surgery as part of standard of care. It does not use radiation, like a standard X-ray or CT scan. Upon arrival you will be asked to fill out some questions regarding your basic health, background history, history and symptoms of back pain and whether you have any metal objects in your body (standard MRI screening form). Following this you will be placed in the MRI scanner for your supine (lying on your back) MRI scan. This will take approximately 60 minutes to complete. This MRI is for research purposes only. It will not be used for any clinical screening or information purposes.

You may be asked to complete questionnaires before undergoing surgery, and 6-months after your surgery. These questionnaires take about 15 minutes to complete, have been designed to obtain information about you and your back condition, and how this condition has affected your daily life. Your study doctor may also complete a questionnaire designed to obtain detailed information about your medical condition before surgery, and the treatment he will perform.

Pre-Operative Exercise:
About 4-24 hours before your surgery, you will be asked to undergo a bout of exercise using a 'dynamometer'. A dynamometer is a device that can measure muscle strength and power by resisting the force you apply and controlling the speed of exercise at a re-selected rate. The dynamometer can instantly detect any change from the pre-selected speed and will increase or decrease its resistance to maintain the same speed. To test spinal muscle strength, you will be asked to bend forward or push backward with your torso (chest region) while strapped to the device (Figure 1). Dynamometers are routinely used in physical therapy for patients with back pain to provide conservative therapy before surgery.

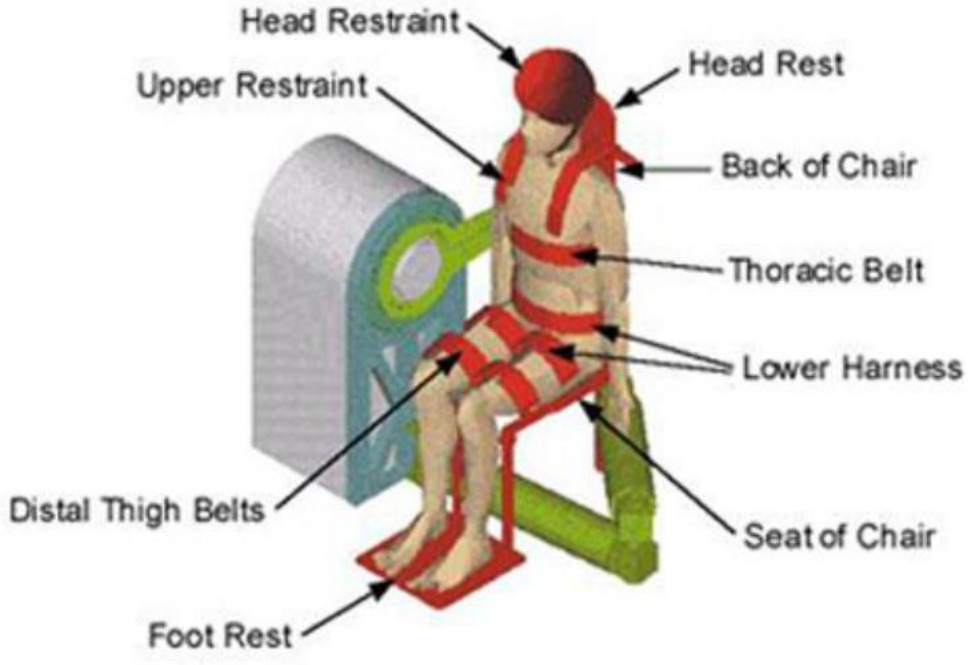

Figure1: Schematic of a Dynamometer to measure muscle strength and power

You will be asked to sit in the dynamometer chair. Straps may be tied around your chest, hips, thighs, and/or calves to stabilize you in the chair, and ensure that you primarily use your back muscles during the activity. To calibrate the system and determine your maximum strength, you will be asked to push against the backrest of the chair with as much force as you can comfortably produce. This may be done two or three times for accuracy. Once calibrated, the device will be set to provide resistance in the 60-80% range of your maximum strength. Speed of the exercise will be controlled at the rate of 5 seconds/rep. The device will be set such that all reps are performed within a range of motion that is comfortable to you. Additionally, you will be asked to target an exertion level ranging from 'very, very light' to 'very light'. You will be asked to complete 20 reps. One rep involves pushing against the backrest of the chair backwards, and then returning back to the original position. This portion of the study is expected to require about 30 minutes of your time.

On the day of your scheduled surgery, you will be admitted to the hospital per your surgical plan. If you choose to participate in this research study, your participation will be for the duration of your pre-surgical procedures (MRI + exercise + questionnaires ~105 minutes), surgery and post-surgical procedures (MRI + exercise + questionnaires~105 minutes) 6-months after the surgery. All tests and procedures except those which involve the research MRI, exercises, biopsy and laser measurement at the time of surgery are part of your normal medical care.

In the traditional open approach to spinal surgery, the back muscles are stripped away from the bones and held out of the ay by retractors (handheld instruments like flat hooks). When less invasive surgery is performed, the muscle is often split and a tubular retractor is used. Depending upon your surgeon's medical opinion, your surgery may involve either the traditional open approach or the minimally invasive approach. In either case, use of retractors allows the surgeon to see the entire area of the spine he is operating on. During this time, measurement of your back muscles will be performed by using laser diffraction. It is to help us measure the length of muscle proteins. This procedure of measurement using laser diffraction is not standard of care and is study related.

This study will also involve removing a small amount of muscle and fat tissue at two different time points during your surgery. The first sample will be biopsied (muscle and fat tissue will be removed and examined) at the beginning of the procedure. Approximately 100mg (size of pencil eraser) will be biopsied by your surgeon. The second sample of muscle and fat will be taken at the end of the procedure. The material for the second sample will be taken from tissue damaged by the retractors. Typically, the volume of this damaged tissue, which is anyway removed before closing the wound as part of standard of care, is approximately 300-500mg. Approximately 100mg of this muscle and fat tissue will be collected and used for the second sample. This will represent tissue that has been fully dissected and retracted during the standard operation. The tissue samples collected will be immediately frozen to avoid degradation and transported to the UCSD Skeletal Muscle Physiology Laboratory where a member of the research team will complete the examination of the muscle and fat tissues. The tissue sample collected will be used to find out more information on normal and post-operative muscles in patients undergoing spinal surgery. Collection of the tissues is not standard of care and is being performed as part of the study.

Post-Operative Research MRI:
About 6-months after your surgery, you will be asked to return for another research MRI of your back. The procedure used for your pre-operative MRI will be observed for the post-operative MRI as well. This procedure is expected to last for about 60 minutes.

Post-Operative Exercise:
About 6-months after your surgery, you will be asked to undergo another bout of exercise using the dynamometer. The procedure used for the pre-operative exercise will be observed for the post-operative exercise as well. This procedure is expected to last for about 30 minutes.

All visit procedures have been summarized in the table below:

Pre-Operative Questionnaires	15 minutes
Pre-operative MRI	60 minutes
Pre-operative Exercise	30 minutes
Biopsy during surgery	--
6-months Post-operative questionnaires	15 minutes
6-months Post-operative MRI	60 minutes
6-months Post-operative exercise	30 minutes

Analysis of Muscle and Fat Tissues and the Risks
By consenting to be a part of this study, the muscle and fat tissue that will be collected from your back will be studied. The microscopic structure of your tissue, as well as its DNA (the genetic material inside your cells) will be evaluated by Dr. Allen, the Principal Investigator, and other members of the research team to learn more about what happens to your back muscles before and after surgery. The specimens will be de-identified (your personal information will not be used to label the specimens) as soon as they are taken. In addition to Dr. Allen, your tissue structure and DNA may also be studied by Dr. Vinko Zlomislic, Dr. Samuel Ward, Dr. Steven Garfin, Dr. Yu-Po Lee, Dr. Bahar Shahidi, and/or Shannon Bremner. Dr. Allen will be responsible for deciding how your DNA will be used. Your muscle may also be used in additional research to be conducted by Dr. Allen and associates. Dr. Allen and associates will be responsible for deciding how it will be used. This genetic information and its derivatives may have significant therapeutic or commercial value. You consent to such uses. The specimens collected from you and the DNA that they contain will be used only for this study. If you decide later that you do not want the specimens collected from you to be used for research, you may tell this to Dr. Allen, who will use his best efforts to stop the use of your DNA for research. However, if analysis of your DNA has already begun, it may be necessary to retain your DNA for the duration of this study. Dr. Allen, his associates, or his successors in this study will keep your DNA specimen long enough to analyze it. The Information derived from your DNA specimen will be kept for up to 50 years. There will be no direct benefit to you from this study wince you will not be provided with any results or information regarding your DNA test. The research team; however, we may learn more about what happens to back muscles before and after surgery. No one else will have access to the DNA sample in the future and the scientists from this study will not use your DNA sample for any other purposes.

Risks of Genetic Testing
Participation in this study does not mean that you have had genetic testing. Genetic testing means having a test performed and the results provided to you and your doctor. If you are interested in having genetic testing performed, you should consult your doctor, as some commercial tests are available. Your doctor can provide you with the necessary information to determine if such a test would be appropriate to you. Also please be aware that there is no absolute legal protection against discrimination on the basis of genetic information. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. Although we are not able to know all of the risks from using genetic information, we believe the risks to you are very low, because your samples will be coded. Research results will not be returned to you or your doctor. Very rarely health or genetic information could be misused by employers, insurance companies, and others. A federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. If you want to learn more about GINA, you can find information about it on the internet or ask the study staff.

Women of Child Bearing Potential
If you are a female and capable of child-bearing, a sample of urine or blood will be collected before the study is begun in order to be as sure as possible that you are not pregnant. It is important to be sure as possible that you are pregnant, since the x-rays may cause harm to an unborn child. This procedure is routinely performed in all such patients who are undergoing spinal surgery and is not part of the study.

Confidentiality
Research records will be kept confidential to the extent allowed by law. If you agree to participate in this research, identifiable health information about you will be shared with and used by members of the research team. For you to be in in this research we need your permission to collect and share this information. Federal law protects your right to privacy concerning this information.

Individually identifiable health information under the federal privacy law is considered to be any information obtained from this study, that can be associated with you, and relates to your past, present, or future physical or mental health or condition. This is referred to as protected health information.

Your protected health information will be kept confidential. Your identity will not be revealed in any publication or presentation of the results of this research.

Who Will Have Access to Study Information
The investigators and their staff will have access to your medical records and study documentation. In addition to the investigators and their staff, the UCSD Institutional Review Board (IRB), and other applicable regulatory bodies have the right to review your study records.

Potential Risks
Participation in this study may involve some added risks or discomforts. These include:

- MRI: There are no known adverse effects from exposure to magnetic fields. However, the imager makes a loud, banging noise while it is taking pictures. Ear plugs will be provided to you to protect against the loud banging noise of the machine. You may feel claustrophobic or as though you need to get out of a small space during imaging. You may become anxious. You may experience some discomfort and fatigue from lying still in a confined space during imaging. If this happens to you, you can stop the procedure at any time. If you have any metal clips or plates in your body or a pacemaker, you should tell the investigator about it. MRI may not be appropriate under certain conditions: A cardiac pacemaker; metal fragments in eyes, skin, body; heart valve replacement, brain clips, venous umbrella; being a sheet-metal worker or welder; aneurysm surgery, intracranial bypass, renal aortic clips; prosthetic devices such as middle ear, eye, joint or penile implants, joint replacements; hearing aid, neurostimulator, insulin pump; shunts/stents, metal mesh/coil implants; metal plate/pin/screws/wires, or any other metal implants; permanent eyeliner, eyebrows. The MRI procedures should take approximately 60 minutes.
- Exercise: The exercise protocol described above is routinely used by physical therapists for conservative therapy for spine patients. Risks will be minimized by ensuring that the exercise protocol is administered by a certified physical therapist or exercise physiologist. Potential risks of this procedure include fatigue, increased pain in the back, and soreness. At any time if you experience any of these, please inform the physical therapist or exercise physiologist and they will work with you to manage your condition per standard of care protocol.
- Participation in research involves a risk of loss of confidentiality. Your research records will be handled as confidentially as is possible within the law. In order to verify the study data, the UCSD Institutional Review Board (IRB) may review some specific records, including yours. No individual identities (such as names) will be used in any reports or publications resulting from this study. If you consent to participate in this research, you understand that every effort will be made to keep your information private and that absolute confidentiality is not a guarantee. Your personal information may be disclosed, if required by law. The IRB may look at and/or copy your research records and other medical records for quality assurance and data analysis.
- During surgery, the added time the wound is open may cause increased risk of infection and/or anesthetic complications. However, because the overall surgical time of typical spinal surgery lasts about 6 hours, the increased risks of adding 10 minutes to the operative time is minimal.
- The small biopsy taken from the muscle of interest at the beginning of the surgery adds a small risk of additional bleeding – approximately 1-2cc (about 2-4 drops of blood). This is a research procedure.
- There is a small risk of bleeding when the tissue is collected at the end of surgery (second sample). However, this risk may occur even if you were not part of the study as the tissue from which we obtain the biopsy would be removed by your surgeon anyway as part of standard procedure. For research purposes, a small amount of tissue sample (about a teaspoon) will be collected).

Unforeseeable and/or unknown risks/discomforts may occur as a result of your participation in this study. You have been told that every effort will be made to ensure that these hazards are avoided; and that the medical personnel conducting the study are well trained in the non-investigational procedures. You will be informed of any significant new findings.

Precaution Taken to Minimize Risks

The following will be performed to minimize the risks of these procedures:

- Standard screening procedures will be performed prior to the MRI scan to minimize risks.
- Exercise will be administered by a trained and certified physical therapist or exercise physiologist.
- Standard operating room procedures will be performed to minimize risks, including use of standard anesthetics, medical history screening for risks, medical history screening for potential allergies to anesthetic agents, standard sterile surgical technique and wound management.
- If complications do arise (such as infection), these will be dealt with in a timely manner to assure your maximal safety.
- Muscle and fat tissue biopsy (removal and examination of muscle and fat tissue) sites will be inspected for bleeding before closure of the incision (cut).
- Research Records, medical records, and other identifiable health information about you will be handled as confidentially as is possible within the law. The investigators will keep their own private files, under lock. Any identifiable patient information will be stored ina locked cabinet in the department of orthopaedic surgery office and will only be accessible to the investigator and his research team.
- Only de-identified information will be disclosed. Study reports presented at scientific forums and publications will be presented without any patient identification.

Potential Benefits
There is no direct benefit to you from participating in this study. You may be helping the investigator to capture information about muscles before and after surgery that may potentially benefit future patient undergoing the similar surgical procedures.

Costs Associated with Participating in this Study
You will not incur any additional costs as a participant in this clinical study beyond those normally associated with your surgery and follow-up visits.

Compensation Associated with Participating in this Study
You will receive $100 in gift cards as compensation for completing the pre-op and post-op visit each. Thus, the total compensation for this study would be no more than $200. You will not be compensated for visits that you miss.

Research Related Injury
If you are injured as a direct result of participation in this research, the University of California will provide any medical care you need to treat those injuries. The University will not provide

any other form of compensation to you if you are injured. You may call the UCSD Human Research Protections Program office at (858) 246-4777 for more information about this, or to inquire about your rights as a research subject, or to report research-related problems.

Alternatives to Participating in this Study
The alternatives to participation in this study are not participating in the study at all. You will still receive the same treatment and care to which you are entitled.

Consent to use DNA data/Moore Clause
The specimens collected from you and the DNA that they contain may also be used in additional research to be conducted by the University of California personnel collaborating in this research. These specimens, DNA, and their derivatives may have significant therapeutic or commercial value. The PI will be responsible for deciding how it will be used and you consent to such uses.

Voluntary Participation
Taking part in this study is entirely voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. Any new information that may affect your health, welfare or willingness to participate will be made available to you.

Withdrawal from the Study
You may be withdrawn from the study for the following reasons: (1) your surgeon has decided you need an alternative treatment; (2) the principal investigator has decided to discontinue the study; (3) your surgeon/clinician believes that it is in your best medical interest. You may also be withdrawn from the study if you do not follow the instructions given you by the study personnel. If you decide that you no longer wish to continue in this study, you will be required to inform your surgeon.

Patient's Consent
Dr. R. Todd Allen, or _____ has explained this study to you and answered your questions. This study and the informed consent have been explained to you and your questions have been answered. You are free to ask whatever questions you have at any time. Your participation in this study is voluntary. You have been informed of the purpose, methods, risks, and benefits of the research study. You are not aware of any medical condition that you have which would render your participation unsafe. You consent to the release of your medical records to the investigators, their staff, and the institutional review board (IRB), but only to be used by these parties in connection with carrying out their obligation relating to this research study or as required by law. You voluntarily give your consent to participate. You will receive a copy of the signed consent form to keep for future reference. By signing this consent form, you have not waived any of the legal rights, which you would otherwise have as a participant in a research study. For information/questions or in the event of research related injury regarding the stud, you should contact Dr. R. Todd Allen at 619-985-389.1

You have received a copy of this consent document and a copy of the Experimental Subject's Bill of Rights to keep. You agree to participate.

_____ _____
SIGNATURE of Subject Date

_____
PRINTED Name of Subject

_____ _____
SIGNATURE of Person Obtaining Consent Date

_____
PRINTED NAME of Person Obtaining Consent