

ADIPOSE DERIVED STEM CELL THERAPY

Disclaimer: The information in the following pages is believed to be correct but does not purport to be all inclusive and shall be used only as a guide. This information is based on our present knowledge and is applicable to the procedure with appropriate safety precautions. This protocol has been designed to focus on the individual characteristics of each patient as to offer the utmost safety and results.

MEDICAL TEAM: Medical team is made up of different healthcare professionals is required to successfully complete the procedures. The team may include: a specialist for the specific condition being treated, a physician trained and certified in cellular medicine techniques and laboratory procedures, a laboratory technician trained and certified in cellular medicine techniques and an office administrator.

The medical team determines the appropriateness of cell based therapy on a case by case basis. Preoperative surgical risk assessment is conducted on each patient.

1. **SAFETY:** Common and minor complications are defined as conditions that do not threaten a patient's life, normal body functions or the ability to work. These include but are not limited to superficial irregularities of the skin, hematomas, or seromas after lipoaspiration.
 - A. Major complications: are defined as conditions, sickness, or incidents that require medical treatment, hospitalization, leave sequela(e), and/or are life threatening. All adverse events are documented and reported to the medical ethics committee.
 - B. Risks of local anesthesia: lidocaine is the safest anesthetic available for liposuction. The tumescent technique is applied by trained physicians. Tumescent liposuction has an unprecedented safety record when used as directed.
 - C. Lidocaine toxicity: occurs with unintended intravascular administration or with administration of an excessive dose. Toxicities may be observed at 6 mcg/ml, but more commonly occur once levels exceed 10 mcg/ml. Blood concentrations of lidocaine in excess of 12 mg/l may produce cardiac toxicity. Common medications that may affect Lidocaine levels include cimetidine, ciprofloxacin, clonidine, phenytoin, and beta-blockers such as propranolol, metoprolol, and nadolol.
2. **PURPOSE:**
 - A. Adipose-Derived Stromal Vascular Fraction Containing Adult Stem Cells: An adult stem cell is an undifferentiated cell, one of the body's most important natural repair mechanisms. They repair organs, muscles, heart, lungs, skin, and nerves by replacing old, dead, or diseased cells throughout the body. Plastic surgeons routinely perform liposuction, acquiring fat along with the embedded stem cells. Tissue dissociation studies demonstrate that adipose stromal vascular compartment is the site of origin of adipose stem cells.

The treatments described in this manual are considered experimental and have not been evaluated or approved by the FDA.

B. The stromal vascular fraction (SVF) is defined as the heterogeneous mixture of cells that are isolated by enzymatic dissociation and density separation, a procedure designed to remove the assortment of cells that reside in the depot from surrounding adipocytes, which float. These stromal vascular cells are a potentially rich resource to examine a variety of questions relevant to regenerative medicine. For within this complex set of cells are adipose-derived stem cells (ADSCs), and also strikingly similar mesenchymal stem cells (MSCs), that can differentiate into a variety of cell types, such as bone, cartilage, muscle, endothelial cells and neurons. The stromal vascular fraction also contains adipose stem cells, possibly a subset of the aforementioned ADSC and MSC populations. There are no ethical or religious issues surrounding adult stem cell removal nor are there concerns of autologous adult stem cell rejection. Procedures for adipose stem cell isolation are already well established, minimally invasive, and safe.

3. EXCLUSION CRITERIA:

- Refusal to provide a signed informed consent
- Severe uncontrolled diseases (chronic renal failure, cardio, pulmonary, etc)
- Any type of medical or psychiatric disease which are considered as exclusion criteria, in the physician's opinion
- Patients with diagnosis of malignant neoplasia, except basal cell or epidermoid carcinoma of the skin or previous history of malignant tumors, except those that have no evidence of relapse for at least 5 years
- Patient had major surgery or serious traumatism within 6 weeks prior to initiating treatment
- Pregnant / possibility of being pregnant or breast-feeding women
- History of current pathology or current laboratory results indicative of any severe uncontrolled diseases (chronic renal failure, cardio, pulmonary, etc)
- Patients with a history of alcohol or other addictive substances abuse within 6 months before inclusion
- Severe cachexia and malnourishment (BMI less than 19)
- Predicted impossibility of a biopsy of at least 30 grams of fat
- Patients with congenital or acquired immunodeficiency
- Positive serology for Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV)
- Patients on chronic immunosuppressive therapy
- Patients awaiting organ transplant / on organ transplant waiting list (kidney, lung, liver, etc)
- Unrealistic expectations about treatment outcome, in the physician's opinion
- Patients who have a history of adverse reactions to local anesthesia or who present with the possibility of health risks if local anesthesia is applied

4. ELIGIBILITY CRITERIA

- 18 years and older (at the physician's discretion, may be younger)
- Gender: either male or female
- Patients with conditions that do not improve with the current standard of care.
- Patients who provide a written consent to receive Autologous Adipose-Derived Stromal Vascular Fraction Containing Adult Stem cell treatment.

5. AD-SVF CONTAINING ADULT STEM CELLS PROCEDURE

- A. Initial patient evaluation: A physician reviews the medical information, lab work, and diagnostic imaging provided by the patient in order to determine the stage of the medical condition and any other secondary conditions.
- B. Pre-op evaluation / post-op medical consultation: A medical specialist to the specific condition to be treated provides a medical consultation at the location where the procedure will be performed.
- C. Harvesting of adipose tissue: Adipose tissue acquisition can be summarized in three steps:
- *Application of anesthetic / injection of tumescent solution*
 - *Waiting time*
 - *Acquisition of adipose tissue*: An area of the body with sufficient adipose tissue is selected; this is usually the periumbilical area. With the patient supine, the physician infiltrates a small amount of local anesthetic. A tissue sample is then obtained using 60 cc syringe(s) to aspirate 50 to 100 cc of adipose tissue. Immediately following lipo-aspiration, adipose tissue sample is processed (minimally manipulated) to separate stem cells for use as graft.
- D. Preparation of Platelet Rich Plasma (PRP) (if applicable): Using a standard phlebotomy technique the patient's own blood sample is obtained. After collection of whole blood, sample is centrifuged to obtain PRP aliquot. The regenerative potential of PRP is based on the release of growth factors / cytokines upon platelet rupture. PRP also enhances stem cell proliferation.
- E. Autologous implant of Ad-SVF: The stem cells obtained from the adipose tissue sample and the PRP are applied to the patient using appropriate protocol for their condition. Autologous Ad-SVF containing adult stem cells may be infused intravenously and / or locally, for example: intra-articular injection, intra-dermal injection.

CONDITIONS TREATED WITH STEM CELL THERAPY

- 1. Alopecia**
- 2. Congestive Heart Failure**
- 3. COPD**
- 4. Diabetes Mellitus**
- 5. Erectile Dysfunction Protocol**
- 6. Macular Degeneration**
- 7. Multiple Sclerosis (MS)**
- 8. Orthopedic (OA and Injuries)**
- 9. Parkinson's Disease (PD)**
- 10. Rheumatoid Arthritis (RA)**
- 11. Spinal Cord Injuries**
- 12. Systemic Lupus Erythematosus (SLE)**