

Fat Grafting: Research Aspects



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**THE PLASTIC SURGERY
FOUNDATION™**

About The Plastic Surgery Foundation (PSF)



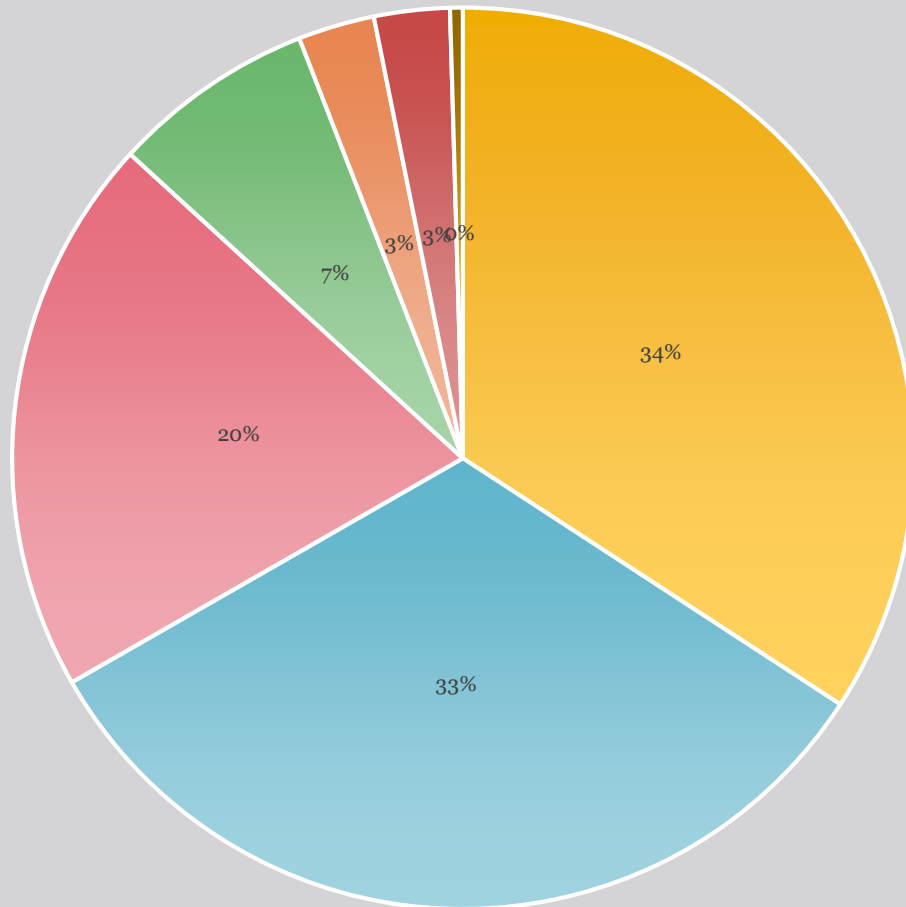
- Founded in 1948, the Mission of The PSF is to
 - Foster innovation in plastic surgery
 - Improve the quality of life of plastic surgery patients through
 - ✦ Research and development
 - Award research grants
 - Develop clinical trials and studies
 - Develop registries for quality improvement
 - ✦ Charity care
 - Breast Reconstruction
 - Pediatric Reconstruction
 - ✦ Public awareness

About The Plastic Surgery Foundation (PSF)



- The PSF fosters the clinical exposure of plastic surgeons by sponsoring
 - Visiting Professors Program
 - International Scholar Program
- Donations to The PSF also support surgeons who volunteer abroad to help the impoverished and foster international outreach through Volunteers in Plastic Surgery.

The Plastic Surgery Foundation (PSF) Budget



- Investigator Initiated Research
- Proactive Research
- Academic Affairs
- Administrative
- Research Education and Workshops
- Fund Development
- Communications and Awards

Total Budget - \$3,157,100

PSF Research Funding



- Investigator-Initiated Grant Program
 - In 2016, The PSF awarded **36** grants totaling nearly **\$800,000** in support to investigators in plastic surgery research.
 - Nearly 20% of the grants funded by The PSF this year, were in Fat Grafting and/or Stem Cells, totaling nearly **\$140,000** awarded.

PSF Funded: Fat Grafting Research

2011-2016



- Investigator-Initiated Grant Program
 - ✦ **25** Grants Funded in Fat Grafting and/or Stem Cells
 - ✦ **\$604,346** Awarded in Fat Grafting and/or Stem Cells
- Basic Science and Clinical Research Grants
 - ✦ **More than \$530,000** Basic Science grants in Fat Grafting and/or Stem Cells
 - ✦ **\$70,000** Clinical Research grants in Fat Grafting and/or Stem Cells
- Research Fellowship Grants
 - ✦ Salary support for young investigators getting formal research training
 - ✦ **3** Fat Grafting Research Fellowships have been awarded to young investigators in the field of Fat Grafting.

PSF: Institutions Funded Research in Fat Grafting and/or Stem Cells since 2011

- Brigham and Women's Hospital
- Case Western Reserve University
- New York University
- Rhode Island Hospital
- Southern Illinois University School of Medicine
- Stanford University
- University of California, Los Angeles
- University of California, San Diego
- University of California, San Francisco
- University of Michigan
- University of Pennsylvania
- University of Pittsburgh
- Wright State University

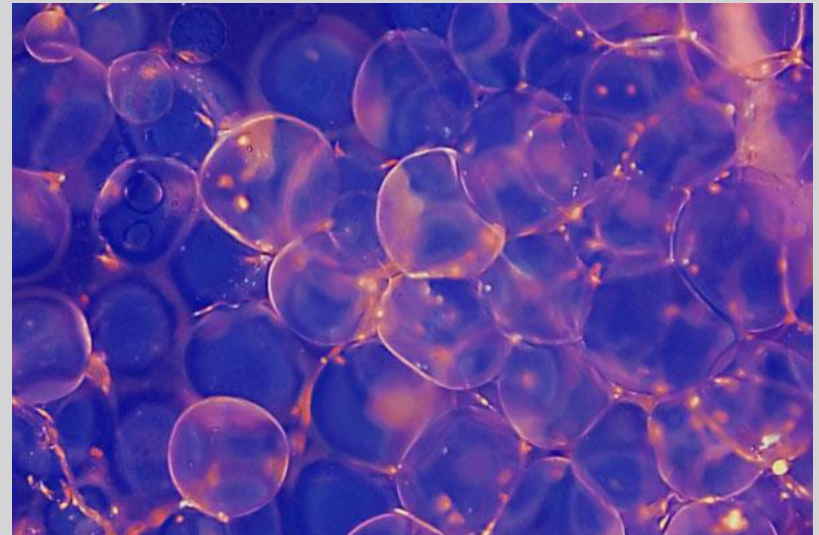
Plastic Surgery Foundation: Funded Research in Fat Grafting and/or Stem Cells since 2011

- Radiated Bone:
 - “Adipocyte Stem Cell Enhancement of Distraction in Radiated Jaws”
- Skin Regeneration;
 - “Skin regenerative potential of ADSCs: in vivo nude mouse model”
- Scleroderma:
 - “Autologous fat grafting for scleroderma induced skin fibrosis”
- Radiated Skin:
 - “ADSC Potentiates Tissue Reorganization/Repair - Radiated Expansion”
- Fracture Healing:
 - “LGR6+ Epithelial Stem Cell Augmentation of Fracture Healing”



Plastic Surgery Foundation: Funded Research in Fat Grafting and/or Stem Cells since 2011

- Peripheral Nerve Repair:
 - “Transfected Adipose Stem Cells for Peripheral Nerve Repair”
- Diabetic Feet:
 - “Autologous fat grafting for pedal fat pad atrophy”
- Aging Tissue:
 - “Sirtuin Regulation of Aging Human Adipose Tissue”
- Breast Reconstruction:
 - “Therapeutic Fat Grafting: Breast Cancer Treatment & Recon”



Lipofilling of the Breast Does Not Increase the Risk of Recurrence of Breast Cancer: A Matched Controlled Study

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Background: Although many plastic surgeons perform autologous fat grafting (lipofilling) for breast reconstruction after oncologic surgery, it has not been established whether postoncologic lipofilling increases the risk of breast cancer recurrence. The authors assessed the risk of locoregional and systemic recurrence in patients who underwent lipofilling for breast reconstruction.

Methods: The authors identified all patients who underwent segmental or total mastectomy for breast cancer (719 breasts) (i.e., cases) or breast cancer risk reduction or benign disease (305 cancer-free breasts) followed by breast reconstruction with lipofilling as an adjunct or primary procedure between June of 1981 and February of 2014. They also then identified matched patients with breast cancer treated with segmental or total mastectomy followed by reconstruction without lipofilling (670 breasts) (i.e., controls). The probability of locoregional recurrence was estimated by the Kaplan-Meier method.

Results: Mean follow-up times after mastectomy were 60 months for cases, 44 months for controls, and 73 months for cancer-free breasts. Locoregional recurrence was observed in 1.3 percent of cases (nine of 719 breasts) and 2.4 percent of controls (16 of 670 breasts). Breast cancer did not develop in any cancer-free breast. The cumulative 5-year locoregional recurrence rates were 1.6 percent and 4.1 percent for cases and controls, respectively. Systemic recurrence occurred in 2.4 percent of cases and 3.6 percent of controls ($p = 0.514$). There was no primary breast cancer in healthy breasts reconstructed with lipofilling.

Conclusions: The study results showed no increase in locoregional recurrence, systemic recurrence, or second breast cancer. These findings support the oncologic safety of lipofilling in breast reconstruction. (*Plast. Reconstr. Surg.* 137: 385, 2016.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Risk, II.

Kronowitz SJ, Mandujano CC, Liu J, Kuerer HM, Smith B, Garvey P, Jagsi R, Hsu L, Hanson S, Valero V. Lipofilling of the Breast Does Not Increase the Risk of Recurrence of Breast Cancer: A Matched Controlled Study. *Plast Reconstr Surg.* 2016 Feb;137(2):385-93.

Fat Injection to the Breast: Technique, Results, and Indications Based on 880 Procedures Over 10 Years



Emmanuel Delay, MD; Sebastian Garson, MD; Gilles Tousson, MD; and Raphael Sinna, MD

BACKGROUND: Fat injection to the breast is not a new idea, but it has always been controversial. In particular, it has been feared that breast augmentation with autologous fat could lead to the formation of calcifications and cysts that might hinder mammographic examinations for detection of possible breast cancer.

OBJECTIVE: The authors report their experience with fat transplantation in the breast (lipomodeling) covering 880 procedures performed over the past 10 years. They review their technique and results, and describe the various indications for which they have found lipomodeling to be appropriate.

METHODS: Lipomodeling was generally performed under general anesthesia. Fat was harvested from the abdomen or in some cases from the inner thighs, depending on the patient's natural fat deposits. The harvested fat was centrifuged to obtain purified fat, which was transferred to 10-mL syringes for injection directly into the breast. Fat was injected in small quantities under light pressure, utilizing a honeycomb of microtunnels and halting when the recipient tissues were saturated to avoid creation of fatty pools that could lead to fat necrosis. To compensate for fat resorption, 140 mL of fat was injected for a desired final volume of 100 mL.

RESULTS: Clinical follow-up shows that the morphologic results of lipomodeling with regard to the volume obtained are stable three to four months postoperatively if the patient's weight remains constant. The postoperative radiologic appearance is usually that of normal breasts, sometimes showing images of fat necrosis that will not confuse the differential diagnosis of cancer for radiologists experienced in breast imaging. Oncologic follow-up at 10 years postoperatively (for the first patients) showed no increased risk of local recurrence of cancer or development of a new cancer. Results were highly satisfactory for both patients and surgeons. Complications included one case of infection at the harvest site, six cases of infection at the injection site, and one case of intraoperative pneumothorax that was successfully treated in the recovery room with no later consequences. The incidence of fat necrosis was 3%, with most cases occurring early in the surgeon's experience.

CONCLUSIONS: Lipomodeling, because of a low complication rate and positive results, presents a new option for plastic, reconstructive, and aesthetic surgery of the breast. Pre- and postoperative examination by a radiologist specialized in breast imaging is necessary to limit the risk that a cancer may occur coincidentally with lipomodeling. (*Aesthet Surg J*;29:360-378.)

Delay E¹, Garson S, Tousson G, Sinna R. Fat injection to the breast: technique, results, and indications based on 880 procedures over 10 years. *Aesthet Surg J*. 2009 Sep-Oct;29(5):360-76.

The Oncologic Safety of Breast Fat Grafting and Contradictions Between Basic Science and Clinical Studies

A Systematic Review of the Recent Literature

Heath J. Charvet, MD,* Hakan Orbay, MD, PhD,† Michael S. Wong, MD,† and David E. Sahar, MD†

Abstract: Fat grafting is increasingly popular and is becoming a common practice in plastic surgery for postmastectomy breast reconstruction and aesthetic breast augmentation; however, concerns over the oncologic safety remains a controversial and hot topic among scientists and surgeons. Basic science and laboratory research repeatedly show a potentially dangerous effect of adipose-derived stem cells on breast cancer cells; however, clinical research, although limited, continually fails to show an increase in breast cancer recurrence after breast fat grafting, with the exception of 1 small study on a subset patient population with intraepithelial neoplasm of the breast. The aim of this review is to summarize the recent conflicting basic science and clinical data to better understand the safety of breast fat grafting from an oncological perspective.

Key Words: breast cancer, fat grafting, mesenchymal stem cells, adipose-derived stem cells

(*Ann Plast Surg* 2015;75: 471–479)

dormant in certain niches in organs, but become activated in the case of injury (ie, surgery) to help tissue regeneration. It has been widely speculated that the growth factors secreted by activated MSCs may stimulate the growth and metastasis of cancer cells. Although clinical studies have yet to show an increased breast cancer recurrence risk after breast fat grafting with the exception of a subset population of epithelial neoplasms of the breast, basic science research is replete with evidence demonstrating that ASCs and breast cancer cells communicate and lead to increased migration and proliferation of breast cancer cells, as well as increased gene expression of typical malignancy markers (epithelial cell adhesion molecule [*EPCAM*], erythroblastosis oncogene B2 [*ErbB2*], lymphoidenhancer-binding factor 1 [*LEF1*], fibroblast growth factor receptor 4 [*FGFR4*], and synucleingamma [breast cancer-specific protein 1; *SNCG*]), and increased tumor growth and metastasis using in vivo xenograft models.^{8–11}

The aim of this review is to evaluate the recent data on clinical

Charvet HJ¹, Orbay H, Wong MS, Sahar DE. The Oncologic Safety of Breast Fat Grafting and Contradictions Between Basic Science and Clinical Studies: A Systematic Review of the Recent Literature. *Ann Plast Surg*. 2015 Oct;75(4):471-9.

A Case-Controlled Study of the Oncologic Safety of Fat Grafting

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Background: Currently, there is no clinical evidence of oncologic risk associated with fat grafting, although its safety has been questioned. The authors investigated the risk of relapse associated with fat grafting in women with a history of breast cancer.

Methods: Of 328 women with previously treated malignant breast disease who underwent fat grafting at the Nottingham Breast Institute, complete data were available for 211 (invasive carcinoma, $n = 184$; ductal carcinoma in situ, $n = 27$). Mean follow-up was 88 months after primary cancer surgery and 32 months after fat grafting. Control subjects were matched 2:1 for date of primary cancer operation (within 2 years), age (within 5 years), type of surgery, tumor histology, estrogen receptor status, and disease-free status by time equivalent to that of fat grafting. Final endpoints were tumor recurrence and death. Outcome results were compared with a systematic review of all patients undergoing fat grafting with adequate follow-up reported in the literature.

Results: No significant excess oncologic events were observed in patients who had fat grafting compared to controls with regard to local (0.95 percent versus 1.90 percent; $p = 0.33$), regional (0.95 percent versus 0 percent; $p = 0.16$), and distant recurrences (3.32 percent versus 2.61 percent; $p = 0.65$). A systematic review identified case series with a total of 1573 women who had fat grafting after primary oncologic breast surgery. The locoregional relapse rate for these patients was 2.92 percent (0.95 percent per year).

Conclusion: This study has found no evidence of increased oncologic risk associated with fat grafting in women previously treated for breast cancer. (*Plast. Reconstr. Surg.* 135: 1263, 2015.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Risk, II.

Gale KL¹, Rakha EA, Ball G, Tan VK, McCulley SJ, Macmillan RD. A case-controlled study of the oncologic safety of fat grafting. *Plast Reconstr Surg.* 2015 May;135(5):1263-75.

Safety of Lipofilling in Patients with Breast Cancer



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Krishna Bentley Clough, MD^d, Isabelle Sarfati, MD^d,
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KEYWORDS

- Lipofilling • Fat transfer • Breast cancer • Mastectomy • Breast conservative treatment
- Breast reconstruction • Oncoplasty • Recurrences

KEY POINTS

- Biological considerations: review of experimental research and translational studies.
- Technique: differentiate the transfer technique with simple purification of the fat or an enrichment technique.
- Clinical evaluation based on a reliable statistical method to limit the risk of bias.
- Randomized trial is the best method but is not realistic in plastic surgery indications (patients refuse to submit to the surgeon choice).
- Prospective studies are more reliable than retrospective studies but require long accrual periods.
- Prospective or retrospective studies should at least be case-control studies.
- Definitive conclusions require large series, control groups with a rigorous matching of the cancer criteria, and at least 5 years' mean follow-up.

Petit JY¹, Maisonneuve P², Rotmensz N², Bertolini F³, Clough KB⁴, Sarfati I⁴, Gale KL⁵, Macmillan RD⁶, Rey P⁷, Benyahi D⁴, Rietjens M⁸. Safety of Lipofilling in Patients with Breast Cancer. Clin Plast Surg. 2015 Jul;42(3):339-44.

Determining the Oncological Risk of Autologous Lipoaspirate Grafting for Post-Mastectomy Breast Reconstruction

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Guido Baroni · Mirco Galiè · Anna Maria Molino ·
Anna Mercanti · Rocco Micciolo · Andrea Sbarbati

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Abstract This study compares the incidence of local and regional recurrence of breast cancer between two contiguous time windows in a homogeneous population of 137 patients who underwent fat tissue transplant after modified radical mastectomy. Median follow-up time was 7.6 years and the follow-up period was divided into two contiguous time windows, the first starting at the date of the radical mastectomy and ending at the first lipoaspirate grafting session and the second beginning at the time of the first lipoaspirate grafting session and ending at the end of the total follow-up time. Although this study did not employ an independent control group, the incidence of local recurrence of breast cancer was found to be comparable between the two periods and in line with data from similar patient populations enrolled in large multicenter clinical trials and

who did not undergo postsurgical fat tissue grafting. Statistical comparison of disease-free survival curves revealed no significant differences in relapse rate between the two patient subgroups before fat grafting and after fat grafting. Although further confirmation is needed from multicenter randomized clinical trials, our results support the hypothesis that autologous lipoaspirate transplant combines striking regenerative properties with no or marginal effects on the probability of post-mastectomy locoregional recurrence of breast cancer.

Keywords Autologous fat grafting · Breast cancer · Adipose-derived stem cells · Reconstructive surgery · Tissue regeneration

Rigotti G, Marchi A, Stringhini P, Baroni G, Galiè M, Molino AM, Mercanti A, Micciolo R, Sbarbati A. Determining the oncological risk of autologous lipoaspirate grafting for post-mastectomy breast reconstruction. *Aesthetic Plast Surg.* 2010 Aug;34(4):475-80.

PSF's Fat Grafting Safety Initiatives



- Cancer Risk After Fat Transfer (CRAFT)
- General Registry of Autologous Fat Transfer (GRAFT)
 - All Procedures Module
 - Breast Module
- Since 2011, The PSF has invested nearly \$400,000 in these two programs to further investigate the safety and efficacy of fat grafting.

Cancer Recurrence After Fat Transfer (CRAFT)



- **Study Sponsor:** The Plastic Surgery Foundation
- **Clinical Coordinating Center:** The Plastic Surgery Foundation
- **Data Coordinating Center:** University of North Carolina, Chapel Hill
- **Participating Centers:**
 - Memorial Sloan-Kettering Cancer Center
 - Washington University, St. Louis
 - MD Anderson Cancer Center
 - University of Chicago

Cancer Recurrence After Fat Transfer (CRAFT)



- **Methodology:**

- Case Cohort Study

- Rationale

- ✦ Fat transfer is an increasingly popular method for refining post-mastectomy reconstructions

- Population:

- ✦ Women with Stage I-III invasive ductal carcinoma, who underwent mastectomy with immediate breast reconstruction.
- ✦ Diagnosed between 2006-2011

- Evaluated:

- ✦ All recurrences

Cancer Recurrence After Fat Transfer (CRAFT)



- **Results:**

- In this population of breast cancer patients who had mastectomy with immediate reconstruction, fat transfer was not associated with a higher risk of cancer recurrence.

- Myckatyn TM, Wagner IJ, Mehrara BJ, Crosby, Park JE, Qaqish BF, Moore DT, Busch EL, Silva AK,, Kaur S, Ollila DW, Lee CN. **Cancer Recurrence After Fat Transfer (CRAFT)- A Multicenter Case-Cohort Study (2016)** *Plastic and Reconstructive Surgery, in Press*

General Registry of Autologous Fat Transfer (GRAFT)



G  **R A F T**

General Registry of Autologous Fat Transfer (GRAFT)



- **Background:**

- Lack of consensus on fat grafting methods and analysis of outcomes
- Wide range of outcomes, complications and patient satisfaction results have been reported
- Majority of studies are case series or retrospective reviews

General Registry of Autologous Fat Transfer (GRAFT)



- Quality Improvement Initiative
- Nationwide Registry of fat grafting for aesthetic and reconstructive surgery
- A web-accessible database in which participating clinical centers contribute their cases

General Registry of Autologous Fat Transfer (GRAFT)



- **Aims of the Registry:**

- Prospectively determine the rates of early and late complications of fat grafting for aesthetic and reconstructive procedures
- Analyze the effects of these procedures on quality of life and patient satisfaction using validated patient reported outcome measures; BREAST-Q

General Registry of Autologous Fat Transfer (GRAFT)



- **All Procedures Module**
 - ✦ Launched in 2015
 - ✦ Capture fat grafting **to all areas of body**, for both aesthetic and reconstructive procedures.
 - ✦ All ASPS members performing Fat Grafting procedures are expected to enter this information.
- **Breast Module**
 - ✦ Launched in 2014
 - ✦ Capture fat grafting to **Breast**, for both aesthetic and reconstructive procedures.

General Registry of Autologous Fat Transfer (GRAFT)



- **Sample Population**

- **Inclusion Criteria:** All cases involving fat grafting to breast following reconstruction or cosmetic procedures
 - ✦ Augmentation with fat grafts or implant
 - ✦ Breast reduction or mastopexy
 - ✦ Cases where fat grafting is used as revision procedure for breast reconstruction or augmentation
- **Exclusion Criteria:** Dermal fat grafting or fat grafts delivered as composite grafts

General Registry of Autologous Fat Transfer (GRAFT)



- **Data Variables Collected**
 - Patient Demographics
 - Fat harvesting/processing technique variables
 - Complications
 - Incidence of new or recurrent breast cancers
 - BREAST-Q – Patient-Reported Outcome Instrument
 - Longitudinal data collection, with 6 week, 6 month and up to 3 year follow up

General Registry of Autologous Fat Transfer (GRAFT)

• Data Collection for Breast Module

Time Point	Demographics and Medical History	Breast Cancer Information	Indication for Graft	Technique	Complications	BREAST-Q	Radiologic Outcomes
Baseline	X	X	X	X		X	
6 weeks post procedure				If necessary	X	X	
6 months post procedure		X		If necessary	X		X
1 year post procedure		X		If necessary	X		X
2-3 years post procedure		X		If necessary	X		X

General Registry of Autologous Fat Transfer (GRAFT)



- **All Procedures Module**

- As of July 14, 2016

- ✦ More than **150** ASPS Members have registered for GRAFT since October 2015.

- Since October 2015, more than 1,500 patient visits have been entered into GRAFT

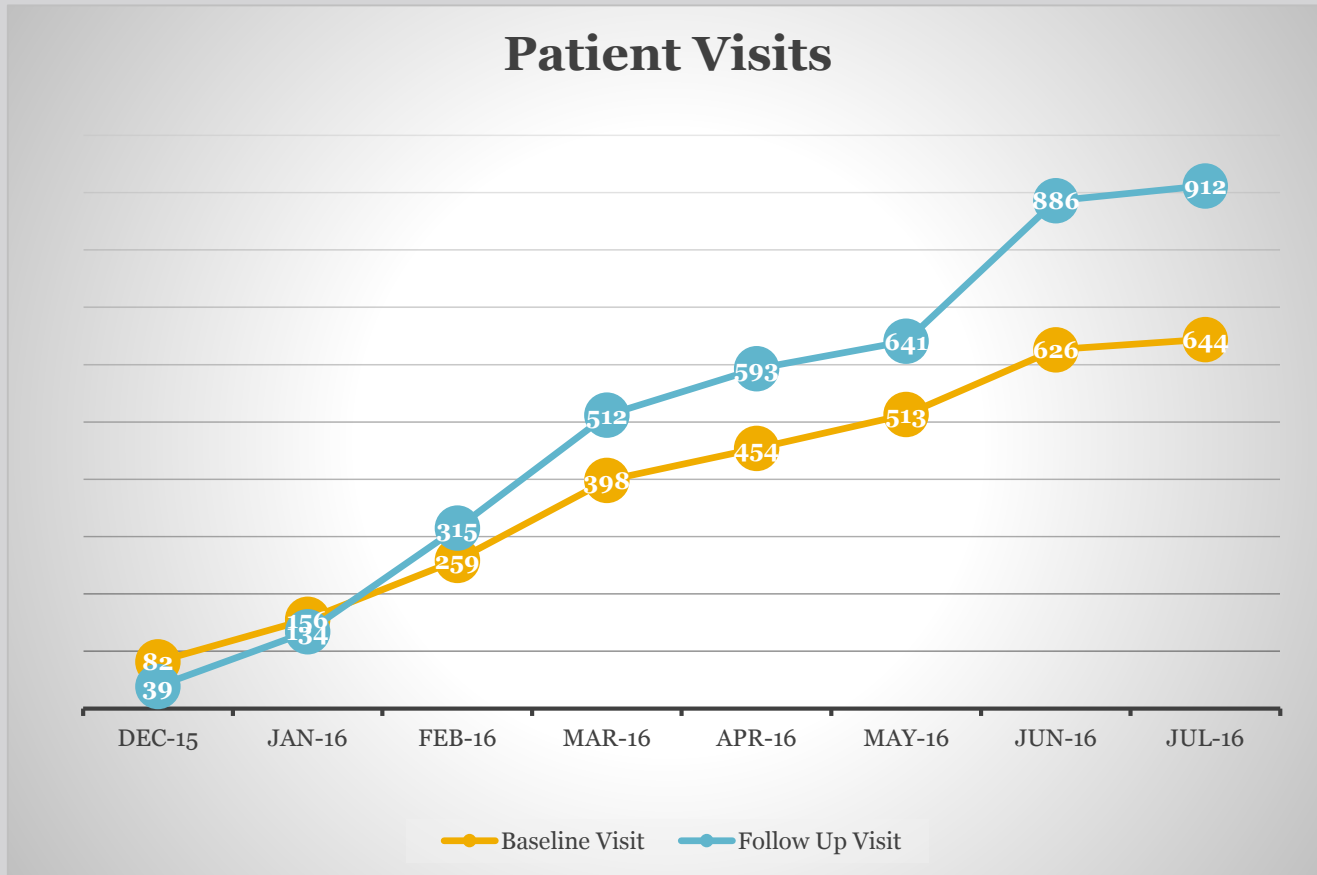
- ✦ **644** Baseline Procedures

- ✦ **912** Follow-up Visits

General Registry of Autologous Fat Transfer (GRAFT)



Patient Visits



PSF's Overall Investment in Fat Grafting Research



- **Since 2011, The PSF has invested more than **ONE MILLION DOLLARS** in fat grafting research!**
- **We are focused on providing the highest quality of safe and effective care possible for our patients.**



- Thank you!