

Study Protocol and Statistical Analysis Plan
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UNIVERSITY of PITTSBURGH

Department of Plastic and Reconstructive Surgery

J. Peter Rubin, MD
University Center Suite 225
UPMC Center for
Innovation in Restorative Medicine
120 Lytton Ave
Pittsburgh, PA 15213
(412) 383-8080
(412) 864-2673 (fax)

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: "Adipose Stromal Cell Enriched Autologous Fat Grafting for Treating Pain at Amputation Sites: A Prospective Randomized Trial"

Research Project Director:	J. Peter Rubin, M.D., Founding Chair Department of Plastic Surgery Professor of Surgery at the University of Pittsburgh School of Medicine University Center 120 Lytton Ave. Suite 225, Pittsburgh, PA 15213; 412.383.8080	
Other Key Research Team Members:	Albert Donnenberg, PhD	Rory Cooper, PhD
	Kacey Marra, PhD	Ian Valerio, MD
	Vera Svobodova Donnenberg, PhD	Annmarie Kelleher, MS, OTR/L, ATP, CCRC
	Carroll Lee, BSN, RN	Sara Peterson, MBA
	Ryan Mitchell, MD	Jeff Gusenoff, MD
	Gretchen Haas, PhD	Patsy Simon, RN, BS, CCRC
	Megan Hendricks, BA, RN	Elizabeth Radomsky, PhD
	Diana Mermon, MS	Peter Adams, BS
	Jacqueline Bliley, BS	Jenelle Mock, BSN, RN
	Brenda Pecora, MS	Wendy Wakefield, CRNP
	Mara Yerk, BS	

Clinical Research Coordinator: Carroll Lee, BSN, RN
412-864-2585

Source of Support: Department of Defense Contract



Conflict of Interest Statement: Dr. Sydney Coleman, a Co-Investigator for this trial is the inventor of the Coleman Cannula System which is being used in the Fat grafting procedure. He has a financial interest in the Coleman Cannula System and receives royalties from this product. Dr. Rubin, the Principal Investigator has addressed this potential conflict of interest (COI) with a standard conflict of interest management plan and will actively monitor this plan during the conduct of the trial. This project has been carefully reviewed to ensure that your well-being holds more importance than any study results. Any questions you about this will be answered fully by Dr. Rubin (412-383-8080) or by the Human Subject Protection Advocate of the University of Pittsburgh (866-212-2668).

Why is this research being done?

We are conducting a clinical trial to assess how minimally invasive fat grafting (a common cosmetic and reconstructive procedure) affects pain at amputation sites. Fat grafting is a procedure in which a person's own fat is taken from areas throughout the body, usually the thighs or abdomen, with a small liposuction tube. The fat is then transferred into the amputation site. The research study is also being done to determine how slightly altering the current fat grafting procedure effects the retention of the fat graft over time and a subject's quality of life.

The goal of this research study is to measure whether the experimental procedure has any affect on pain at the amputation site(s). Additional goals of the study include evaluating the fat graft over time, and to measure the quality of life of a subject during a 24 months post-surgical follow-up period. The total duration of participation is approximately 26-27 months. Even though fat grafting has been commonly done for other indications, the proposed surgical procedure is experimental for the indication in traumatic amputations. This is a completely new, experimental application of a conventional treatment.

Who is being asked to take part in this research study?

This study will be conducted at the University of Pittsburgh enrolling approximately 30 adults, male or female, civilian or military personnel, and ages 18 years of age and older.

What treatments or procedures are available if I decide not to take part in this research study?

If you decide to not participate in this experimental study, there are several other treatments or procedures you may wish to consider:

- Getting fat grafting procedure without being in this, or any, study
- Participating in another study
- No surgical treatment

What procedures will be performed for research purposes?

If you decide to participate in this study, we will do some or all of the following tests to see if you are eligible for the study. The following procedures will be completed after you have discussed the study with your physician and signed the informed consent. These procedures are considered to be research; neither you nor your insurance company will be billed for these procedures. These procedures may occur over several sessions and at different locations within the UPMC system. We



will discuss this information in further detail at the time of the your visit which will take place at the Aesthetic Plastic Surgery Center located at 3380 Boulevard of the Allies, Pittsburgh, Pa. 15213.

Screening Visit/Pre-Graft Visit 1 (S/PGSV1):

All screening procedures will be performed at the UPMC Aesthetic Plastic Surgery Center in a private room and at the UPMC laboratory located on the 5th floor at Montefiore University Hospital. These screening procedures will take approximately 3.5-4 hours and may occur on different dates.

All the following activities are research procedures and are being completed for the purpose of this clinical trial. If you agree to participate, you will be asked to complete the following research procedures to determine whether you are eligible:

- Review of medical records related to the injury, past surgeries, prosthetic history, health care, and medications
- Medical history and physical exam inclusive of your limb (including your height, weight, BMI calculation) and current medications to include prescription and vitamins / supplements you are presently on.
- The investigator will rate the appearance of the graft site using a standardized chart
- Basic vital signs measurement (such as blood pressure, respirations, pulse, and temperature)
- Collection of demographic information to include date of birth, gender, race, ethnicity, level of education, current relationship and employment status, religion and living arrangements.
- Urine pregnancy test (for females of child bearing potential)
- Blood tests approximately 30mls (2 tablespoons) for hematology (test that checks how your blood is able to fight infection), chemistry panel (test to check how well your kidneys and liver are working), and coagulation study (test to check how well your blood clots).
- Standard digital (2D) photographs
- CT Scan (sometimes called a CAT Scan) of the amputation stump
- Patient questionnaires - questions for your completion pertaining to satisfaction with your appearance/surgical outcomes and satisfaction with the medical /health services that you have previously and are presently receiving.
- You will be asked to complete a series of questions (questionnaire) that will evaluate the presence or absence of a psychiatric disorder. The questionnaire will include your demographic history and will be completed by a research technician who is an experienced member of the psychiatric clinical team. This SCID will take approximately 45-60 minutes of your time to complete.
- Nutritional Assessment/Education (an evaluation of your current nutritional habits)
- Prosthetic Evaluation to include Occupational Therapy - these evaluations may include physical examination and measurements of the amputation site(s), evaluation of your use of prosthetics and related issues/concerns. This assessment may also include a 6 Minute walk test (6MWT) for lower extremity amputees or other tools to evaluate your functional exercise capacity or your physical endurance, Amputee Mobility Predictor (AMP) and Prosthetics Evaluation Questionnaire (PEQ) etc.



- Pain evaluation -Assessment of pain at your pre-surgical amputation stump

Should a **clinically significant and/or unexpected disease or condition be found during these screening procedures**, the research team will notify you and, with your permission, discuss those findings with your primary care physician for further evaluation.

Upon completion of your screening visit the study investigator will determine your eligibility to participate in this study. The research procedures for this study are as follows:

Pre-Graft Study Visit 2 (PGSV2):

If you meet eligibility criteria for this study, you will return to UPMCs Aesthetic Plastic Surgery Center prior to the fat graft surgery procedure. Procedures for pre-graft visit 2 may occur on the same day or, due to the coordination of your schedule and travel distance the procedures, may be performed on different days as long as the completion of the procedures do not exceed a length of 4 days. This visit will require approximately 3-4 hours of your time. During this visit the following research procedures will be completed:

- Standard digital (2D) photographs
- Medical history and physical exam inclusive of your limb, vital signs (Blood Pressure, pulse, respirations and temperature, weight and BMI calculation), collection of medication profile, medical record review, and collection of any medical problems you are experiencing..
- The investigator will rate the appearance of the graft site using a standardized chart
- Urine pregnancy test (for females who could become pregnant)
- Pre operative blood tests -approximately 30mls (2 tablespoons) for hematology (test that checks for anemia and how your blood is able to fight infection), chemistry panel (test to check how well your kidneys and liver are working), and coagulation study (test to check how well your blood clots).
- EKG (Electrocardiogram—a test that traces the electrical activity of your heart) if indicated
- Chest X-ray if medically indicated
- You will be given a Diary Card/Pain Log to record your daily assessment of pain and other symptoms at your **post**-surgical amputation stump. You will complete these logs starting 24hours after the surgery and continue until Post Op study visit 3-6days after the surgery or until the next visit if there are any concerns.
- Pain evaluation- Your assessment of pain at your **pre** -surgical amputation stump site
- In this study, you will be randomized (like a flip of a coin) to receive either a concentrated fat graft procedure (15 subjects) or a standard fat graft procedure (15 subjects). You will be followed over 24 months post operatively to measure outcomes.

Surgical Procedure:

Your fat grafting surgical procedure will be performed at UPMC Shadyside Hospital surgical suites. One of the nurses from the surgical team will telephone you the night before the procedure and review your medications, time to arrive at the hospital and tell you not to have anything to eat or drink for approximately 12 hours before the surgical procedure. The day of the surgery someone from the Anesthesia Department will meet with you. You will be given either twilight anesthesia and spinal



anesthesia, or general anesthesia so that you will be unconscious during the surgery: you will not feel or remember anything that happens. Generally, surgery patients will be given a combination of drugs through a vein in their arm and/or gases that they will breathe through their nose. You will be given a separate consent document to sign for the surgery – which is a standard clinical procedure, and both the anesthesiologist (doctor who administers anesthesia) and surgeon will go over the risks of this surgery. The surgical procedure will take approximately 4-5 hours to complete.

For the 15 subjects randomized to the Standard fat graft procedure, the following will occur: The plastic surgeon, using small narrow tube-like instruments called cannulas will remove fat from various places throughout your body (commonly the abdomen and thighs). The plastic surgeon will collect the fat through multiple small incisions (less than ½ inch) using hollow tubes and place the fat into a centrifuge (spinning device in operating room), where it is prepared in a specific way before placing it back into your body. The plastic surgeon will then use the small hollow tubes with varied shapes and tip sizes that will deliver small amounts of fat to fill the injured areas of your amputation stump. The incisions that will be made to place the fat to these areas are less than ¼ inch.

For the 15 subjects randomized to the experimental Concentrated Fat Graft procedure, the following will occur: The plastic surgeon will remove the fat the same way the standard fat grafting procedure is done. The fat that is removed from your body will be separated into two parts. One portion of this fat will be taken to the Hillman Stem cell lab and prepared in a specific way to concentrate the fat cell. The other part of the fat will stay in the operating room, separated using a centrifuge (machine that spins the fat). This process is done to separate the fluid and cells of the fat. The portion of fat from the Stem Cell Lab will then come back to the operative suites to be combined with the cells of the fat that remained in the operating suites to place it back into your body. This portion of the procedure will add no more than 30 minutes to the overall operating time compared to Autologous Standard fat graft processing. Using small hollow tubes with varied shapes and tip sizes, the surgeon will deliver small amounts of this fat to fill the injured areas of your amputation stump. The incisions that will be made to place the fat to these areas are less than ¼ inch.

During this surgical procedure, the study investigator will obtain a sample portion of your fat for laboratory testing. This sample is approximately 25-50mls (1-3 tablespoons). The research samples will be transported to the University of Pittsburgh's Plastic Surgery Research laboratory. The research samples will remain under the oversight of Kacey Marra, PhD, Co-Investigator, on the 16th floor of the Biomedical Science Tower, University of Pittsburgh. These samples will be de-identified and labeled with a unique study ID number only. All these samples may be used for this study and shared with secondary investigators (investigators not listed on the first page of this consent document) without identifiers for other studies.

FOLLOW UP STUDY VISITS:

As part of this study, you will also complete a series of medical follow-up visits in the weeks and months following surgery. A detailed schedule of these visits will be provided to you. You can expect to make approximately 7 post operative visits starting at 3-6 days post-op and will extend over a 24-26 month period. Your visits will require approximately 1 ½ to 3 hours of your time.



Post-Op Study Visit (Day 3-6)

- Limited physical exam with a limb exam completed by the PI and /or the Co-investigator
- Collection of any medical problems you are experiencing as a result of the study procedures.
- Review of your medications to include prescription and vitamins / supplements, vital signs (Blood Pressure, pulse, respirations, temperature)
- Collection of Diary Card and Pain Log

Study Visits 1 -6 or SV 1-6:

These study visits will occur with the study investigator or research team and will take place at 7-21 days, month 2, 3, 4, 6, 12 and 2 years after the surgical fat grafting procedure. The duration of time for each visit will be approximately 2-3 hours. All visits will be scheduled by the research coordinator and discussed with the subject prior to the fat graft procedure. The following research procedures will be completed at these visits:

- Review of your medications to include prescription and vitamins / supplements
 - Collection of vital signs (Temp, pulse, Resp, BP) and weight/BMI
 - Diary Card and Pain Log collection (V1 only if required)
 - Adverse event reporting.
 - Pain evaluation -Assessment of pain after the surgery to your amputation stump
 - Limited physical exam with limb exam completed by the PI and /or the Co-investigator.
 - The investigator will rate the appearance/volume of the graft site using a standardized chart
 - Medical chart review
 - Nutritional Evaluation (Visit 1 PO, Visit 3 PO ONLY)
 - Prosthetic Evaluation to include Occupational Therapy evaluations as indicated
- Visit 2 and or 3 will only include amputation site assessment to evaluate readiness in collaboration with the physician for weight bearing and readiness for check socket. The check socket and permanent socket is to be obtained in conjunction with your primary prosthetist as standard of care. You may be asked to attend an additional visit at 4-5 months PO if the standard of care procedures for check socket and permanent socket fall out of the 2-3 month range. You are not to wear the prosthetic device until seen by the study team and clearance is received to utilize these devices which will usually occur at Visit 3 or 4 PO. We will ask you to bring any new prosthetic parts to your next scheduled visit after they are obtained to evaluate fit /comfort.

Visit 4, 5 and 6 - these evaluations may include physical examination and measurements of the amputation site(s), evaluation of your use of prosthetics and related issues/concerns. This assessment may also include a 6 Minute walk test (6MWT) for lower extremity amputees or other tools to evaluate your functional exercise capacity or your physical endurance, Amputee Mobility Predictor (AMP) and Prosthetics Evaluation Questionnaire (PEQ) etc.



- Urine pregnancy test (for females who could become pregnant) (Visit 4 PO, Visit 5 PO and Visit 6 PO)
- CT Scan with 3D renderings Visit 4 PO, Visit 5 PO and Visit 6 PO)
- Psychosocial assessment (Visit 1 PO, Visit 3 PO ,Visit 4 PO, Visit 5 PO and Visit 6 PO)
- Structured Clinical Interview (SCID) -Visit 4, 5, and 6 PO only)
- 2D Photographs
- Biopsy - a small amount of tissue (approximately the width of a pencil point) collected called a biopsy (the removal of a sample of tissue). This collection of tissue sample will be completed using a very small tube. This biopsy procedure will occur after your surgery during your 3 month (Visit 3 PO) and 1 year (Visit 5 PO) visit. This will only be done with subjects where it is determined by the PI that the biopsy will not interfere with the desired outcome

We will be digitally recording (i.e. photography or video) any and all portions of your pre-operative, operative, and post-operative course of treatment. These may include, but not be limited to, videos of personal interviews, functional assessment testing and clinical exams or photos of follow up clinical course, etc. We are using these digital recordings and/or photos for medical education and training, publication, and media reports – and they may occur in any mode of transmission, including and not limited to: print, email, television, internet, etc. While some recordings will be de-identified, some recordings will remain identifiable (interviews). You do not have to undergo digital taping in order to participate in this study. There is a place at the end of the consent document to indicate if you agree to participate in digital taping or not.

Telephone Interviews 1 and 2 – (These will occur at 48-72 hours after biopsies) the phone interviews will consist of a collection of your current medications and any concerns or problems experienced after your biopsies (20-30minutes)

Telephone Interview 3- (at approximately 18 months after surgery)- The phone interviews will consist of a collection of your current medications and any concerns or problems as well as pain assessment related to use of your prosthesis (20-30minutes)

What are the possible risks, side effects, and discomforts of this research study?

You may experience a number of side effects or complications or discomforts that are associated with participating in this research study. Members of the research team can describe these risks in more detail and you are encouraged to ask questions about study-related risks. As with any research or clinical procedure, there may be side effects that are currently unknown and certain of these unknown risks could be permanent, severe or life threatening. You will be watched carefully for any side effects. You should inform your study doctor about any side effects you experience while taking part in the study.

This procedure is experimental and there is no guarantee that the procedure will work. It is possible that additional treatments may be needed to maintain the desired volume of the transferred fat and resulting appearance.



Fat Graft surgical procedure may be associated with risks that vary depending on your age, weight, preoperative condition, and other factors.

Common risks may include a change in appearance. Typically the transferred fat loses some of its volume over time and then becomes stable. Bruising and swelling may occur due to the movement of the instruments used to remove and place fat during the liposuction and fat grafting procedures. Your skin contour may change; it is possible that some or all of the fat may become firm, hard or lumpy. If some of the fat does not survive the transfer, it may result in firmness and discomfort and pain. Cysts may also form at the site of the transferred fat. Asymmetry, or difference in appearance between the right and left side, may be present after treatment. Pain may occur after fat removal or grafting procedures. Pain associated with the surgical procedure is expected to resolve within the immediate postoperative period. You may also experience pain and/or muscle soreness with physical evaluations, manipulation and testing of the stump site post op; please let the study staff know if you feel discomfort and we will adjust tests accordingly. Some patients experience embarrassment or have emotional responses to photographs or physical exams that focus on the injury and/or with psychological testing. All efforts will be made to maximize your comfort, including use of private exam rooms, minimizing time of potentially embarrassing exams, and providing clinical psychologists as needed.

Infrequent risks may include infection, which may occur due to the multiple small incisions from the liposuction procedure. Infection is unusual after the fat graft procedure. Should infection occur, additional treatment including antibiotics or surgery may be necessary. You may experience bleeding during or after this procedure. Seroma (a collection of fluid) may appear at the site where the fat was removed. All invasive procedures produce scars, some more visible than others. Additional treatment, including surgery, may be needed to treat scarring.

Serious risks are extremely rare and may include severe complications that may include blood clots, pulmonary embolism (blood clots in the lung), fat embolism (fat globules that affect circulation), stroke, loss of vision, and/or death. Regarding tissue loss, in rare cases, the grafted fat may cause the skin over the transferred area to be injured resulting in loss of the skin and surrounding tissue. Damage to deeper structures such as nerves, blood vessels and muscles may occur during the course of this procedure. The injury to deeper structures may be temporary or permanent.

General anesthesia affects the whole body and is more likely to cause side effects such as nausea and/or vomiting and sore throat, which are minor and can be easily managed.

Infrequent Risks: Aspiration during anesthesia and surgery is very uncommon. Aspiration occurs when the anesthesia suppresses the normal throat reflexes such as swallowing, coughing, or gagging. Insertion or removal of airways may cause respiratory problems such as coughing; gagging; or muscle spasms in the voice box, or larynx (laryngospasm), or in the bronchial tubes in the lungs (bronchospasm) and may cause an increase in blood pressure (hypertension) and heart rate (tachycardia). Incorrect placement of the tube can cause hypoxia (lack of oxygen). Other complications may include damage to teeth and lips, swelling in the larynx, sore throat, and hoarseness, temporary or permanent vocal cord damage, drug reactions, and/or death. Although all



types of anesthesia involve some risk, major side effects and complications from anesthesia are uncommon. Your specific risks depend on your health, the type of anesthesia used, and your response to anesthesia. Other serious risks of General anesthesia include severe drop in body temperature, changes in blood pressure or heart rate or rhythm, heart attack, or stroke. Death or serious illness or injury due solely to anesthesia is rare and is usually also related to complications from the surgery.

Other medical procedures conducted as part of this research also have risks associated with them. The **electrocardiogram** (EKG) uses sticky pads which sometimes causes redness on the skin after removal.

The small **core needle biopsy** has a risk of bleeding, bruising, redness, swell, and pain; less common are scarring and infection. There may be a risk of nerve or vessel damage, due to changes in the physical structure of the injured extremity during the biopsy procedure. The application of **lidocaine** to numb the skin during the biopsy very rarely affects heart rate.

CT and standard x-ray tests will expose you to radiation. There is no known minimum level of radiation exposure that is recognized as being totally free of the risk of causing genetic defects (cellular abnormalities) or cancer, but we will make every effort to minimize the number of these tests conducted solely for research purposes. The amount of radiation exposure that you will receive from this CT scan is about 1.3 rem (rem is a unit of radiation exposure) to your affected limb, with minimum exposure of other areas of your body. You will receive a total of 5.2 rems for the entire study. For comparison, radiation workers are permitted, by federal regulation, a maximum radiation exposure of 50 rems per year to any single body organ. The risk associated with the amount of radiation exposure that you will receive from taking part in this study is felt to be low and comparable to everyday risks. In addition, if you are a female of childbearing potential participating in this study, you will be asked to have a urine dip stick pregnancy test to verify you are not pregnant prior to all CT scans being obtained. All results of this test will be recorded to your research chart. Because CT scans require you to lay still or flat in a small confined space for a period of time, you may experience a feeling of becoming closed in or uncomfortable (claustrophobic). Should this experience occur, you can immediately contact the technician and stop the procedure.

Your participation in this research study does potentially involve **a risk of a breach of confidentiality** of the medical record information and associated privacy. The study investigators will take steps to reduce these risks by: 1) removing direct participant identifiers (i.e., names, social security numbers, medical record numbers) from information stored in the study records; 2) securing the study records in a separate location, and limiting access to information linking codes assigned to the study record information with direct participant identifiers; and 3) limiting access to information contained within the study records to study investigators only.

You will also have a **blood draw** as part of this study (and as part of your medical care). **Risks are generally slight**, but may include pain, excessive bleeding, fainting, or feeling lightheaded, bruising, infection, and multiple punctures to locate veins.



You will be counseled to avoid pregnancy during the study and if you are a female participant who is of child bearing potential, you will receive a urine pregnancy dip test prior to each CT scan. If we learn of any new information about study risks that could cause you to change your mind about continuing to participate, we will notify you promptly.

What are the possible benefits from taking part in this research study? You may not benefit from your participation in this study. There is the possibility that you will experience a positive result of your fat grafting procedure (including improvement of limb pain, improved appearance, and/or better prosthetic fit); however, we cannot guarantee a positive outcome from the procedure. In addition, this study may help us to understand the effects of fat grafting over time.

Will I or my insurance provider be charged for the costs of any procedures performed as part of this research study? Neither you nor your insurance company will be charged for any medical tests, surgical procedures, or follow-up evaluations. You will, however, need a standard of care evaluation by your prosthetist for socket fit, check socket and new permanent socket after the operative procedure to assure proper fit of your prosthetic device. This would be charged in the usual manner to your insurance provider. All study procedures that are specifically being performed for the purpose of this study (i.e., Fat Grafting procedure, CT scans, collection of blood and research samples, questionnaires and EKG's) are being covered under a contractual agreement with the Department of Defense. If you receive a bill or believe that your health insurance has been billed for something that is part of this research study, immediately notify a member of the research team or UPMC Patient Billing Services.

Will I be paid if I take part in this research study?

You will receive payment for your participation in this research study. You will be compensated for your participation at a per diem total rate of \$104.00/day upon completion or partial completion of each study visit. Your reasonable travel expenses will be reimbursed for round trip air fare coverage or mileage coverage at \$0.55 per mile round trip per visit from your place of residence to the UPMC Anesthetic Plastic Surgery Center or UPMC hospital/ overnight housing facility. The details of reimbursement will vary from person to person and will be discussed during this visit.

Your participation may lead to new inventions or products. If the investigators are able to develop new products from the research use of your tissue or biological sample, there are currently no plans to share with you any money or other rewards that may result from the development of these new products.

Also, Department of Defense personnel may receive compensation for research activities only if the research activities take place outside of scheduled work hours.

Who will pay if I am injured as a result of taking part in this research study?

If you believe that the research procedures have resulted in an injury to you, immediately contact Dr. Rubin or the Study Coordinator (see first page). Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of



those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation.

Who will know about my participation in this research study?

To protect your privacy and maintain the confidentiality of information we obtain from you and from your medical records, we will keep all information about you in a secure location. All paper records that could identify you will be stored in locked file cabinets, and all electronic records will be stored in password-protected files. Access to this information will be limited to research team members and to those health care professionals who are providing clinical services as part of this research study.

Will this research study involve the use or disclosure of my identifiable medical information?

Although we will do everything in our power to protect your privacy and the confidentiality of your records, just as with the use of your medical information for health care purposes, we cannot guarantee the confidentiality of your research records, including information that we obtained from your medical records. However, **no third party**, including relatives, personal physicians or insurance companies, or other researchers **will have access to your identifiable** information, with three exceptions. First, staff at the hospitals of UPMC will have access to your identifiable information related to clinical activities, including the laboratory or diagnostic procedures and surgical procedures. Second, authorized representatives of the hospitals of UPMC may have access to identifiable information only for handling internal hospital operations. Third, authorized representatives of the Food and Drug Administration (FDA), the Department of Defense (which is providing funding for this study), and the University of Pittsburgh Research Conduct and Compliance Office may review your identifiable information for monitoring the appropriate conduct of this research study. This research study will result in identifiable information that will be placed into your medical records held at UPMC. The nature of the identifiable information resulting from your participation in this research study that will be recorded in your medical record will be derived from the medical/surgical (fat grafting procedure). Psychiatric interview information will be entered into the medical record only if it is important to ensure your medical/physical safety.

It is possible that we may use the information – including stored biological specimens – obtained from this study in other research studies to examine the effects of the cellular fat grafting procedure process. This information and specimens may also be shared with other researchers here, and at other research centers, but those researchers will never be provided with any personal identifiers that would allow them to learn who you are.

As part of this study, we are also requesting your authorization or permission to review your medical records to obtain past, current, and future medical information from hospital and other medical facilities. We will obtain information concerning your diagnosis, age, past medical history, diagnostic or surgical procedures, prosthetic history and results of the tissue biopsy and blood tests that may have been done as part of your care. We will use this information to determine whether you meet the conditions for participation in this study, to compare your earlier test results to the findings from this study and, if possible, to use your previous exam results in place of or in addition to some of the exams



needed for this study.

Who will have access to identifiable information related to my participation in this research study?

This identifiable information will be made available to members of the research team for an indefinite period of time. That medical information, as well as information obtained during this research study, may be shared with other groups, possibly including authorized officials from the FDA, Department of Defense, the University of Pittsburgh Research Conduct and Compliance Office, and contracted entities for the purpose of monitoring the study. Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g., laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) assessing internal hospital operations (i.e. quality assurance). Any information that is entered into your medical records will be available to you, in accordance with the UPMC Notice of Privacy Practices.

Your doctor may also be involved as an investigator in this research study, but you are not under any obligation to participate in any research study offered by your doctor. Before agreeing to participate in this research study, or at any time thereafter, you may wish to discuss participation in this study with another health professional, to obtain a 'second opinion' about study participation.

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Is my participation voluntary?

Your participation in this research study is completely voluntary. Whether or not you participate in this research study it will have no effect on your current or future relationship with the University of Pittsburgh, UPMC or its affiliated health care providers or health care insurance providers

May I withdraw, at a future date, my consent for participation in this research study?

If you decide you no longer wish to continue to participate after you have signed the consent form, you should contact Dr. J. Peter Rubin or his research colleagues (412-383-8080). You may also withdraw, at any time, your authorization to allow the research team to review your medical records, but if you do so, you will no longer be permitted to participate in this study. Any information obtained from you up to that point will, however, continue to be used by the research team. Should you decide to withdraw or be withdrawn from study participation, the already collected samples will be kept and rendered anonymous, (i.e., the link between the code (your study ID#) and your identity will be destroyed. Any samples taken during surgery will remain the property of the University of Pittsburgh and will be stored indefinitely in a de-identified manner at University of Pittsburgh's Adipose Stem Cell under the oversight of Kacey Marra, PhD, Co-Investigator, on the 16th floor of the Biomedical Science Tower. Your decision to withdraw will have no effect on your current or future relationship with the University of Pittsburgh or with UPMC or its affiliate health care and insurance operations.



If I agree to participate in this research study, can I be removed from the study without my consent?

If the investigators feel that you cannot complete the study requirements safely (for example, positive pregnancy test, experience severe side effects, unable to complete physical therapy), they may withdraw you from the study. At the time of your withdrawal, the investigator will discuss with you the appropriate and requested follow up based on the specific event.

OPTIONAL CONSENT FOR DIGITAL RECORDINGS OF PROCEDURES

The research team is requesting permission to digitally record (i.e. photography or video) any and all portions of your pre-operative, operative, and post-operative course of treatment. These may include, but not be limited to, videos of personal interviews, functional assessment testing and clinical exams or photos of follow up clinical course, etc. These digital recordings and/or photos may be used for medical education and training, publication, and media reports – and, in any mode of transmission, including and not limited to: print, email, television, internet, etc. While some recordings will be de-identified, some recordings will remain identifiable (interviews). Regarding the use of these digital recordings for education, training, publication and storage purposes, you will not be identified by name, only by a unique code number. Your identifiable features in these photographs will be blacked out (i.e., eyes, facial features, tattoos etc.). Regarding the use of your digital recordings for media purposes, you may be identified by name, but permission from you will be obtained in a separate consent document prior to the recordings being obtained. You are not required to give this permission and can refuse at any time after giving consent to these digital recordings being obtained. You can still participate in this study without permitting these recordings.

I consent to the digital recording, as described above:

Participant's Signature

Date

I **do NOT** consent to the digital recording:

Participant's Signature

Date



VOLUNTARY CONSENT FOR STUDY PARTICIPATION

The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified member of the research team or by Dr. Rubin, at 412-383-8080. I understand that I may always request that my questions, concerns or complaints be addressed to Dr. Rubin. At any time I may also contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations in the event that the research team is unavailable. By signing this form I agree to participate in this research study, and allow the use and disclosure of my medical record information for the purposes described above. A copy of this consent form will be given to me.

Printed name of Participant

Participant's Signature

Date / Time

CERTIFICATION OF INFORMED CONSENT:

I certify that I have explained the nature and purpose of this research to the above individual and I have discussed the potential risks and possible benefits of study participation. Any questions the individual has about this study have been answered, and I will be available to address future questions as they arise. I further certify that no research procedures were begun until after this consent form was signed.

Printed Name of Person Obtaining Consent

Role in Research Study

Signature of Person Obtaining Consent

Date / Time

