Protocol Title: Structural Fat Grafting for Craniofacial Trauma using manual technique for processing fat graft material (BTI++)

NCT02267187

Study Protocol including statistical plan

Approved 04/04/2017

Triage Section

Provide a short title for this study (200 characters or less)**:**

BTI++

T1.0 **Select the type of application:**New Research Study

T2.0 **Is the proposed research study limited to the inclusion of deceased individuals?** * No

The review and approval of proposed innovative practices are ***not*** subject to IRB review and approval. The introduction of innovative procedures or therapies into clinical practice (i.e., independent of a research activity approved by the IRB) should be reviewed with the applicable department chairperson and the UPMC Technology Assessment Committee/Innovative Practices Sub-Committee prior to their implementation. The contact person is **Mary Gardner at 412-647-6883.**

T2.1 **Are any research activities being conducted at the VA Pittsburgh Healthcare System or with VA funds?** * No

Respond to the following questions to determine the IRB-of-record:

Research is conducted using only VA records and/or subjects recruited thru the VA:
University or UPMC facilities are not engaged in research:
University or UPMC funds are not expended in direct support of research:

If all **true**, then the VA is the IRB-of-record and UPitt IRB review is not required.If all **false**, only UPitt IRB review is required.Otherwise, dual review from both the VA and UPitt IRB is required.

Read carefully- Studies are **not eligible for NCI Central IRB** review if any of the following are required: • review by the Institutional Biosafety Committee (IBC) • waiver of HIPAA authorization • conduct of any research procedures at a site outside of the Commonwealth of Pennsylvania • enrolling prisoners
Please select the external IRB of record:

Provide the name of the Central IRB:

Quality assurance projects are ***not*** subject to IRB review and approval. UPMC has adopted an oversight process that requires the submission of all quality assurance projects for review. At UPMC, submissions are reviewed by the Quality Improvement Review Committee (QRC). You can contact the QRC at askqrc@upmc.edu.

Research studies that are limited to the inclusion of deceased individuals are ***not*** subject to IRB review and approval. Research performed on individuals who have been declared legally dead

and/or research involving the collection of tissues from deceased individuals is not subject prior review and approval by the University of Pittsburgh IRB.

There are, however, ethical issues associated with research conducted on or involving deceased individuals. To address these ethical issues, all University faculty who desire to perform research on or involving deceased individuals must submit a project application for review and approval by the Committee for Oversight of Research and Clinical Training Involving the Dead Research Involving the Dead (CORID). Note that, as per UPMC policies, research involving the medical records of deceased individuals is subject to obtaining the written consent of the decedents' next-of-kin or the executors of the decedents' estates.

For studies that include **BOTH** living and deceased subjects, IRB review and approval **is required**.

Emergency Use is the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval [21 CFR312.310]. Detailed information on the submission process is available on the IRB website under the A-Z Guidance, Emergency Use.

All of the following conditions must exist to justify the emergency use of an unapproved investigational drug, biologic, or device. Check all the boxes that apply:

Selections
There are no items to display

View: T3.0

Triage Section

T3.0 What is the anticipated risk to the research participants?

Greater Than Minimal Risk

T3.1 **Why do you feel that all aspects of this research study, including screening and follow-up, involve no more than minimal risk to the research subjects?**

T4.0 **Does the proposed study qualify for 'exempt' IRB review or for a determination of either 'not research' or 'no human subject' involvement?**

*

T5.0 **Does the proposed research study qualify for 'expedited' IRB review status?**

*

View: CS01.0 - 01.1.1

Cover Sheet Section

CS1.0 **What is the reason for this submission?**

New Research Protocol Submission

CS1.1 **Has this research study been approved previously by the University of Pittsburgh IRB?**

* No

If the **study expired**, you are required to upload the completed Renewal Report Form and a Data and Safety Monitoring Report.

Upload the Renewal Report Form and Data and Safety Monitoring Report:
Name Modified Date

Previous IRB #:

CS1.1.1 **Has this research study (or a substantially similar research study) been previously disapproved by the University of Pittsburgh IRB or, to your knowledge, by any other IRB?**

* No

If **Yes**, identify the IRB, IRB number if Pitt IRB disapproved, and the primary reasons for disapproval:

View: CS02.0 - 02.1

Cover Sheet Section

CS2.0 **Title of Research Study:**

Structural Fat Grafting for Craniofacial Trauma using manual technique for processing fat graft material

CS2.0.1 Use the textbox below to list any language or documents to be displayed in the approval letter. List only those items submitted for review with ***this submission***.

Documents to be displayed may include items such as versions of investigator brochures, consent forms, and advertisements.

If specific language is not required in the approval letter, leave the textbox blank (**do not write 'None'**).

Requested approval letter wording: Protocol Informed Consent

CS2.1 **Research Protocol Abstract:**Clinical use of autologous fat grafting in humans was described as early as 1893, when Neuber published his report of transferring multiple small particles of fat to fill a soft tissue depression (1). Over the past three decades, autologous fat grafting has

become a common procedure in clinical plastic surgery, and is also employed by clinicians in other specialties. The refinement of liposuction techniques in the 1980's made it possible to harvest the adipose grafts with low risk and without the need for a significant incision. The liposuction aspirate could simply be re-injected at a different site. Specialized equipment has been developed for fat grafting and is commercially available from a number of sources. The American Society of Plastic Surgeons 2007 procedural statistics show that over 65,000 fat grafting procedures were performed in the United States (www.plasticsurgery.org) during the previous year.Fat grafting may represent a superior method of facial reconstruction after severe trauma, but the results can be impacted by resorption of fat volume over time. The specific aims of the study are:1) Assess facial appearance and soft tissue volume before and after autologous fat grafting using CT scans and 3D photography.2) Assess cellular properties of the cells within the fat graft3) Comparison of cotton rolling to centrifugation method of autologous fat grafting4) Measure of quality of life in patients before and after autologous fat grafting using validated psychosocial measures. Ten (10) subjects 18 years of age and older will be enrolled to this trial. This study will examine the impact of the fat grafting procedure on facial appearance and quality of life over time by precisely measuring soft tissue volume with CT scans, assessing appearance with 2D and 3D photography and standard photography and evaluating quality of life through various validated psychosocial measures. This study will be a very important evaluation of the effectiveness of this therapy, and will help guide clinicians in applying this technique. Additionally, laboratory testing of the injected fat material will be performed so that the results may be correlated with clinical outcomes in the future.The study endpoints include the analysis of the graft site via study procedures at different time points, the comparison of cotton rolling to centrifugation method of autologous fat grafting, as well as the correlation of cell behavior of the laboratory assays with clinical outcomes.

CS2.2 **Select the category that best describes your research:**

View: CS03.0 - 03.9

Cover Sheet Section

CS3.0 **Name of the Principal Investigator:**

J. Peter Rubin

Note: Adjunct faculty of the University, including lecturers and instructors, are not permitted to serve as a PI or Faculty Mentor but may serve as co-investigators. Refer to Chapter 4 on the HRPO website for more information.

CS3.1 **Affiliation of Principal Investigator:**

UPitt faculty member

If your answer was **Other**, fill in the Principal Investigator's affiliation:

If you chose any of the **Pitt options**, please indicate the specific campus:Main Campus - Pittsburgh

If you chose the UPitt faculty member option, provide the PI's **University Faculty Title**:Professor of Plastic Surgery

CS3.1.1 **Indicate below the name of the qualified University faculty member or UPP or UPMC staff member who will serve as a mentor and provide supervision or guidance regarding the conduct of this research study.**

CS3.2 **Address of Principal Investigator:**UPMC Center for Innovation in Restorative Medicine6B Scaife Hall, Room 690 3550 Terrace StreetPittsburgh, PA 15213

CS3.3 **Recorded Primary Affiliation of the Principal Investigator:**

U of Pgh | School of Medicine | Plastic Surgery

CS3.4 **Identify the School, Department, Division or Center which is responsible for oversight of this research study:**

U of Pgh | School of Medicine | Plastic Surgery

CS3.5 **Telephone Number of Principal Investigator:**

412-383-8080

CS3.6 **Recorded Current E-mail Address of Principal Investigator to which all notifications will be sent:**rubinjp@upmc.edu

CS3.7 **Fax Number:**

412-383-9053

CS3.8 **Does this study include any personnel from Carnegie Mellon University, and/or use any CMU resources or facilities (e.g., Scientific Imaging and Brain Research Center (SIBR)?**

* No

CS3.9 **Is this your first submission, as PI, to the Pitt IRB?**

* No

View: CS04.0

Cover Sheet Section

CS4.0 **List of Co-Investigators:**

Last	First	Organization
Acarturk	Tahsin Oguz	U of Pgh | School of Medicine | Plastic Surgery
Amar	Dalit	UPMC | Physician Services Division | UPP | Surgery
Bliley	Jacqueline	Other
Bourne	Debra	UPMC | Other
Branstetter	Barton	U of Pgh | School of Medicine | Radiology
Bykowski	Michael	UPMC | Physician Services Division
Coleman	Sydney	U of Pgh | School of Medicine | Plastic Surgery
czerniak	sharona	Other
DiBernardo	Gabriella	U of Pgh | School of Medicine | Plastic Surgery
Donnenberg	Albert	U of Pgh | School of Medicine | Medicine
Donnenberg	Vera	U of Pgh | School of Medicine | Surgery | Thoracic Surgery

Fishman	Jordan	UPMC | Physician Services Division | UPP | Medicine
Foley	Karen	U of Pgh | School of Medicine | Plastic Surgery
Grybowski	Damian	U of Pgh | School of Medicine | Plastic Surgery
Gusenoff	Jeffrey	U of Pgh | School of Medicine | Plastic Surgery
Haas	Gretchen	U of Pgh | School of Medicine | Psychiatry
James	Isaac	U of Pgh | School of Medicine | Surgery | Plastic Surgery
Lee	Jessica	U of Pgh | School of Medicine | Surgery | Plastic Surgery
Ma	Irene	U of Pgh | School of Medicine | Plastic Surgery
Marra	Kacey	U of Pgh | School of Medicine | Plastic Surgery
Mermon	Diana	U of Pgh
Minteer	Danielle	U of Pgh | School of Medicine | Plastic Surgery
Pang	John Henry	U of Pgh | School of Medicine | Plastic Surgery
Radomsky	Elizabeth	UPMC | Hospital Divisions
Ruane	Edward	U of Pgh | School of Medicine | Plastic Surgery
Schusterman	Mark	U of Pgh | School of Medicine | Plastic Surgery
Simon	Patsy	U of Pgh | School of Medicine | Plastic Surgery
Steele	Amy	U of Pgh | School of Medicine | Plastic Surgery

View: CS05.0 - CS06.3

Cover Sheet Section

CS5.0 **Name of Primary Research Coordinator:**Amy Steele

CS5.1 **Address of Primary Research Coordinator:**

UPMC Center for Innovation in Restorative MedicineDepartment of Plastic Surgery University of PittsburghIsaly Building 3380 Blvd. of the Allies, Suite 158Pittsburgh, Pa. 15213

CS5.2 **Telephone Number of Primary Research Coordinator:**

412-641-3728

CS6.0 **Name of Secondary Research Coordinator:**

Karen Foley

CS6.1 **Address of Secondary Research Coordinator:** 3380 Blvd. of the AlliesSuite 158Pittsburgh, PA 15213

CS6.2 **Telephone Number of Secondary Research Coordinator:** 412-641-3726

CS6.3 **Key Personnel/Support Staff (Only list those individuals who require access to OSIRIS):**

Last	First	Organization
Simon	Patsy	U of Pgh | School of Medicine | Plastic Surgery

View: CS07.0

Cover Sheet Section

CS7.0 **Will this research study use any Pediatric PittNet or Clinical and Translational Research Center (CTRC) resources?**

No

CS7.1 **Please select the sites you intend to use:**

There are no items to display

View: CS08.0

Cover Sheet Section

CS8.0 **Select the entity responsible for scientific review.**

Department Review - (a dean, department chair, division chief, or center head) Note: **DoD funded studies** require departmental review

CS8.1 **Select the school, department or division which is responsible for scientific review of this submission.**

U of Pgh | School of Medicine | Plastic Surgery

CS8.1 **Select the CTRC which is responsible for scientific review of this submission**

View: CS09.0 - 10.0

Cover Sheet Section

CS9.0 **Does this research study involve the administration of an investigational drug or an FDA-approved drug that will be used for research purposes?**

* No

CS9.1 **Do you plan to utilize the Investigational Drug Service (IDS) to dispense the drug?**

*

CS10.0 Is this research study being conducted under a University of Pittsburgh-based, sponsor-investigator IND or IDE application?

* No *If YES, you are required to submit the IND or IDE application and all subsequent FDA correspondence through the Office for Investigator-Sponsored IND and IDE Support (O3IS). Refer to applicable University policies posted on the O3IS website (www.O3IS.pitt.edu).*

CS10.1 **Append to this application**:

(1) Copy of the current version of the clinical protocol submitted with the IND or IDE application which corresponds to this IRB submission:
Name Modified Date

(2) Copy of the FDA's letter which acknowledges receipt of the application and assignment of the IND or IDE number:

Name Modified Date

View: CS11.0

Cover Sheet Section

CS11.0 **Use the 'Add' button to upload one or more of the following:**

- **the sponsor protocol (including investigator initiated studies) and/or other brochures**
- **the multi-center protocol and consent form template, *if applicable***

Name Modified Date

Is this research study supported in whole or in part by industry? This includes the provision of products (drugs or devices). * No

Is this a multi-centered study?* No

View: CS12.0 - 14.0

Cover Sheet Section

CS12.0 **Does your research protocol involve the evaluation or use of procedures that emit ionizing radiation?*** Yes

HUSC GUIDANCE REQUIREMENTS FOR THE REVIEW OF HUMAN SUBJECT RESEARCH PROTOCOLS BY THE HUMAN USE SUBCOMMITTEE (HUSC), RADIATION SAFETY COMMITTEE

For Research Protocols Involving the Evaluation of Use of **Diagnostic Procedures** that Emit Ionizing Radiation: Formal HUSC review/approval is required if the research protocol involves **any** of the following:

1. The use or evaluation of a radioactive agent or procedure that is not currently approved (i.e., for any clinical indication) by the FDA
2. The evaluation (i.e., for safety and/or effectiveness) of a FDA-approved radiopharmaceutical or procedure for an "off label" indication[1]; or the use of a FDA-approved radiopharmaceutical or procedure for an "off label" indication if such use is experimental (i.e., not routinely performed in clinical practice).
3. Individuals (e.g., healthy volunteers) who would not be undergoing the procedure in association with the diagnosis or treatment of a disease or condition

Formal HUSC review/approval is not required if the diagnostic procedure is being performed, in a standard clinical manner and frequency, for screening or to evaluate the outcome of a treatment regimen. This would include diagnostic procedures for off- label uses that are routinely performed in clinical practice. [2,3]

For Research Studies Involving the Use or Evaluation of **Therapeutic Procedures** that Emit Ionizing Radiation:

Formal HUSC review/approval is required if parameters (e.g., total radiation dose, dose fractionation scheme, etc.) of the radiation therapy procedure(s) are defined by the research protocol.

[1]An "off-label" indication is a clinical indication which is not currently specified in the FDA-approved product labeling.[2]The risks of radiation exposure associated with the diagnostic procedure must continue to be addressed in the protocol and consent form using the HUSC-accepted wording.[3]The University of Pittsburgh IRB, at its discretion, may request formal HUSC review of the research protocol.

For any questions related to these requirements or their application, contact the Chair of the HUSC (412-383-1399) or the University's Radiation Safety Office (412-624-2728)

CS12.1 **After reviewing the HUSC guidance above, does your research protocol require HUSC review?** (Note: University of Pittsburgh's Radiation Safety Committee oversight is limited UPMC Presbyterian-Shadyside, Magee Women's Hospital of UPMC, Children's Hospital of Pittsburgh-UPMC, and Hillman Cancer Center. If other sites, you will be required to obtain approval from your radiation safety officer. Please contact askirb@pitt.edu for more information.)

Yes

Upload Radiation Forms:

Name	Modified Date

CS13.0 **Does this research study involve the deliberate transfer of recombinant or synthetic nucleic acid molecules into human subjects?**

* No

Upload Appendix M of NIH Guidelines:

Name	Modified Date

CS14.0 **Are you using UPMC facilities and/or UPMC patients during the conduct of your research study?**

* Yes If Yes, upload completed Research Fiscal Review Form:

Name	Modified Date
BTI++ Initial FRIAR Draft Mod 3	7/24/2015 10:31 AM

View: CS15.0 - CS15.0.1(a)

Cover Sheet Section

CS15.0 **Indicate the sites where research activities will be performed and/or private information will be obtained.**

Choose all sites that apply and/or use **Other** to include sites not listed:

Sites:
UPMC

University of Pittsburgh
Campus:
There are no items to display

List university owned off-campus research sites if applicable:

UPMC
Sites:
UPMC Presbyterian
UPMC Magee Women's Hospital
UPMC Montefiore
UPMC Shadyside
Other UPMC Site- Specify below:

UPMC Aesthetic Plastic Surgery Center 3380 BLVD of the Allies suite 158Pittsburgh, PA. 15213

UPMC Cancer Network Sites:
Site
There are no items to display

If you selected **School**, **International** or **Other**, list the sites:UPMC Aesthetic Plastic Surgery Center3380 Boulevard of the Allies, Suite 158

***For research being conducted at non Pitt or UPMC sites, upload a site permission letter granting the researcher permission to conduct their research at each external site:**
Name Modified Date

CS15.1 **Have you, J. Peter Rubin , verified that all members of the research team have the appropriate expertise, credentials, and if applicable, hospital privileges to perform those research procedures that are their responsibility as outlined in the IRB protocol?**

* Yes

CS15.2 **Describe the availability of resources and the adequacy of the facilities to conduct this study:**

* UPMC Facilities have the resources necessary to perform this clinical trial. UPMC Operative suites and clinics provide the support necessary to

see and perform surgical procedures to meet the collection of data to assess the objectives of the study.

View: CS16.0

Cover Sheet Section

CS16.0 **Special Research Subject Populations:**

Categories
None

View: CS17.0

Cover Sheet Section

CS17.0 **Does your research involve the experimental use of any type of human stem cell?*** No

View: Clinical Trial Study

NIH Definition of a Clinical Trial

A research study[1] in which one or more human subjects[2] are prospectively assigned[3] to one or more interventions[4] (which may include placebo or other control) to evaluate the effects of those interventions on health related biomedical or behavioral outcomes.[5]

[1] See Common Rule definition of research at 45 CFR 46.102(d) .

[2] See Common Rule definition of human subject at 45 CFR 46.102(f) .

[3] The term "prospectively assigned" refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.

[4] An intervention is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.

[5] Health-related biomedical or behavioral outcome is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects' biomedical or behavioral status or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.

CS18.0 *** Based on the above information, does this study meet the NIH definition of a clinical trial?** ○ ○ Yes ○ ○ No

If Yes, click Save and then Click Here For Study Team's CITI Training Records . Please ensure all personnel's training is up to date

View: 1.1 - 1.4

Section 1 - Study Objective, Specific Aims, Background and Significance

1.1 **Objective: What is the overall purpose of this research study?** (Limit response to 1-2 sentences.)The Objective of this study is to evaluate the changes in facial appearance over time in craniofacial deformity subjects who are post injury and/or post surgery (e.g. tx of aneurism, intercranial bleed, and tumor resections that do not involve radiation and would be analogous to trauma population requiring craniotomy) following autologous fat graft procedure.

1.2 **Specific Aims: List the goals of the proposed study (e.g., describe the relevant hypotheses or the specific problems or issues that will be addressed by the study).**Facial trauma injuries, especially those sustained in military combat and severe automobile crashes, are characterized by destruction of bone and soft tissue anatomy. While the bony skeleton can often be reconstructed, the overlying soft tissue is difficult to restore. Similar deformities typically seen after treatment of facial trauma.Importantly, it is the structure of the soft tissue that imparts the normal human form, and adequate reconstruction of soft tissue defects allows trauma victims to reintegrate into society. Accepted procedures for soft tissue reconstruction of the face involve tissue flap reconstruction procedures and autologous fat grafting. Tissue flap operations are extensive, often including microvascular surgery, and do not precisely correct the deformities. Fat grafting is a less invasive technique that allows for more precise shaping of the reconstructed tissues. However, autologous fat grafts may undergo resorption that can affect the appearance of the reconstruction over time. The degree of change in appearance after fat grafting has not been well studied for facial trauma patients. We hypothesize that initial results from fat grafting for facial trauma will show good restoration of tissue volume, and that a majority of the fat tissue will remain in place over time. Additionally, we hypothesize that the cellular properties of the fat precursor cells (preadipocytes) may correlate with fat graft retention.The specific aims of the study are:1) Assess facial appearance and soft tissue volume before and after autologous fat grafting using CT scans, standard photography and 3D photography.2) Assess cellular properties of the cells within the fat graft3) Measure of quality of life in patients before and after autologous fat grafting using validated psychosocial measures. 4) Compare the cotton rolling to centrifugation method of autologous fat grafting. This will be accomplished by analyzing outcomes of facial appearance and soft tissue volume in subjects in this study compared to those subjects enrolled in protocol PRO09060101.

1.3 **Background: Briefly describe previous findings or observations that provide the background leading to this proposal.** Autologous fat grafting is a common procedure in clinical plastic surgery. Clinical use of autologous fat grafting in humans was described as early as 1893, when Neuber published his report of transferring multiple small particles of fat to fill a soft tissue depression (1). Over the past three decades, autologous fat grafting has become a common procedure in clinical plastic surgery, and is also employed by clinicians in other specialties. The refinement of liposuction techniques in the 1980's made it possible to harvest the adipose grafts with low risk and without the need for a significant incision. The liposuction aspirate could simply be re-injected at a different site. Specialized equipment has been developed for fat grafting and is commercially available from a number of sources. The American Society of Plastic Surgeons 2007 procedural statistics show that over 65,000 fat grafting procedures were performed in the United States (www.plasticsurgery.org)Autologous fat grafting has often been used in the craniofacial regionOf the anatomic sites that autologous fat grafting can be applied to, a significant experience

has been accrued in the craniofacial region. Indications include post-traumatic reconstruction, congenital deformities, post-surgical deformities (e.g. cancer resection), facial atrophy associated with HIV treatment, acne scars, and cosmetic correction of facial aging (2-25). Adipose tissue is injected into the subcutaneous planes and into deep fat pads. Volumes of adipose tissue injection in the facial region tend to range from several ml to over 100 ml. Procedures are often performed in a single stage, but staged fat injections are not uncommon.Advantages of autologous fat grafting for craniofacial reconstructionAutologous fat grafting has many advantages for craniofacial reconstruction compared with alternative treatments. Other standard methods of restoring soft tissue volume involve the surgical transfer of tissue flaps, either on a vascular pedicle or by microvascular technique. These flap procedures are much more invasive, carry a risk of donor site morbidity, and do not allow for precise. We have had significant and successful improvement in all subjects, with retention of volume in the range of 65%. Our basic science team recently published a paper in Plastic and Reconstructive Surgery Journal demonstrating in an animal model that a manual processing technique for separating the aqueous layer from the fat graft material without centrifugation provides superior volume retention after healing. This manual separation method requires less equipment in the operating room, making it more applicable for a variety of clinical settings in the military health system. Craniofacial Injuries Have Serious Psychosocial Sequele and Affect Quality of LifeMany individuals who suffer significant facial disfigurement from injury experience psychological distress and impairment in functioning not limited to the acute phase of injury but over a longer term period of treatment, recovery and adjustment (26, 27). Symptoms of anxiety and depression and post-traumatic stress disorder are common—both before and after surgery (28, 29). In their study of individuals with severe facial lacerations and disfigurement, Levine and colleagues (30) noted the “powerful [influence] of facial appearance and body image on the quality of life” of these individuals. Clinical studies of facial trauma victims, using structured interview and self-report instruments, also document the common experience of social anxiety and social withdrawal—problems that can significantly compromise social and occupational functioning and engagement in social and leisure time activities--ultimately impacting the overall quality of life (31, 32). Facial burn victims report that interactions with strangers and with children and adolescents can be particularly discomfiting in response to visible non-verbal communications of negative affect (e.g. surprise, disgust) (27). Results of outcome studies of burn patients suggest that personal adjustment and quality of life are better predicted by psychosocial factors than site of injury (33). Pre- and post-surgical psychosocial factors such as social support, coping skills, and satisfaction with surgical outcomes are significant predictors of personal and social adjustment and quality of life outcomes, in addition to the physical outcomes of surgical intervention for disfigurement (34-36). Significant is the fact that there are few studies of the psychosocial impact of complex CMF battle injuries and post-surgical changes in psychosocial well-being and quality of life.

1.4 **Significance: Why is it important that this research be conducted? What gaps in existing information or knowledge is this research intended to fill?** Fat grafting may represent a superior method of facial reconstruction after severe facial deformity, but the results can be impacted by resorption of fat volume over time. This study will examine the impact of the fat grafting procedure on facial appearance and quality of life over time by precisely measuring soft tissue volume with CT scans, assessing appearance with 2D and 3D photography and standard photography and evaluating quality of life through various validated psychosocial measures. This study will be a very important evaluation of the effectiveness of this procedure, and will help guide clinicians in applying the technique. Additionally, laboratory testing of the injected fat material will be performed so that the results may be correlated with clinical outcomes in the future.The study is also demonstrating the application of a minimally invasive injectable technique to a very difficult reconstructive problem. The concentration of the cotton roll technique for autologous fat processing has the potential to further improve clinical outcomes while simplifying the procedure.

View: 2.01

Section 2 - Research and Design Methods

2.1 **Does this research study involve the *use* or evaluation of a drug, biological, or nutritional (e.g., herbal or dietary) supplement?**

* No

2.1.1 **Does this research study involve an evaluation of the safety and/or effectiveness of one or more marketed nutritional (e.g., herbal or dietary) supplements for the diagnosis, prevention, mitigation or treatment of a specific disease or condition or symptoms characteristic of a specfic disease or condition?**

*

2.1.1.1 **List each of the marketed nutritional supplements being evaluated in this research study. Specify for each supplement the corresponding IND number or attach FDA correspondence specifying that an IND is not required.**

Marketed nutritional supplement	IND number
There are no items to display	

Upload FDA correspondence specifying that an IND is not required, if applicable:

Name Modified Date Version

View: 2.02

Section 2 - Research Design and Methods

2.2 **Will this research *use* or evaluate the safety and/or effectiveness of one or more devices?**

* No

2.2.1 **Does this research study involve an evaluation of the safety and/or effectiveness of one or more devices not currently approved by the FDA for general marketing?***

If **YES**, describe your **plan to prevent unauthorized use of the investigational device**:

2.2.1.1 **List each of the unapproved devices being evaluated in this research study.** Specify for each listed device the corresponding Investigational Device Exemption (IDE) number or provide a justification for why you feel that this device and its use, as proposed in this research study constitute a non-significant risk (i.e., to include potential failure of the device) to the research subjects:

Unapproved device	IDE #	Non-significant risk justification
There are no items to display		

View: 2.03 - Summarize general classification

Section 2 - Research Design and Methods

2.3 **Summarize the general classification (e.g., descriptive, experimental) and methodological design (e.g., observational, cross-sectional, longitudinal, randomized, open-label single-blind, double-blind, placebo-controlled, active treatment controlled, parallel arm, cross-over arm) of the proposed research study, as applicable.**

This is an experimental intervention study with an observational component assessing clinical outcomes following the fat graft reconstructive surgery procedure using a manual separation process of the fat grafting material.

2.3.1 **Does this research study involve a placebo-controlled arm?**

* No

View: 2.04

Section 2 - Research Design and Methods

2.4 **Will any research subjects be withdrawn from known effective therapy for the purpose of participating in this research study?**

* No

2.4.1 **Provide a justification for discontinuing subjects from known effective therapy for the purpose of study participation.**

2.4.2 **Describe the risks to subjects associated with discontinuing them from known effective therapy for the purpose of study participation.**

View: 2.05

Section 2 - Research Design and Methods

2.5 **Will screening procedures (i.e., procedures to determine research subject eligibility) be performed specifically for the purpose of this research study?**

* Yes

2.5.1 **List the screening procedures that will be performed for the purpose of this research study. Do NOT include the inclusion/exclusion criteria in this section as they will be addressed in section 3; questions 3.13 and 3.14.**

Obtain Informed Consent, assignment of subject unique identifierMedical and surgical history review: The PI and/ or co-investigator will perform a medical and surgical history review inclusive of past medical and surgical procedures pertaining to the craniofacial trauma, laboratory tests, radiological tests, and consults pertaining to trauma event. If medical records do not accompany the subject or are not available at the time of screening evaluation for investigator review, the investigator in lieu of direct medical record review will accept direct report from the referring physician, and/or other referral source and /or subject self-report and will document this reported information to research chart. This report will consist of past medical /surgical history pertaining to the craniofacial defect and trauma. The Principal Investigator will base determination of study eligibility on a combination of evaluation criteria to include physical examination, referral physician/other source direct report and /or subject self-report and psychological (SCID) assessment all pertaining to past injury and current status of the area of interest.Performance of a medical history and physical exam inclusive of participant's height and

weight, Body mass index (BMI) calculation and craniofacial exam will be completed by PI and /or a co-investigator. Collection of subject's vital signs (Temperature, heart rate (HR), respiratory rate, blood pressure (BP), medication profile to include prescription and vitamins / supplements. Collection of demographic information to include date of birth, gender, race and ethnicity, smoking history, relationship status, educational level, dominant handedness, and allergies. 2D Photographs: Pictures will be taken of the entire face (only) with a professional-grade camera creating images with high resolution and excellent detail. The pictures that will be taken may include following views: 1. Front view2. AP three-quarter Right 3. AP three-quarter Left 4. Lateral Right5. Lateral Left Dependent on investigator evaluation we may opt to obtain the following views: 1. Inferior view2. Superior viewThe pictures will be taken at the UPMC Aesthetic Plastic Surgery Center in a private room and will take approximately 10 minutes. 2D photographs will be taken by the PI, Co-Investigator or a research coordinator.A Structured Clinical Interview for DSM-IV (SCID) will be included in the baseline to evaluate the presence/absence of psychiatric disorders. This evaluation will be completed using a standard psychiatric diagnostic interview that enables determination of DFSM-IV-based diagnoses. As part of the clinical interview a demographic history will be completed. Participants who are women of child bearing potential will receive a urine pregnancy dip test. All screening procedures will be performed at the UPMC Aesthetic Plastic Surgery Center in a private room and will take approximately 2-3 hours of the participant's time. Eligibility Determination: Upon the completion and evaluation of all screening procedures subject eligibility determination for continued study participation will be completed by the Principal Investigator (PI),.Due to participant's schedule, travel distance and/or coordination of the screening study visit, procedures may be performed on different days as long as the screening procedures do not exceed a length of 2 weeks for completion. The principal investigators eligibility determination will occur up to 45 days post the date of completion of the last screening visit procedure date.

2.5.2 **What steps will be taken in the event that a clinically significant, unexpected disease or condition is identified during the conduct of the screening procedures?**

Addressed below:

Upon discovery the PI and/ or co-investigator will notify the subject of any event that could be of clinical significance needing further evaluation, or of a diagnosis of any unexpected disease or condition that occurred during the conduct of the study's research procedures. The study investigator will at the time of discovering the event contact the referring physician or primary physician for further evaluation of the event. Should the event be of a critical nature needing immediate intervention, the study investigator or co-investigator will proceed with immediate clinical intervention and screening procedures will be concluded.

View: 2.06

Section 2 - Research Design and Methods

2.6 **Provide a detailed description of all research activities (e.g., all drugs or devices; psychosocial interventions or measures) that will be performed for the purpose of this research study.** This description of activities should be complete and of sufficient detail to permit an assessment of associated risks. At a minimum the description should include:

- **all research activities**
- **personnel (by role) performing the procedures**

- **location of procedures**
- **duration of procedures**
- **timeline of study procedures**

Upon the completion of screening procedures and if tests are within normal range (including a negative pregnancy test for women), the investigator will invite the subject to participate in the study. The research procedures for this clinical trial are as follows:Pre-Graft Study Visit (PGSV)Collection of subject's vital signs (Temperature, heart rate (HR), respiratory rate, blood pressure (BP), medication profile to include prescription and vitamins / supplements, allergies, weight, Body mass index (BMI) calculation and Adverse Event Assessment.3-Dimensional imageThe investigator or study staff will take photographs of the entire face (only) with the Canfield 3D camera system. The camera takes 2 simultaneous photographs of the face from different angles and makes a 3-dimensional image. The 3D camera system is not a medical device and is not regulated by the FDA. The pictures will be taken at the UPMC Aesthetic Plastic Surgery Center in a private room and will take approximately 10 minutes. Limited medical history and physical exam with a craniofacial exam by the investigator. The investigator will rate the appearance/volume of the graft site using a craniofacial volume and appearance grading scale. 2D Photographs the pictures will be taken at the UPMC Aesthetic Plastic Surgery Center in a private room and will take approximately 10 minutes. 2D photographs will be taken by the PI, Co-Investigator on the study or a research coordinator.Digital Recordings: for subjects who consent, digital recordings (photography or video) will be collected at any and all portion's of the subject's pre-operative, operative and post-operative study participation. These may include but not be limited to, videos of personal interviews, functional assessment testing and study physical exams or photos of the subject's follow-up course, biopsies, etc. We will ask the subject's permission to allow Dr. J. Peter Rubin and research team to use any and all these digital recordings for medical education and training, publication and media reports-and, in any mode of transmission, including but not limited to: print, email, television, internet, etc. Serial Computed Tomography Imaging A high resolution Computed Tomography (CT) Scan of the face will be performed at Presbyterian Hospital and will take approximately 60 minutes. This scan will be pre-procedural and will serve as a baseline. All CT scans will be performed on a 64-slice scanner (LightSpeed, GE Healthcare), using collimation of 0.625mm and slice interval of 0.3mm, resulting in approximately 50% overlap between adjacent slices. kVp, mA, and FOV will be optimized to the subject, but will approximately be kVp = 120; mA = 320, FOV = 18cm. Soft tissue and bone kernels will be employed. These images will be volumetrically reformatted into coronal and sagittal planes for confirmation of findings. Additionally, surface-rendered volumetric reformats will be created emphasizing both bony structures and soft tissues. Images will be reviewed by a dedicated head and neck radiologist with 9 years of experience in CT of the face. Volume measurements of the implanted material will be made on all post-procedural CTs. These volumetric measurements are expected to be precise to within 5% of the actual volume of material. Trends in volume of tissue will be analyzed over time across the multiple CT scans. Both linear and volumetric measurements will be used to quantify implanted material.Psychosocial AssessmentAt baseline, patients will be asked to complete a psychosocial battery that includes: a) self-report measures of satisfaction with physical appearance, anxiety and depressive symptoms, social functioning and social avoidance and distress and; b) questionnaires that assess significant predictors of quality of life outcomes from post-trauma craniofacial surgery: perceived social support, self-esteem, coping style and pre-surgical expectations of/post-surgical outcomes. A research technician experienced in psychosocial interviewing with patients (DM) will meet with each patient during the baseline evaluation to administer the self-report battery of psychosocial questionnaires. A comprehensive battery of tests for evaluation of quality of life has been assembled for this study. It is important to properly determine the impact of the surgical changes and the investigators have selected Psychosocial

assessment instruments to evaluate four domains:a) Satisfaction with appearance/surgical outcomes: The Satisfaction with Appearance (SWAP) scale is a 14-item questionnaire with good internal consistency and test-retest reliability that measures both subjective and social–behavioral aspects of body image and has been used in populations with significant physical disfigurements or deformities. b) Satisfaction with Medical/Health Services - Patient Satisfaction with Health Services – the Client Satisfaction Questionnaire (CSQ-8) (38) is a widely used brief inventory of satisfaction with services (amount of help, kind of help, availability of help) provided by a medical service or program. This 8-item self-report questionnaire will be administered at each of the post-surgery visits.c) Social Distress, Depression and Avoidance: Social Distress and Avoidance - Individuals with facial disfigurement can suffer extreme anxiety and avoidance in interpersonal interactions. The Social Anxiety and Distress (SAD) Scale (40) is a widely used measure of social avoidance and distress that has shown to be sensitive to pre-/post- surgical improvement in recent studies of patients undergoing reconstructive surgery for significant physical deformity. Anxiety and Depressive Symptomatology will be monitored using the Patient Health Questionnaire (PHQ-Brief) (41) and the PCL-S (Brief) (42), a self-report questionnaire that taps PTSD symptoms for use among individuals. Self-esteem will be assessed by the Rosenberg Self Esteem Inventory (SES)(43), a brief (10-item), self-report inventory has been widely used in research on reconstructive surgery for facial trauma. Coping Style will be assessed with the Brief COPE inventory (44) an abbreviated version of the situation-specific coping inventory (45) that has been effectively used to characterize psychological coping with physical illness and disability. An extensive body of research on clinical and psychosocial outcomes from surgical and medical interventions has yielded evidence that psychosocial coping style is an important factor that contributes to psychological well-being, physical health and quality of life outcomes. Presence of d epression will be captured in a self-report inventory, one of the most widely used instruments for measuring the severity of depression. The Beck Depression Inventory is composed of 21 items relating to symptoms of depression such as hopelessness and irritability, cognitions such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, and lack of interest in sex.Perceived Social Support will be analyzed by the Perceived Social Support Questionnaires(PSSQ)-Family and Friends (46). This 6-item self-report inventory with satisfactory internal reliability and construct validity regarding the perceived availability of social support for needs for support, information and feedback. Social support, along with psychosocial coping cognitions and behaviors contributes significantly to psychological well-being, physical health and quality of life outcomes. Each of these may be important covariates that contribute to variance in quality of life outcomes in this study. d) Quality of Life and General Functioning Outcomes - Quality of life and general functional status will be evaluated using the SF-36 (47, 48), a self-report inventory widely used in medical outcome research with self-rated indices of health, quality of life, energy, role limitations due to physical problems or emotional problems, and functionality in everyday physical, emotional, and social function domains. A brief (shortened) demographic history form will be completed as part of the psychosocial assessments. These baseline clinical and psychosocial evaluation will take an estimated 1 hour and will take place at the UPMC Plastic Surgery Center in a private room. A research coordinator or research technician certified with psychosocial assessment experience will administer these questionnaires.PRE-OP Laboratory blood tests will be obtained via a peripheral stick performed by laboratory personnel located on the 5th floor of the UPMC MUH building to include CBC with Differential,Platlets Comprehensive Chemistry panel, and PT/ PTT/ INR. If the subject is a female of child bearing potential, we will obtain a urine pregnancy dip test. If the test result is positive the subject will not continue participation in this research study. Electrocardiogram (EKG) Chest X-ray as indicated by past medical history and/or physician discretionA coordinator note will be completed summarizing the study visit and placed into the subject's chart. The total time duration for subject participation for this visit is estimated to be approximately 3-4 hours in length. FAT GRAFT Surgical Procedure: For the purpose of

this study the fat grafting procedure is a research procedure. It is very important to note that this research procedure is not an experimental procedure. Fat grafting is a minimally invasive clinical procedure that has been widely used by plastic surgeons within reconstructive surgery for many years. Fat grafting is known as a filler providing an accurate means to restoring facial soft tissue structure. The fat grafting procedure will occur at UPMC Magee or Montefiore Hospital Surgical Suites. On the day of the surgical procedure, prior to entering the operating room, the Investigator physician will mark the subject's facial area(s) intended for fat grafting procedure. 2D pictures may also be obtained for research purposes at this time. With the fat graft procedure the subject will be given general anesthesia, a medicine that will relax and assist to in keeping the subject unconscious (in a sleep like state) during the entire procedure. Once unconscious, the plastic surgeon, using small narrow tube-like instruments called cannulas, will remove fat from various places throughout the body (commonly the abdomen and thighs). The processing of the fat graft material is done using a Tefla non-adherent gauze pad in a rolling technique that separates the aqueous and oil layers from the injected component. The plastic surgeon will then use the Coleman cannulas (specialized smaller cannulas with varied shapes and tip sizes specifically made to deliver smaller amounts of fat) to fill the desired area. The facial areas which are known to have tight spaces with varying angles and can have scarring bands (scar tissue) makes the Coleman cannula appropriate for this type of fat delivery. The Coleman Cannula System is also associated with less graft re-absorption than other techniques. The Coleman Cannula System is not experimental and is commercially available in the United States and in compliance with Federal regulations. During the Fat grafting reconstructive surgery the PI and /or Co-investigator will obtain a portion of the fat (lipoaspirate) up to 80ccs specimen will be collected as a research sample. If the subject refuses to give consent for this sample, the subjects will not be able to participate in the clinical trial. The sample will remain under the oversight of Kacey Marra, PhD, Co-Investigator examined for cellular information in the Plastic surgery lab located on the 16th floor of the Biomedical Science Tower, University of Pittsburgh. The samples will be de-identified, labeled with the subject's study ID number. Once the surgical procedure has been completed the subject will go to the recovery room where he /she will be monitored until stable enough to be released to home. There might be a possibility that the subject would be admitted to the hospital overnight for observation as deemed necessary by the plastic surgeon. The following lab process will take place in the University of Pittsburgh Adipose Stem Cell Center lab:Up to 80cc of the lipoaspirate specimen will be used to obtain preadipocytes. The specimen will be digested in balanced salt solution containing 1 mg/ml collagenase and 3.5% fatty acid free BSA in a 37°C shaking water bath until fragments are no longer visible and digest has a milky appearance. Digests are filtered and centrifuged at 1000 rpm for 10 minutes. Floating adipocytes are removed and the remaining digests are treated with an erythrocyte lysis buffer. Plating media will be changed every two days until confluence (~4 days to reach 90% confluence). 1x106 adiposed-derived stem cells/patient will be stored at -80°C. Remaining cells will be utilized in the experiments below. We have been successfully culturing human preadipocytes in our laboratory for the past 7 years.[1-12]Preadipocyte yield: The number of cells isolated per gram of adipose tissue will be determined using a hemacytometer. Comparison of isolated cells from gentle centrifugation of lipoaspirate at 200 rpm for 3 minutes to adipose-derived stem cells will be determined.Preadipocyte Viability: Cell viability will be determined using the Live/Dead assay. The live cells will be stained with fluorescein diacetate (FDA, Green) and dead cell nuclei will be stained with propidium iodide (PI, Red). Preadipocyte Proliferation: Cellular proliferation of preadipocytes will be assessed with the CyQUANT Cell Proliferation Assay Kit (Invitrogen, Carlsbad, CA) at 48 and 96 hours. Media will be changed every 48 hours.Preadipocyte Differentiation: To assess the potential of the preadipocytes to differentiate into the adipogenic cell type within the HA gels, cells will be treated plating media containing 0.2 nM dexamethasone, 0.5 uM insulin, 0.2 nM triiodothyronine, antibiotics, and 540 uM IBMX in addition to their current media. To confirm adipogenesis, lipid inclusions cells will be confirmed

by staining with Oil Red-O. Additionally, protein expression of PPAR and FABP4 will be determined using western blot analysis, and RNA expression of these adipogenic markers will be determined using PCR.Preadipocyte characterization. We will characterize preadipocytes from each patient for stem cell surface antigens using flow cytometry. Passage zero preadipocytes isolated (as described above) from the abdominal subcutaneous tissue will be divided into aliquots of 5x105 cells and stained with selected monoclonal antibodies (mAbs) against progenitor cell surface markers. The antibodies include mAbs against CD34, CD45, CD90, CD133, CD105 and CD166. Rationale for these surface markers includes the following: 1) these markers are routinely examined for bone marrow stem cell markers, and have also been examined as adiposed-derived stem cells markers,[13]and 2) we will be able to discern stem cell purity by testing for these markers. The cells will be incubated with mAbs for 30 min at 4 ?C, and washed in PBS. At least 100,000 viable cells based on 7AAD(-) staining in each sample will be acquired and analyzed using a FACSAria fluorescence-activated cell sorter (Becton-Dickinson).The samples will remain 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, University of Pittsburgh

2.6.1 **Will blood samples be obtained as part of this research study?**

* Yes *If submitting a protocol for expedited review, it should be clear that the planned blood draws are within the parameters described here: http://www.hhs.gov/ohrp/policy/expedited98.html (see Expedited Research Category #2)

If **Yes**, address the frequency, volume per withdrawal, the total volume per visit, and the qualifications of the individual performing the procedure:Laboratory blood tests will be obtained via a peripheral stick performed by laboratory personnel located on the 5th floor of the UPMC MUH building to include CBC with Differential, Comprehensive Chemistry panel, and PT/ PTT/ INR

The purpose of the flowchart is to enhance and not replace the detailed description for all research activities in question 2.6.

It is the ***responsibility of the PI to ensure consistency of the content within the entire IRB application*** which includes all uploaded documents (e.g., sponsor protocol, consent, flow charts).

Study Flow Chart:

Name	Modified Date
BTI++ Study Schema	7/2/2015 1:17 PM

View: 2.07 - 2.07(b)

Section 2 - Research Design and Methods

2.7 **Will follow-up procedures be performed specifically for research purposes? Follow-up procedures may include phone calls, interviews, biomedical tests or other monitoring procedures.*** Yes

Detailed procedures listed in the textbox below:

Post graft study visits:POST op study visit (Day 3-6)This study visit will occur with the study investigator or research team and will take place approximately in 3-6 days post surgical procedure for the purpose of incision assessment and suture removal. The entire visit will take approximately 30-45 mins and will be scheduled with the subject prior to hospital discharge post fat graft procedure. 1.) Limited medical history and physical exam with craniofacial exam 2.) Collection of any Adverse events (Should an adverse medical event occurred prior to the visit and be reported by the subject, the research team will do due diligence to collect information pertaining to the event through subject report and /or medical record review and /or referring physician report)3.) Collection of current medications, allergies and vital signs. Study visits (V1-V3): This study visit will occur with the study investigator or research team and will take place 7-21 days (+2 weeks) after the fat grafting surgical procedure, the entire visit will take approximately 2-3 hours. This visit will be scheduled by the research coordinator and discussed with the subject prior to the fat graft procedure. These research procedures will be repeated at both 3 months after the fat grafting procedure [Visit 2 (V2)] and at 9 months after the fat grafting procedure [Visit 3 (V3)]. The following research procedures will be completed:1.) Subject weight and BMI measurement calculation 2.) 3-Dimensional photographs 3.) Limited medical history review and physical exam with a craniofacial exam completed by the PI and /or the Co-investigator 4.) 2D Photographs5.) Psychosocial questionnaires assessment 6.) Collection of subject's vital signs (Temperature, heart rate (HR), respiratory rate, blood pressure (BP), medication profile to include prescription and vitamins / supplements, and allergies.7.) The investigator will rate the appearance/volume of the graft site using a craniofacial volume and appearance grading scale 8.) A urine pregnancy test will be given to women of child bearing age prior to the CT scan. 9.) CT Scan with 3D renderings10.) Structured Clinical Interview for DSM-IV (SCID) (Visit 3 V3 only) A Structured Clinical Interview for DSM-IV (SCID) will be included to evaluate the presence/absence of psychiatric disorders. This evaluation will be completed using a standard psychiatric diagnostic interview that enables determination of DFSM-IV-based diagnoses. The information contained in the SCID will be collected by a research technician, a member of Dr. Gretchen Haas's clinical team who is experienced in psychosocial interviewing with patients. This SCID will take approximately 45-60 minutes of the subject's time to complete. 11.) Adverse Event Reporting (Should an adverse medical event occurred prior to the visit and be reported by the subject, the research team will do due diligence to collect information pertaining to the event through subject report and /or medical record review and /or referring physician report)Due to the subjects traveling distances who are enrolled into this trial, we have included a (+/-) of 14 days (2 weeks) for the completion of Visit 2 and Visit 3 as a convenience for the coordination of schedules.

View: 2.08

Section 2 - Research Design and Methods

2.8 **Does this research study involve the use of any questionnaires, interview or survey instruments?*** Yes

Upload a copy of all materials except for the SCID or KSADS which are on file at the IRB. The use of all instruments must be addressed in question 2.6 and/or question 2.7 (except for an exempt submission where they should be addressed on the appropriate uploaded exempt form).

Name	Modified Date
QOL demographic baseline form	2/25/2015 10:12 AM
Beck Depression Inventory	2/24/2015 3:25 PM
Rosenburg Self-esteem	2/24/2015 3:17 PM

Social Avoidance (SAD)	2/24/2015 3:16 PM
PCL-S	2/24/2015 3:21 PM
CSQ-8	2/24/2015 3:21 PM
Perceived Social Support Questionnaire (PSSQ)	2/24/2015 3:22 PM
SWAP	2/24/2015 3:16 PM
Coping Scale	2/24/2015 3:18 PM
SF_36.pdf	2/24/2015 3:17 PM
PHQ_Brief.pdf	2/24/2015 3:22 PM
Brief Demographic Form	2/24/2015 3:17 PM

Previously the name and publisher for commercially available materials were listed in the textbox below but effective 9/1/2015, all materials (except for the SCID and KSADS) must be uploaded using the Add button above.

View: 2.09 - 2.10

Section 2 - Research Design and Methods

2.9 **If subjects are also patients, will any clinical procedures that are being used for their conventional medical care also be used for research purposes?*** no

If **Yes,** describe the clinical procedures (and, if applicable, their frequency) that will be used for research purposes:

2.10 The blood sample question was moved to 2.6.1.

View: 2.11

Section 2 - Research Design and Methods

2.11 **What is the total duration of the subject's participation in this research study across all visits, including follow-up surveillance?*** Approximately 12-13 months

View: 2.12

Section 2 - Research Design and Methods

2.12 **Does this research study involve any type of planned deception?** If Yes, you are required to request an alteration of the informed consent process (question 4.7)

* No

2.12.1 **Describe the planned deception:**

*

2.12.2 **Provide a justification for this planned deception:**

*

2.12.3 **Describe when and how subjects will be debriefed:**

*

View: 2.13 HB

Section 2 - Research Design and Methods

2.13 **Does this research study involve the use of UPMC/Pitt protected health information that will be de-identified by an IRB approved "honest broker" system?**

* No

2.13.1 **Identify the name of the honest broker system:**

2.13.2 **Specify the IRB-assigned honest broker system number (e.g., HB123456):**

2.13.3 **Specify the names of the individuals who will provide the honest broker services:**

Last	First	Organization
There are no items to display		

Previous inputted information for Question 2.13.3:

2.13.4 **Upload the signed honest broker assurance agreement:**

Name	Modified Date
There are no items to display	

View: 2.14

Section 2 - Research Design and Methods

2.14 **Will protected health information from a UPMC/Pitt HIPAA covered entity be accessed for research purposes or will research data be placed in the UPMC/Pitt medical record?*** Yes

If you answer **Yes**, you are required to submit this study to the Center for Assistance in Research using e-Record (CARe). Per UPMC Policy HS-RS0005, all research projects that access or involve UPMC electronic protected health information (e-PHI) must be submitted to CARe, with the exception of clinical trials that are contracted through the UPMC Office of Sponsored Programs and Research Support (OSPARS). Complete the online submission form at https://care.upmc.com/request.aspx. After the study is submitted in OSIRIS, a CARe representative will conduct a review. You will be notified once your CARe review is complete or if anything further is needed. Studies that will access only paper-based medical records (not in combination with any electronic records) do not need to be submitted to CARe.For additional information, please see https://care.upmc.com.

Describe the medical record information that will be collected from the UPMC/Pitt HIPAA covered entity and/or the research-derived information that will be placed in the medical records. The medical record information that may be extracted from the medical chart during a review are only those items pertaining to the subject's history of the trauma and all surgical procedures, consults, medications, lab values leading up to and after the fat graft procedure. Pre-procedure blood tests, including but not limited to blood clotting, red blood cell, electrolytes and cultures, history /physical exams of the face and body, MRI and CT scans, menstrual status and/or the results of pregnancy tests, and any medical record information that could adversely impact the outcome of the fat grafting reconstructive surgery procedure.This research study will result in identifiable information that will be placed into the subject's medical records held at UPMC. The nature of the identifiable information resulting from the

subject's participation in this research study that will be recorded in their 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 the subject's medical/physical safety.

2.14.1 **Will protected health information from a non-UPMC/Pitt HIPAA covered entity be obtained for research purposes or will research data be placed in the non-UPMC/Pitt medical record?** * No

If Yes, describe how the HIPAA requirements will be met:

I, J. Peter Rubin **, certify that any member of my research team accessing, reviewing and/or recording information from medical records have completed HIPAA Researchers Privacy Requirements (Formerly RPF Module 6) training. The HIPAA certificates must be available for review if audited but do not need to be uploaded into this OSIRIS application.**

* Yes

2.14.2 **Are you requesting a waiver of the requirement to obtain written HIPAA authorization for the collection of the PHI from a UPMC/Pitt covered entity?** ***Note that the University of Pittsburgh IRB cannot grant a HIPAA waiver for entities outside of UPMC/Pitt.*** * No

View: 2.15

Section 2 - Research Design and Methods

2.15 **Does this research study involve the long-term storage (banking) of biological specimens?**

* Yes

2.15.1 **Broadly describe the intended future use of the banked biological specimens:** To assess cellular properties of the grafted material in each patient for future correlation of the clinical outcomes.

2.15.2 **Indicate the planned length of storage of the banked biological specimens:**

* Indefinite

2.15.3 **Will biological specimens be stored without identifiers or linkage codes?**

If you answer Yes, the samples *will not* be stored with any identifiers or linkage codes and it is highly unlikely to be linked back to the individual.

If you answer No, the samples *will be* stored with an identifier or linkage code and can be linked back to the individual.

* No

View: 2.15.4

Section 2 - Research Design and Methods

2.15.4 **Will subjects (including family members, if applicable) be informed of their personal results from analyses performed on their biological specimens?**

* No

View: 2.15.4.1

Section 2 - Research Design and Methods

2.15.4.1 **Justify why the personal results will <u>not</u> be disclosed to the research subjects at this time. Under what conditions, if any, might personal results be disclosed to research subjects in the future?**

Personal results of analyses performed on the banked samples will not be disclosed to the research subjects because the involved research laboratory is not CLIA certified and the analysis/ results of future testing can not yet be interpreted or applied in a clinically relevant or meaningful manner.

View: 2.15.4.7 - 2.15.4.9

Section 2 - Research Design and Methods

2.15.4.7 **Describe the procedures that will be employed to protect the confidentiality of subjects' private information associated with use of biological specimens:**Unique subject identifiers will be used to label all data and research samples. All samples and data will be stored using codes assigned by the investigators or their designee, and any information linking these code numbers to the corresponding subjects' identities, medical and research information and all subject personal information collected from all study participants will be kept in a separate, locked file within the offices of the Department of Plastic Surgery, University of Pittsburgh. Stored specimens will be de-identified and may be provided to secondary investigators. Any information obtained from or for this research study will be kept as confidential as possible. All records pertaining to the subjects' involvement in this research study, including the lipoaspirate specimens, will be indicated by a code number only. The specimens will be kept indefinitely and stored in a –80 degree freezer on the 16th floor of the Biomedical Science Tower under the supervision of Kacey Marra, PhD. The specimens will be rendered anonymous, so no identifiers can be linked back to the subjects. Upon subject withdrawal, storage of the specimens will continue and only the PI will have access to the linkage code to the subject's identity. Data will be maintained and monitored in a password protected computer system. Printed data will be stored in the research study binders in a locked filing cabinet within the Department of Plastic Surgery office. Information linking the code numbers to the subjects will be kept in a separate locked filing cabinet that can only be accessed by the investigators and their research study staff. Subjects will not be identified by name in any publication of the research results unless they sign a separate release form giving permission.

2.15.4.8 **Will the banked biological specimens or data derived from them be provided <u>with subject identifiers</u> to any secondary investigators or external entities?*** No

2.15.4.9 **Will research subjects be remunerated in the event of the future commercial development of inventions or products based on the research use of their biological specimens?*** No

View: 2.16

Section 2 - Research Design and Methods

2.16 **Will research participants be asked to provide information about their family members or acquaintances?**

* No

2.16.1 **Describe what information about the third party will be obtained from the participant:**

2.16.2 **If the information about the third party is of a private nature, can the identity of the third party be readily ascertained or associated with this information?**

*

Describe the **private information** that will be collected and recorded about the third party:

View: 2.17 - 2.18

Section 2 - Research Design and Methods

2.17 **What are the main outcome variables that will be evaluated in this study?**

Analysis of all 2D and 3D Photographs, CT scans, Psychosocial assessments, outcomes of manual vs. centrifuged method of separating the aqueous portions of the fat graft material.Basic assays of adipose cell behavior to elucidate the functional properties of adipose cells used for grafting, with correlation to outcomes.

2.18 **Describe the statistical approaches that will be used to analyze the study data.**

* Addressed below:

Serial computed tomography imaging will be performed to assess the total soft tissue volume before fat grafting and afterwards at three time points: immediately post-grafting, three months post-graft and nine month post-graft. Comparisons of the post-graft tissue volume to pre-treatment volume will be performed using a paired t-test model. Repeated measures analysis of variance will be used to evaluate change over time in all outcome measures. Using standard conventions of alpha=0.05 and beta=0.8, an enrollment of ten patients will provide sufficient power to detect a clinically meaningful differences in the volume of soft tissue between groups.. Based on published effect sizes for clinically significant medical outcomes on the SF-36 (i.e., 0.5 to 0.7), e.g., following surgery for dentofacial deformities (d = 0.6) (64), and medium (0.5 – 0.79) to large (0.8 to > 3.0) effect sizes on SF-36 social functioning outcomes of neck surgery (65) and orthopedic surgery (66), it is expected that a sample of 10 patients will provide sufficient power to detect a medium effect size (d = 0.5) on SF-36 measures of social functioning and quality of life, applying standard conventions of alpha = 0.05 and beta = 0.8. The cotton rolling fat processing technique takes place in the Operative Room during the study surgery directly following the collection of the lipoaspirate. Outcome of facial appearance and soft tissue volume in subjects who were injected with fat grating material processed by the cotton rolling technique in this protocol will be compared to those subjects in protocol PRO09060101 who were injected with fat grafting material using the centrifuged technique. Significance level (adjusted for sidedness) =.025, standard deviation = 15 (15%), number of patients = 10, power= .0.8, difference in means = undefined, location of mean in one group as a percentile of the other group = undefined. The variable calculated was the minimum detectable difference. The probability is 80 percent that the study will detect a treatment difference at a two-sided 0.05 significance level, if the true difference between the treatments is 19.881 units or 19.8%. This is based on the assumption that the standard deviation of the response variable is 15 units or a 15% inter-individual coefficient of variation.

View: 2.19 - 2.19.6

Section 2 - Research Design and Methods

2.19 **Will this research be conducted in (a) a foreign country and/or (b) at a site (e.g., Navajo Nation) where the cultural background of the subject population differs substantially from that of Pittsburgh and its surrounding communities?*** No

Note that copies of training records, licenses, certificates should be maintained in the study regulatory binder and are subject to audit by the Research Conduct and Compliance Office (RCCO).

In addition, individuals planning to conduct human subject research outside the United States must complete an optional module on the CITI training website: International Studies. Click here to access the instruction sheet for accessing optional CITI modules.

2.19.1 **Address the following for each of the foreign/culturally different sites where this research will be conducted:**• Name of site• Name of authorized individual (e.g., IRB Chair) from the local IRB or other human subject protections entity that is responsible for the review and approval of the project; upload approval letter with an English translation, if applicable • Name and qualifications of the site collaborator responsible for the conduct of the research (e.g., site PI)• The anticipated number of subjects that will be enrolled at that site • If Federally funded, provide the Federalwide Assurance number (FWA) assigned to the site *

Site	Date Modified
There are no items to display	

2.19.1.1 **Provide a description of the context of cultural norms and local laws and highlight differences between U.S. culture in all areas relevant to your study, including, at a minimum:**

• Age of majority of participants to be enrolled• If study includes minors or decisionally impaired subjects, summarize laws on guardianship • If your study involves any invasive medical procedure (including blood draws), provide assurance that the individuals undertaking those procedures for research purposes are appropriately credentialed. • If your study involves the administration of a drug, device or biologic for research purposes, describe the process for shipping, labeling, storing and dispensing, and indicate how these are consistent with all relevant local (and US) laws, including those requiring import / export permits.• If your study involves collection of biological specimens, describe the process for shipping, labeling, storing and using such samples. Identify any special local consent requirements, and any special permits that may be required by local law.

*

2.19.1.2 **Describe any aspects of the local cultural, political or economic climate that might increase the risks of harm for either local participants or researchers. Describe the steps you will take to minimize these risks. UPitt Faculty, Staff, and Students must access the Travel Registry page. Go to my.pitt.edu and the link is displayed under My Resources.**

*

2.19.2 **Will all individuals being recruited to participate in this research study be able to read and comprehend English***

If **No**, describe how consent will be obtained. Explain provisions for culturally appropriate recruitment and consent accommodations such as, translations or involvement of native language speakers, especially if literacy is not widespread in this country.

2.19.2.1 **If translated documents are used, upload a signed translator certification form and back translations (if applicable):**(Translator Certification Form is available under the ***Resources*** tab located to right of this item)

Name Modified Date
There are no items to display

2.19.3 **Will all of the research procedures described in this IRB application be conducted at the foreign/culturally different sites?**

* ○ ○ Yes ○ ○ No

If **No**, describe the subset of research procedures to be performed at the sites:

2.19.4 **To what extent do the local site requirements to protect subject confidentiality and privacy differ from US standards. If applicable, explain how those will be addressed by this research team:***

2.19.5 **If the researcher is a student, describe how the student will communicate with the advisor during the conduct of the research and how the advisor will oversee the research:**

View: 2.21

Section 2 - Research Design and Methods

2.21 **Will this research study be conducted within a nursing home located in Pennsylvania?**

* No

2.21.1 **Does this research involve a medical procedure or an experimental treatment?***

2.21.2 **Does the research study involve the exposure of nursing home residents to pain, injury, invasion of privacy, or ask the resident to surrender autonomy?**

*

If **Yes to either question**, upload the Pennsylvania Department of Health approval letter. 28 PA Code Section 201.29 (o) specifies that prior to the initiation of research, and in addition to IRB approval, any study that includes experimental research or treatment conducted in a nursing home must be approved by the Pennsylvania Department of Health. A signed consent form from nursing home resident-subject is also required.

Name Modified Date

View: 3.01 - 3.04(a)

Section 3 - Human Subjects

3.1 **What is the age range of the subject population?** 18 years of age and older.

3.2 **What is their gender?*** Both males and females Provide a justification if single gender selected:

3.3 **Will any racial or ethnic subgroups be explicitly excluded from participation?*** No If **Yes**, identify subgroups and provide a justification:

3.4 **For studies conducted in the U.S., do you expect that all subjects will be able to comprehend English?**

* Yes

If **No**, identify what languages will be understood by subjects and describe your plan to manage communication with non-English speaking subjects during all phases of the study:

3.4.1 **If translated documents are used, upload a signed translator certification form and back translations (if applicable):**

Name Modified Date
There are no items to display

View: 3.05 - 3.05(a)

Section 3 - Human Subjects

3.5 **Participation of Children: Will children less than 18 years of age be studied?*** No

If **No**, provide a justification for excluding children: Children will be excluded because any active growth of the craniofacial complex will obscure our ability to detect changes due the surgical procedure over time.

3.5.1 **Specify the age range of the children to be studied.** (Check all that apply below:)

*

Choices
There are no items to display

3.5.2 **Provide a rationale for the specific age ranges of the children to be studied:**

3.5.3 **Describe the expertise of the study team for conducting research with children within this age range:**

3.5.3.1 **Have you obtained the following clearances from all research staff who may have direct contact with children under the age of 18? Direct contact under the law includes face-to-face, and telephonic or electronic, contact with minors. Please see the Child Clearances guidance document for further explanation?**

Pennsylvania Department of Public Welfare Child Abuse History Clearance;Pennsylvania State Police Criminal Record Check; andFBI Criminal Background Check

Note: If No, once all clearances are obtained, a modification must be submitted.**If you selected N/A, please explain:**

It is important to note that "direct contact" refers not only to face-to-face meetings but also extends to communication via phone (including text messaging), social media or internet. Direct contact also includes the care, guidance, supervision or control, or routine interaction with, minors. Conversely, a participating investigator or support staff member who does not have direct contact, either electronically or in person, with children does not need to obtain clearances (e.g., statistician, non-clinical laboratory personnel, etc.). If your research study provides babysitting services, the babysitters must have the required child clearances. * **Note:** It is the **responsibility of the principal investigator** to ensure that all research staff have these clearances prior to any interaction with children. Contact Human Resources at 412-624-8150 for assistance with this process.

3.5.4 **Describe the adequacy of the research facilities to accommodate children within this age range:***

3.5.5 **Permitted Categories of Research: The Federal Policy and FDA regulations governing human subject protections specify that research involving children must fall into one of the following permitted categories.**

*

45 CFR 46.406

- The risk represents only a minor increase over minimal risk.
- The research procedures present experiences to the subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.
- The research procedures are likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for understanding or amelioration of the subjects' disorder or condition.

45 CFR 46.407

- The risk is justified by the anticipated benefit to the subjects; and the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.

Provide a justification which **must address all considerations** related to the designated category of research:

3.6 **Does this research study involve prisoners, or is it anticipated that the research study may involve prisoners?*** No

3.6.1 **The Federal Policy and FDA regulations specify that research involving prisoners must fall into one of the following permitted categories.**

*

*Provide a justification for your designation:

General Requirements: The Federal Policy and FDA regulations specify that research involving prisoners must also conform to each of the following general requirements. Describe how your study **meets each of the following regulations**.

3.6.2 **Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in the prison are not of such a magnitude that the prisoner's ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired.** ***[45 CFR 46.305 (a)(2)]****

3.6.3 **The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers.*****[45 CFR 46.305 (a)(3)]*** *

3.6.4 **The procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners.*****[45 CFR 46.305 (a)(4)]*** *

3.6.5 **Information regarding the research is presented to the potential prisoners-subjects in a language which is understandable to them.*****[45 CFR 46.305 (a)(5)]****

3.6.6 **Adequate assurance exists that the parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole.** ***[45 CFR 46.305 (a)(6)]*** *

3.6.7 **Where there may be a need for follow-up examination or care of the prisoners-subjects after the end of their participation in the research, adequate provision has been made for such examination or care; taking into account the varying lengths of individual prisoners' sentences, and the prisoners have been informed of this fact.** ***[45 CFR 46.305 (a)(7)].*** *

View: 3.07

Section 3 - Human Subjects

3.7 **Will pregnant women be knowingly and purposely included in this research study?**

* No

General Requirements: The Federal Policy **[45 CFR 46, Subpart B]** specify that research involving pregnant women and/or fetuses must also confirm to each of the following criteria. Describe how your study meets each of the requirements.

3.7.1 **Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and**

provide data for assessing potential risks to pregnant women and fetuses. ***[45 CFR 46.204 (a)]*** [Include references]*

3.7.2 **The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the women or the fetus; or, if there is no such prospect of direct benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.** ***[45 CFR 46.204 (b)]***

*

3.7.3 **Any risk is the least possible for achieving the objectives of the research.** ***[45 CFR 46.204 (c)]****

3.7.4 **No inducements, monetary or otherwise, will be offered to terminate the pregnancy.** ***[45 CFR 46.204 (h)]***

*

3.7.5 **Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.** ***[45 CFR 46.204 (i)]***

*

3.7.6 **Individuals engaged in the research will have no part in determining the viability of a neonate.** ***[45 CFR 46.204 (j)]***

*

View: 3.08

Section 3 - Human Subjects

3.8 **Does this research study involve neonates of uncertain viability or nonviable neonates?**

* No

General Requirements: The Federal regulations **[45 CFR 46.205]** specify that research involving neonates of uncertain viability and nonviable neonates must conform to each of the general requirements. Describe how each of the following requirements will be met.

3.8.1 **Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates (include references).** *[45 CFR 46.205 (a)(1)]* *

3.8.2 **Individuals engaged in the research will have no part in determining the viability of the neonate.** *[45 CFR 46.205 (a)(3)]**

3.8.3 **Does this research study involve neonates of uncertain viability?** [45 CFR 46.205(b)]*

3.8.3.1 **The Federal regulations specify that, until it is ascertained whether or not a neonate is viable, a neonate may <u>not</u> be involved in research unless one of the following conditions is met.** *

*Provide a justification for your selection:

3.8.4 **Does this research study involve nonviable neonates?** [45 CFR 46.205(c)]*

General Requirements: The Federal regulations specify that, after delivery, a nonviable neonate may not be involved in research unless each of the following additional conditions are met [**45 CFR 46.205(c)**].

3.8.4.1 **Vital functions of the neonate will not be artificially maintained.** *[45 CFR 46.205 (c)(1)]**

3.8.4.2 **The research will not terminate the heartbeat or respiration of the neonate.** *[45 CFR 46.205 (c)(2)]**

3.8.4.3 **There will be no added risks to the neonate resulting from the research.** *[45 CFR 46.205 (c)(3)]* *

3.8.4.4 **The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means.** *[45 CFR 46.205 (c)(4)]**

View: 3.09

Section 3 - Human Subjects

3.9 **Fetal Tissues: Does this research involve the use of fetal tissues or organs?*** No

General Requirements: In accordance with the Pennsylvania Abortion Control Act, fetal tissues or organs may only be obtained for use in research subsequent to obtaining the written informed consent of the mother. The Pennsylvania Abortion Control Act specifies that research involving the use of fetal tissue or organs must also conform to **each** of the following requirements. [Indicate how you will conform to each requirement]

3.9.1 **Informed consent for the research use of fetal tissue derived from an abortion will be obtained separate from, and after, the decision and consent to abort has been made.**

*

3.9.2 **No consideration of any kind (i.e., monetary or otherwise) will be offered to the mother in obtaining her consent for the research use of the fetal tissue or organs.**

*

3.9.3 **The mother will not be permitted to designate a recipient of the fetal tissue or organs for use in research.**

*

3.9.4 **All persons who participate in the procurement or use of the fetal tissue or organs will be informed as to the source of the tissue (e.g., abortion, miscarriage, stillbirth, ectopic pregnancy).**

*

View: 3.10 - 3.12(a)
--->

Section 3.0 - Human Subjects

3.10 **What is the total number of subjects to be studied at this site, including subjects to be screened for eligibility?**Note: The number below is calculated by summing the data entered in question 3.11. Any additions or changes to the values entered in 3.11 will be reflected in 3.10.* 20

3.11 **Identify each of the disease or condition specific subgroups (include healthy volunteers, if applicable) that will be studied.**

Click on the "Add" button and specify for <u>each</u> subgroup:

1) how many subjects will undergo research related procedures at this site; and

2) if applicable, how many subjects will be required to undergo screening procedures (e.g., blood work, EKG, x-rays, etc.) to establish eligibility. Do Not include subjects who will undergo <u>preliminary telephone screening</u>.*

	Subgroup	Number to undergo research procedures	Number to undergo screening procedures
View	Study group	10	20

3.12 **Provide a statistical justification for the total number of subjects to be enrolled into this research study at the multicenter sites or this site.*** Described below: Serial computed tomography imaging will be performed to assess the total soft tissue volume before fat grafting and afterwards at three time points: immediately post-grafting, three months post-graft and nine month post-graft. Comparisons of the post-graft tissue volume to pre-treatment volume will be performed using a paired t-test model. Repeated measures analysis of variance will be used to evaluate change over time in all outcome measures. Using standard conventions of alpha=0.05 and beta=0.8, an enrollment of ten patients will provide sufficient power to detect a clinically meaningful differences in the volume of soft tissue between groups.. Based on published effect sizes for clinically significant medical outcomes on the SF-36 (i.e., 0.5 to 0.7), e.g., following surgery for dentofacial deformities (d = 0.6) (64), and medium (0.5 – 0.79) to large (0.8 to > 3.0) effect sizes on SF-36 social functioning outcomes of neck surgery (65) and orthopedic surgery (66), it is expected that a sample of 10 patients will provide sufficient power to detect a medium effect size (d = 0.5) on SF-36 measures of social functioning and quality of life, applying standard conventions of alpha = 0.05 and beta = 0.8. Outcome of facial appearance and soft tissue volume in subjects in this protocol will be compared to those subjects in PRO09060101. Significance level (adjusted for sidedness) =.025, standard deviation = 15 (15%), number of patients = 10, power= .0.8, difference in means = undefined, location of mean in one group as a percentile of the other group = undefined. The variable calculated was the minimum detectable difference. The probability is 80 percent that the study will detect a treatment difference at a two-sided 0.05 significance level, if the true difference between the treatments is 19.881 units or 19.8%. This is based on the assumption that the standard deviation of the response variable is 15 units or a 15% inter-individual coefficient of variation.

View: 3.13 - 3.15(a)

Section 3.0 - Human Subjects

3.13 **Inclusion Criteria: List the specific criteria for inclusion of potential subjects.**1. Aged 18 years or older and able to provide informed consent2. Who are post injury and/or post surgery (e.g. tx of aneurism, intercranial bleed, and tumor resections that do not involve radiation and would be analogous to trauma population requiring craniotomy) resulting in craniofacial volume defect which could be treated with a graft volume of between 5 and 150 cc of lipoaspirate3. Be at least 3 months post-injury or post-surgery (from trauma procedures) so that acute edema is resolved4. Volume defects are covered by intact skin and do not communicate with oral cavity or sinuses5. The three dimensional geometry of the volume defect(s) would allow for treatment with lipoaspirate injection that at least a single distinct treated area can be discerned on gross examination.6. Willing and able to comply with follow up examinations, including radiographic studies

3.14 **Exclusion Criteria: List the specific criteria for exclusion of potential subjects from participation.**1. Age less than 18 years2. Inability to provide informed consent3. Craniofacial defects intended for treatment have open wounds or communicate with oral cavity or sinus (note: presence of such a defect in the setting of another defect(s) that meets treatment criteria will not exclude the patient from participating).4. Active infection anywhere in the body5. Diagnosed with cancer within the last 12 months and /or presently receiving chemotherapy or radiation treatment6. Known coagulopathy7. Pregnancy8. Subjects with an Axis I DSM-IV diagnosis (e.g., Schizophrenia, Bipolar disorder) who are found to be clinically (i.e. medically) unstable at baseline. Individuals who manifest either: 1) evidence of currently active alcohol or psychoactive drug abuse or dependence on the SCID interview, or 2) a GAF score of 40 or lower due to any acute psychiatric symptomatology (e.g. suicidality, psychosis, severe depression or mania) will be reviewed by the Co-I for Psychosocial Assessment with the PI for determination of possible medical instability. Final determination of medically unstable status will be made by the PI on the basis of overall medical status and appropriateness for medical procedures; the patient may be considered ineligible for study participation per the Physician's discretion.

3.15 **Will HIV serostatus be evaluated specifically for the purpose of participation in this research study?*** No If **Yes**, provide a justification:

View: 4.01 - Version 2

Section 4 - Subject Recruitment and Informed Consent Procedures

4.1 **Select all recruitment methods to be used to identify potential subjects:**
Advertisements
CTSI Research Participant Registry

Advertisements

Upload the advertisements for review:

Name	Modified Date
BTI++ pull of tab advertisement	4/11/2014 11:29 AM
UPMC - Facial Reconstruction Study - R1.mp4	7/23/2014 1:43 PM
BTI++ audio and visual TV advertisement	8/24/2015 11:03 AM
BTI++ Recruitment flyer Mod 7.2.15	7/2/2015 1:23 PM
BTI ++ TV advertisement_script 7.23.2015	7/23/2015 4:44 PM
Facial study script 5 27 14revised (2)pas.doc	7/23/2014 3:01 PM

Honest Broker

Identify the name of the honest broker system and name of the specific individuals who will provide those services:

Specify the IRB-assigned honest broker system number (e.g., HB123456):

Upload the signed honest broker assurance agreement:
Name Modified Date
There are no items to display

Recruitment Letters and Scripts

Upload recruitment letters/scripts/text:

Name Modified Date

Research Registry

List the IRB approval number and title for each registry source:

4.2 **Provide a detailed description of your recruitment methods, including identifying and initiating contact with participants:**

Potential subjects will also be recruited using advertisements (see section 4.1) placed throughout the local Oakland and Pittsburgh area, through registration of the study with the CTSI Research Participant Registry, through TV and digital advertising (inclusive of social networking sites i.e. facebook, etc.), clinicaltrials.gov, the Center for Innovation in Restorative Medicine (CIRM) website, and via our existing contacts with support groups, and Plastic surgery clinics and Physicians throughout the University of Pittsburgh area and nationally. The research coordinator, utilizing a telephone script (attached section 4.5) will obtain and document into the research binder, the verbal consent of the potential subject for participation for the pre-screening activity. The research coordinator will only pre-screen potential subjects for exclusion criteria by phone. The research coordinator will also obtain information specific to the registration of the potential subject for the screening visit. Upon completion of the telephone interview, qualified and interested subjects will be instructed to come to the UPMC Aesthetic Plastic Surgery Center for the scheduled screening visit. At the time of the screening visit if the potential subject, after review of the informed consent document and upon resolution of any questions, then verbalizes continued interest in study participation, the PI and/or Co-investigator who is a physician will obtain informed consent. A copy of the informed consent will be given to the subject for his/ her files. Original consent will placed to the research chart. This consenting process will minimize the possibility of coercion and undue influence. No research related activities would be conducted until a fully executed informed consent document is obtained.

Note: Questions jump from 4.2 to 4.6 as questions 4.3-4.5 have been removed and the information is now captured in 4.1

View: 4.06

Section 4 - Subject Recruitment and Informed Consent Procedures

4.6 **Are you requesting a <u>waiver to document</u> informed consent for any or all participants, for any or all procedures? (e.g., a verbal or computerized consent script will be used, but the subjects will not be required to sign a written informed consent document.** ***This is not a waiver to obtain consent.***

* Yes

4.6.1 **Identify the specific research procedures and/or the specific subject populations for which you are requesting a waiver of the requirement to obtain a signed consent form.**

Addressed below:

If not all, identify the specific procedures and/or subject populations for which you are requesting a waiver: A telephone screening interview script will be utilized for potential craniofacial trauma subject that are calling in to inquire about the advertisements.

4.6.2 **Indicate which of the following regulatory criteria is applicable to your request for a waiver of the requirement to obtain a signed consent form.**

45 CFR 46.117(c)(2)

45 CFR 46.117(c)(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

45 CFR 46.117(c)(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

4.6.2.1 **Address why the specific research procedures for which you are requesting a waiver of the requirement to obtain a signed consent form present no more than minimal risk of harm to the research subjects:**

This telephone screening process within the research study presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. We believe the information being obtained during the screening phone call is the same type of information that would be collected on patients setting up an appointment for a routine well visit.

4.6.2.2 **Justify why the research listed in 4.6.1 involves no procedures for which written informed consent is normally required outside of the research context:**

We have requested and obtained a waiver of the requirement to obtain signed informed consent for the screening process, which will take place over the phone. We believe we meet the following criteria: The respective research procedures present no more than minimal risk of harm to the involved subjects and involve no procedures for which written consent is normally required outside of the research context. We believe the information being obtained during the screening phone call is the same type of information that would be collected on patients setting up an appointment for a routine well visit.If the subject does not meet inclusion criteria, all the information collected during the screening process will be destroyed and the subject will be

informed of this activity at the time of telephone screening. In addition, written informed consent will be obtained at the screening visit prior to any research activities. The investigator or co-investigator will obtain written informed consent.

4.6.3 **Address the procedures that will be used and the information that will be provided (i.e., script) in obtaining and documenting the subjects' verbal informed consent for study participation:**

Potential subjects will call the research coordinator in response to the advertisement. The research coordinator will read from the the screening script with the pre screening criteria being reviewed. If the potential subject meets this criteria the potential subject's information will be reviewed with the PI for further action. The PI will make a final determination on continuing the evaluation process and the potential subject will be contacted for further coordination of a screening visit. Upon completion of the telephone interview, qualified and interested subjects will be instructed to come to the Aesthetic Surgery Center for the scheduled screening visit. At the time of the screening visit if the potential subject, after review of the informed consent document and upon resolution of any questions, then verbalizes continued interest in study participation, the principal investigator or co-investigator who is on the Investigational Review Board (IRB) approved research protocol and consent documents, and is a physician will obtain subject signature. The physician will then sign the Certification of Informed Consent Statement ensuring a Health Insurance Portability and Accountability Act (HIPAA)- compliant informed consent document for the study, thereby minimizing the possibility of coercion and undue influence. No research related activities would be conducted until a fully executed informed consent document is obtained.

Upload Scripts:

Name	Modified Date
BTI++ telephone script	7/2/2015 8:22 AM

View: 4.07 - Version 2.0

Section 4 - Subject Recruitment and Informed Consent Procedures

4.7 **Are you requesting a waiver to obtain informed consent or an alteration of the informed consent process for any of the following?**

* No

4.7.1 **If Yes, select the reason(s) for your request:**

There are no items to display

General Requirements: The Federal Policy **[45 CFR 46.116 (d)]** specifies in order for a waiver of consent to be approved, the request must meet four criteria. For each request, you will be asked to provide a justification addressing how each of these criterion is met.

Medical record review for the identification of potential subjects:

The research involves no more than minimal risk to the subjects; **[45 CFR 46.116 (d)(1)]**

The waiver or alteration will not adversely affect the rights and welfare of the subjects;**[45 CFR 46.116 (d)(2)]**

The research could not practicably be carried out without the waiver or alteration;**[45 CFR 46.116 (d)(3)]**

Whenever appropriate, the subjects will be provided with additional pertinent information after participation; **[45 CFR 46.116 (d)(4)]**

Review of identifiable medical records: [Note: A waiver of HIPAA Authorization must be requested (2.14.2)] **Include the approximate number of medical records and/or specimens that will be accessed and enter -1 in question 3.11 for the number of subjects to be enrolled.**

The research involves no more than minimal risk to the subjects;**[45 CFR 46.116 (d)(1)]**

The waiver or alteration will not adversely affect the rights and welfare of the subjects;**[45 CFR 46.116 (d)(2)]**

The research could not practicably be carried out without the waiver or alteration;**[45 CFR 46.116 (d)(3)]**

Whenever appropriate, the subjects will be provided with additional pertinent information after participation.**[45 CFR 46.116 (d)(4)]**

Parental Permission and/or Child Assent

The research involves no more than minimal risk to the subjects;**[45 CFR 46.116 (d)(1)]**

The waiver or alteration will not adversely affect the rights and welfare of the subjects;**[45 CFR 46.116 (d)(2)]**

The research could not practicably be carried out without the waiver or alteration;**[45 CFR 46.116 (d)(3)]**

Whenever appropriate, the subjects will be provided with additional pertinent information after participation.**[45 CFR 46.116 (d)(4)]**

Alteration of informed consent process

The research involves no more than minimal risk to the subjects;**[45 CFR 46.116 (d)(1)]**

The waiver or alteration will not adversely affect the rights and welfare of the subjects;**[45 CFR 46.116 (d)(2)]**

The research could not practicably be carried out without the waiver or alteration;**[45 CFR 46.116 (d)(3)]**

aWhenever appropriate, the subjects will be provided with additional pertinent information after participation.**[45 CFR 46.116 (d)(4)].**

Other Minimal Risk activity

The research involves no more than minimal risk to the subjects;**[45 CFR 46.116 (d)(1)]**

The waiver or alteration will not adversely affect the rights and welfare of the subjects;**[45 CFR 46.116 (d)(2)]**

The research could not practicably be carried out without the waiver or alteration;**[45 CFR 46.116 (d)(3)]**
Whenever appropriate, the subjects will be provided with additional pertinent information after participation.**[45 CFR 46.116 (d)(4)].**

4.7.2 **Under what circumstances (if any) will you obtain consent from some of these subjects?**

View: 4.08

Section 4 - Subject Recruitment and Informed Consent Procedures

4.8 **Are you requesting an exception to the requirement to obtain informed consent for research involving the evaluation of an 'emergency' procedure?Note:** This exception allows research on life-threatening conditions for which available treatments are unproven or unsatisfactory and where it is not possible to obtain informed consent.* No

View: 4.09 Informed Consent

Section 4 - Subject Recruitment and Informed Consent Procedures

4.9 **Upload all consent documents for watermarking:**Draft Consent Forms for editing:

Name	Modified Date
BTI++ RUBIN Mod 10	12/2/2016 12:07 PM

Approved Consent Form(s):

Name	Modified Date
BTI++ RUBIN Mod 10	12/2/2016 12:07 PM

View: 4.10

Section 4 - Subject Recruitment and Informed Consent Procedures

4.10 **Will all potential adult subjects be capable of providing direct consent for study participation?** * Yes

Indicate why direct consent is not possible:

4.10.1 **Provide a justification for the inclusion of adult subjects who are unable to provide direct consent for study participation.**

4.10.2 **Specify the criteria used to determine that a potential adult subject is not able to provide direct consent for participation and identify who will be responsible for that determination.**

4.10.3 **Will you obtain the potential adult subject's assent for study participation?**

*

If **No**, provide a justification for not obtaining assent:

4.10.4 **Identify who will provide proxy consent for the participation of the decisionally impaired adult:**

View: 4.11 - 4.11(b)

Section 4 - Subject Recruitment and Informed Consent Procedures

4.11 **At what point will you obtain the informed consent of potential research subjects or their authorized representative?**Prior to performing any of the screening procedures

If **Other**, address below:

4.11.1 **Address why you feel that it is acceptable to defer obtaining written informed consent until after the screening procedures have been performed.**

4.11.2 **Taking into account the nature of the study and subject population, indicate how the research team will ensure that subjects have sufficient time to decide whether to participate in this study. In addition, describe the steps that will be taken to minimize the possibility of coercion or undue influence.**

A screening visit will be scheduled during the telephone pre-screening conversation with the study coordinator and the potential subject. This screening visit will take place at UPMC Aesthetic Plastic Surgery Center located at 3380 Boulevard of the Allies, Suite 158, Pittsburgh Pa. 15213 and will include review of the informed consent. The study investigator or co-investigator will discuss with the subject the nature of the research study, design schema, the risks and benefits, cost and payments and their rights as a research subject. The potential subject will review the informed consent document allowing ample time to review all information and ask questions. Should the potential subject wish to take the consent and review it outside of the office setting or discuss with other family, medical personnel he/she will be able to leave the office and return at a later date. The study investigator will provide the potential subject a private area to conduct this study document review prior to signing the informed consent. After this detailed discussion of the study and conclusion of any and all questions, the study investigator, who is a physician, will obtain informed consent. The research coordinator will document the consenting process and prior to beginning any research activities provide a copy of the fully executed informed consent document to the subject for his or her records. No research related procedures, including but not limited to the screening procedures or the review of medical records will be performed before the informed consent has been obtained.

View: 4.12 - 4.14(a)

Section 4 - Subject Recruitment and Informed Consent Procedures

4.12 **Describe the <u>process</u> that you will employ to ensure the subjects are fully informed about this research study. *** Addressed below: **This description must include the following elements:**

- who from the research team will be involved in the consent process (both the discussion and documentation);
- person who will provide consent or permission;
- information communicated; and

- any waiting period between informing the prospective participant about the study and obtaining consent

In addition, address the following if applicable based on your subject population:

- process for child assent and parental permission
  - continued participation if a child subject turns 18 during participation
- process for obtaining proxy consent and assent for decisionally impaired subjects
  - continued participation if subject regains capacity to consent

The study investigator or co-investigator will discuss with the subject the nature of the research study, design schema, the risks and benefits, cost and payments and their rights as a research subject. The potential subject will review the informed consent document allowing ample time to review all information and ask questions. The study investigator will provide the potential subject a private area to conduct this study document review prior to signing the informed consent. After this detailed discussion of the study and conclusion of any questions, the study investigator, who is a physician, will obtain informed consent. The research coordinator will document the consenting process and prior to beginning any research activities provide a copy of the fully executed informed consent document to the subject for his or her records. No research related procedures, including but not limited to the screening procedures or the review of medical records will be performed before the informed consent has been obtained.If a re-consenting process is required based on regulatory guidance, the subject will be re-consented at their next scheduled visit or at an interim visit determined to be necessary for subject safety. The research member will highlight all changes with the subject while providing opportunity for the subject to review these changes at their leisure and make an informed decision to continue or discontinue study participation based on these changes.

4.13 **Are you requesting an exception to either IRB policy related to the informed consent process?**

- For studies involving a drug, device or surgical procedures, a *listed physician* investigator is required to obtain the written informed consent unless an exception to this policy has been approved by the IRB
- For all other studies, a *listed* investigator is required to obtain consent (Note: In order to request an exception to this policy, the study must be minimal risk)

* No

If **Yes**, provide a justification and describe the qualifications of the individual who will obtain consent:

4.14 **Will you inform research subjects about the outcome of this research study following its completion?*** No If **Yes**, describe the process to inform subjects of the results:

View: 5.01.1 - 5.01.2 Version 2

Section 5 - Potential Risks and Benefits of Study Participation

5.1 **Describe potential risks (physical, psychological, social, legal, economic or other) associated with screening procedures, research interventions/interactions, and follow-up/monitoring procedures performed specifically for this study: ***

View

Research Activity:	Chest X-ray
Common Risks:	The chest x-ray is one of the lowest radiation exposure medical examinations performed today. The effective radiation dose from this procedure is about 0.1 mSv, which is about the same as the average person receives from background radiation in 10 days.
Infrequent Risks:	*No Value Entered*
Other Risks:	*No Value Entered*

View

Research Activity:	CT Scan-Risks of Radiation Exposure
Common Risks:	Experimental Interventions: This study will involve exposure to radiation. The amount of radiation exposure that each patient will receive will be about 1.3 rem per scan (a total of 5.2 rem) with minimum exposure of other areas of the body. There is no Follow up Procedures: This study will involve exposure to radiation. The amount of radiation exposure that each patient will receive will be about 1.3 rem per scan (a total of 5.2 rem) with minimum exposure of other areas of the body. There is no minimum amount of radiation exposure that is recognized as being totally free of the risk of causing genetic mutations or cancer. However, the risk associated with the amount of radiation exposure is felt to be low and comparable to everyday risks.
Infrequent Risks:	*No Value Entered*
Other Risks:	*No Value Entered*

View

Research Activity:	Medical History Assessment, Medical chart review and Physical Exam
Common Risks:	Screening Procedures: Breach of Confidentiality
Infrequent Risks:	*No Value Entered*
Other Risks:	*No Value Entered*

View

Research Activity:	Photographs
Common Risks:	Experimental Interventions: There may be feelings of embarrassment during the photographs.
Infrequent Risks:	Experimental Interventions: Loss of Confidentiality.
Other Risks:	*No Value Entered*

View

Research Activity:	Psychosocial Assessment
Common Risks:	Experimental Interventions: Anxiety and depressive symptoms are common among individuals who have experienced significant facial trauma and disfigurement and among individuals who have been in military combat. Follow up Procedures: Anxiety and depressive symptoms are common among individuals who have experienced significant facial trauma and disfigurement and among individuals who have been in military combat.
Infrequent Risks:	*No Value Entered*
Other Risks:	*No Value Entered*

View

Research Activity:	Risk of Breach of Confidentiality
Common Risks:	All Follow up Procedures: Participation in this research study does involve the potential risks of a breach of confidentiality of the medical record information and associated privacy of the participants. 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, 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.
Infrequent Risks:	*No Value Entered*
Other Risks:	Screening Procedures: Participation in this research study does involve the potential risks of a breach of confidentiality of the medical record information and associated privacy of the participants. The study investigators will take steps to reduce the Experimental Interventions: Participation in this research study does involve the potential risks of a breach of confidentiality of the medical record information and associated privacy of the participants. 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, 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.

View

Research Activity:	Risk of the Clinical Interview (SCID)
Common Risks:	Screening Procedures: Anxiety and depressive symptoms are common among individuals who have experienced significant facial trauma and disfigurement and among individuals who have been in military combat.
Infrequent Risks:	*No Value Entered*
Other Risks:	Screening Procedures: A feeling of emotional discomfort for the participant while answering questions during the interview process.

View

Research Activity:	Risk of Venipuncture (blood draw)
Common Risks:	*No Value Entered*
Infrequent Risks:	Experimental Interventions: Infrequent (Occurs in 1% to 10% or 1 to 10 out of 100 people): mild pain and discomfort at the injection or needle insertion site as well as possible infection, bleeding, bruising and soreness.
Other Risks:	Experimental Interventions: Rare (Occurs in less than 1% or less than 1 out of 100 people): severe pain; swelling; possibly an infection from the actual injection; fainting.

View

Research Activity:	Risks from reactions to anesthetic medicines
Common Risks:	*No Value Entered*
Infrequent Risks:	*No Value Entered*
Other Risks:	Experimental Interventions: Some anesthetic medicines may cause allergic or other abnormal reactions in some people, but these are rare. If you suspect you may have such a problem, you should tell both your surgeon and anesthesia specialist well before your surgery. Testing will then be arranged as necessary. A rare, potentially fatal condition called malignant hyperthermia (MH) may be triggered by some anesthetics. The anesthetics most commonly associated with malignant hyperthermia include the inhalation anesthetics and the muscle relaxant medicines.

View

Research Activity:	Risks of Echocardiogram (EKG)
Common Risks:	Experimental Interventions: It is common (Occurs in 10-25% of people (10 to 25 out of 100 people) that you may experience irritation or redness at the sites where small adhesive disks are placed on the chest skin to hold the wires that are hooked to the computer that measures heart rhythm.
Infrequent Risks:	*No Value Entered*
Other Risks:	*No Value Entered*

View

Research Activity:	Surgical Anesthesia
Common Risks:	Experimental Interventions: 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. Some people who are going to have general anesthesia express concern that they will not be completely unconscious but will "wake up" and have some awareness during the surgical procedure. Awareness during general anesthesia is very rare because anesthesia specialists devote careful attention and use many methods to prevent this.
Infrequent Risks:	Experimental Interventions: Infrequent Risks: General anesthesia suppresses the normal throat reflexes that prevent aspiration, such as swallowing, coughing, or gagging. To help prevent aspiration, an endotracheal (ET) tube may be inserted during general anesthesia. When an ET tube is in place, the lungs are protected so stomach contents cannot enter the lungs. Aspiration during anesthesia and surgery is very uncommon. To reduce this risk, people are usually instructed not to eat or drink anything for a specific number of hours before anesthesia so that the stomach is empty. Anesthesia specialists use many safety measures to minimize the risk of aspiration. 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). Insertion of airways also may cause an increase in blood pressure (hypertension) and heart rate (tachycardia). Other complications may include damage to teeth and lips, swelling in the larynx, sore throat, and hoarseness caused by injury or irritation of the larynx.

Other Risks:	Experimental Interventions: Other serious risks of General anesthesia: These include 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. Death occurs in about 1 in 250,000 people receiving general anesthesia, although risks are greater for those people with serious medical conditions. Serious side effects of general anesthesia are uncommon in people who are otherwise healthy. But because general anesthesia affects the whole body, it is more likely to cause side effects than local or regional anesthesia. Most side effects of general anesthesia are minor and can be easily managed.

View

Research Activity:	Surgical Fat Grafting procedure
Common Risks:	Experimental Interventions: Change in appearance: Typically the transferred Fat loses some of it's volume over time and then becomes stable. It is possible that more treatments maybe needed to maintain the desired volume of the transferred fat and resulting appearance. Less commonly, if you experience significant weight gain, the transferred fat may increase in volume and cause an undesirable appearance. Skin Contour: While most transferred fat results in a natural feel, 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 fat necrosis (fat tissue death) caussing firmness and discomfort and pain. Cysts may also form at the site of the transferred fat. Asymmetry: symmetrical body appearance may not result from a fat graft procedure. Factors such as skin tone, fatting deposits, boney prominences, and muscle tone may contribute to normal asymmetry in body features. Pain: Chronic pain may occur rarely after fat removal or graft.
Infrequent Risks:	Experimental Interventions: Bleeding: It is possible, though unusal to experience a bleeding episode during or after this procedure. Should bleeding occur, it may require emergency treatment to drain accumulated blood (hematoma). Seroma: Although unlikely, a collection of fluid may appear at the site where the fat was removed. This is usually treated by draining the fluid with a needle. Infection: Infection is unusual after this procedure should infection occur additional treatment including antibiotics or surgery may be necessary. 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. This may leave scars and disfigurement. Damage to deeper structures: Deeper structures such as nerves, blood vessels and muscles may be damaged during the course of this procedure. The potential for this to occur varies according to where on the body the procedure is being performed. The injury to deeper structures may be temporary or permanent. serous complications may include blood clots, partial collapse of lungs, pulmonary embolism, fat embolism, stroke, infection, blindness loss of vision, and/or death.
Other Risks:	Experimental Interventions: Scarring: All invasive procedures produce scars, some more visible than others. although good wound healing after a procedure is expected, abnormal scars may occur both within the skin and within the deeper tissues. Scars may be unattractive and of different color than the surrounding skin. There is the possibility of visible marks from sutures used to close the wound. Scars may also limit motion and function. Additional treatment including surgery may be needed to treat scarring. Long term effect: subsequent changes in the shape or appearance of the area were the fat was removed or placed may occur as a result of aging, weight loss or gain, or other circumstances not related to the Fat grafting procedure. Unsatisfactory result: There is a possibility of unsatisfactory result from the procedure resulting in unacceptable visible deformities, loss of function, wound disruption, skin death and loss of sensation. Allergic reaction: In rare cases local allergies to tape, suture material, or topical preparations have been reported. Systemic reactions, which are more serious, may result from drugs used during the procedure.

5.1.1 **Describe the steps that will be taken to prevent or to minimize the severity of the potential risks:** Screening Procedures:Subject will be in a private room. All Study materials will be assigned a study ID code. No personal information will be on said study materials. All paper files will be in a locked file cabinet within the Department of Plastic and Reconstructive Surgery offices. All computer based files will be password protected. Experimental Interventions:The plastic surgeons performing the fat graft procedures are highly trained and skilled with years for surgical procedures inclusive of grafting. The anesthesiologists are highly trained and skilled with many years of clinical surgical procedures with the use of various methods of sedation. All research staff are trained in research conduct and compliance having completed all required research modules and have education in Good Clinical Practice in research. All research staff are

trained in the use of the 3D and 2D cameras. The pictures will be taken in a timely manner so as not to prolong any possible discomfort for the subject. Also, the photographs will labeled with subject ID only and will not be stored with any additional identifiable information. The photographs will be located within a secure database within a locked office. Only the Study Investigators and associated research staff will have access to these photographs.In addition to our screening and subsequent pregnancy tests, the CT technicians are well-versed in the risks and thoroughly question the subject prior to each exam, including excess exposure to radiation. All exams will be terminated as soon as the subject expresses any discomfort. The psychosocial evaluations will be conducted by the research technician. A clinically significant symptom elevation or increase on these measures will direct the technician to contact the clinical psychologist on the team (GLH) who will visit with the patient on-site to ascertain need for further evaluation and possible referral for mental health support services. Follow up Procedures:All research staff are trained in the use of the 3D and 2D cameras. The pictures will be taken in a timely manner so as not to prolong any possible discomfort for the subject. Also, the photographs will be de-identified and labeled with subject ID only. The photographs will be located within a secure database within a locked office.In addition to our screening and subsequent pregnancy tests, the CT technicians are well-versed in the risks and thoroughly question the subject prior to each exam, including excess exposure to radiation. All exams will be terminated as soon as the subject expresses any discomfort. The psychosocial evaluations will be conducted by the research technician. A clinically significant symptom elevation or increase on these measures will direct the technician to contact the clinical psychologist on the team (GLH) who will visit with the patient on-site to ascertain need for further evaluation and possible referral for mental health support services.

5.2 **What steps will be taken in the event that a clinically significant, unexpected disease or condition is identified during the conduct of the study?* Addressed below:**

Upon discovery the PI and/ or co-investigator will notify the subject of any event that could be of clinical significance needing further evaluation, or of a diagnosis of any unexpected disease or condition that occurred during the conduct of the study's research procedures. The study investigator will at the time of discovering the event contact the referring physician or primary physician for further evaluation of the event. Should the event be of a critical nature needing immediate intervention, the study investigator or co-investigator will proceed with immediate clinical intervention and screening procedures will be concluded.

5.3 All the risk questions (screening, intervention/interaction, follow-up) have been merged into one question (5.1).

View: 5.04

Section 5 - Potential Risks and Benefits of Study Participation

5.4 **Do any of the research procedures pose a physical or clinically significant psychological risk to women who are or may be pregnant or to a fetus?*** Yes

5.4.1 **List the research procedures that pose a risk to pregnant women or fetuses:**

Ct scan and anesthesia for the fat graft surgery

5.4.2 **Describe the steps that will be taken to rule out pregnancy prior to exposing women of child-bearing potential to the research procedures that pose a risk to pregnant women or fetuses:**

All participants who are women of child bearing potential will receive a urine pregnancy dip test at screening and prior to any CT scan and surgical procedure. Educate the subject that during participation in this clinical trial they are not to become pregnant and that pregnancy will result in their removal from the clinical trial.

5.4.3 **Describe the measures to prevent pregnancy, and their required duration of use, that will be discussed with women of child-bearing potential during and following exposure to research procedures:**

All participants who are women of child bearing potential will receive a urine pregnancy dip test at screening and prior to any CT scan and surgical procedure. Educate the subject that during participation in this clinical trial they are not to become pregnant and that pregnancy will result in their removal from the clinical trial.

View: 5.05

Section 5 - Potential Risks and Benefits of Study Participation

5.5 **Do any of the research procedures pose a potential risk of causing genetic mutations that could lead to birth defects?*** Possibly or Definitely

5.5.1 **List the research procedures that pose a potential risk of genetic mutations/birth defects:**

CT Scans and Anesthesia used for Fat grafting procedure

5.5.2 **Describe the measures to prevent pregnancy, and their required duration of use, in female subjects and female partners of male subjects during and following exposure to research procedures:**

All participants who are women of child bearing potential will receive a urine pregnancy dip test at screening and prior to any CT scan and surgical procedure. Educate the subject that during participation in this clinical trial they are not to become pregnant and that pregnancy will result in their removal from the clinical trial.

View: 5.06 - 5.06(a)

Section 5 - Potential Risks and Benefits of Study Participation

5.6 **Are there any alternative procedures or courses of treatment which may be of benefit to the subject if they choose not to participate in this study?*** Yes - Describe below:

If **Yes**, describe in detail:- Receive fat grafting procedure as standard of care- Receive another plastic surgery procedure to address their injury and/or appearance.

View: 5.07 - 5.07(a)

Section 5 - Potential Risks and Benefits of Study Participation

5.7 **Describe the specific endpoints (e.g., adverse reactions/events, failure to demonstrate effectiveness, disease progression) or other circumstances (e.g., subject's failure to follow study procedures) that will result in discontinuing a subject's participation?*** Describe below:

Noncompliance of study visits (including but not limited to completion of screening and study visit procedures). Development of complications that obscures evaluation of the fat graft results, i.e. severe infection at the graft site resulting in a need for further surgery.

View: 5.08 -5.08(a)

Section 5 - Potential Risks and Benefits of Study Participation

5.8 **Will any individuals <u>other</u> than the investigators/research staff involved in the conduct of this research study and authorized representatives of the University Research Conduct and Compliance Office (RCCO) be permitted access to research data/documents (including medical record information) associated with the conduct of this research study?*** Yes

5.8.1 **Identify the 'external' persons or entity who may have access to research data/documents and the purpose of this access:**

Department of Defense and their contracted entities will review and/or obtain identifiable information; which may include the subject's identifiable medical information related to participation in this research study for the purpose of monitoring the accuracy and completeness of the research data and for preparing required scientific analyses of the research data. Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include the subject's identifiable medical information) related to their participation in this research study for the purpose of (1) fulfilling orders, made by investigators, for hospital and health care services (e.g. laboratory tests) associated with this research study participation, (2) addressing correct payment for tests and procedures ordered by the investigators, and/or (3) for internal hospital operations (i.e. quality assurance).This research study will result in identifiable information that will be placed into the subject's medical records held at UPMC. The nature of the identifiable information resulting from the subject's participation in this research study that will be recorded in their 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 the subject's medical/physical safety. In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable medical information) related to your participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

5.8.2 **Will these 'external' persons or entity have access to identifiable research data/documents?**

*Yes - Describe below:

If **Yes**, describe how they will protect the confidentiality of the research data:While the study funding source, Department of Defense (DOD), understands the importance of maintaining the confidentiality of the identifiable research and medical information, the UPMC and the University of Pittsburgh cannot guarantee the confidentiality of this information after it has been obtained by the Department of Defense.

5.9 **Has or will a Federal Certificate of Confidentiality be obtained for this research study?**

* No

5.10 **Question has been moved to 5.17**

5.11 **Question has been moved to 5.16**

View: 5.12 - 5.13

Section 5 - Potential Risks and Benefits of Study Participation

5.12 **Does participation in this research study offer the potential for direct benefit to the research subjects?**Yes - Describe the direct benefit that subjects may receive as a result of study participation. Indicate if all, or only certain, of the subjects may derive this potential benefit. Describe the benefit:Historically fat grafting procedures performed for clinical purposes have supported positive cosmetic and surgical results in patients. Although we cannot guarantee a positive outcome from this research fat grafting procedure, there may be a direct benefit to the research subject from his/her participation in this research study. In addition, this research may provide a greater understanding of the effects of fat grafting over time.

5.13 **Describe the data and safety monitoring plan associated with this study. If the research study involves multiple sites, the plan must address both a local and central review process.**Data Safety Monitoring PlanThe Data Safety and Monitoring Plan for this trial will consist of two parts. A Local Data and Safety Monitoring Plan will be implemented by the Principal Investigator to ensure that there are no changes in the risk/benefit ratio during the course of the study and that confidentiality of research data is maintained. This DSMB will consist of the PI, Co-Investigators and study personnel who will meet and discuss monthly the study (e.g., study goals and modifications of those goals; subject recruitment and retention; progress in data coding and analysis; documentation, identification of adverse events or research subject complaints; violations of confidentiality) and address any issues or concerns at that time. Minutes will be kept for these meetings and will be maintained in the study DSMB binder. Any instances of adverse events will be reported immediately to the University of Pittsburgh IRB in accordance with the guidance on the IRB website. The annual IRB renewal for this study will include a summary report of the Data and Safety Monitoring Plan findings from the study for the prior year. We will include the following information at the time of the IRB renewal regarding the frequency of the monitoring, the dates that the monthly meetings took place, a summary of the cumulative adverse events, external factors or relevant information that might have an impact on the safety or ethics of the study, and final conclusions regarding changes to the anticipated risk/benefit ratio to study participation and final recommendations related to the continuation, changing, or termination of the study. The protocol will be not be initiated until written notification of approval of the research project is issued by the HRPO. A copy of the approved continuing review report and the local IRB approval notification will be submitted to the USAMRMC ORP HRPO as soon as these documents become available. A copy of the approved final study report and local IRB approval notification will be submitted to the USAMRMC ORP HRPO as soon as these documents become available. Substantive modifications to the research protocol and any modifications that could potentially increase risk to subjects must be submitted to the HRPO for approval prior to implementation. The USAMRMC ORP HRPO defines a substantive modification as a change in Principal Investigator, change or addition of an institution, elimination or alteration of the consent process, change to the study population that has regulatory implications (e.g. adding children, adding active duty population, etc.), significant change in study design (i.e. would prompt additional scientific review), or a change that could potentially increase risks to subjects. All other amendments must be submitted with the continuing review report.All unanticipated problems involving risk to subjects or others must be promptly reported by phone (301-619-2165), by email (HRPO@amedd.army.mil), or by facsimile (301-619-7803) to the HRPO. A complete written report will follow the initial notification. In addition to the methods above, the complete report can be sent to the US Army Medical Research and Materiel Command, ATTN: MCMR-RP, 504 Scott Street Fort Detrick, Maryland 21702-5012 Suspensions, clinical holds (voluntary or involuntary), or terminations of this research by the IRB, the institution, the sponsor, or regulatory

agencies will be promptly reported to the USAMRMC ORP HRPO.A copy of the continuing review report and the re-approval notification by the UP IRB must be submitted to the HRPO as soon as possible after receipt of approval. Please note that the HRPO also conducts random audits at the time of continuing review and additional information and documentation may be requested at that time.The final study report submitted to the UP IRB, including a copy of any acknowledgement documentation and any supporting documents must be submitted to the HRPO as soon as all documents become available.The knowledge of any pending compliance inspection/visit by the Food and Drug Administration (FDA), Office for Human Research Protections, or other government agency concerning this research; the issuance of inspection reports, FDA Form 483, warning letters, or actions taken by any regulatory agencies including legal or medical actions; and any instances of serious or continuing noncompliance with the regulations or requirements must be reported immediately to the HRPO.Accurate and complete study records will be maintained and made available to representatives of the USAMRMC as a part of their responsibility to protect human subjects in research. All research records are stored in a confidential manner so as to protect the confidentiality of subject information.Per DoD Directive 3216.02, all greater than minimal risk studies require a Medical Monitor. The USAMRMC ORP HRPO also reserves the authority to require assignment of a Medical Monitor for those protocols assessed as presenting no greater than minimal risk to the subjects participating in the study. The second part of the DSMP will be the inclusion of an Independent Data Safety Monitoring Board (IDSMB). This IDSMB will convene once a year or as needed for review of all unanticipated events, adverse events, and serious adverse events affecting the risk to the human subject or others. The members of the IDSMB include Drs. Ernest Manders and James Russavage who are all present faculty members within the Department of Plastic Surgery at the University of Pittsburgh, without any involvement in this research protocol, they are not under the supervision of the PI or have a conflict of interest. Dr Manders, a member of the Independent Data Safety and Monitoring Board (IDSMB) will act as the Research Monitor for this study; he is available on site to respond to any urgent or emergency situations that may arise during the study and to serve as the subject advocate. The Research Monitor is required to review all unanticipated problems involving risk to subjects or others, serious adverse events and all subject deaths associated with the protocol and provide an unbiased written report of the event. At a minimum, the Research Monitor must comment on the outcomes of the event or problem and in case of a serious adverse event or death, comment on the relationship to participation in the study. The Research Monitor must also indicate whether he/she concurs with the details of the report provided by the principal investigator. The Medical Monitor has the authority to stop the research at any time; he /she can remove individuals from the study, and take any steps necessary to protect the safety and well being of participants until the IRB has time to assess the study. This IDSMB will evaluate any adverse events and research staff adherence to subject confidentiality and de-identification processes. The IDSMB members will discuss, if necessary, any changes to the risk/benefit ratio of this study for the PI’s report to the local IRB of all reporting adverse events, external factors or relevant information that might have an impact on the safety or ethics of the study, and final conclusions regarding changes to the anticipated risk/benefit ratio to study participation and final recommendations related to the continuation, changing, or termination of the study as outlined by the University of Pittsburgh IRB.

View: 5.14 - 5.17

Section 5 - Potential Risks and Benefits of Study Participation

5.14 **What precautions will be used to ensure subject privacy is respected?** (e.g. the research intervention will be conducted in a private room; the collection of sensitive information about subjects is limited to the amount necessary to achieve the aims of the research, so that no

unneeded sensitive information is being collected, drapes or other barriers will be used for subjects who are required to disrobe)

All aspects of the study will be performed in a private room, including the consenting process, exams, photographs, CT scan, laboratory blood draw and the fat grafting procedure. The collection of sensitive information about subjects is limited to the amount necessary to achieve the aims of the research, so that no unneeded sensitive information is being collected, drapes or other barriers will be used for subjects who are required to disrobe.

5.15 **What precautions will be used to maintain the confidentiality of identifiable information?** (e.g., paper-based records will be kept in a secure location and only be accessible to personnel involved in the study, computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords, prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information, whenever feasible, identifiers will be removed from study-related information, precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys, audio and/or video recordings of subjects will be transcribed and then destroyed to eliminate audible identification of subjects)

Participation in this research study does involve the potential risks of a breach of confidentiality of the medical record information and associated privacy of the participants. 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, 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. Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study, computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords, prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information, whenever feasible, identifiers will be removed from study-related information, precautions are in place to ensure the data is secure by using password restrictions and folder level access by permission only on UPMC servers.Reference to sample: All research samples will be stored to include assigned code numbers, and any information linking these code numbers to the corresponding subjects' identities will be kept in a separate, secure location located in the security manned Biomedical Science Tower. Should the subject decide to withdraw or be withdrawn from study participation, the already collected samples will be kept and not destroyed. It is the Principal Investigator's intention to make stored samples and subject de-identified information available to secondary investigators (investigators not listed on the front page of this consent document) after all research study testing has been completed. These stored samples and associated subject information will not include subject identifiers.The photographs will be housed as electronic files within the Canfield camera system. The system is password protected and is located within the locked offices of the Aesthetic Plastic Surgery Center located at 3380 Boulevard of the Allies, suite 180 Pittsburgh pa 15213. While the photographs will be labeled with an ID code, there is a risk of loss of confidentiality. The digital recordings are being collected for the purpose of medical education and training, publication, and media reports – and, in any mode of transmission, including and not limited to: print, email, television, internet, etc. All digital records (i.e. photography or video) obtained during any or all of the subject's pre-operative, operative, and post-operative period, may include, but not be limited to videos of personal interviews, functional assessment testing and clinical exams or photos of follow up, biopsies, etc. will be given a specific code and stored without any additional identifiable

information. These recordings will be stored indefinitely in a secure, password protected location on the UPMC server.

5.16 **If the subject withdraws from the study, describe what, if anything, will happen to the subject's research data or biological specimens.**

Any identifiable research or medical information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent will continue to be used and disclosed by the investigators for the purposes described above. All research samples will be stored to include assigned code numbers, and any information linking these code numbers to the corresponding subjects' identities will be kept in a separate, secure location located in the Department of Plastic and Reconstructive Surgery at the University of Pittsburgh. Should the subject decide to withdraw or be withdrawn from study participation, the already collected samples and all digital recordings will be kept and not destroyed. We are not collecting or storing any samples for any use in future research studies with this clinical trial; samples will not be retained for testing in future studies. All samples and digital recordings collected during your participation in this clinical trial, upon your early withdraw from the study, will be kept and not destroyed, but processed specifically as outlined as stated in the research design for this trial. It is the Principal Investigator's intention to make stored samples and subject information de-identified available to secondary investigators (investigators not listed on the front page of this consent document) after all research study testing has been completed. These stored samples and associated subject information will not include subject identifiers. Subjects will be instructed that they may choose to withdraw from this study at any time, but it is important that they continue to be monitored by a physician after they receive the research Fat grafting procedure in order to ensure their safety. It is also important for the subject to contact study personnel if they later experience any side effects that they might feel are related to the research study.

5.17 **Following the required data retention period, describe the procedures utilized to protect subject confidentiality.** (e.g., destruction of research records; removal of identifiers; destruction of linkage code information; secured long-term retention)

Any information about the subject obtained from or for this research study will be kept as confidential (private) as possible. All records related to the subject's involvement in this research study will be kept in a locked file cabinet or in a password protected computer database accessible only to study personnel as described above. The identity on these records will be indicated by a unique study number, rather than by name, and the information linking this study number with the subject's identity will be kept separate from the research records. The digital recordings are being collected for the purpose of medical education and training, publication, and media reports – and, in any mode of transmission, including and not limited to: print, email, television, internet, etc. All digital records (i.e. photography or video) obtained during any or all of the subject's pre-operative, operative, and post-operative period, may include, but not be limited to videos of personal interviews, functional assessment testing and clinical exams or photos of follow up, biopsies, etc. and will be will be given a specific code and stored without any additional identifiable information. The digital recordings will be stored indefinitely in a secure password protected, location on the UPMC server. The subject will not be identified in any publication of the research study.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 the subject. At most, the website will include a summary of the results. The subject can search this website at any time.

View: 6.1

Section 6 - Costs and Payments

6.1 **Will research subjects or their insurance providers be charged for any of the procedures (e.g., screening procedures, research procedures, follow-up procedures) performed for the purpose of this research study?*** No

6.1.1 **Specify what research procedures will be billed to the subject or insurance provider:**

6.1.2 **Provide a justification for billing subjects or insurance providers for procedures that are performed solely for the purpose of the research study.**

6.1.3 **Will subjects or insurance providers be billed for the investigational drug or device being evaluated or used in this research study?**

*

Provide assurance that the FDA has given approval for the sponsor of this research study to charge investigators for the investigational drug or device.

If this is an investigational device, indicate if the Health Care Financing Administration has designated it as a Class B medical device.

*

6.1.4 **Address the contingencies that are in place to ensure that potential subjects, who may desire to participate in this research study but are not able to bear this personal financial risk, will be afforded access to study participation.**

View: 6.2

Section 6 - Costs and Payments

6.2 **Will subjects be compensated in any way for their participation in this research study?*** Yes

6.2.1 **Describe the amount of payment or other remuneration offered for complete participation in this research study.**Study subjects will be remunerated for their participation in the research study a per diem total rate of $104.00/day. The subjects will receive the remuneration upon completion of each study visit. The subject's reasonable travel expenses are reimbursed at 50.0 cents per mile round trip. Travel may include air fare coverage round trip booked through the University of Pittsburgh travel agency "People's Travel". Proper supporting documentation for mileage reimbursement is demonstrated by trip tickets or a Mapquest inquiry from the subject's place of residence to the study site displaying round trip mileage. Subjects will be reimbursed using the UPMC "WE PAY" system at the time of each visit.

6.2.2 **Describe the amount and term of payment or other remuneration that will be provided for partial completion of this research study.**Study subjects will be remunerated for their participation in the research study a per diem total rate of $104.00/day. The subjects will receive the remuneration upon completion of each study visit.

View: 7.1

Section 7 - Qualifications of Investigators and Sources of Research Study

7.1 **Summarize the qualifications and expertise of the principal investigator and listed co-investigators to perform the procedures outlined in this research study.** J. Peter Rubin, MD is Chair, Department of Plastic Surgery and a Professor of Surgery. He is Board certified in plastic surgery and an expert in the areas of upper and lower extremity surgery, body contouring surgery as well as adipose research. He is the Co-Director of the Aesthetic Plastic Surgery Center, the Director and founder of the Life After Weight Loss Center. He is also the co-director of the Plastic Surgery research lab. He will actively perform the research procedures and provide medical oversight for all study subjects. He is responsible for review and meeting of subject research study eligibility criteria, consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP. Sydney Coleman, MD is a renowned plastic surgeon having over 20 years of expertise in the Fat grafting procedure. Dr. Coleman is the inventor of the Coleman Cannula System which is the instrumentation being used with this research surgical procedure. He will serve as a technical consultant where his expertise will be use to enhance this project.T. Oguz Acarturk, MD finished his Plastic Surgery Residency (Integrated) at the University of Pittsburgh in 2004. He then served a year in the Turkish Military at the Gülhane Military Medical Academy in Ankara, Turkey. He later joined the Çukurova University Department of Plastic Surgery in Adana, Turkey in 2005 and has been there since, as an Associate Professor. T. Oguz Acarturk, MD joined the UPMC Department of Plastic Surgery in November 2011, where is main appointment will be in the area of head and neck reconstruction. His clinical interests include microsurgery, general reconstruction and aesthetic surgery. In addition, he has experience in burn reconstruction, pediatric plastic surgery, orthognatic surgery and craniofacial trauma. His research interest includes prefabricated flaps, flap physiology and perforator flaps. As a Co-Investigator, he will provide clinical oversight for study subjects, will be responsible for collection of information assessing the research study eligibility criteria, consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP.Jeffrey Gusenoff, MD is Co-Director of the Life After Weight Loss Program and Visiting Associate Professor of Surgery in the Department of Plastic Surgery at UPMC. He completed his undergraduate and medical school training at The Johns Hopkins University in 1998 and 2002. His residency in General and Plastic Surgery was at the University of Rochester School of Medicine in Rochester, NY, and he graduated in 2007. This was followed by a fellowship in Post-Bariatric Body Contouring with J. Peter Rubin, MD at the University of Pittsburgh Medical Center. From 2008 until 2012, Dr. Gusenoff was an Assistant Professor of Surgery and Director of the Life After Weight Loss Program at the University of Rochester Medical Center. His research experience includes extensive clinical outcomes research. As a principle/co-investigator, he will provide clinical oversight for study subjects, will be responsible for collection of information assessing the research study eligibility criteria, consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP.Albert Donnenberg, PhD, Since 1998, Dr. Donnenberg has also been the director of University of Pittsburgh Cancer Institute's (UPCI) Flow Cytometry Facility. Additionally, he is currently the Deputy Director of the Stem Cell Transplantation (SCT) Program and Director of UPCI Bone Marrow Processing Laboratory. Dr. Donnenberg graduated with a B.A. in Philosophy from the University of Colorado in 1973. Following the completion of his Ph.D. in Infectious Disease Epidemiology from Johns Hopkins University School Public Health in 1980, Dr. Donnenberg served as a Research Fellow in Oncology at Johns Hopkins University School of Medicine until 1982. Dr. Donnenberg is the recipient of multiple awards for his research efforts at

the university. Among his honors are induction into the Delta Omega Honorary Public Health Society and his receipt of a 1988 - 1993 Carter-Wallace Fellowship for AIDS Research. Most recently, he was honored as a visiting fellow at the Institute Pasteur in Paris in 1994. As the director of University of Pittsburgh Cancer Institute's (UPCI) Flow Cytometry Facility and Deputy Director of the Stem Cell Transplantation (SCT) Program and Director of UPCI Bone Marrow Processing Laboratory, he will have oversight of the cell processing of the adipose tissue, and oversee the flow cytomety studies within the GMP hematopoietic stem cell laboratory, analyze the data, and assist in manuscript preparation.Vera Svobodova Donnenberg, PhD, Assistant Professor of Surgery, University of Pittsburgh, is a co-investigator who will oversee the flow cytometry analysis of the cell product and will directly supervise all technical aspects of the flow cytometry studies and ensure quality control. Dr. Donnenberg research focuses on flow cytometry, broncho-alveolar lavage fluid, and the analysis of dendritic cell subsets. Dr. Donnenberg has written over 75 publications, abstracts and other scientific presentations. Dr. Donnenberg is a member of several professional and scientific societies including the American College of Clinical Pharmacology, American Association for Cancer Research, and the International Society for Analytical Cytology.Kacey Marra, PhD is an expert in the area of adipose research experience. The Co-director of the Plastic Surgery research lab, Dr. Marra has almost 10 years of adipose research. She will be responsible for the oversight of all lab processing, maintenance and storage of all research biological samples collected for this study. Barton Branstetter, MD is an experienced radiology clinician of 10 years. He will be responsible for the physician review and reporting of the radiological CT scans tests conducted in this study. Gretchen Haas, PhD is a psychologist who has extensive experience working with veterans, and specializes in measures of social function. She is responsible for the initial and ongoing evaluation of potential participant's clinical interview and quality of life assessments conducted in this study. Patsy Simon, RN, BS, CCRC, CCRA Director, Regulatory and Clinical Affairs University of Pittsburgh, Department of Plastic Surgery at the UPMC Center for Innovation in Restorative Medicine. Ms. Simon has over 30 years of clinical nursing expertise with 17 years of research trial conduct and compliance expertise inclusive of Federal, Industry and Investigator Sponsored IND and IDE clinical trials experience. Ms. Simon’s role on this project will consist of the regulatory and clinical oversight and management of this department of defense trial. This role includes guidance on the development, execution and adherence of good clinical practice and clinical procedure development to ensure compliance with trial execution.Diana Mermon, MS has a Master's degree in Counseling with a Certification in Education – master’s level. Diana has over 10 years of research experience and will conduct the subject's clinical interview and the quality of life assessments. Elizabeth Radomsky, PhD, is a clinical psychologist with extensive experience and specific training and expertise in the use of neuropsychological assessments and diagnostic and psychopathology rating instruments. She has over 25 years of research experience. She will be responsible for conducting the subject's clinical interview and the quality of life assessments at baseline and follow-up assessments. Paul Afrooz, MD is a plastic surgery resident and is responsible for review and meeting of subject research study eligibility criteria, consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP. Jacqueline Bliley, MS, has over a year of clinical experience and over seven years laboratory experience. She will be responsible for providing clinical oversight for study subjects, and obtaining research specimens for storage. She will also provide insight into research study procedures and the overall protection of human subject risks and benefits. Isaac James, MS has a year of laboratory experience within the BST Adipose Stem Cell Laboratory. As co-investigator on this study he will be responsible for obtaining lipoaspirate from the operative area and transporting specimens to the laboratory (BST and HSC) for processing and analysis. Jordan Fishman, MD is employed by UPMC and a member of the Department of Plastic Surgery. As a co-investigator, he is responsible for collection of information assessing the research study eligibility criteria and consenting process, research study procedures, overall protection of human subject risks and

benefits, performance of clinical trial conduct and compliance maintaining GCP.Debra Smith, MD is employed by UPMC and a member of the Department of Plastic Surgery. As a co-investigator, she is responsible for collection of information assessing the research study eligibility criteria and consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP.Amy Steele, RN, MSN, CCRC has over 15 years of regulatory and clinical research experience. Her study role will be to actively perform research related activities, access medical records and databases, as well as submission of regulatory documents to the University of Pittsburgh IRB associated with the conduct and compliance of a clinical trial.Karen Foley, RN, BSN, CCRC has several years of regulatory and clinical research experience. Her study role will be to actively perform research related activities, access medical records and databases, as well as submission of regulatory documents to the University of Pittsburgh IRB associated with the conduct and compliance of a clinical trial.John Pang, MD is employed by UPMC and a member of the Department of Plastic Surgery. As a co-investigator, he is responsible for collection of information assessing the research study eligibility criteria and consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP.Mark Asher Schusterman, MD is employed by UPMC and a member of the Department of Plastic Surgery. As a co-investigator, he is responsible for collection of information assessing the research study eligibility criteria and consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP.Michael Bykowski, MD, MS is employed by UPMC and a member of the Department of Plastic Surgery. As a co-investigator, he is responsible for collection of information assessing the research study eligibility criteria and consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP.Dalit Amar, MD is employed by UPMC and a member of the Department of Plastic Surgery. As a co-investigator, she is responsible for collection of information assessing the research study eligibility criteria and consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP.Jessica Lee, MD is employed by UPMC and a member of the Department of Plastic Surgery. As a co-investigator, she is responsible for collection of information assessing the research study eligibility criteria and consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP.Damien Grybowski, MD is a Research Fellow in the Adipose Stem Cell Center. As co-investigator on this study he will be responsible for obtaining lipoaspirate from the operative area and transporting specimens to the laboratory (BST and HSC) for processing and analysis. Gabriella DiBernardo, BS is a Research Fellow in the Adipose Stem Cell Center. As co-investigator on this study she will be responsible for obtaining lipoaspirate from the operative area and transporting specimens to the laboratory (BST and HSC) for processing and analysis. Danielle Minteer, PhD is employed by University of Pittsburgh, Department of Plastic Surgery as a Research Data Manager. As a co-investigator, she will be responsible for data collection and building and managing research databases. Edward Ruane, MD is employed by UPMC and a member of the Department of Plastic Surgery. As a co-investigator, she is responsible for collection of information assessing the research study eligibility criteria and consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP.Sharona Czerniak, MD is employed by UPMC and a member of the Department of Plastic Surgery. As a co-investigator, she is responsible for collection of information assessing the research study eligibility criteria and consenting process, research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP.Irene Ma, MD is employed by UPMC and a member of the Department of Plastic Surgery. As a co-investigator, she is responsible for collection of information assessing the research study eligibility criteria and consenting process,

research study procedures, overall protection of human subject risks and benefits, performance of clinical trial conduct and compliance maintaining GCP.

View: 7.2

Section 7 - Qualifications of Investigators and Sources of Study Support

7.2 **Indicate all sources of support for this research study.***

Selections

Federal: Upload a copy of the entire grant application **(including the cover sheet)** if our site is the awardee institution; for federal contracts, upload a copy of the research plan

If **Federal** support, provide the sponsor information:

	Federal sponsor	Grant Title	Grant number	Awardee institution	Federal grant application
View	DOD	structural fat grafting for craniofacial trauma	W911QY-09-C-0209	University of Pittsburgh	COA 09 25 13 without budget information.pdf(0.01)

For projects not supported by a federal grant, upload the research plan that was submitted for funding:

Name Modified Date

If **Industry** support, provide the sponsor information and level of support:

If **Foundation** support, provide the sponsor information:

If **Other** support, provide the support information and level of support:

View: 7.3

Section 7 - Qualifications of Investigators and Sources of Research Study

Please contact the Conflict of Interest Office if you have any questions related to this section.

7.3 **Is this study funded in part or whole by a PHS Agency?**

* No

Does any investigator* involved in this study (select all that apply):

Name

- ☐ **A.** Have a financial interest (aggregated value of equity and remuneration** during the past or next twelve months) in a **publicly-traded entity** that either sponsors*** this research or owns the technology being evaluated or developed that exceeds **$5,000 but not $10,000**?
- ☐ **B.** Have a financial interest (aggregated value of equity and remuneration during the past or next twelve months) in a **publicly-traded entity** that either sponsors this research or owns the technology being evaluated or developed that exceeds **$10,000**?

- ☐ **C.** Receive remuneration (during the past or next twelve months) from a **non-publicly traded entity** that either sponsors this research or owns the technology being evaluated or developed that exceeds **$5,000 but not $10,000**?
- ☐ **D.** Receive remuneration (during the past or next twelve months) from a **non-publicly traded entity** that either sponsors this research or owns the technology being evaluated or developed that exceeds **$10,000**?
- ☐ **E.** Have equity in a **non-publicly traded entity** that either sponsors this research or owns the technology being evaluated or developed?
- ☐ **F.** Receive reimbursement or sponsorship of travel expenses (for one trip or a series of trips during the past or next twelve months) by an outside entity that either sponsors this research or owns the technology being evaluated or developed that exceeds **$5,000**?
- ☐ **G.** Have rights as either the author or inventor of **intellectual property** being evaluated or developed in this research that is the subject of an issued patent or has been optioned or licensed to an entity?
- ☐ **H.** Have an officer or management position**** with a **Licensed Start-up Company** overseen by the COI Committee that either sponsors this research or owns the technology being evaluated or developed?
- ☐ **I.** Receive compensation of any amount when the value of the compensation would be affected by the outcome of this research, such as compensation that is explicitly greater for a favorable outcome than for an unfavorable outcome or compensation in the form of an equity interest in the entity that either sponsors this research or owns the technology being evaluated or developed?
- ☐ **None** of the above options apply and there are no other financial conflicts of interest in the conduct of this research.

***Investigator** means the PI, co-investigators, and any other member of the study team, regardless of title, who participates in the design, conduct, or reporting of this research, as well as his/her spouse, registered domestic partner, dependents, or other members of his/her household. **The PI is responsible for ensuring that s/he and all other relevant members of the study team review the above questions describing Significant Financial Interests.**

**such as salary, consulting fees, honoraria, or paid authorship

***through the provision of funds, drugs, devices, or other support for this research

****Such as serving on the Board of Directors or Board of Managers or a position that carries a fiduciary responsibility to the company (e.g., CEO, CFO, CTO, or CMO).

Does any investigator* involved in this study (select all that apply):

Name

- ☐ **A.** Have equity in a **publicly-traded entity** that either sponsors** this research or owns the technology being evaluated or developed that exceeds a **5% ownership interest** or a current value of **$10,000**?
- ☐ **B.** Have equity in a **non-publicly-traded entity** that either sponsors this research or owns the technology being evaluated or developed?

- [x] **C.** Receive salary, consulting fees, honoraria, royalties or other remuneration from an entity that either sponsors this research or owns the technology being evaluated or developed that is expected to exceed **$10,000** during the past or next 12 months?
- [ ] **D.** Have rights as either the author or inventor of **intellectual property** being evaluated or developed in this research that is the subject of an issued patent or has been optioned or licensed to an entity?
- [ ] **E.** Have an officer or management position**** with a **Licensed Start-up Company** overseen by the COI Committee that either sponsors this research or owns the technology being evaluated or developed?
- [ ] **F.** Receive compensation of any amount when the value of the compensation would be affected by the outcome of this research, such as compensation that is explicitly greater for a favorable outcome than for an unfavorable outcome or compensation in the form of an equity interest in the entity that either sponsors this research or owns the technology being evaluated or developed?
- [ ] **None** of the above options apply and there are no other financial conflicts of interest in the conduct of this research.

***Investigator** means the PI, co-investigators, and any other member of the study team, regardless of title, who participates in the design, conduct, or reporting of this research, as well as his/her spouse, registered domestic partner, dependents, or other members of his/her household. **The PI is responsible for ensuring that s/he and all other relevant members of the study team review the above questions describing Significant Financial Interests.**

****through the provision of funds, drugs, devices, or other support for this research

*****Such as serving on the Board of Directors or Board of Managers or a position that carries a fiduciary responsibility to the company (e.g., CEO, CFO, CTO, or CMO).

7.3.1 **Provide the name of the investigator(s) and describe the nature of the Significant Financial Interest(s):**Dr. Sydney Coleman conflict of interest involves the receipt of royalties and consulting fees for the Coleman cannules.

7.3.2 If you selected **A, B, C, or E**, please complete a **Standard Conflict of Interest Management Plan** and submit it with your protocol. Please provide all of the requested information, including the correct protocol number and title. **Incomplete, inaccurate, or unsigned forms will have to be edited and replaced.**

For all other financial interests **(D or F)**, the COI Office will work with you to develop an appropriate COI Management Plan.

7.3.2 If you selected **B, D, E, or H**, please complete a **Standard Conflict of Interest Management Plan** and submit it with your protocol. Please provide all of the requested information, including the correct protocol number and title. **Incomplete, inaccurate, or unsigned forms will have to be edited and replaced.**

For all other financial interests **(A, C, F, or G)**, the COI Office will work with you to develop an appropriate COI Management Plan.

*

Name	Modified Date
BTI++ COI management plan	5/8/2014 2:12 PM

View: Other Attachments

Supporting Documentation Section

References and Other Attachments

Additional documents:

Name	Modified Date	Version
References	4/25/2014 9:36 AM	0.01

View: Clinical Trials Registration

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

"Applicable clinical trials" are required **by federal law** to be registered in ClinicalTrials.gov.

Applicable Clinical Trials (ACTs) are studies that meet the following criteria:

- The study is an interventional study AND
- The study intervention is a drug, biologic, medical device, radiation or genetic AND
- The Study is not Phase 0 or 1 AND
- The study has at least one site in the United States or is conducted under an investigational new drug application or investigational device exemption

NIH Policy

Effective January 18, 2017, revised NIH Policy requires that all clinical trials funded in whole or in part by the NIH be registered and results information posted on ClinicalTrials.gov.

As defined by the NIH, a clinical trial is:

A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health related biomedical or behavioral outcomes.

The NIH Policy extends beyond the Food and Drug Administration Amendment Act (FDAAA 801) requirements in that it requires registration and results reporting of:

- clinical trials of behavioral, surgical and other types of health and medical interventions
- phase 1 studies of drugs and biological products

- small feasibility studies of device products

Failure to submit all required registration and results information requested on ClinicalTrials.gov can jeopardize University grant funding, the future funding of the grantee and subject the University of Pittsburgh to future monetary penalties.

In addition, to promote transparency of the clinical trials process, the International Committee of Medical Journal Editors (ICMJE) has established a policy requiring the entry of clinical trials in a public registry, such as ClinicalTrials.gov, prior to subject enrollment as a condition of consideration for publication of the trial results.

* **Based on the above information, will this study be registered in ClinicalTrials.gov?**Yes

Who will serve as the Responsible Party? UPMC/Pitt Investigator or IND/IDE Pitt Sponsor **Why are you registering your study?** (Check all that apply)

It is required for publication by the **International Committee of Medical Journal Editors** (*Registration is required in a publically available, searchable database system prior to informed consent being obtained from the first study participant*)

If you are not yet registered and need to establish an account for the PI or other research staff that may need to access the record, please send an email to the University of Pittsburgh PRS administrator at ctgov@pitt.edu with the following information for each individual:

- Full name
- Telephone number
- Pitt or UPMC email address

If you have any questions or concerns, please email us at ctgov@pitt.edu.

To find out additional information about how to register your study go to: https://www.clinicaltrials.gov/ct2/manage-recs/how-register

View: Conclusion for Application

Completion of Application and Submission

Congratulations, you have completed the IRB on-line application! Click on '**Finish**' to return to the main page of the application. Your study has ***not been submitted*** for review at this point.

Remember**:** **Only the Prinicipal Investigator** is permitted to submit a study for review or submit a response to comments.

If you are the PI and wish to submit the study for review:

- Go the main study page by clicking on '**Finish**'

- Click on the **'Submit Application'** button located on the left side of the main page under **'My Ac vities'**