Preliminary Report

A Preliminary Clinical Trial Comparing Split Treatments to the Face and Hand With Autologous Fat Grafting and Platelet-Rich Plasma (PRP): A 3D, IRB-Approved Study

Gordon H. Sasaki, MD, FACS

Abstract

Background: Numerous methodologies have been suggested to enhance fat graft survival, but few long-term studies are available.

Objectives: The authors of this institutional review board-approved study investigated the safety and efficacy of utilizing platelet-rich plasma (PRP).

Methods: Each of 10 patients received equal volumes of syringe-harvested, centrifuged fat to opposing midfaces with a lateral submuscular aponeurotic system-plication or no face lift and hands that were combined with equal volumes of either concentrated PRP or normal saline. Comparable assessments of fat retention/baseline values by 3D Vectra Analysis, VISIA, and Cortex facial skin analyses were performed. Clinical results were judged on a visual analogue scale.

Results: The average percent change in mean volume assessments at the fat/PRP sites from baseline values, as profiled by 3D Vectra Analysis, demonstrated a higher, but statistically nonsignificant value over 1 year than the percent value changes at the fat/normal saline sites in the opposing face or hand. Three independent evaluators were able to assess volume restorations to the malar fat pad, naso-jugal groove, and nasolabial fold as well as to intermetacarpal hollowness with reduction of visible veins and tendons in the anterior midface and hands with both treatments. No adverse events were observed over the year-long study. Perioperative edema, erythema, bruising, and tenderness lasted up to 1 to 2 weeks at most.

Conclusions: Autologous fat grafting continues to be a safe and effective adjunct in facial and hand aesthetic surgery. This study will require more patients and longer follow-up periods to determine whether PRP has a potential role to increase fat graft retention in aesthetic patients.

Level of Evidence: 3
fate of fat grafting is due to both adipocyte survival within the transplanted fat and its replacement by a population of ischemic-resistant adipose stem cells that proliferate and differentiate into new adipocytes and endothelial cells. A recent transgenic mouse study traced the differentiated donor adipose-derived stem cells (ADSCs) with labelled green fluorescent protein signals into endothelial cells of new vessels and newly differentiated adipocytes, both of which integrated themselves with the surviving recipient tissue for increased graft retention after cell-assisted lipo-transfer. Despite numerous cell culture, translational, and tissue investigations, no consensus algorithm exists that ensures superior or reliable results by refining existing techniques and standardization of clinical protocols.

In the past 2 decades, the use of platelet-rich plasma (PRP) has emerged as a possible strategy to improve overall fat graft survival. Multiple growth factors are released from a concentrated number of platelets obtained by an uncomplicated, cost-effective processing method utilizing FDA-cleared devices. Although some clinical publications have reported significant benefits of improved fat retention after PRP therapy, other investigations have not observed significant effects in comparison trials.

This clinical investigation was designed to clarify the benefits of PRP by evaluating the safety and efficacy of PRP for improved retention of fat volume and skin elasticity to split midfaces and hands within a well-defined but limited healthy patient cohort.

**METHODS**

**Study Overview**

This investigator-initiated, single-center study was designed and implemented as a preliminary, case-controlled, clinical trial investigating the safety and efficacy of equivalent volumes of combined fat:PRP or fat:normal saline to opposing sides of the face with or without a Baker-designed lateral submuscular aponeurotic system-plication face lift and dorsum of hands at the author’s American Association for Accreditation of Surgery Facilities surgical center under local anesthesia from February 2015 to May 2018.

**Candidate Inclusion and Exclusion Criteria**

Of more than 100 evaluated patients (30-65 years of age), only 35 candidates qualified for enrollment in this study based on the same inclusion/exclusion criteria that were similarly applied in the author’s previous publication. Candidates were required to exhibit topographical changes of ptosis and deflation of the malar fat pad compartments (deepened naso-jugal and nasolabial grooves and descension towards the nasolabial line), to have never experienced any midface surgery, or had any lower lid procedure with anterior translocation of orbital fat within 2 years. Candidates were considered for midface inclusion after 2 years from receiving temporary fillers/volumizers and neurotoxins, noninvasive procedures (deep chemical peels, nonablative, ablative resurfacing; external ultrasound or radiofrequency skin tightening procedures), or minimally invasive lifting surgeries (micro-needling with radiofrequency; suture lifting; subdermal radio-frequency or laser procedures). Candidates were excluded if they presented with active systemic or local facial infections, significant facial scarring, pregnancy, active immune disease, uncontrolled diabetes mellitus and hypertension, hemorrhagic disorders, or midface augmentation with boney or alloplastic implants or filled with permanent fillers.

Specific primary hand inclusion criteria were observed in candidates who demonstrated aging skin (crepiness; pigmentations; laxity), intermetacarpal hollowness, and prominent vessels and tendons. Secondary inclusion criteria were included for candidates who did not undergo any chemical or laser treatments, fillers, fat grafting, non-surgical device treatments, or surgical procedures to the dorsum of the hand within 2 years. Candidates who previously underwent any of these treatments within 2 years were excluded from participation in the trial.

**Informed Consent**

All candidates were required to have 3 separate consultation sessions with the author, surgical registered nurse, and office manager until the candidate acknowledged and understood the offered procedures that would attempt to meet their clinical expectations and safety requirements. Each candidate was informed there would be only one fat-grafting session without any additional fat-grafting session or the use of any other volumetric material during the study. Each candidate was informed no other face or hand rejuvenating procedures were permitted during the study. Corrective procedures or management of complications (bleeding, infections, nerve injuries, and tissue loss) would be managed according to the office guideline policies. The trial protocol complied with the Declaration of Helsinki and was approved by an investigational review board (IRB; February 5, 2015, Allendale IRB, Old Lyme, CT). All patients provided written informed consents.

**Subject Randomization**

Patients were asked to draw blindly from a nontransparent jar that contained a mixture of 5 red and 5 black identically sized strips of paper. The red strip indicated that fat:normal saline would be the treatment to the right midface and right hand, whereas a black strip indicated that fat:PRP would be delivered to the right midface and right hand. Accordingly,
patients 1, 2, 4, 5, and 8 were selected to be grafted with fat (up to 10 mL) mixed with normal saline to the right side of the midface and right hand. The left side of the midface and left hand were grafted with an equivalent volume from the same batch of processed fat combined with an identical volume of PRP instead of normal saline. Patients 3, 6, 7, 9, and 10 were selected to be grafted in a similar manner, except the same volumes of fat (up to 10 mL) and PRP were injected to the right side of the midface and right hand, whereas the left side of the midface and left hand received an identical volume of processed fat plus normal saline.

**Clinical Evaluation Methods**

Baseline facial and hand studies were performed with the Complex VISIA Investigational Facial Skin Analysis and Facial Vectra XT 3D Volumetric Analysis Imaging (Canfield Imaging, Parsippany, NJ) and Cortex Facial Skin Analysis (Cortex Technology, Hadsund, Denmark). These studies were repeated at 3, 6, and 12 months in follow-up sessions. At the end of the study, 3 independent evaluators were asked to estimate levels of improvement in volume retention and skin changes in the area of the anterior midface and also volume changes, degree of tendon and vessel presence, and textural improvements in the hand between baseline photos and photos at the 3-, 6-, and 12-month treatment intervals. Levels of change were based on a visual analogue scale that estimated degrees of change (0 = no change; 1 = slight improvement; 2 = improvement; 3 = much improvement; 4 = significantly improvement). Adverse event analyses were recorded at the same intervals when photographic analyses were obtained up to 1 year.

**Surgical Protocol**

**Study Preparation and Follow-Up Studies**

Prior to surgery, each patient’s medical history, surgical clearance, blood and chemical panels, and electrocardiogram were obtained. Measurements of body mass index (BMI), baseline high-resolution digital facial and hand photography, VISIA/Cortex/ and 3D Vectra Imaging were performed by the same technician throughout the study. Oral antibiotics and pain medication were prescribed for 3 days after surgery. Patients at risk of a viral skin infection received a course of prophylactic antiviral medication for 3 days after the procedure. Women of childbearing potential had a urine pregnancy test performed immediately before the procedure.

**Surgical Markings**

With the patient in a sitting position, the location and outline of the key 3 deep compartments (deep medial cheek fat compartment, medial sub-orbicularis fat compartment, and lateral sub-orbicularis fat compartment) and 2 superficial compartments (nasolabial compartment and medial fat compartment) of the malar fat pad were marked on both midfaces, as shown in Figure 1A,B.

As depicted in Figure 1C,D, a transverse line was drawn across the wrist at the caudal border of the ulnar tuberosity. At its midpoint, the midpoint of the transverse line, a 2.5-cm perpendicular line was dropped to mark the cannula proximal entry point on the dorsal skin of the hand. Other distal entry points at the 4 web spaces were used for more uniform distribution of graft. The metacarpal bones, intercarpal atrophic hollows, visible extensor tendons, and prominent veins were delineated for fat graft enhancement.

**Fat-Harvesting Cannula and Centrifuge Processing System**

Fat was harvested from the anterior abdomen, utilizing tumescent technique with a solution containing 50 mL 0.5% lidocaine, 1 mg epinephrine, and 20 mL of 8.4% sodium bicarbonate per liter of warm saline. Each of four 20-mL syringes was prefilled with 2 mL of normal saline, reducing the aspiration pressure (<500 mm Hg), and connected to a blunt tip, multiport, 2.1 mm × 10 cm cannula for fat aspiration. The content from each 20-mL syringe was spun for 3 minutes at 1000 g in the AdiPrep Adipose Transfer System (Harvest TerumoBCT, Inc., Lakewood, CO) process disposables of the centrifuge. After decantation of the tumescent fluid, tissue debris, and oil, the concentrated processed fat from all syringes was collected and gently combined in one 60-mL syringe. The fat-filled syringe was capped and placed in a sterile plastic bag, which was submerged in a cold-water bath for use within 2 to 4 hours after preparation.

**Preparation of Platelet-Rich Plasma**

The FDA-cleared automated device (SmartPreP2 System, Harvest-TerumoBCT, Inc, Lakewood, CO) isolated a buffy coat containing high concentrates of platelets, as reported in the Quality Assurance Testing by Kevy and Jacobson. A total of 54 mL of whole blood was withdrawn from an antecubital arm vein mixing with 6 mL of adenosine-citrate-dextrose within a 60-mL syringe. Through floating shelf and double spin centrifuge technology, platelet-poor plasma was used to resuspend the buffy-coat pellet to a final volume suspension of approximately 7 mL PRP.

**PRP Cell-Counting Analyses**

A 1-mL aliquot of the 7 mL PRP was transported overnight to BioScience Research Associates, Cambridge, MA, for analysis of baseline platelet count from whole blood and Harvest PRP using a Coulter ACT DIFF 2 Series Analyzer (Beckman Coulter, Inc., Miami, FL). The final platelet concentration...
Figure 1. (A) Diagrammatic location and outline of the 3 key deep fat compartments (DLSC, deep lateral suborbicularis compartment; DMC, deep medial compartment; DMSC, deep medial suborbicularis compartment) and 2 superficial fat compartments (MFC, medial fat compartment; NLC, nasolabial compartment). (B) Preoperative drawings on this 53-year-old female patient’s left anterior midface outlining the location of the 3 deep compartments with the nasojugal groove separating the DMC from the DMSC. (C) Diagrammatic location and outline of the visible extensor tendons, intermetacarpal hollows, and veins. The yellow dots at midpoint of the wrist line and at the web sites represent the cannula entry points for retrograde linear fan-shaped deposition of fat, sparing the thenar and hypothenar bulges. (D) Preoperative mapping of the dorsal hand is based on the topographical assessment. A horizontal line distal to the ulnar tuberosity indicates the most proximal area for fat grafting. The purple circle 2.5 cm distal to horizontal line designates the proximal cannula entry point from which the fat is distributed in a fan-shaped pattern from the thumb extensor pollicis longus tendon across to the extensor digiti quinti tendon (usually sparing the thenar and hypothenar bulges) up to the intercarpal web sites. Other entry points at the web sites were available for a more even fat distribution. Fat grafting was not injected over the proximal phalanges.
in 6 mL of Harvest-processed PRP (1 × 10⁶ particles/µL) was calculated by multiplying the base platelet counts with the dilution ratio used for each sample. Because the final prepared PRP volume was 6 mL, the total number of platelets could be derived by multiplying the baseline platelet concentration (10⁶ particles/µL) by 6 to obtain the number of particles/µL (1 × 10⁹/µL) injected per site.

**Preparation of Fat:PRP and Fat:Normal Saline Injections**

A total of 6 mL of PRP was mixed thoroughly with a 20-mL portion of the processed fat. This 26-mL mixture was divided into two 10-mL allotments. Each of the 10-mL blended allotments was injected into one anterior midface and to the dorsum of one hand. As a control, 6 mL of normal saline was mixed with a 20-mL portion of the remaining batch of processed fat. The 26-mL mixture was similarly divided into 10-mL allotments. Each 10-mL blended allotment was injected into the contralateral anterior midface and the opposite hand. The ratio of fat:PRP or fat:normal saline was approximately 3:1 in the presence of 33% PRP. The PRP was not activated by thrombin or calcium chloride to release growth factors from the platelets’ α-granules in this study.

**Graft Injection Technique**

After completion of the facelift under local anesthesia or no facelift, approximately 2 mL of buffered lidocaine and epinephrine-containing solution in tuberculin syringes was distributed into the compartments of the anterior malar fat pad of each midface through an injection site at the lateral oral commissure with a 1-inch, 30-gauge needle and a longer 2-inch, 25-gauge needle. As described in the author’s previous publication, each midface received as close as possible to a total volume up to 10 mL that was distributed into 1- to 2-mL aliquots into each of the 5 midface compartments. A needle puncture to the lateral cheek was used for deposition of small volumes of fat transversely below the orbital rim inferior to the orbital malar ligaments to treat the upper boundary of the compartments that were not adequately addressed from the commissure approach. The sites were then gently massaged and covered temporarily with a cold pack.

Each hand was injected with a total of 2 mL of buffered lidocaine and epinephrine-containing solution at multiple sites in the subdermal space. The anesthetic solution was gently massaged from the proximal wrist crease to the distal metacarpal heads, sparing the dorsal thenar and hypothenar eminences. An 18-gauge needle punctured the marked entry points to allow subdermal passage of a 1.3-mm (18-gauge) blunt cannula attached to a 1-mL syringe filled with fat mixed with either PRP or normal saline. The harvested fat was injected by increments of < 0.1-mL droplets in proximity to one another. Progressive retrograde threading was performed by passing the cannula to the undersurface of the skin in a fan-shaped fashion throughout the demarcated expanse of the dorsal hand. Grafting was focused on filling interosseous hollows, spaces along the radial aspect of the fifth metacarpal and ulnar border of the first metacarpal, and web space depressions. Very gentle massaging was used to smooth any irregular deposits rather than to spread the grafts to unfilled areas. Patients were advised to minimize aggressive hand movements and elevate hands as much as possible to reduce edema for 1 week.

**Statistical Analysis**

A sensitivity power analysis was performed to the predetermined size of 10 patients. The values used to calculate the analysis were an alpha of 0.05, power of 0.80, computing the mean difference between 2 independent means (2 groups). The analysis used the G* Power 3.1.9.2 software (Universität Kiel, Germany) to conduct the analysis.

**RESULTS**

As listed in Table 1, the 10 patients (4 Hispanic females and 6 Caucasian females) averaged 54.4 years of age (range, 46-67 years) and exhibited an average baseline BMI value of 22.4 (range, 20.5-24.6). Subsequent BMI values for each patient did not significantly change during the study duration (not shown). The average baseline platelet count ± SD was 242.7 ± 76.0 × 10³/µL, PRP concentration ± SD was 1.214 ± 3.9 × 10⁶/µL, and average number of total platelets/3 mL was 3.6 ± 1.9 × 10⁵ (range, 3.0-4.8 × 10⁵/mL). Patients were injected with an average of 9.1 ± 1.0 mL of blended fat that contained either PRP (average, 3.0 ± 0.1 mL) or saline (average, 3.0 ± 0.1 mL). For midface restoration, patients received nearly comparable percentage ratios of PRP:fat (33.5 ± 7.9%). For hand restoration (Table 1), the platelet counts, PRP concentration, and total PRP cells per milliliter were identical to that used in the face, because each patient’s PRP was divided into equal batches. Each hand received the same fat volume (10 ± 0 mL) mixed with equivalent volumes of either PRP (3.0 ± 0.1 mL) or normal saline (3.0 ± 0.1 mL) and contained the same percentage of PRP:fat (33.5 ± 7.9%). The dorsum of each hand easily accommodated a 10-mL volume in contrast to that of smaller facial compartments.

As shown in Figure 2A, the average percent 3D Vectra changes ± SDs from baseline measurements in both hands and faces were higher in the PRP-blended fat than those in the saline-blended fat at 3, 6, and 12 months, but the differences were not statistically significant.

Three evaluators, who were not involved in any aspect of the study, were asked to grade the degree of improved
volumetric changes (Visual analogue; 0-4 improvement scale) after either PRP-fat or saline-fat was injected into the palpebral-malar/naso-jugal grooves and anterior malar fat pad. The evaluators also graded the degree of filling the second through fourth interosseous spaces and reduction in the appearance of dorsal veins and tendons within each set of baseline and 3-, 6-, and 12-months postoperative photographs for each patient (Figures 3 and 4). In Table 2, baseline evaluations of the degree of volume loss in face and hands were rated as “mild to moderate volume loss” (Grade −2). Posttreatment volume restoration by either PRP-fat or saline-fat was rated as “improvement” (Grade +2) in face and hand sites at months 3, 6, and 12.

VISIA facial results (not shown) recorded no significant differences in pigmentation spots, wrinkles, texture, pores, UV spots, and porphyrin spots at any assessment interval in facial and hand treated sites in PRP or saline treatment groups. Cortex facial and hand measurements (not shown)

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* a Hispanic. b Caucasian. Plts, platelets; PRP, platelet-rich plasma; Pt, patient.

Figure 2. (A) The average percent of change ± standard deviation from baseline by 3D Vectra Analysis after saline:fat or platelet-rich plasma:fat to split-face at 3, 6, and 12 months. (B) The average percent change ± standard deviation from baseline by 3D Vectra Analysis after saline:fat or platelet-rich plasma:fat to opposing hands at 3, 6, and 12 months.
Figure 3. Preoperative photos of this 53-year-old Hispanic female patient (patient 1, Table 1) with a body mass index of 24.0 presented with hollowness to each anterior midface with deepening nasojugal groove in (A) frontal, (C) left oblique, and (E) right oblique views. Postoperative photos of patient who received 10 mL of combined fat and saline to the right midface 5 compartments in (B) frontal, and (F) right oblique views. After 1 year, the fat:normal saline grafts have resorbed to almost baseline appearance. Postoperative photos of this patient who received 10 mL of combined fat and platelet-rich plasma to the left midface 5 compartments in (B) frontal and (D) left oblique views. After 1 year, volume restoration of the left midface has maintained in all grafted compartments. (G, I) Both hands of this patient demonstrated intercarpal hollows, prominent outline of extensor tendons, and veins. (J) After 1 year, there is modest improvement of the intercarpal hollows and visible prominence of extensor tendons and veins in the right hand after 10 mL of combined fat:saline grafting. (H) After 1 year, restoration of volume and camouflaging of the tendons and veins in the left hand after 10 mL of combined fat:platelet-rich plasma and maintained to a greater degree compared with those observed in the right hand.
Figure 4. Preoperative photos of this 53-year-old Hispanic female patient (patient 2, Table 1) with a body mass index of 22.3 presented with prominent pseudo-herniated fat in the lower lids, hollowness to each palpebral-malar groove, and anterior midface with deepening nasojugal and nasolabial grooves in (A) frontal, (C) right oblique, and (E) left oblique views. Postoperative photos of this non-facelift patient who underwent transconjunctival approach to reduce lower lid fat deposits and received 8 mL of combined fat and normal saline to the right midface 5 compartments in (B) frontal and (D) right oblique views. After 1 year, the fat:normal saline grafts have almost completely resorbed to baseline appearance. Postoperative photos of this patient who received 8 mL of combined fat and platelet-rich plasma to the left midface 5 compartments in (B) frontal and (F) oblique views. After 1 year, the fat:platelet-rich plasma grafts have restored volume loss in her anterior midface compartments. (G,J) Both hands of this patient demonstrated intercarpal hollows, prominent outline of extensor tendons, and veins. (H) After 1 year, there is modest improvement of the intercarpal hollows and visible prominence of extensor tendons and veins in the right hand after 10 mL of combined fat:saline grafting. After 1 year, restoration of volume and camouflaging of the tendons and veins (J) in the left hand after 10 mL of combined fat:platelet-rich plasma are maintained to a greater degree compared with those observed (H) in the right hand.
also recorded no significant changes in elasticity, transepidermal water loss, hydration, melanin, and erythema at each assessment period in the face and hand treated sites in PRP and saline groups.

There were no complications or adverse events observed during the year-long study to the face or hands. All patients demonstrated minimal perioperative edema, erythema, slight bruising, firmness, and tenderness lasting for up to 1 to 2 weeks. Two patients who initially received fat/normal saline to their midfaces were regrafted with fat/PRP at the end of the study to achieve symmetry. The presence of fat nodules or infections was not observed.

**DISCUSSION**

PRP has been exploited in various medical disciplines for the past 4 decades on the premise that they contain a natural reservoir of growth factors in platelets, concentrated higher than in the original collected blood, to treat various diseases and aging processes.\(^{17,24}\) Primary factors included platelet-derived growth factors and transforming growth factor \(\beta_1\), which have been involved mostly in cell proliferation, differentiation, chemotaxis, and extracellular matrix production/angiogenesis.\(^{25}\) Activated platelets also discharged other growth factors such vascular endothelial growth factors, epidermal growth factor, insulin-like growth factor, and fibroblast growth factor known to play critical roles in the hemostasis, proliferation, and remodeling phases of wound healing.\(^{26,27}\) To date, the question of whether PRP’s entire cocktail of growth factors or the presence of fewer proangiogenic, proliferative, differentiative, and antiapoptotic growth factors is needed to increase fat cell survival in patients has yet to be defined.

In most culture studies,\(^{17,24,28-31}\) 5% to 50% concentrations of PRP have consistently demonstrated enhanced ADSC proliferation in a dose-dependent pharmacologic manner, while either inhibiting ADSC differentiation or maintaining their capability to eventually differentiate to adipocytes during the crucial postproliferation phase.\(^{32,33}\) Conversely, other in vitro investigations have shown that, although lower PRP concentrations were stimulatory, higher concentrations resulted in a reduction in human ADSCs and fibroblasts,\(^{34}\) which could contribute negatively to end-graft volume. A similar reciprocal relation was seen in the majority of in vitro studies\(^ {25-27,31}\) that demonstrated positive effects with higher PRP concentrations on endothelial cells and network formation in a dose-dependent fashion, whereas other investigations\(^ {31}\) observed significantly decreased expression of vascular endothelial growth factor at higher PRP concentrations. With few exceptions,\(^ {35}\) the use of PRP in most animal studies\(^ {36,36-38}\) observed improved graft survival, possibly through increased vascularization. In contrast, clinical efficacy of combining PRP with only fat grafting has been highly variable, raising concerns about its reliability to support graft-take in patients despite overall positive findings in experimental investigations.\(^ {39}\) One of the ongoing

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**Table 2. Evaluation Per Assessors**

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Baseline visual analogue evaluation scale

0 = Loss of volume
-1 = Slight loss of volume
-2 = Mild-moderate loss of volume
-3 = Moderate presence of loss of volume
-4 = Severe loss of volume

Post Tx visual analogue improvement scale

0 = No change
+1 = Slight improvement
+2 = Improvement
+3 = Much improvement
+4 = Significant improvement
clinical challenges in establishing PRP as an adjunct with fat grafting remains the lack of protocol standardization, uniform platelet characterization, and quantification by different processing devices, dosing, outcome measurements, and control presence.

The goal of this case-controlled IRB study was to implement as much as possible uniform treatments to opposing sites in each patient by a single surgeon (G.S.). The harvesting and processing methods to procure fat or PRP, as well as PRP concentrations, cell numbers, and PRP/fat ratios, were performed as nearly alike as possible in all patients. The double-spin device recovered comparable platelet concentrations from which analogous numbers of total cell particles per milliliter were delivered at 2 separate sites (face or hand) with each patient’s contralateral saline sides serving as controls. Because similar baseline PRP counts per microliter were found amongst the 10 patients, comparison of results was possible by means of equal volumes and ratios of fat:PRP and fat:normal saline.

The present study demonstrated that the addition of nonactivated PRP to fat resulted in greater, but statistically nonsignificant, percent volume changes from baseline than after the addition of saline to fat over their baseline values in opposing sides of the face and hands at 3, 6, and 12 months. The addition of PRP to lipo-grafts did not significantly improve skin elasticity or other measurements of skin rejuvenation over fat alone, as measured by the VISIA and Cortex measurements during 1 year. The present controlled split-face PRP data provide, however, further evidence to support the results obtained in my previous publication that observed statistically significant changes over baseline values at 1 year in patients receiving equal volumes of fat and depot injections of PRP to both sides of their anterior midface. Both the present and aforementioned study were comparable in: (1) average baseline platelet counts (281,692 cells/µL vs 254,200 cells/µL), respectively; (2) average PRP concentrations (1.214 × 10^6 cells/µL vs 1.262 × 10^6 cells/µL), respectively; (3) analogous syringe suctioning technique with similarly designed #19-gauge harvesting cannulas; (4) same technique for processing lipo-aspirated fat by centrifugation (3 minutes @ 1100-1200 g); (5) comparable injected volumes of centrifuged processed fat (total 9-10 mL/midface) to the same 5 anterior midface compartments, and (6) a single PRP-assisted fat grafting in conjunction with or without a submuscular aponeurotic system-facelift. However, the present and aforementioned studies differ in the following: (1) total number of injected cells (3.6 × 10^8 cells/mL vs 2.0 × 10^8 cells/mL, respectively); (2) dissimilar ratios of PRP:fat percentages (1:3 vs 1:5, respectively); and (3) different methods to combine PRP to fat (mixing vs depot injection, respectively). The significance of the mentioned differences and their relevance to the observed clinical outcomes are unclear and remain to be determined. Nevertheless, it could be speculated that a higher total number of injected platelets (in this study) may have resulted in a reduced graft retention by 3D Vectra analysis than that observed when a lower total number of platelets was injected (previous study), or that a 1:3 PRP-to-fat ratio rather than a 1:5 PRP-to-fat ratio resulted a lower retention effect by 3D Vectra analysis. Other critical factors that must be considered for the different outcomes involve the viability of the harvested and processed adipocytes, the characteristic of the quality of recipient bed, and the impact of activated or nonactivated platelets to induce neovascularization and fat survival. To the best of my knowledge, no controlled studies exist comparing the effects of PRP to lipografts vs fat alone in the hands.

In conclusion, I observed a modest improvement utilizing PRP with fat over a saline control fat group in facial and hand fat restoration. The results emphasize the possibility that each site for fat grafting may have different requirements of PRP concentrations, total cells numbers, and optimal ratios to maximize adipocyte proliferation, maturation, and neovascularization. One of the limitations of this study is the small number of patients from whom I obtained data, which lessened the intent and hypothesis. The number of patients was limited to 10 in this preliminary trial because of practical factors. Based on these promising preliminary findings, a multi-center study is being discussed to extend this preliminary study to confirm whether the current use of PRP elicits an effective clinical role in fat grafting.

**CONCLUSIONS**

Autologous fat grafts remained at the sites of implantation but diminished in volume after a year as determined by 3D Vectra Analyses and subjective assessments by independent evaluators. The addition of PRP at concentrated levels between 4 and 6 × beyond baseline serum platelet values to near-identical fat volumes to one side of the face and hand sites resulted in higher but statistically nonsignificant changes over equal volumes of fat and normal saline to the opposite midfaces and hands at 3, 6, and 12 months. Evaluator assessments were able to distinguish almost identical benefits on a visual analogue scale in specific areas of the face and hand after either fat:PRP or saline:fat treatments. Fat grafting with PRP was safe and associated with minimal side effects at 1 year.

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