Journal of Clinical and Cosmetic Dermatology
ISSN 2576-2826 | Open Access

RESEARCH ARTICLE

Volume 8 - Issue 1

# Effect of Topical Platelet Extract for Post-Procedural Skin Recovery with Fractional Carbon Dioxide Skin Laser Resurfacing

## *Platelet Regenerative Technology and Fractional $CO_2$ Laser*

**Michael Somenek[1,*], Chelsea Handfield[2], Atta Behfar[3], and Saranya Wyles[4]**

[1]Facial Plastic and Reconstructive Private Practice, Washington DC, USA
[2]Mayo Clinic Department of Dermatology, Rochester, MN, USA
[3]Mayo Clinic Department of Cardiovascular Diseases, Van Cleve Cardiac Regenerative Medicine Program, Rochester, MN, USA
[4]Mayo Clinic Department of Dermatology, Rochester, MN, USA

***Corresponding authors:** Michael Somenek, Facial Plastic and Reconstructive Private Practice, Washington DC, USA E-mail: msomenek@gmail.com

**Received:** 07 Feb, 2024 | **Accepted:** 23 Feb, 2024 | **Published:** 29 Feb, 2024

**Citation:** Somenek M, Handfield C, Behfar A, Wyles S (2024) Effect of Topical Platelet Extract for Post-Procedural Skin Recovery with Fractional Carbon Dioxide Skin Laser Resurfacing. J Clin Cosmet Dermatol 8(1): dx.doi.org/10.16966/2576-2826.182



## Abstract

**Background:** Fractional Carbon Dioxide ($CO_2$) laser resurfacing is an effective treatment option for skin rejuvenation, yet the healing process of post-laser skin can contribute to significant downtime. Topical Human Platelet Extract (HPE), containing Renewosome™ regenerative technology, can accelerate skin restoration after laser resurfacing.

**Aims:** To determine the adjuvant effect of regenerative topical HPE application on skin recovery post-fractional Carbon Dioxide ($CO_2$) laser resurfacing.

**Methods:** This prospective, randomized, double-blinded study investigated the effect of topical HPE following fractional $CO_2$ laser resurfacing on the bilateral forearms. Blinded investigator assessment included post-treatment redness, bruising, and hypo/hyperpigmentation on standard photography on days 4, 7, 14, and 30 post-laser resurfacing. Patient reported outcomes for potential laser-induced adverse effects including pain, redness, irritation due to itching, and dryness were recorded daily for 10 days following laser procedure.

**Results:** Adjuvant application of topical HPE following fractional $CO_2$ laser resurfacing resulted in significant reduction in post-procedural redness ($p$=0.02) and an accelerated time to improvement ($p$=0.0237). Additionally, participants reported significant reduction in post-procedural sensation of irritation due to itching ($p$<0.001) and dry skin ($p$<0.001).

**Conclusion:** Topically applied platelet-derived regenerative nanotechnology, HPE, following fractional $CO_2$ laser resurfacing for skin rejuvenation accelerated skin restitution and overall skin health.

## Introduction

Photoaging, resulting from chronic skin exposure to Ultraviolet (UV) radiation [1], is characterized by epidermal and dermal alteration, leading to wrinkles, mottled pigmentation, telangiectasia, and extracellular matrix degradation including collagen, elastin, and proteoglycans [2]. Since the late 1980s, carbon dioxide ($CO_2$) laser resurfacing has been considered a suitable cosmetic treatment approach for skin rejuvenation, although associated with longer healing times and possible side effects including hypo/hyperpigmentation [3]. Therefore, its use is often limited to fractional laser instead of full ablative laser resurfacing to reduce complications while maintaining results. Briefly, the technique of fractional $CO_2$ laser consists of tissue water vaporization, generating epidermal ablation and dermal heating (called microscopic treatment zones) while sparing islands of healthy skin to accelerate recovery and to produce new extracellular matrix components [4].

Platelets are a natural reservoir of growth factors that facilitate fibroblast collagen production, keratinocyte proliferation, and hyaluronic acid generation to increase dermal elasticity [5]. Indeed, Platelet-rich Plasma (PRP) has been reported to play a synergistic effect to ultra-pulsed fractional $CO_2$ laser, contributing to epidermal regrowth and dermal remodeling [6].

Herein we investigated the topical application of regenerative platelet technology after fractional $CO_2$ laser treatment for skin rejuvenation. Human Platelet Extract (HPE) is a leukocyte-depleted allogenic product made from U.S-sourced, pooled, apheresed platelets that exhibits consistent batch purity. This over-the-counter topical

HPE product is safe and well-tolerated. Prior studies have reported that topical HPE promotes skin rejuvenation by reducing redness, brown spots, and promoting luminosity and color evenness [7]. We evaluated the effect of topical HPE application after cosmetic $CO_2$ laser resurfacing on the ventral forearm skin.

## Materials and Methods

The study was approved by the Sterling IRB. Ten participants were enrolled in the study conducted at a single center private practice in Washington D.C. All participants were screened to ensure that they met all inclusion criteria and none of the exclusion criteria before enrollment in the study. Participants recruited were not pregnant, fully understood the requirements and needs to comply with the study testing and volunteered willingness to discontinue any other anti-aging topical or parenteral treatments for the duration of the study.

The study aimed to enroll adults 18 years of age and older with Fitzpatrick skin types I to III. Individuals who had active dermatologic disease or cutaneous markings on the experimental area were excluded, as were participants with asymmetric photodamage due to environmental exposures. Additionally, those with diabetes or severe peripheral neuropathy were also excluded.

Participants underwent $CO_2$ laser resurfacing treatment (30-50 millijoules fluence with ablation up to 900 microns in depth and spot diameter 150 microns) to the bilateral ventral forearms. After $CO_2$ laser procedure, participants were instructed to apply 2 fingertip units (FTU, approximately 1 g) of topical HPE (Plated Gold, Rion Aesthetics, Inc., Rochester, MN) to one forearm *vs*. 2 FTU of control (Aquaphor, Beiersdorf, Inc., Stamford, CT) to the contralateral forearm as an internal control twice daily for one month duration. The distribution of the treatment *versus* control to the right or left forearm was randomized. Patients underwent standardized 2D photography on days 4, 7, 14, and 30 post-treatment (visits 2, 3, 4, and 5, respectively). Participants also completed a diary questionnaire, evaluating the perception of pain, redness, irritation related to itching, and dryness daily for the 10 days immediately following $CO_2$ laser procedure.

The primary endpoint was improvement in the appearance of topical HPE treated forearm skin compared to placebo-control as assessed on 2D photography at each post-procedural visit. The investigator was blinded to the product application arm. Redness, bruising, and hypo/hyperpigmentation were rated on 0-5 severity scale (0=none, 1=mild, 3=moderate, 5=severe). The secondary endpoints of the study were potential adverse effects as measured on participant reported outcomes for both arms. Pain, redness, irritation related to itching, and dryness were rated on 0-5 scale (0-none, 1=mild, 3=moderate, 5=severe). The investigator score for each variable (redness, bruising, and hypo-hyperpigmentation) was evaluated as a continuous response (0-5) and analyzed using mixed model that included day, product application, and product application* day as fixed effects, and a random effect for participants. Participant reported outcome score for each variable (pain, redness, irritation due to itching, and dryness) was evaluated as a continuous response (0-5) and analyzed using mixed effect analysis that included day, product application, and product application* day as fixed effects, and a random effect for participants. Findings are based on the significance of the fixed effects in each model. Statistics were conducted using JMP Pro 16.2.

## Results

Ten participants (all females) aged 21 to 51 years old (average age 31.9 years) and Fitzpatrick skin types I-III were enrolled in this study (Table 1). The primary endpoint was improvement in skin appearance following $CO_2$ laser treatment after daily application of topical HPE compared to placebo as visualized on 2D photography. At the first post-treatment visit (Visit 2), all participants scored between 2 and 4 for redness (Figure 1a), and by Visit 5 (30 days post procedure) ratings had decreased to 0 to 3. Using a mixed model there was a significant reduction in redness with HPE product application (F ratio 5.36, p=0.02) (Table 2). The photographic comparation of a 51-year-old female forearm redness comparing control *vs*. treated arms on day 7 is shown in Figure 1b. There was no difference in redness at visit 1 however by visit 5 the difference is nearly a point on the 6-point scale (Figure 1c), suggesting that decrease in redness with topical HPE was detected over time in later stages. In this study, fractional $CO_2$ laser treatment did not produce bruising or hypo/hyperpigmentation as all ratings at all visits for both arms were 0. One participant missed visit 3, otherwise all data is complete.

The secondary endpoints included patient-reported outcomes recorded daily for the first 10 days post-treatment. Using a mixed model, there was moderate to no perceived pain following laser treatment; however, if present, perceived pain was significantly reduced in the HPE product application arm (F ratio 10.26, p=0.001) and resolved quicker (Table 2).

**Table 1:** Demographics.

| | Number | % |
|---|---|---|
| **Sex** | | |
| **Female** | 10 | 100 |
| **Male** | 0 | 0 |
| **Race/Ethnicity** | | |
| **Caucasian** | 8 | 80 |
| **Asian** | 1 | 10 |
| **Other** | 1 | 10 |
| **Fitzpatrick Skin Phototype** | | |
| **I** | 0 | 0 |
| **II** | 10 | 100 |
| **III** | 0 | 0 |
| **Age (years)** | **Mean** | **Range** |
| | 31.9 | 21-51 |

**Table 2:** Evaluation of Post-procedural Effects on Skin Recovery.

| Area | Source | F Ratio | Prob>F |
|---|---|---|---|
| **Redness** | Product Application | 0.82105 | 0.3682 |
| | Day | 69.0155 | <.0001* |
| | Product Application* Day | 5.3612 | 0.0237* |
| **Perceived pain** | Product Application | 2.3857 | 0.1241 |
| | Day | 58.5596 | <.0001* |
| | Product Application* Day | 10.2578 | 0.0016* |
| **Irritation due to Itch** | Product Application | 16.3738 | <.0001* |
| | Day | 0.2791 | 0.5979 |
| | Product Application* Day | 1.6461 | 0.0211 |
| **Dryness** | Product Application | 21.0754 | <.0001* |
| | Day | 0.3485 | 0.5359 |
| | Product Application* Day | 4.6994 | 0.0314* |

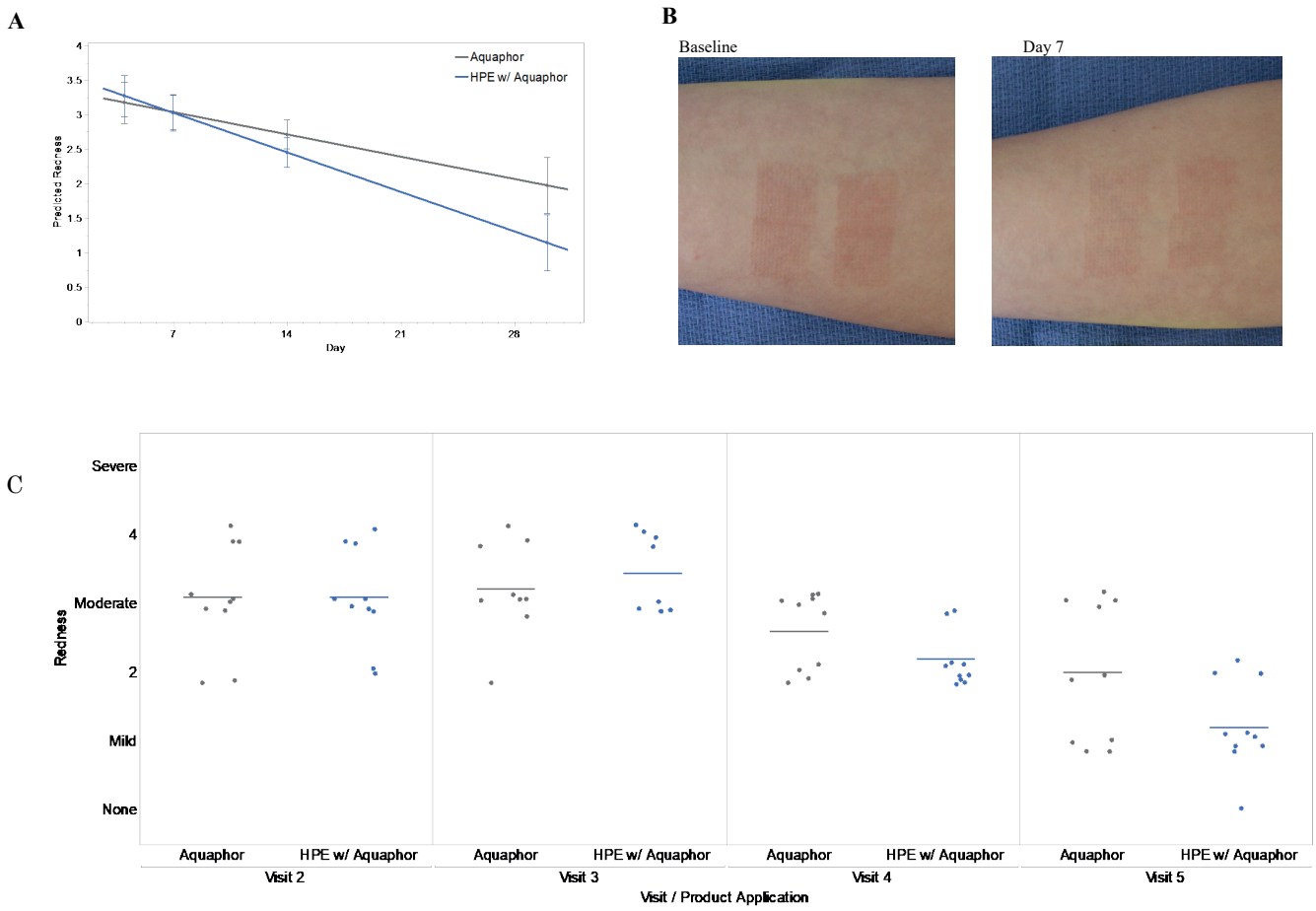


**Figure 1:** Evaluation of Post-$CO_2$ Laser Resurfacing Redness following Topical HPE+Aquaphor *vs*. Topical Aquaphor only. Subject level plots of redness scores by product application over time (1a). Baseline and post-topical HPE photographs from a 51 year-old female subject at visit day 7 (1b). Redness ratings across subjects within each product application within visit (1c). The difference in post-recovery product application increases with time.

Redness was rated at 4 and below at day 1 and significantly decreased over time regardless of post-procedural product (F ratio 99.06, p<0.0001) excluding one subject who reported increasing redness on the control arm.

Patient reports of perceived pain, irritation due to itch, and dryness varied but were significantly lower with topical HPE (Figures 2a-2c). Irritation due to itch scores ranged from 0-5 with six participants (60%) experiencing irritation due to itch over the 10 days, particularly on the control arm. Using a mixed model, irritation due to itch was significantly reduced with adjuvant HPE (F ratio 16.37, p<0.0001) (Table 2). All participants reported dryness at some point over the 10 days following product application, but again this was significantly decreased with application of HPE (F ratio 21.08, p<0.0001) and resolved quicker on the HPE product application arm (F ratio 4.70, p<0.03) (Table 2).

## Discussion

Fractional $CO_2$ laser resurfacing is a reliable tool for skin rejuvenation. However, ablative laser treatments are frequently associated with a longer recovery relative to other non-ablative modalities. Fractional laser treatment produces microablative columns of vaporized epidermis and dermis and delivers thermal energy to surrounding tissues. This results in collagen remodeling, tissue shrinkage, and skin tightening [8]. During the recovery period, laser-induced redness, dyspigmentation, and discomfort slowly resolve. In rare cases, adverse effects can become permanent. Additionally, multiple sessions may be required to achieve desired results. Therefore, there has been a drive to optimize fractional ablative $CO_2$ laser treatment to augment outcomes, hasten recovery, and minimize unwanted events.

Platelet-rich Plasma (PRP) is a small volume of plasma with highly concentrated platelets typically obtained from autologous whole

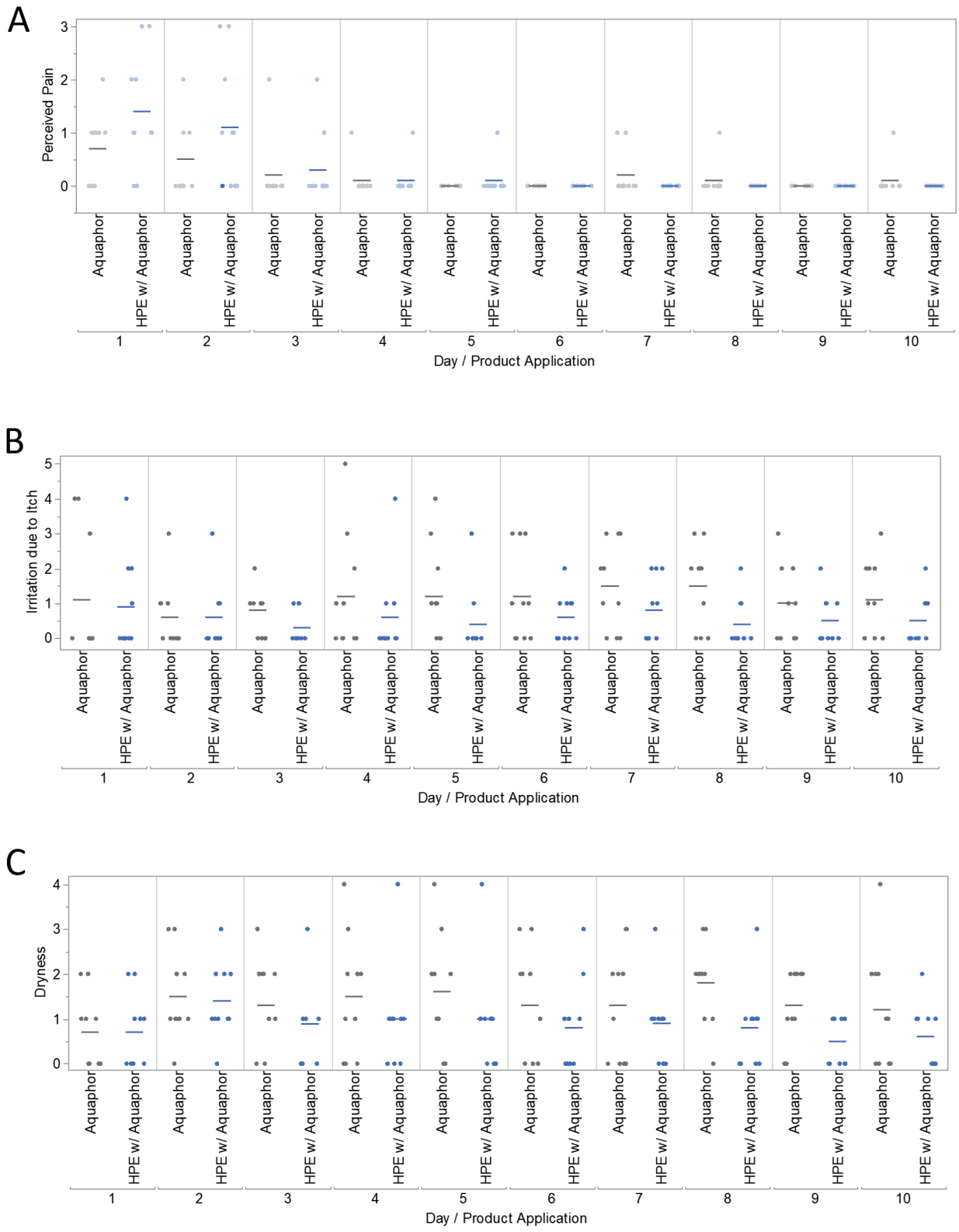


**Figure 2:** Post-Procedural Recovery Parameters following Topical HPE+Aquaphor *vs*. Topical Aquaphor only. Perceived pain ratings (2a), irritation due to itch ratings (2b), and dryness ratings (2c) across subjects within each post-procedural product application on a daily basis from day 1-10 as logged in daily patient diary.

blood processed by centrifugation. PRP promotes skin healing by releasing growth factors that induce cellular migration, proliferation, and angiogenesis [9]. Adjuvant application of PRP following ultra-pulsed fractional $CO_2$ for skin rejuvenation on the face and forearms has demonstrated improvement in post-laser therapy erythema, crusting, and associated with shorter recovery time [10,11]. However, PRP preparation has not been standardized. There exists considerable variability in PRP processing and efficacy.

Mesenchymal Stem Cells (MSCs) are multipotent stem cells that can self-renew and differentiate into many different cell types [12]. Adipose Derived Stem Cells (ADSCs) have similar properties with different tissue-specific differentiation abilities [13]. Adjuvant application of ADSC conditioned medium following fractional $CO_2$ laser resurfacing for acne scars was found to produce better treatment results with a lower incidence of adverse effects [14]. However, there are several complications to mesenchymal or adipose-derived stem cells including limited engraftment ability, potential for tumor formation, and inherent difficulty to maintain quality control given external biomanufacturing process [15].

Recent regenerative strategies using exosomes, or extracellular vesicles, offer benefits from the host cell with fewer complications [16-28]. Similar to ADSC, adjuvant application of ADSC-exosomes (ADSC-E) can deliver anti-inflammatory and regenerative growth factors resulting in rapid healing [12,29-32]. Fractional $CO_2$ laser therapy followed by application of ADSC-E for acne scarring resulted in faster recovery time, decreased erythema, and improved appearance of scar [33].

Herein we investigated the regenerative platelet technology. Compared to stem cells, platelets are an inherent component of the wound healing process. The dynamism of wound healing consists of inflammation, proliferation, and remodeling phases. Formation of a platelet plug to stop bleeding is the first step in the inflammatory phase [34]. Therefore, platelets are an ideal source to promote skin healing and recovery. Indeed, the topical HPE product is safe and well-tolerated under normal conditions of use [7]. This study found that applying topical HPE after fractional $CO_2$ laser produced significantly reduced post-laser adverse effects, and an overall shortened skin recovery period.

Study limitations include small sample size and inability to blind participants which could have biased participant reported outcomes. Additionally, the study was conducted with a short follow-up duration. The previous study investigating topical HPE found improvement in luminosity and color evenness with reduction in redness, wrinkles, and brown spots after 6 weeks of twice daily product application [7]. Therefore, it is likely that continued surveillance would have demonstrated a synergistic effect between fractional $CO_2$ treatment and topical HPE regarding treatment outcome. Further studies are needed to elucidate the potential of this novel mediator.

## Conclusion

The field of regenerative aesthetic medicine continues to search for novel mediators to reverse and prevent skin aging. Additionally, these bioregenerative agents could serve as adjuvant topical options to expedite their recovery. In this study, we used topically applied regenerative platelet nanotechnology, HPE, following fractional $CO_2$ laser therapy for skin rejuvenation. The results in this study demonstrate the potential to produce a shorter and more tolerable recovery period, potentially changing the landscape of post-procedure downtime.

## Funding

This study was partially financed by Rion Aesthetics, LLC (Rochester, MN).

## Ethical Consideration

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to and the appropriate ethical review committee approval has been received. Approval was obtained from Sterling IRB on February 11, 2022. Informed consent was obtained from all participants. All participants provided photography consent.

**Photo consent statement:** All subjects granted permission for the use of their photograph(s) or electronic media images for educational and research purposes by signing photo consent form.

**Statement of contribution:** M.S. contributed to the design and implementation of the clinical study. All authors contributed to the analysis of the results and writing of the manuscript.

## Acknowledgements

Karen Copeland, PhD, Boulder Statistics.

## Disclosure of Interest

Dr. Behfar has ownership interest in Rion Inc and Rion Aesthetics, LLC. The other authors have nothing to disclose.

## References

1. Uitto J, Bernstein EF (1998) Molecular mechanisms of cutaneous aging: connective tissue alterations in the dermis. J Investig Dermatol Symp Proc 3: 41-44.
2. Scharffetter-Kochanek K, Wlaschek M, Brenneisen P, Schauen M, Blaudschun R, et al. (1997) UV-induced reactive oxygen species in photocarcinogenesis and photoaging. Biol Chem 378: 1247-1257.
3. Berlin AL, Hussain M, Phelps R, Goldberg DJ (2009) A prospective study of fractional scanned nonsequential carbon dioxide laser resurfacing: a clinical and histopathologic evaluation. Dermatol Surg 35: 222-228.
4. Clementoni MT, Galimberti M, Tourlaki A, Catenacci M, Lavagno R, et al. (2013) Random fractional ultrapulsed $CO_2$ resurfacing of photodamaged facial skin: long-term evaluation. Lasers Med Sci 28: 643-650.
5. Yuksel EP, Sahin G, Aydin F, Senturk N, Turanli AY (2014) Evaluation of effects of platelet-rich plasma on human facial skin. J Cosmet Laser Ther 16: 206-208.
6. Hui Q, Chang P, Guo B, Zhang Y, Tao K (2017) The Clinical Efficacy of Autologous Platelet-Rich Plasma Combined with Ultra-Pulsed Fractional $CO_2$ Laser Therapy for Facial Rejuvenation. Rejuvenation Res 20: 25-31.
7. Proffer SL, Paradise CR, DeGrazia E, Halaas Y, Durairaj KK, et al. (2022) Efficacy and Tolerability of Topical Platelet Exosomes for Skin Rejuvenation: Six-Week Results. Aesthet Surg J 42: 1185-1193.
8. Hantash BM, Bedi VP, Kapadia B, Rahman Z, Jiang K, et al. (2007) *In vivo* histological evaluation of a novel ablative fractional resurfacing device. Lasers Surg Med 39: 96-107.
9. Freymiller EG, Aghaloo TL (2004) Platelet-rich plasma: ready or not? J Oral Maxillofac Surg 62: 484-488.

10. Hui Q, Chang P, Guo B, Zhang Y, Tao K (2017) The Clinical Efficacy of Autologous Platelet-Rich Plasma Combined with Ultra-Pulsed Fractional $CO_2$ Laser Therapy for Facial Rejuvenation. Rejuvenation Res 20: 25-31.

11. Na JI, Choi JW, Choi HR, Jeong JB, Park KC, et al. (2011) Rapid healing and reduced erythema after ablative fractional carbon dioxide laser resurfacing combined with the application of autologous platelet-rich plasma. Dermatol Surg 37: 463-468.

12. Shin TH, Kim HS, Choi SW, Kang KS (2017) Mesenchymal Stem Cell Therapy for Inflammatory Skin Diseases: Clinical Potential and Mode of Action. Int J Mol Sci 18: 244.

13. Mohamed Ahmed S, Fristad I, Lie SA, Suliman S, Mustafa K, et al. (2018) Adipose-derived and bone marrow mesenchymal stem cells: a donor-matched comparison. Stem Cell Res Ther 9: 168.

14. Zhou BR, Zhang T, Jameel AAB, Xu Y, Xu Y, et al. (2016) The efficacy of conditioned media of adipose-derived stem cells combined with ablative carbon dioxide fractional resurfacing for atrophic acne scars and skin rejuvenation. J Cosmet Laser Ther 18: 138-148.

15. Lou G, Chen Z, Zheng M, Liu Y (2017) Mesenchymal stem cell-derived exosomes as a new therapeutic strategy for liver diseases. Exp Mol Med 49: e346.

16. Zhang B, Yeo RWY, Lai RC, Sim EWK, Chin KC, et al. (2018) Mesenchymal stromal cell exosome-enhanced regulatory T-cell production through an antigen-presenting cell-mediated pathway. Cytotherapy 20: 687-696.

17. Pittenger MF, Mackay AM, Beck SC, Jaiswal RK, Douglas R, et al. (1999) Multilineage potential of adult human mesenchymal stem cells. Science 284: 143-147.

18. Kordelas L, Rebmann V, Ludwig A-K, Radtke S, Ruesing J, et al. (2014) MSC-derived exosomes: a novel tool to treat therapy-refractory graft-*versus*-host disease. Leukemia 28: 970-973.

19. Mendt M, Kamerkar S, Sugimoto H, McAndrews KM, Wu C-C, et al. (2018) Generation and testing of clinical-grade exosomes for pancreatic cancer. JCI Insight 3: e99263.

20. O'Loughlin AJ, Woffindale CA, Wood MJ (2012) Exosomes and the emerging field of exosome-based gene therapy. Curr Gene Ther 12: 262-274.

21. Qin J, Xu Q (2014) Functions and application of exosomes. Acta Pol Pharm 71: 537-543.

22. Sun L, Xu R, Sun X, Duan Y, Han Y, et al. (2016) Safety evaluation of exosomes derived from human umbilical cord mesenchymal stromal cell. Cytotherapy 18: 413-422.

23. Golan K, Kumari A, Kollet O, Khatib-Massalha E, Subramaniam MD, et al. (2018) Daily Onset of Light and Darkness Differentially Controls Hematopoietic Stem Cell Differentiation and Maintenance. Cell Stem Cell 23: 572-585 e7.

24. Pelizzo G, Avanzini MA, Cornaglia AI, De Silvestri A, Mantelli M, et al. (2018) Extracellular vesicles derived from mesenchymal cells: perspective treatment for cutaneous wound healing in pediatrics. Regen Med 13: 385-394.

25. da Fonseca Ferreira A, da Silva Cunha P, Carregal VM, de Cássia da Silva P, de Miranda MC, et al. (2017) Extracellular Vesicles from Adipose-Derived Mesenchymal Stem/Stromal Cells Accelerate Migration and Activate AKT Pathway in Human Keratinocytes and Fibroblasts Independently of miR-205 Activity. Stem Cells Int. 2017: 9841035.

26. Phinney DG, Pittenger MF (2017) Concise Review: MSC-Derived Exosomes for Cell-Free Therapy. Stem Cells 35: 851-858.

27. Lai RC, Yeo RWY, Lim SK (2015) Mesenchymal stem cell exosomes. Semin Cell Dev Biol 40: 82-88.

28. Park JE, Tan HS, Datta A, Lai RC, Zhang H, et al. (2010) Hypoxic tumor cell modulates its microenvironment to enhance angiogenic and metastatic potential by secretion of proteins and exosomes. Mol Cell Proteomics 9: 1085-1099.

29. Ha DH, Kim H-K, Lee J, Kwon HH, Park G-H, et al. (2020) Mesenchymal Stem/Stromal Cell-Derived Exosomes for Immunomodulatory Therapeutics and Skin Regeneration. Cells 9: 1157.

30. Heo JS, Choi Y, Kim HO (2019) Adipose-Derived Mesenchymal Stem Cells Promote M2 Macrophage Phenotype through Exosomes. Stem Cells Int 2019: 7921760.

31. Li X, Xie X, Lian W, Shi R, Han S, et al. (2018) Exosomes from adipose-derived stem cells overexpressing Nrf2 accelerate cutaneous wound healing by promoting vascularization in a diabetic foot ulcer rat model. Exp Mol Med 50: 1-14.

32. McBride JD, Rodriguez-Menocal L, Badiavas EV (2017) Extracellular Vesicles as Biomarkers and Therapeutics in Dermatology: A Focus on Exosomes. J Invest Dermatol 137: 1622-1629.

33. Kwon HH, Yang SH, Lee J, Park BC, Park KY, et al. (2020) Combination Treatment with Human Adipose Tissue Stem Cell-derived Exosomes and Fractional $CO_2$ Laser for Acne Scars: A 12-week Prospective, Double-blind, Randomized, Split-face Study. Acta Derm Venereol 100: adv00310.

34. Lee HJ, Jang YJ (2018) Recent Understandings of Biology, Prophylaxis and Treatment Strategies for Hypertrophic Scars and Keloids. Int J Mol Sci 19: 711.