

# ORIGINAL ARTICLE

Cosmetic

# Evaluation of Platelet-rich Plasma and Microneedling for Facial Skin Rejuvenation

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**Background:** The regenerative properties of platelet growth factors make plateletrich-plasma (PRP) an attractive modality for treatment of aging skin. The main objective of this study was to determine efficacy and safety of PRP injections and microneedling compared with saline injections in women with aging skin of the face.

**Methods:** In this prospective, randomized clinical trial, 18 women with facial aging were randomized to receive either PRP injections to the unilateral face and saline injections to the contralateral side, or vice versa. Microneedling was performed after injections on the entire face. Physician assessment, photographs, and treatment satisfaction questionnaires were used for outcome assessment at baseline and 16- and 24-week follow-ups.

**Results:** There was no evidence of improvement and suggestion of worsening in skin laxity and rhytides from baseline to weeks 4, 16, and 24 for PRP and saline (all  $P \le 0.004$ ) and no notable difference in skin roughness between baseline and follow-up time points for PRP or saline (all  $P \ge 0.19$ ). The degree of change in skin laxity, rhytides, and skin roughness from baseline to follow-up time points was similar for PRP and saline. All patients experienced some degree of pain/discomfort and burning/stinging sensation at treatment weeks 4, 8, and 12 for both saline and PRP.

**Conclusions:** PRP injections did not seem to be effective for treatment of aging skin of the face in women, with no notable macroscopic improvement in appearance when compared with baseline or saline injections. Advanced age of study participants (>45 years) and less-sensitive methods of evaluation may be potential contributing factors to the lack of detected response. (*Plast Reconstr Surg Glob Open 2024; 12:e5829; doi: 10.1097/GOX.00000000005829; Published online 20 May 2024.*)

# **INTRODUCTION**

Skin aging is characterized by various clinical and histological changes. The most common signs of aging include but are not limited to, fine lines, wrinkles, altered skin texture, and loss of subcutaneous fat around the mouth and temples. Histological changes include flattening of the dermal-epidermal junction, decreased epithelial cell turnover, progressive disappearance of

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Copyright © 2024 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The American Society of Plastic Surgeons. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal. DOI: 10.1097/GOX.00000000005829 elastic tissue, decrease in collagen fibers, and loss of fibroblasts.<sup>1,2</sup> In recent years, there has been an increased interest in treatments focused on improvement of skin appearance. In the cosmetic field, most rejuvenating procedures are easily accessible and quick, with minimal side effects and downtime.<sup>3</sup> Current therapies available for aesthetic facial rejuvenation approved by the Food and Drug Administration include topical antiaging products such as tretinoin, microdermabrasion, chemical peels, laser therapy, intense pulsed light, botulinum toxin, and filler injections.<sup>4</sup>

Microneedling is a minimally invasive skinrejuvenating procedure in which fine needles create micropunctures in the skin and promote tissue regeneration. These microscopic injuries induce release of growth factors and cytokines, and may result in increased collagen and elastin deposition, and dermal remodeling.<sup>5–7</sup> The goal of microneedling is to improve overall skin texture and appearance. It can be used to treat acne

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scarring, fine lines, wrinkles, skin texture, pore size, and pigmentary disorders.

Platelet-rich-plasma (PRP) is an autologous concentration of human platelets in a small volume of plasma that has a four to seven times higher platelet concentration than baseline.<sup>8,9</sup> Activated platelets secrete several cytokines and growth factors, which are believed to promote upregulation of genes responsible for tissue repair, cellular proliferation, angiogenesis, and extracellular matrix synthesis. This may represent an attractive option to promote collagen regeneration in the aging skin, potentially leading to overall improvement of skin appearance.<sup>6</sup>

Recent investigators have explored the use of PRP as a treatment modality in the aesthetic and rejuvenation field, with available studies to date showing positive results.<sup>7,10-12</sup> In a randomized clinical trial, Alam et al studied the effects of PRP on facial skin and found significant improvement in skin texture.<sup>10</sup> We further explore this premise in our study. A recent review on the available literature regarding PRP treatment for cosmetic indications identified 22 articles describing the use of PRP, 14 of which were used on the face. Even though all studies reported beneficial effects of PRP on facial skin, indicating a positive response to treatment, only a minority of these were controlled trials. The predominant criticisms of trials to date are the lack of a consensus protocol regarding the exact concentration, dosing parameters, depth of injections, and required frequency of sessions.<sup>7</sup> Furthermore, the scarcity of studies using split-face comparisons as controls was also emphasized. The use of splitside studies would allow each subject to serve as their own control, minimizing intersubject variability and enabling a better assessment of the efficacy of PRP treatments. Nonetheless, PRP seems to be a useful tool for treatment of skin aging, and there is a need for randomized controlled studies with reproducible protocols to better study clinical efficacy.

The objective of this randomized, single-blinded study was to assess the effects of PRP and microneedling on aging facial skin.

# **METHODS**

#### **Study Subjects**

Eighteen women seen at the dermatology department at Mayo Clinic in Jacksonville, Florida between July 2019 and December 2020 were included in this prospective, randomized, single-blinded study. Patients' median age was 59 years (range: 47–72 years), all patients were women, and had signs of facial skin aging (wrinkles, skin atrophy, and laxity). Information was collected regarding baseline patient characteristics (demographics, medical history, medications, contraceptive measures, and previous treatments for skin rejuvenation). The most common previous treatments for skin rejuvenation were topical retinoids (77.8%), followed by neuromodulators (50.0%) and injectable fillers (44.4%). Patients were randomized to receive either PRP on the right side of their face and saline on the left side, or saline on the right side and PRP

### **Takeaways**

**Question:** Platelet-rich-plasma (PRP) has been largely used as a treatment modality for facial rejuvenation. The study aimed at assessing the effects of PRP and microneedling on aging facial skin.

**Findings:** This prospective randomized clinical trial showed no evidence of improvement in skin laxity and rhytides after treatment with injectable PRP and no notable difference in skin roughness between PRP and saline.

**Meaning:** PRP injections were not effective for treatment of facial skin aging in women aged 45 years and older, with no notable improvement in skin appearance compared with baseline or to saline injections.

on the left side of their face. Exclusion criteria included the following: abnormal platelet count, serum chemistry, or screening laboratory results; patients who had had any cosmetic procedures for facial skin aging 3 months before enrollment; patients who had had facial resurfacing laser 1 year before enrollment; pregnant or lactating women; patients with infectious diseases, uncontrolled diabetes, history of keloid, active skin disease or skin infection on the intended treatment areas; patients on anticoagulant or antiaggregating therapy; and patients participating in a study of an experimental drug or medical device within 30 days of study entry. During the study, patients were not allowed to make any changes to their routine skin care habits; on the contrary, all facial skin care products were strictly standardized, including facial wash and sunscreen, and no retinoid-containing products were allowed during the entire duration of the study.

#### Methods

PRP was prepared using a standard benchtop centrifuge, as described below. For PRP preparation, 60 mL of blood was collected from a peripheral vein using a standard venipuncture technique and combined with 8 mL of citrate dextrose solution A as an anticoagulant. Blood was processed using standard dual spin centrifugation. Spin protocol included an initial 10-minute centrifugation (1500 rpm) followed by the removal of the red cell layer. An additional centrifugation at 3500 rpm for 10 minutes was performed (G force of 684 and radius of 50) followed by the removal of 5 mL of platelet-poor plasma with an 18-gauge blunt-tipped aspirating needle, resulting in 5 mL of PRP, which was transferred to five 1-mL sterile syringes. One million platelets per microliter was established as the preferred platelet dose in our PRP preparations. Using a 30-gauge needle, PRP or saline was injected into the malar area in 0.05 mL aliquots, for a total of 20 injection points about 0.5 cm apart. The nasolabial/melolabial fold areas and periorbital areas were injected in a similar manner, with approximately 10 injection points in each area, with a total volume of 2.0 mL. Using a 25-gauge 38-mm cannula, PRP or saline was injected into the nasolabial folds, periorbital and tear trough areas (1.0 mL per injection point) with a total volume of approximately 2.0 mL. PRP or saline application was followed by microneedling.

Microneedling was performed using an Food and Drug Administration-approved device (Skin Pen by Bellus Medical) containing 36 needles of 0.3-mm diameter. The patient's face was divided into four quadrants, and microneedling was performed six times in four different directions perpendicular and diagonal to each other in a to-and-fro motion. Immediately afterward, the half of the face that received PRP was draped by a thin gauze-sponge soaked with Platelet-poor plasma from the residual PRP, placed on the face for 15 minutes, as an additional topically applied element of the plasma therapy. The saline half-face was draped using saline-soaked gauze that remained on the face for 15 minutes. Water and glycerinbased rescue gel (SkinFuse by Bellus) was used after the procedure, and patients were instructed to avoid chemical sunscreens on the treated areas.

Clinical skin examination information (skin roughness, skin laxity, and rhytids) was collected at baseline and weeks 4, 16, and 24; treatment satisfaction questionnaire at weeks 16 and 24; clinical assessment of injection sites at weeks 4, 5, 8, and 12; patients' impressions during injections at weeks 4, 8, and 12, and patients' impressions during microneedling at weeks 4, 8, and 12. Outcomes were assessed through a clinical skin examination using two grading scales, the Allergan Skin Roughness Scale, and the Wrinkle Severity Rating Scale at baseline and weeks 4, 16, and 24. Clinical photographs were obtained at the same time points, and a treatment satisfaction questionnaire was used at weeks 16 and 24. All post week-4 missing data were imputed using the last observation carried forward method.

### **Statistical Analysis**

Continuous variables were summarized with the sample median and range. Categorical variables were summarized with number and percentage of patients. Comparisons of outcomes between baseline and follow-up visits within the separate PRP and saline treatment groups were made using a paired Wilcoxon signed rank test. Comparisons of outcomes between PRP and saline treatments were made using a paired Wilcoxon signed rank test (continuous outcomes) or a paired McNemar test (categorical outcomes). *P* values of less than 0.05 were considered as statistically significant, and all statistical tests were two-sided. Statistical analysis was performed using R Statistical Software (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria).

#### **RESULTS**

Baseline patient characteristics are shown in Table 1. Table 2 compares skin roughness, skin laxity, and rhytids between PRP and saline through a clinical skin examination assessment. There was no evidence of improvement and interestingly, with a suggestion of slight worsening in skin laxity from baseline to weeks 4, 16, and 24 for both saline and PRP (all  $P \le 0.004$ ), with no difference noted between saline and PRP (all P = 1.00). Similarly, there was no evidence of improvement and a suggestion of slight worsening in rhytids from baseline to weeks 16 and 24 for

# **Table 1. Patient Characteristics**

	N	Median (Minimum, Maximum) or No. (%) Patients
Variable	N	Patients
Demographic Information		
Age (y)	18	59 (47, 72)
Sex (male)	18	0 (0.0%)
Race (White)	18	17 (94.4%)
Randomized face	18	
PRP on left side, saline on right side		10 (55.6%)
PRP on right side, saline on left side		8 (44.4%)
Medical History		
Hypertension	18	4 (22.2%)
Diabetes	18	0 (0.0%)
Hyperlipidemia	18	5 (27.8%)
Cardiovascular disease	18	1 (5.6%)
Stroke/TIA	18	0 (0.0%)
Breast cancer	18	0 (0.0%)
Liver cancer	18	0 (0.0%)
Kidney cancer	18	0 (0.0%)
Brain cancer	18	0 (0.0%)
Blood cancer	18	0 (0.0%)
Lung cancer	18	0 (0.0%)
Colon cancer	18	0 (0.0%)
Skin cancer	18	1 (5.6%)
Medication use		
Antiaggregant use	18	2 (11.1%)
Antihypertensive use	18	4 (22.2%)
Antidyslipidemic drug use	18	3 (16.7%)
Antidiabetic drug use	18	0 (0.0%)
Hormone replacement drugs	18	4 (22.2%)
Contraceptive Measure		
Oral	18	0 (0.0%)
Injection	18	0 (0.0%)
Implant Implant	18	0 (0.0%)
Transdermal patch	18	0 (0.0%)
Vaginal ring	18	0 (0.0%)
Intrauterine device	18	1 (5.6%)
Tubal ligation	18	4 (22.2%)
Partner's vasectomy	18	2 (11.1%)
Condom	18	0 (0.0%)
Previous Treatment for Skin Rejuvenation		, , , , , , , , , , , , , , , , , , ,
Topical retinoids	18	14 (77.8%)
Chemical peels	18	5 (27.8%)
Injectable fillers	18	8 (44.4%)
Laser	18	4 (22.2%)
Surgical lifting	18	4 (22.2%)
Neuromodulators	18	9 (50.0%)
	10	0 (00.070)

both saline and PRP (all  $P \le 0.040$ ), as noted in Figures 1 and 2, with similar but not quite significant trends at week 4 (P = 0.095 and 0.065, respectively). The degree of worsening in rhytids from baseline did not differ between PRP and saline (all  $P \ge 0.18$ ). There was not a notable difference in skin roughness between baseline and follow-up time points for either PRP or saline (all  $P \ge 0.19$ ), with a similar degree of change between the two treatments (all  $P \ge 0.081$ ).

dutemine         N         No. (%) Patients         Pressus Basetine         N         No. (%) Patients         Pressus Basetine         N         No. (%) Patients           %)         1         0.034         13         0.034         13           %)         0.00%)         11/5         0.034         14           %)         0.00%)         10.01%         9.00%         9.00%           %)         10.68.9%         0.00%         10.00%         9.00%           %)         10.68.9%         0.019         18         0.00%         9.00%           %)         10.68.9%         0.016%         10.00%         0.00%         0.00%           %)         10.68.9%         0.016%         11.61.1%         0.00%         0.00%           %)         10.68.9%         0.00%         0.00%         0.00%         0.00%           %)         10.00%         0.00%         0.00%         0.00%         0.00%           %)         10.00%         0.00%         0.00%         0.00%         0.00%           %)         10.00%         0.00%         0.00%         0.00%         0.00%           %)         10.00%         0.00%         0.00%         0.00%         0	lable z. comparison of clinical skin examination Outcomes between FKP and Saline Baseline Week 4		Baseline		utcomes between Week			Week 16	16		Week 24
upper         uppe         upper         upper <thu< th=""><th>Outcome</th><th>z</th><th>No. (%) Patients</th><th>z</th><th>No. (%) Patients</th><th>Pversus Baseline</th><th>z</th><th>No. (%) Patients</th><th>Pversus Baseline</th><th></th><th></th></thu<>	Outcome	z	No. (%) Patients	z	No. (%) Patients	Pversus Baseline	z	No. (%) Patients	Pversus Baseline		
18         17         10         0.10         1         0.04         18         0.04         18           10         11 <th< th=""><th>Skin roughness</th><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th></th></th<>	Skin roughness										
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	PRP	18		17		0.19	18		0.34	18	0.82
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	None		0 (0.0%)		0 (0.0%)			1 (5.6%)		4 (22.2	%)
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Minimal		1(5.6%)		1 (5.9%)			2(11.1%)		9 (50.0	%)
ctr         2 (1.1%)         5 (2.9.4%)         0 (0.0%)         0 (0.0%)         0 (0.0%)           ltm         l         0 (0.0%)         1 (2.2.%)         0 (0.0%)         0 (0.0%)         0 (0.0%)           ntmal         1 (5.6%)         1 (5.6%)         1 (5.6%)         0 (0.0%)         2 (1.1%)         0 (0.0%)           ntmal         1 (5.6%)         1 (5.6%)         1 (5.9%)         2 (1.1%)         1 (1.1%)         0 (0.0%)           ntmal         1 (5.6%)         1 (5.9%)         2 (1.1%)         1 (1.1%)         0 (0.0%)           ntmal         1 (5.6%)         0 (0.0%)         1 (5.6%)         0 (0.0%)         0 (0.0%)           ntmal         0 (0.0%)         1 (5.6%)         0 (0.0%)         0 (0.0%)         0 (0.0%)           ntmak         0 (0.0%)         1 (5.6%)         0 (0.0%)         0 (0.0%)         0 (0.0%)           ntmak         0 (0.0%)         1 (5.6%)         0 (0.0%)         0 (0.0%)         0 (0.0%)           ntmak         0 (0.0%)         1 (5.6%)         0 (0.0%)         0 (0.0%)         0 (0.0%)           ntmak         0 (0.0%)         1 (5.6%)         0 (0.0%)         0 (0.0%)         0 (0.0%)           ntmak         0 (0.0%)         1 (5.6%	Moderate		15(83.3%)		10(58.9%)			11 (61.1%)		5 (27.8	%)
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Severe		2(11.1%)		5(29.4%)			4(22.2%)		0.0) 0	%)
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met         0.00%	Saline	18		17		0.19	18		0.28	18	0.82
Image         1 (5.6%)         1 (5.9%) <t< td=""><td>None</td><td></td><td>0 (0.0%)</td><td></td><td>0 (0.0%)</td><td></td><td></td><td>0 (0.0%)</td><td></td><td>3 (16.7</td><td>(%)</td></t<>	None		0 (0.0%)		0 (0.0%)			0 (0.0%)		3 (16.7	(%)
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Minimal		1(5.6%)		1(5.9%)			2(11.1%)		11 (61.1	(%)
term         2 (11.%)         5 (93.4%)         2 (11.%)         0 (00%)	Moderate		15 (83.3%)		10(58.9%)			13 (72.2%)		4 (22.2	%)
$ \begin{array}{c ccccc} \mbox{trends} & 0 (0.0\%) & 1 (5.9\%) & 0 (0.0\%) & 0 (0.0\%) \\ \mbox{trends} & N/A & 1.00 & 0.02 & 18 & 0.04 & 18 & 0 (0.0\%) \\ \mbox{trends} & 1 & 0 (0.0\%) & 0 (0.0\%) & 0 (0.0\%) & 0 (0.0\%) & 0 (0.0\%) \\ \mbox{trend} & 9 (50.0\%) & 1 (5.0\%) & 0 (0.0\%) & 0 $	Severe		2 (11.1%)		5 (29.4%)			2 (11.1%)		0.0) 0	%)
true         N/A         100         0.081           alinge from baseline         1         0.002         1         0.003           sty         1         0.005         1         0.005         0.005           sty         0.005         1 (59%)         0.002         0.005         0.005           sty         0.005         1 (59%)         0.005         0.005         0.005           calted         9 (5005)         1 (59%)         0.005         0.005         0.005           calted         9 (5005)         1 (59%)         0.004         1 (75.85)         0.005           state         0 (005)         1 (41.25%)         0.004         1 (75.85)         0.005           state         9 (5005)         1 (51.86)         0.0165         0.005         0.005           state         9 (5005)         1 (41.25%)         0.005         0.005         0.005           state         0 (005)         1 (41.25%)         0 (005)         0.005         0.005           state         0 (005)         1 (55.60)         0 (005)         0 (205)         0 (205)           state         0 (005)         1 (41.25%)         0 (005)         0 (205)         0 (205)	Extreme		0(0.0%)		1(5.9%)			1(5.6%)		0.0) 0	(%)
model         10         0.002         18         0.004         18         0.004         18         0.005         0.004         18         0.005         0.005         0.004         18         0.005	PRP versus saline: Pvalue for change from baseline		N/A		1.00			0.081			1.00
mod         18         7         0.002         18         0.004         18           med         0         0.00%         1         0.00%         0         0.00%         0         0.00%           med         9         0.00%         7         7         41.5%         0 <td>Skin lavity</td> <td></td>	Skin lavity										
me         0 (00%)         0 (00%)         0 (00%)         0 (00%)         0 (00%)           calized         9 (300%)         1 (3.5%)         0 (00%)         0 (00%)         0 (00%)           calized         9 (300%)         7 (4.2%)         1 (61.1%)         13 (72.2%)         0 (00%)           cripted         0 (00%)         7 (4.2%)         0 (00%)         0 (00%)         5 (27.8%)         0 (00%)           refet         0 (00%)         0 (00%)         0 (00%)         0 (00%)         0 (00%)         0 (00%)         0 (00%)           refet         9 (500%)         9 (22.9%)         13 (72.2%)         0 (00%)	PRP	18		17		0.009	18		0 004	18	0.001
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Interf         0 (0.0%)	Deep		0 (0.0%)		7 (41.2%)			0 (33.3%)		5.12) C	%0)
IB         I         0.002         IS         0.004         IS         0.004         IS           calized         9 (50.0\%)         1 (5.9\%)         0 (0.0\%)         0 (0.0\%)         0 (0.0\%)         0 (0.0\%)           calized         9 (50.0\%)         9 (50.0\%)         9 (52.9\%)         1 (5.6\%)         0 (0.0\%)         0 (0.0\%)           oninent         9 (50.0\%)         0 (0.0\%)         0 (0.0\%)         1 (5.5%)         1 (7.2\%)         1 (7.2\%)           weed         0 (0.0\%)         0 (0.0\%)         0 (0.0\%)         0 (0.0\%)         0 (0.0\%)           stas salue:         Value         1.00         1.00         4 (22.2\%)         1 (22.2\%)           hange from baseline         N/A         1.00         1.00         1.00         1.00           constance         0 (0.0\%)         0 (0.0\%)         0 (0.0\%)         0 (0.0\%)           hange from baseline         N/A         1.00         1.00         1 (22.2\%)           constance         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)           intal         1 (22.5%)         1 (22.5%)         1 (22.5%)         1 (22.5%)           intal         0 (0.0%)         0 (0.0%)         0 (0.0%)         0 (0.0%)	Marked	,	0 (0.0%)	ļ	0 (0.0%)	00000	0	0 (0.0%)			
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Is         17         0.065         18         0.040         18           18         17         0.065         18         0.040         18           19         0.005         0.005         18         0.005         0.005           10         0.005         0.006         0.005         0.005         0.005           10         0.005         0.005         0.005         0.005         0.005           10         0.55.6%         6         35.3%         17.6%         0.005%           1         5.6%         8         47.1%         12         66.7%         8         44.4%           1         5.6%         0.005         18         4         12.25%         8         14.4%           1         0.005         1         0.005         18         4         12.56%         6         13.3.3%           18         17         0         0.005         18         0.005         16         16.7%           10         0.006         0         0.005         18         0.005         16.6.7%           10         0.006         0         0.005         16         16.6.7%         16.4.4.5%	PRP versus saline: <i>P</i> value		N/A		1.00			1.00			1.00
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	for change from baseline Rhytids (WSRS)										
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	PRP	18		17		0.065	18		0.040	18	0.015
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Absent	2	0 (0.0%)		0 (0.0%)	0000	2	0 (0.0%)	01 010		
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Minimal		0 (0.0%)		0 (0.0%)			0 (0.0%)		0 (0.09	(2) (2)
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Mild		10(55.6%)		6(35.3%)			2 (11.1%)		4 (22.2	%)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Moderate		7 (38.9%)		8 (47.1%)			12 (66.7%)		8 (44.4	%)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Severe		1(5.6%)		3(17.6%)			4 (22.2%)		6 (33.3	%)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Saline	18		17		0.095	18		0.015	18	0.015
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Absent		0(0.0%)		0(0.0%)			0(0.0%)		0 (0.0)	(%)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Minimal		0(0.0%)		1 (5.9%)			0(0.0%)		1 (5.6)	(%)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Mild		10(55.6%)		5(29.4%)			5(27.8%)		3(16.7)	(%)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Moderate		8 (44.4%)		7 (41.2%)			11(61.1%)		11 (61.1	(%)
N/A 0.18 0.53	Severe		0 (0.0%)		4 (23.5%)			2(11.1%)		3 (16.7	(%)
	PRP versus saline: <i>P</i> value		N/A		0.18			0.53			1.00
	Pvalues result from a paired Wilcoxon signed rank test.	IS UOXO	igned rank test.								

Table 2. Comparison of Clinical Skin Examination Outcomes between PRP and Saline

4

*P*values result from a paired Wilcoxon signed rank test. WSRS, Wrinkle Severity Rating Scale.

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**Fig. 1.** Baseline clinical photograph of face before saline and PRP treatment demonstrating mild to moderate skin roughness, skin laxity, and rhytids.

The treatment satisfaction questionnaire is summarized in Table 3, and clinical assessment of injection sites is displayed in Table 4. Erythema was very common for both PRP and saline at weeks 4, 8, and 12 ( $\geq$ 72.2%), but was not reported in any patients at week 5. Findings were similar, though less common, for edema ( $\geq$ 55.6% for both PRP and saline at weeks 4, 8, and 12). There were no significant differences in clinical assessment of injection sites at any week between the saline and PRP groups (all  $P \geq 0.13$ ).

Table 5 conveys patient impressions during injections. All patients experienced pain/discomfort and burning/ stinging sensation at weeks 4, 8, and 12 for both saline and PRP. Patients' impressions during microneedling are displayed in Table 6; pain/discomfort and burning/stinging sensations were reported in approximately half of the study patients at each time point.

# **DISCUSSION**

Although there are limited literature on split-face studies using PRP, recent studies have demonstrated promising results with use of PRP in tissue regeneration and revitalization.

In the present study, the Allergan Skin Roughness scale and Wrinkle Severity Rating Scale were used to assess skin



**Fig. 2.** Week 24 follow-up photograph after saline and PRP injections to the face, demonstrating no appreciable difference in skin roughness, skin laxity, and rhytids when compared with baseline, with suggestion of slight worsening in skin laxity.

roughness and rhytids. The assessment using these scales was performed by a blinded investigator to minimize bias, and additional clinical photographs taken at each time point were assessed by a third blinded dermatologist. The results of our study demonstrated lack of improvement in signs of skin aging after treatment with PRP. A possible explanation for the lack of noticeable response could be the advanced age of study participants. Younger patients with less-severe wrinkles have demonstrated easierto-appreciate results in previous studies.<sup>13</sup> With increasing age, the decline in number of fibroblasts and loss of regenerative capacity of the skin leaves less surface area for growth factors to act upon. Elnehrawy et al<sup>13</sup> reported that younger participants responded better to PRP injections when compared with their older counterparts. Lower platelet quality and higher grades of wrinkles in older age groups could potentially be another hindering factor. PRP has shown significant efficacy in the treatment of atrophic acne scars, and it has been observed that the improvement in skin rejuvenation is age dependent.<sup>12,14-16</sup> Similarly, the lack of visible improvement suggested by some of our results could possibly be explained by the ongoing intrinsic and extrinsic aging that continued to occur as anticipated, throughout the time of the study.

# **Table 3. Treatment Satisfaction Questionnaire**

	Wk 16		Wk 24	
Variable	N	No. (%) Patients	Ν	No. (%) Patient
Did you notice improvement in the skin of your right	13		13	
face after treatment with PRP?				
Not at all		1 (7.7%)		4 (30.8%)
A little bit		8 (61.5%)		4 (30.8%)
Somewhat		4 (30.8%)		3 (23.1%)
Quite a bit		0 (0.0%)		1 (7.7%)
Very much		0 (0.0%)		1 (7.7%)
Extremely		0 (0.0%)		0 (0.0%)
Did you notice improvement in the skin of your left face after treatment with PRP?	13		13	
Not at all		4 (30.8%)		3 (23.1%)
A little bit		3 (23.1%)		5 (38.5%)
Somewhat		5 (38.5%)		3 (23.1%)
Quite a bit		0 (0.0%)		1 (7.7%)
Very much		1 (7.7%)		1 (7.7%)
Extremely		0 (0.0%)		0 (0.0%)
Do you feel you look younger after facial treatment with PRP?	13	· · · · · ·	13	
Not at all		4 (30.8%)		6 (46.2%)
A little bit		7 (53.8%)		3 (23.1%)
Somewhat		2 (15.4%)		3 (23.1%)
Quite a bit		0 (0.0%)		0 (0.0%)
Very much		0 (0.0%)		1 (7.7%)
Extremely		0 (0.0%)		0 (0.0%)
Do you feel overall satisfied with the PRP treatment on your face?	13	· · · ·	13	
Not at all		2 (15.4%)		3 (23.1%)
A little bit		5 (38.5%)		3 (23.1%)
Somewhat		4 (30.8%)		4 (30.8%)
Quite a bit		1 (7.7%)		1 (7.7%)
Very much		1 (7.7%)		2 (15.4%)
Extremely		0 (0.0%)		0 (0.0%)
When compared with previous treatments for facial skin rejuvenation, would you consider PRP superior overall?	12	· · · · · ·	12	i
Not at all		5 (41.7%)		4 (33.3%)
A little bit		2 (16.7%)		4 (33.3%)
Somewhat		2 (16.7%)		3 (25.0%)
Quite a bit		1 (8.3%)		1 (8.3%)
Very much		2 (16.7%)		0 (0.0%)
Extremely		0 (0.0%)		0 (0.0%)

Alam et al<sup>10</sup> studied the effects of PRP on facial skin by using the needle technique for injection and outcome assessments were done through photoaging and participant self-assessment scores. Different techniques and methods of PRP administration could play a role in the degree of change identified on the skin. The use of needles in PRP administration causes a localized tissue reaction which may result in collagen stimulation and a transient improvement in facial skin appearance. It is possible that the use of a cannula in the present study may have eliminated needle pricking effect on the skin as a potential confounding factor, making it more difficult for subtle changes to be appreciated. Similarly, if more time had been allowed between injections and assessments, eventual changes may have become more apparent. Anecdotally, three study subjects recently seen in our clinic for unrelated reasons, two years after study completion, were able to readily appreciate which side of their face had received PRP injections. The same impression was shared by their treating dermatologist during the visit. Furthermore, the lack of sufficiently sensitive evaluation methods may be another possible explanation for the absence of detected response. For example, had skin biopsies been used to assess treatment outcomes, some microscopic degree of improvement could potentially have been identified. Unfortunately, utilization of skin biopsies as an assessment tool, although scientifically optimal, would be less than ideal in this context. Regarding tolerability of injections, the sensation

Regarding tolerability of injections, the sensation of pain and discomfort experienced by some subjects, although transient, was intense enough for them to state they would avoid repeat treatment sessions in the future. However, if significantly positive skin changes had been

		No. (\$	%) Patients	
	Ν	Face Side Treated with PRP	Face Side Treated with Saline	P
Week 4	18			
Erythema		18 (100.0%)	16 (88.9%)	0.48
Edema		17 (94.4%)	16 (88.9%)	0.48
Hematoma		2 (11.1%)	0 (0.0%)	0.48
Signs of active infection	·	0 (0.0%)	0 (0.0%)	1.00
Other		0 (0.0%)	0 (0.0%)	1.00
Week 5	18			
Erythema		0 (0.0%)	0 (0.0%)	1.00
Edema		1 (5.6%)	0 (0.0%)	1.00
Hematoma		5 (27.8%)	3 (16.7%)	0.13
Signs of active infection		0 (0.0%)	0 (0.0%)	1.00
Other		0 (0.0%)	0 (0.0%)	1.00
Week 8	18			
Erythema	·	14 (77.8%)	14 (77.8%)	1.00
Edema		14 (77.8%)	10 (55.6%)	0.13
Hematoma		2 (11.1%)	1 (5.6%)	1.00
Signs of active infection		0 (0.0%)	0 (0.0%)	1.00
Other		0 (0.0%)	0 (0.0%)	1.00
Week 12	18			
Erythema		13 (72.2%)	13 (72.2%)	1.00
Edema		13 (72.2%)	10 (55.6%)	0.25
Hematoma		3 (16.7%)	1 (5.6%)	0.48
Signs of active infection		0 (0.0%)	0 (0.0%)	1.00
Other		0 (0.0%)	0 (0.0%)	1.00

Pvalues result from a paired McNemar test.

# **Table 5. Patient Impression during Injections**

		No. (%	) Patients	
Patient's Impression during Injections	Ν	Face Side Treated with PRP	Face Side Treated with Saline	P
Week 4	18			
Pain/discomfort		18 (100.0%)	18 (100.0%)	1.00
Burning/stinging sensation		18 (100.0%)	18 (100.0%)	1.00
Other		0 (0.0%)	0 (0.0%)	1.00
Week 8	18			
Pain/discomfort		18 (100.0%)	18 (100.0%)	1.00
Burning/stinging sensation		18 (100.0%)	18 (100.0%)	1.00
Other		0 (0.0%)	0 (0.0%)	1.00
Week 12	18			
Pain/discomfort		18 (100.0%)	18 (100.0%)	1.00
Burning/stinging sensation		18 (100.0%)	18 (100.0%)	1.00
Other		0 (0.0%)	0 (0.0%)	1.00

Pvalues result from a paired McNemar test.

noted, some patients may have considered repeat injections, despite the discomfort.

The main limitation of this study is the small sample size, which although appropriate for a pilot study such as this one, results in a lack of power to detect differences. The reduced sample size (18 women) was a significant limitation of the present study. Therefore, the possibility of a type II error (ie, a false-negative finding) is important to be considered, and we cannot conclude that a true difference does not exist simply due to the occurrence of a nonsignificant P value in our small pilot study. It is recommended that more split-face studies be carried out with longer follow-up times in different age groups to better

understand the effects of PRP on facial skin rejuvenation. Another limitation would be generalizability because this study did not include male or non-White patients.

# **CONCLUSIONS**

In our pilot split-face randomized clinical trial, the use of PRP injections was not found to demonstrate an improvement in signs of facial skin aging in women during a 24-week follow-up period. Factors influencing these results could have been advanced age of study participants with fairly significant baseline facial aging, low sensitivity of assessment tools used, reduced age-related platelet

Patient's Impression during Microneedling	Ν	No. (%) Patients
Week 4	18	
Pain/discomfort		10 (55.6%)
Burning/stinging sensation		10 (55.6%)
Other		0 (0.0%)
Week 8	18	
Pain/discomfort		9 (50.0%)
Burning/stinging sensation		8 (44.4%)
Other		0 (0.0%0
Week 12	18	
Pain/discomfort		11 (61.1%)
Burning/stinging sensation		11 (61.1%)
Other		0 (0.0%)

**Table 6. Patient's Impression during Microneedling** 

quality, and short follow-up time periods. These results are preliminary and difficult to extrapolate with the small sample size, but provide a basis for further trials. Prospective studies with greater follow-up time periods to observe and verify any long-term effects of PRP should be considered. Future studies should also focus on comparisons between patients of different age groups, to assess for age-related differences in response to PRP treatment.

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#### DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article. None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this article.

### PATIENT CONSENT

The patient provided written consent for the use of her image.

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