Lasers, Microneedling, and Platelet-Rich Plasma for Skin Rejuvenation and Repair

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KEYWORDS

• Platelet-rich plasma • Microneedling • Facial rejuvenation • Laser therapy • Facial scar

KEY POINTS

- Skin resurfacing for rejuvenation and repair continues to evolve with the development of noninvasive or minimally invasive, surgical substitutes and adjuvants within facial plastic surgery.
- Restoring tone and reversing the effects of environmental and genetic aging through nonsurgical modalities have attracted a great deal of attention for their reduced downtime, risk of complication, and sufficient treatment outcomes.
- Advances in optical and laser therapy, microneedling, and platelet-rich plasma have reinvigorated research in wound repair and regenerative science.

INTRODUCTION

Skin resurfacing for the purpose of rejuvenation and repair continues to evolve with the development of noninvasive or minimally invasive surgical substitutes and adjuvants within facial plastic surgery. Restoring tone and reversing the effects of environmental and genetic aging through nonsurgical modalities have attracted a great deal of attention for their reduced downtime, risk of complication, and sufficient treatment outcomes. Advances in optical and laser therapy, microneedling, and platelet-rich plasma (PRP) have reinvigorated research in wound repair and regenerative science. This article summarizes each of these modalities alone and reviews the potential additive benefits of combining these treatments to optimize facial rejuvenation.

LASER THERAPY IN FACIAL REJUVENATION

Laser resurfacing has long been an effective treatment in improving skin tone and texture, reestablishing a more youthful skin appearance. Founded on the basis of selective photothermolysis, ablative carbon dioxide (CO_2) laser treatment allows for destruction of specific layers of the epidermis and dermis with a controlled depth of thermal injury (chromophore, 10,600 nm).[1] Thermal vaporization within the dermis induces remodeling with new collagen synthesis, contraction, and subsequent tone, with good to excellent reported results in the treatment of photoaging and scar.[2–6]

Although effective in skin repair, prolonged adverse events using pure CO_2 laser therapy are common, occurring in 10% to 15% of patients and lasting up to 4.5 months.[7] These posttreatment adverse events include: edema, erythema, crusting, herpes simplex virus infection, and dermatitis.[8] Additionally, patients may experience long lasting pigmentary changes and scarring. Less ablative, more superficial lasers (Er:YAG; 2940 nm) have been used, although they are less effective because of reduced dermal collagen

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remodeling.[9] Ongoing efforts in balancing adverse symptoms with treatment efficacy have resulted in the development of a concept termed fractional photothermolysis (FP).

Fractional Photothermolysis

Fractional ablative technologies create microscopic thermal wounds, conservatively sparing tissue surrounding each wound.[10] Because of small regions of tissue injury surrounded by normal skin, a macroscopic treatment effect is tailored by the arrangement and shape of the microscopic treatment zones (MTZ). Additionally, recent interest in FP technology has resulted in investigations for its possible use as a topical drug delivery system.[11]

The dermal stimulation achieved by using ablative FP has allowed for the successful treatment of scars, rhytides, and photodamaged skin.[12,13] The greatest advantage of avoiding confluent epidermal damage, in contrast to pure ablative laser resurfacing, is the reported lower incidence of scarring and pigment changes, with reported hyperpigmentation rates of 30% in pure laser therapy.[12,14,15] Despite the reduction in adverse symptoms, post-treatment events still arise and include: acneiform eruptions, temporary hyperpigmentation, and persistent erythema, with an incidence of 13% to 17% in recent studies with long-term follow-up.[16–18] Investigations to further improve outcomes following fractional laser therapy have used PRP as a pretreatment and post-treatment adjuvant and are summarized in **Table 1**.

MICRONEEDLING IN FACIAL REJUVENATION

Unlike energy-based laser therapy, microneedling, also known as percutaneous collagen induction, relies on focused areas of mechanical injury to disrupt the dermal skin layer. The ensuing inflammatory and wound healing cascade is then triggered with the release of growth factors and subsequent collagen deposition.[28,29] Patient-derived histologic results have corroborated translational research with the up-regulation of transforming growth factor (TGF)-β1-3 and increased collagen and elastin deposition at 1-year follow up.[30–32] These encouraging results are clinically demonstrated in the treatment of acne scar, photodamage, skin rejuvenation, and androgenetic alopecia.[33–35] The use of combination topical products with needling seems to be a natural progression of this treatment modality. Given the endogenous growth factors found within platelet granules, we have reviewed the literature for possible improvements in outcome and reductions in adverse treatment symptoms (**Table 2**).

PLATELET-RICH PLASMA IN FACIAL REJUVENATION

PRP has recently garnered growing interest as an effective modality for acute and chronic wound repair in several surgical and medical fields.[41–44] Harboring growth factors and cytokines, PRP has been viewed as an elixir of youth. The ease with which it is harvested, grafted, and activated has resulted in wide ranging publications as an adjuvant to conventional treatment modalities. Through topical application or injection, PRP is aimed to replenish the depleted local levels of growth factors and propagate healing through a myriad of chemotactic pathways.[45–47] With similar parallels between wound healing and regeneration of aging skin, the potential to enhance recovery and improve results following skin resurfacing is promising.

Platelet-Rich Plasma: Role in Cutaneous Regeneration

Over the past two decades, a boon in literature attempting to maximize the intrinsic potential of platelet-derived growth factors has resulted in a better understanding of the biologic and molecular pathways for skin repair. Following activation, platelets release alpha-granules containing growth factors and cytokines including platelet-derived growth factor, TGFs, vascular endothelial growth factor, insulin-like growth factor, epidermal growth factor, and interleukin-1.[48,49] These signaling proteins are integral to the remodeling that occurs within the extracellular matrix during aging and repair. Several of the investigations used within this article, and original investigations using PRP alone, confirm the potential of PRP to induce and promote collagen synthesis, regulated by fibroblasts.[50,51] These include the ability to reverse the effects of collagenases, increase collagen levels, and decrease tissue inflammation.[52]

Skin Repair and Scar

Wound healing is initiated by the recruitment of circulating inflammatory cells to the wound site, initiating re-epithelialization, tissue contraction, and an angiogenic response. These processes are coordinated by locally released and locally acting growth factors that control cell growth and proliferation, namely: platelet-derived growth factor, vascular endothelial growth factor, TGF-β, and tissue inhibitor of metalloproteinases.[47] The remodeling that occurs following wound repair stimulates new collagen, elastin, and glycosaminoglycans.[53] These matrix components are diminished in aging skin and abnormally organized in scar formation.[54,55]

Table 1
Platelet-rich plasma adjuvant to laser therapy

Author, Year	Number of Patients Enrolled (M/F)	Condition Treated	Adjuvant Effect of PRP Investigated	Site Treated	Type of Resurfacing	PRP Delivery	Activated In Vitro (Y/N)	Timing of PRP	Treatment Interval and Duration	Control Group	Follow-up After Final Treatment	Objective Outcomes	Subjective Outcomes	Patient Survey	Histology
Na et al,[19] 2011	25	NA	Postlaser symptoms	Inner arm	FCL	Topical	Yes $CaCl_2$	Immediately following laser treatment	Laser: once	Saline topical	4 wk	SS reductions in waterloss, E-index, and M-index with PRP therapy compared with control group	Reduced erythema and pigmentation in PRP group	ND	H&E: thicker epidermis, more organized stratum corneum, higher density of collagen in PRP group
Lee et al,[20] 2011	10/4	Atrophic acne scar	Scar repair	Face	FCL	Intradermal	ND	Immediately following laser treatment	Laser: 1 tx/1 mo Duration: 2 tx	Split-face Saline injection	4 mo	SS reduction in E-index on Day 4	SS reduction in duration of tx symptoms: erythema, edema SS greater improvement in repair of scar	ND	ND
Shin et al,[21] 2012	0/22	Aging skin	Rejuvenation	Face	Fractional erbium laser	Topical	Yes $CaCl_2$	Immediately following laser treatment	Laser: 1 tx/4 wk Duration: 3 tx	Laser alone	1 mo	Roughness: SS decrease compared with baseline, not with control Elasticity: SS increase in control compared with PRP group Hydration: no SSD between groups E-index: SS reduction in PRP group compared with control M-index: no SSD between groups	Improved overall appearance in PRP group compared with control but no SSD	Improvements with PRP compared with control: skin texture (100% vs 58%), elasticity (92% vs 67%) No SSD compared with control in pain, or erythema scales	SS improvement compared with control in the number of fibroblasts, dermal-epidermal junction length, and average area fraction of collagen

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Table 1
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Author, Year	Number of Patients Enrolled (M/F)	Condition Treated	Adjuvant Effect of PRP Investigated	Site Treated	Type of Resurfacing	PRP Delivery	Activated In Vitro (Y/N)	Timing of PRP	Treatment Interval and Duration	Control Group	Follow-up After Final Treatment	Objective Outcomes	Subjective Outcomes	Patient Survey	Histology
Gawdat et al,[22] 2013	12/18	Atrophic acne scar	Scar repair	Face	FCL	Intradermal and topical	Yes $CaCl_2$	Immediately following laser treatment	Laser: 1 tx/1 mo Duration: 3 tx	Split-face Saline injection	3 mo	Optical coherence tomography: SS greater improvement in scar depth with PRP than control	SS improvement with PRP compared with control in skin smoothness	SS reduction in side effects and down-time with PRP. PRP improved scar in >60% of patients, compared with 26.7% of control patients	ND
Kim and Gallo,[23] 2015	15	NA	Postlaser symptoms	Forearm	FCL	Subcutaneous	ND	Immediately following laser treatment	Laser: 1tx	Saline injection	18 d	ND	SS reduction in erythema and edema compared with control	PRP improved posttreatment erythema (71%), edema (67%), pain (67%), and pruritus (89%)	ND
Faghihi et al,[24] 2016	4/12	Atrophic acne scar	Scar repair	Face	FCL	Intradermal	Yes $CaCl_2$	Immediately following laser treatment	Laser: 1 tx/1 mo Duration: 2 tx	Split-face Saline injection	4 mo	ND	PRP improved outcomes at 1 mo (68.8% vs 50%) and 5 mo (87.5% vs 68.8%) compared with control	PRP treatment improved outcomes at 1 mo (50% vs 31.2%) and 5 mo (56.2% vs 43.8%) compared with control	ND
Abdel Aal et al,[25] 2017	18/12	Atrophic acne scar	Scar repair	Face	FCL	Intradermal	Yes $CaCl_2$	Immediately following laser treatment	Laser: 1 tx/3–4 wk Duration: 2 tx	Split-face Laser alone	6 mo	ND	Blinded clinician scoring: SS improvement of scar, duration of laser symptoms, incidence of PIH, in PRP group compared with control	SS greater patient satisfaction with the PRP compared with control side	ND

Hui et al,[26] 2017	0/13	Aging skin	Rejuvenation	Face	FCL	Intradermal and topical	Yes CaGluc	Prelaser injection Postlaser topical	Laser: 1 tx/3 mo Duration: 3 tx	Split-face Saline injection and topical	3 mo	VISIA Complexion Analysis System: SS improvement in wrinkles, textures, and elasticity	Improvements in experimental group but not SSD compared with control	SS improvement in facial wrinkles, skin texture, and skin elasticity	ND
Min et al,[27] 2017	25	Atrophic acne scar	Scar repair	Face	FCL	Intradermal	Yes $CaCl_2$	Immediately following laser treatment	Laser: 1 tx/4 wk Duration: 2 tx	Split-face Saline injection	3 mo	SS reduction in E-index with PRP	SS improvement in IGA and ECCA scaring scores with combination therapy compared with control for all scar subtypes	SS higher patient satisfaction scores for PRP combination therapy at 7 and 84 d following treatment	SS increase in fibrogenetic molecules (c-myc, TIMP, HGF, p-AKT, collagen 1 and 3) with PRP; time and dose dependent

Manuscripts reviewed are listed. Study designs and results are summarized.

Abbreviations: CaGluc, calcium gluconate; ECCA, Echelle d'Evaluation clinique des Cicatrices d'acné; E-index, erythema index; FCL, fractional CO_2 laser; H&E, hematoxylin and eosin; IGA, Invesetigator's Global Assessment Scale; M-index, melanin index; NA, not applicable; ND, not disclosed; PIH, postinflammatory hyperpigmentation; SS, statistically significant; SSD, statistically significant difference; tx, treatment.

Table 2
Platelet-rich plasma adjuvant to microneedling therapy

Author, Year	Number of Patients Enrolled (M/F)	Condition Treated	Adjuvant Effect of PRP Investigated	Site Treated	Type of Resurfacing	PRP Delivery	Activated In Vitro (Y/N)	Timing of PRP	Treatment Interval and Duration	Control Group	Follow-up After Final Treatment	Objective Outcomes	Subjective Outcomes	Patient Survey	Histology
Chawla,[36] 2014	19/8	Atrophic acne scar	Scar repair	Face	MN	ND	Yes CaGluc	ND	MN: 1 tx/4 wk Duration: 4 tx	Split-face Topical vitamin C	4 wk	ND	Improved reduction in scar with PRP compared with vitamin C following microneedling	SS greater patient satisfaction in outcome with use of PRP than vitamin C	ND
Asif et al,[37] 2016	25/25	Atrophic acne scar	Scar repair	Face	MN	Intradermal PRP Topical fibrin gel	Yes $CaCl_2$	Following MN	MN: 1 tx/4 wk Duration: 3tx	Split-face Saline injection	3 mo	ND	SS improvement compared with baseline in both groups; greater frequency of excellent improvement with PRP than control	Greater patient satisfaction and frequency of excellent improvement with PRP than with control	ND
El-Domyati et al,[38] 2017	6/24	Atrophic acne scar	Scar repair	Face	MN	Topical	Yes CaGluc	Following MN	MN: 1 tx/2 wk Duration: 6 tx	Split-face MN alone	3 mo	ND	SS improvement of scar with PRP compared with control	ND	SS increase in epidermal thickness (54.91 ± 1.08 μm vs 50.93 ± 4.692 μm; $P = .032$); subjective increase in collagen density and organization

Ibrahim et al,[39] 2017	35	Atrophic acne scar	Scar repair	Face	MN	Topical	Yes CaGluc	Following MN	MN: 1 tx/3 wk Duration: 4 tx	Split-face MN alone	3 mo and 12 mo	ND	SS reduction in symptom duration compared with control SS improvement compared with baseline, not to control	SS improvement compared with baseline but no SSD compared with control	ND
Ibrahim et al,[40] 2017	44/46	Atrophic scars	Scar repair	Any site	MN	Intradermal	Yes $CaCl_2$	Alternating treatments biweekly	MN: 1 tx/2 wk PRP: 1 tx/2 wk Duration: $\leq$6 tx	MN alone PRP alone	3 mo	ND	SS improvement in scar repair compared with isolated treatments	SS greater patient satisfaction compared with either treatment alone	ND

Manuscripts reviewed are listed. Study designs and results are summarized.

Abbreviations: CaGluc, calcium gluconate; MN, microneedling; ND, not disclosed; SS, statistically significant; SSD, statistically significant difference; tx, treatment.

Aging Skin

Skin aging is a dynamic process attributed to intrinsic (genetically determined, age-associated factors) and extrinsic (environmental factors, ultraviolet radiation, cigarette smoke) processes.[56] A progressive, age-degeneration of connective tissue therefore may be hastened by overlapping molecular mechanisms.[57] Through the breakdown of collagen and elastin fibers, characteristic findings of photoaged and chronoaged skin are apparent and include loss of elasticity, atrophy, xerosis, and rhytides.[52,58] Histologically, these changes are demonstrated by reduced dermal thickness, number of papillae, collagen concentration, and vascularity.[59,60] These changes have been associated with reduced levels of growth factors and effective fibroblast function.[61]

Harvesting Techniques

A review of the methods and techniques of PRP harvest is found throughout this special edition of *Facial Plastics Clinics of North America*. In brief, the production of platelet concentrates for platelet-rich solutions begins with the harvest of peripheral venous blood. The collected specimen are centrifuged in one or two steps depending on the processing system.[62–64] The initial, low force, centrifugation allows the blood components to separate into three weight-dependent layers: (1) a top, supernatant, layer of platelet-poor plasma; (2) a "buffy coat" middle layer rich in platelets and containing white blood cells; and (3) a bottom, red blood cell layer.[65] The second step varies among the numerous protocols; however, in concept it is an attempt to discard the red blood cell and platelet-poor plasma layers. This is mediated by harvesting the platelet-poor plasma and buffy coat layers following the first centrifugation into a separate test tube. Under high centrifugal force, the platelet-rich layer and plasma supernatant are further separated improving the precipitant yield of platelets from plasma. The final liquid platelet suspension coined PRP aims to be enriched four to seven times that of whole blood to be considered therapeutically effective, shown to be approximately 1 to 1.5 million platelets/μL to induce mesenchymal stem cell proliferation.[66,67] Values greater than 1.5 million platelets/μL have been found to decrease angiogenesis.[68]

PLATELET-RICH PLASMA: AN ADJUVANT TO LASER THERAPY

Techniques aimed at reducing post-treatment adverse symptoms and improving outcomes following proven laser therapies have resulted in a natural progression of the use of PRP as an adjuvant to fractional laser therapy. Several recent studies have designed prospective short- and long-term investigations described in **Table 1**. This review summarizes their treatment outcomes.

Platelet-Rich Plasma Improves Postlaser Symptoms

Attempts at mitigating the adverse effects following fractional laser skin treatment have resulted in a myriad of patient-reported and clinician-validated studies. In the peritreatment acute setting, Lee and colleagues[20] found reductions in post-treatment laser symptoms when PRP was injected immediately following laser therapy. Four-days following fractional CO_2 laser (FCL) therapy, statistically significant differences in clinician-rated erythema scores were evident ($P<.01$) and the total duration of symptoms in the combination therapy group were significantly reduced; specifically, erythema (8.6 ± 2.0 days; $P = .047$), edema (6.1 ± 1.1 days; $P = .04$), and crusting (5.9 ± 1.1 days; $P = .04$).

Similar improvements in laser symptoms were achieved when PRP was applied before and following FCL. Where the total duration of erythema (8.31 ± 0.85 vs 9.08 ± 0.64 days; $P = .025$), edema (7.31 ± 0.48 vs 7.92 ± 0.64 days; $P = .013$), and crusting (7.15 ± 0.38 vs 7.85 ± 0.80 days; $P = .032$) were all reduced.[26] Reducing the duration and severity of laser therapy symptoms allows patients to return to their daily routine and reduce their post-procedure downtime as demonstrated by Gawdat and colleagues[22] with the use of PRP following photothermolysis (4.37 ± 1.52 days vs 2.27 ± 0.69 days; $P = .02$).

Although patient-reported outcomes and experience is one of the strongest indicators of treatment success, attempts to correlate objective data with patient experience have also been demonstrated. Following FCL treatment to the inner arm of 25 patients, Na and colleagues[19] noted significant reductions in transepidermal water loss, erythema index, and melanin index when evaluated by spectrophotometer and compared with the placebo-controlled group ($P<.05$). Similar reductions in erythema index and melanin index following topical facial application of PRP have been reported with the use of 1550-nm fractional erbium laser (erythema-index: 8.4 ± 0.9 vs 7.1 ± 0.9; $P = .005$; melanin-index: 32.9 ± 1.5 vs 31.1 ± 1.4; $P>.05$).[21]

The effects of PRP on postlaser hyperpigmentation are difficult to assess given the unpredictable nature of such adverse events. However, Abdel Aal and colleagues[25] reported five occurrences

of postinflammatory hyperpigmentation in their study of patients with Fitzpatrick phototype 3 to 4. All five patients were observed in the control (non-PRP) group. Gawdat and colleagues[69] also demonstrated two events of postinflammatory hyperpigmentation in control, but not in the PRP-treated group.

Platelet-Rich Plasma Enhances Laser Rejuvenation Outcomes

Ablative fractional laser therapy is a current standard in the treatment of facial rhytides and photodamaged skin. The clinical outcomes are founded in the rapid healing and re-epithelialization that occurs between MTZ areas of tissue injury. Improving wound healing following skin damage may therefore result in improved treatment outcomes. This hypothesis has been tested in recent studies. Shin and colleagues[21] studied the effect of topical PRP applied to the facial cheek skin of 22 Korean women (Fitzpatrick scale 4 and 5) followed by fractional erbium laser. Patient-reported improvements in skin texture and elasticity were much higher than the saline-control group. A total of 100% of patients reported improvements in skin texture and 92% reported improvements in elasticity, compared with 58% and 67% in the control group, respectively. Biomechanical outcomes also demonstrated significant improvements of elasticity in the PRP group compared with control (10.3% vs 6.4%); however, they did not identify statistically significant differences in roughness, or hydration. The effect of injected intradermal PRP following FP was then investigated by Hui and colleagues.[26]

In their 2017 split-face, double-blinded, saline-placebo controlled study, Hui and colleagues[26] injected PRP and saline into opposing sides of the periorbital and forehead skin of 17 Fitzpatrick 3 and 4 women. Following FCL treatment, topical PRP and saline was applied to the experimental and control sides, respectively. Over a 3-month three-treatment duration, VISIA Complexion Analysis System (Canfield Imaging Systems, Fairfield, NJ) recorded objective age-related skin changes on each side of the patient's face. Following clinician ranking, the experimental side found significant improvements in skin wrinkles (1.72 ± 0.58 and 1.94 ± 0.55; $P = .145$), texture (0.99 ± 0.33 and 1.21 ± 0.42; $P = .010$), and elasticity (1.41 ± 0.43 and 1.54 ± 0.47; $P = .026$) compared with the contralateral face. Patients, blinded to the experimental side of their face, found significant improvements with PRP injection in facial wrinkles ($P = .039$), skin texture ($P = .039$), and skin elasticity ($P = .040$).

Platelet-Rich Plasma Enhances Laser Atrophic Scar Treatment

Fractional laser therapy has significantly remodeled the depressed and disorganized floor of atrophic scars through elevation of the collagenous dermal matrix.[70,71] Given the natural growth factors found in PRP, combination therapy may aid in improving laser scar treatment. Gawdat and colleagues prospectively investigated the combined efficacy and safety of FCL with PRP in a randomized split-face comparative single-blind clinical trial in the treatment of atrophic acne scars with that of FCL alone. At 6-month follow-up, faces treated with PRP (intradermal or topical) following laser therapy demonstrated significantly greater improvements in scar depth measured by optical coherence tomography (28.9 ± 8.3 μm vs 48.8 ± 16.4 μm; $P = .01$), increased patient satisfaction (60% vs 27%), and reductions in postlaser adverse symptoms and down-time ($P = .02$) compared with the saline-controlled group. Clinician-graded outcomes have also demonstrated subjectively improved outcomes for the use of atrophic acne scar at 4 months.[20]

Platelet-Rich Plasma Imparts Favorable Molecular, Cellular, and Tissue Remodeling

Ablative fractional laser therapy resurfaces skin through tissue contraction in areas of MTZ. Several studies have demonstrated improvements in dermal thickness, neocollagenesis, and collagen contraction following laser therapy. The use of PRP may supplement these favorable histologic outcomes. Following 1550-nm fractional erbium laser treatment, Shin and colleagues[21] applied topical PRP and analyzed biopsy specimens 1 month following treatment. Cheek skin sites demonstrated significantly greater changes in the number of fibroblasts formed (delta +65.4% vs delta −19.4%), dermal-epidermal junction length (delta +67% vs delta +46.9%), and fraction of collagen formed (delta +2.8% vs delta −24.3%) compared with laser alone. Na and colleagues[19] found similarly positive histologic results 4 weeks following combination therapy when pretreated with PRP. Their study demonstrated a thicker epidermis layer, more organized stratum corneum layer, and higher collagen density.

Further investigation of skin with immunohistochemistry has demonstrated significantly increased molecular concentrations of fibrinogenic molecules with the use of PRP following laser therapy.[27] A positive time-dependent (4 week) response of protein cytokines and collagen was noted, specifically of TGF-β, epidermal growth factor receptor, tissue inhibitor of metalloproteinases, and collagen 1 and

3. Additionally, in vitro studies of irradiated fibroblast cells demonstrated more rapid recovery and increased proliferation at 24 hours when cultured in PRP compared with serum alone.[27]

PLATELET-RICH PLASMA AS AN ADJUVANT TO MICRONEEDLING

Considered a noninvasive device, microneedling has a low rate of post-treatment adverse symptoms. When present, these include: erythema, pinpoint bleeding, transient crusting, and localized edema, all of which typically resolve within 72 hours.[33,72] Histologic examination taken 24 hours after therapy demonstrates an intact epidermis and no change in melanocyte number, resulting in limited downtime and minimal risk of dyspigmentation.[28] The most severe post-treatment complication has been associated with the use of topical cosmeceuticals, specifically vitamin C and post-treatment granuloma formation.[73] Given the autogenous harvest of PRP the likelihood of such hypersensitive reactions is further diminished.

Platelet-Rich Plasma Improves Postmicroneedling Symptoms

Ibrahim and colleagues[39] prospectively studied the effects of topical PRP following microneedling in a split-face study of 35 individuals with mild to moderate acne scores 2 to 4 (Goodman-Baron scoring).[74,75] Their study demonstrated significantly reduced durations of erythema and edema on the side treated with skin needling followed by topical PRP (4.3 vs 6.2 days and 1.05 vs 3.3 days; $P<.001$). Similar subjective results were found by El-Domyati and colleagues[38] with early resolution in erythema, edema, and crusting in combination therapy. However, in a 90-patient prospective study, Ibrahim and colleagues[40] demonstrated greater severity of erythema in patients receiving intradermal PRP following microneedling than control groups, which consisted of PRP alone and needling alone ($P<.001$); however, duration and timing of symptom evaluation were not documented.

Platelet-Rich Plasma Improves Microneedling Outcomes in Atrophic Scar

Microneedling has most extensively been studied for acne scar treatment, with a recent systematic review demonstrating moderate efficacy among 10 heterogeneously designed investigations.[33] The ability to remodel atrophic scars is founded in the ability to induce neocollagenesis within the papillary dermis and epithelium.[72] However, scar type seems to be a factor because deep-seated atrophic ice pick scars are found to be less responsive than boxcar or rolling scars with microneedling.[33,40,76] Given the ease with which topical therapies may be transcutaneously delivered, and the low risk of hypersensitivity in autologous PRP, several studies have investigated the augmented effect of needling with platelet-rich concentrates.

In the earliest investigation, Chawla[36] designed a split-face prospective 4-week trial of microneedling and PRP in 27 patients with mild to severe atrophic acne scar. The study found PRP treatment to increase the number of "excellent" responders (18.5% vs 7%), whereas those treated with vitamin C incurred a greater frequency of "poor" improvement results (37% vs 22.2%). El-Domyati and colleagues followed microneedling with topical PRP in a 30-patient split-face trial for atrophic acne scars. When compared with Derma Roller alone, the PRP group demonstrated significantly improved clinician-rated outcomes at 3-month follow-up (64.87 ± 28.67 vs 29.12 ± 22.52; $P = .015$) compared with control outcomes; no difference was found between the PRP and the TCA experimental group. When comparing all forms of atrophic scars (acne and traumatic) Ibrahim and colleagues[40] found a significantly greater improvement with PRP and Dermapen treatment compared with PRP or Dermapen alone (chi-square test, 20.58; $P<.001$). On subgroup analysis, boxcar and ice pick acne scars demonstrated greater response than rolling acne scars ($P<.028$); however, nonacne scars had a greater response to treatment than acne scars ($P<.023$). Furthermore, a significant negative correlation between age of patient and duration of scar with response to treatment was also identified, indicating that younger patients with new scars showed higher response to treatment than patient with old scars. Patient satisfaction has also been reviewed noting consistently greater improvements with PRP therapy than without.[36,37,40]

Platelet-Rich Plasma Influences Postmicroneedling Histology

Microneedling alone has demonstrated increased epidermal thickness and stimulation of neocollagenesis with improvements in collagen organization and bundle patterns.[30–32] The investigations detailed in this article have all demonstrated improvements in skin thickness and collagen bundling when histology is available for combination and control groups. El-Domyati and coworkers[38] assessed histologic features 3 months following 6 treatments with microneedling and PRP (applied topically immediately following microneedling). All specimens demonstrated

improvements compared with baseline; however, combination PRP therapy significantly increased epidermal thickness greater than needling alone (54.91 ± 1.08 μm vs 50.93 ± 4.692 μm; $P = .032$). Combination therapy also demonstrated an increase in deposition of more organized and parallel collagen bundles compared with control. The thicker epidermal layer has also demonstrated a greater numbers of rete ridges, and a greater concentration of elastic fibers, compared with baseline and needling alone.[40]

DISCUSSION

The potential of using an autogenous source of easily attainable growth factors to stimulate cellular regeneration, restore youth, and remodel scar has contributed to a growing number of clinical investigations. As an adjunct to laser and needling therapies, the topical and intradermal application of PRP to skin traumatized by mechanical and thermal microchannels seems to be feasible with no added side effects. Overall, PRP may be an effective means of enhancing wound healing, reducing transient unwanted effects, improving skin tightening, and delivering greater patient satisfaction to traditional modalities alone. All histologic studies reviewed demonstrate a greater concentration of organized collagen bundles with a thicker epidermal layer when compared with control groups. However, there exists only a small number of controlled clinical trials that provide evidence of its use in combination with long-standing methods of rejuvenation. Furthermore, wound healing is a dynamic process that occurs over long periods of time. Caution should be exercised when evaluating the results of each of these studies because the study design, treatment schedule, and patient population are heterogenous.

Research of novel modalities to improve outcomes over established technologies requires the standardization of current research endeavors. In facial plastic surgery, this may be difficult because there is no single set of treatment parameters that can be used in most patients to achieve a predicted outcome; skin varies among anatomic locations and patient background. Regarding PRP, known variations exist in platelet yield, kit manufacturer, and efficiencies between centrifuge system.[77–81] Documentation of these known confounders was found to be a critical limitation of current PRP research by Frautschi and colleagues,[82] noting inaccurate description of PRP composition, dosing, activation, and the use of subjective outcome measures. Additionally, the broad variation in cause, duration, and severity of scar and aged skin, Fitzpatrick phototype, duration of treatment used, and scheduling of treatment interval between each study cohort limits the ability to summarize the overall positive results from each of these studies independently.

Standardization of treatment-dosing protocols, site/area of injection, and injection technique are areas of future investigation. Additional randomized clinical trials with reproducible methods and those contrasting the effects of post-treatment cosmeceuticals will aid in powering larger cohort analyses with reduced study heterogeneity. Further evidence for the establishment of PRP as a supplement to traditional methods of skin rejuvenation and repair is needed to elucidate the therapeutic mechanism and optimal dosing by which PRP rejuvenates skin. Despite additional needed research, PRP has shown significant potential as a stand-alone or combined therapy along with laser or microneedling techniques to optimize facial rejuvenation.

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