



Research article

Volume 6 Issue 4 - April 2025

DOI: 10.19080/JOJDC.2025.06.555694

JOJ Dermatol & Cosmet

Copyright © All rights are reserved by Irene Fusco

Preclinical Results of the Potential Role of Exolight Exosomes as Adjuvant Therapy of CO₂ Laser Application for Skin Aging Management

Fusco I^{1*}, Zingoni T¹, Madeddu F¹, Colombo C², Amato S³, Greco ME³, Rizzuto G³, Zappia E⁴, Bonan P⁵ and Nisticò S³

¹El.En. Group, 50041 Calenzano, Italy

²Lem Compounding Research, Via Oberdan 60 - 20823 Lentate Sul Seveso (MB), Italy

³Dermatology unit, Department of Clinical Internal Anesthesiological and Cardiovascular Sciences, "Sapienza" University of Rome, 00161 Rome, Italy

⁴Department of Health Sciences, Magna Graecia University, Catanzaro 88100, Italy

⁵Laser Cutaneous Cosmetic & Plastic Surgery Unit, villa Donatello clinic, Florence, Italy

Submission: April 12, 2025; **Published:** April 24, 2025

***Corresponding author:** Irene Fusco, El.En. Group, 50041 Calenzano, Italy. (ORCID: 0000-0001-7264-8808).

Abstract

Background: Exosomes represent one of a series of skin-boosting products that have received a lot of attention on its use in skin rejuvenation. Aim: to evaluate the efficacy of a skin collagen booster contained exosomes and other products as an adjuvant therapy after application of a recent CO₂ laser fractional treatment for skin aging.

Material and Methods: A total of 20 skin test were performed on the anterior portion of the forearm of a healthy adult: 10 skin tests were performed with CO₂ fractional laser treatment only and other 10 skin samples with CO₂ fractional laser treatment and subsequent application of the skin collagen booster. The Optical Coherence Tomography (OCT) system was used to analyze the vascularization of treated areas during the healing phase. The outcomes for each set of skin tests were photographically documented and the speed of the skin healing process was also monitored observing the exfoliation process of the crusts.

Results: The areas treated with the CO₂ laser and the skin collagen booster show a reduced vascularisation compared to that obtained with CO₂ laser alone. The photographic documentation revealed that the combination of CO₂ laser with skin collagen booster-containing exosomes accelerates crust expulsion as compared to CO₂ treatment alone. The quantitative assessment of the percentage of crust disappearance showed a greater acceleration of skin healing process with the synergy between skin collagen booster and laser fractional treatment.

Conclusions: exosomes are on the horizon as an exciting adjuvant therapeutic approach for laser application in aging skin management.

Keywords: Exosomes; CO₂ laser; Preclinical data; Skin aging

Abbreviations: HA: Hyaluronic Acid; DOTs: Spaced columns of thermal damage; OCT: Optical Coherence Tomography; MRI: Magnetic Resonance Imaging

Introduction

The original concept of "skin boosters" has evolved, representing a departure from the conventional application of hyaluronic acid (HA) fillers, which was limited to increasing the volume of the skin, to a more varied use intended to improve dermal complication [1]. Skin boosters are a class of substances that increase the dermal extracellular matrix to improve skin quality and reduce the aging process of the skin.

Skin aging is characterized by a decrease in the number of epidermal and dermal cells, a reduction in the height of rete ridges, a decrease in collagen and elastin and a loss in glycosaminoglycans. In order to show their beneficial effects, skin boosters enhance and reinforce the extracellular environment, ameliorate pigmentation disorders, vasodilation and reduce inflammation. Among these, exosomes represent one of a series of skin-boosting products that have received a lot of attention recently and its use in dermatology.

gy and aesthetics has significantly increased in the past few years [2]. Exosomes, which are the tiniest extracellular vesicles and range in size from 30 to 110 nm, play a major role in the phases of wound healing and regeneration of the skin by encapsulating proteins, lipids, mRNA, and miRNA within a lipid bilayer that is generated from the cell membrane. In this way they are responsible for extensive intercellular communication in the form of these cellular components [3]. Exosomes facilitate the communication between skin cells and fibroblast function, enhance collagen and elastin synthesis, and increase dermal fat, thus promoting the regenerative and restorative capacity for skin anti-aging. These results improved skin texture and a reduction in the appearance of wrinkles and fine lines. Exosomes also play a role in elastin production; this elastic property is essential for maintaining a youthful and firm skin appearance [4]. Additionally, as an alternative to cell-free therapy, exosomes have several advantages over stem cell transplantation, including stability, low toxicity, biocompatibility, immune rejection and tumorigenesis risk avoidance, and skilled exchange of molecular goods, making them an ideal candidate for tissue engineering and regenerative medicine [5-8]. Particularly, it is known that milk exosomes are nature's abundant drug delivery carriers, and these exosomes exhibit superior stability, biocompatibility, half-life, and very low immunogenicity [9]. Since exosome treatment is relatively new, the majority of the research demonstrating its effectiveness has been carried out in animal and cell models of disease [10], emphasizing the need for additional clinical trials to evaluate its safety and efficacy in humans. Another crucial point regarding exosomes therapy in the aesthetic field, is that in the United States exosomes may only be topically applied and not injected into the skin, as is permitted in many countries worldwide [11]. For this reason, exosome therapy is combined with techniques such as microneedling, radiofrequency and laser to reach the deeper layers of the skin and as a procedure for promote faster skin repair. Indeed, it was demonstrated that the application of exosomes directly after skin rejuvenation treatments like fractional laser, microneedling, radiofrequency micro-needling, and microdermabrasion aids in the healing process helping to mitigate symptoms associated with these procedures, including erythema, edema, and discomfort [12,13]. Among these techniques, the fractional CO₂ laser treatment is a popular and effective skin rejuvenation treatment with minimal downtime and side effects. This technology is able to create very thin and spaced columns of thermal damage (DOTs) surrounded by healthy tissue, which allows faster healing than traditional ablative resurfacing with the same source [14]. Based on existing literature, we present a collection of preclinical data focused on the evaluation of the efficacy of a skin collagen booster (Exolight, DEKA M.E.L.A Srl, Florence, Italy) contained exosomes and other products (e.g vitamins, Hyaluronic acid, Glycerin, Aminoacids) as an adjuvant therapy after application of a recent CO₂ laser fractional treatment for skin aging management. Primarily the purpose of this study.

was to evaluate the delivery of the collagen skin booster through the micro-channels generated by the CO₂ laser at different parameters in order to verify a possible benefit in the healing and inflammatory process by monitoring with OCT analysis the vascular network and through photographic assessment the full expulsion of fibrin plugs of skin for 18 days following treatment.

Materials and Methods

A total of 20 skin test were performed on the anterior portion of the forearm of a healthy adult, using 5 different energies for DOT values and two different CO₂ scanners allowing for the creation of micro-ablation areas of different sizes. In particular, 10 skin tests were performed with CO₂ fractional laser treatment only and other 10 skin samples with CO₂ fractional laser treatment and subsequent application of the skin collagen booster. These tests were planned to evaluate the response in terms of ablation depth and vehicularity of the product to maximize the effects of the synergy between the laser and the collagen booster. Maintaining the spacing (distance between DOTs) at 500 µm, the following energies/DOT were set: 15 mJ, 20 mJ, 25 mJ, 40 mJ and 50 mJ. The first series of 5 skin tests were carried out irradiating the skin with CO₂ laser (SmartXide Tetra PRO, DEKA M.E.L.A Srl, Florence, Italy) equipped with this dedicated scanner system (DOT PRO scanner, DEKA M.E.L.A, Florence, Italy) [14]. The second series of 5 skin tests were carried out irradiating the skin with CO₂ laser (same CO₂ scanner and same energy for DOT values) combined with skin collagen booster (Exolight, DEKA M.E.L.A Srl, Florence, Italy). The third series of 5 skin tests were performed irradiating the skin with CO₂ laser equipped with SCAR3 PRO scanner (DEKA M.E.L.A, Florence, Italy). The fourth series of 5 skin tests were carried out irradiating the skin with CO₂ laser equipped with SCAR3 PRO scanner (same CO₂ scanner and same energy for DOT values) combined with skin collagen booster. As mentioned before, these scanners create microthermal zones of ablation and coagulation (DOTs), separated from healthy tissue by a spacing parameter (Spacing) and they can be equipped with a contact sensor to ensure greater safety during treatment. Specifically, the SCAR3 PRO scanner has a smaller spot size and a greater ablation depth than the other scanner. In particular, the DOT PRO scanner has an optical spot size of approximately 290 µm while that of the SCAR3 PRO scanner is approximately 210 µm [15]. Tests were carried out with both scanners to monitor possible clinical differences due to the different spot sizes and different penetration depths. The vascularisation of areas treated with CO₂ laser alone or with CO₂ laser and skin collagen booster was analysed by Optical Coherence Tomography (OCT) analysis for a short follow-up: immediately after treatment (T0), 4 hours after treatment (T1), 1 day after treatment (T2) and 7 days after treatment (T3).

This analysis allowed to obtain images of the vascular network at different depths, which were analysed with ImageJ software to obtain quantitative and easily comparable results.

Since the forearm skin was monitored until the complete expulsion of fibrin plugs, the outcomes for each set of skin tests were photographically documented over several days to over two weeks. In summary, the speed of the skin healing process after

the different types of treatment was monitored by observing the vascular network for a short follow-up and the exfoliation process of the crusts for longer follow-up. (Figure 1)

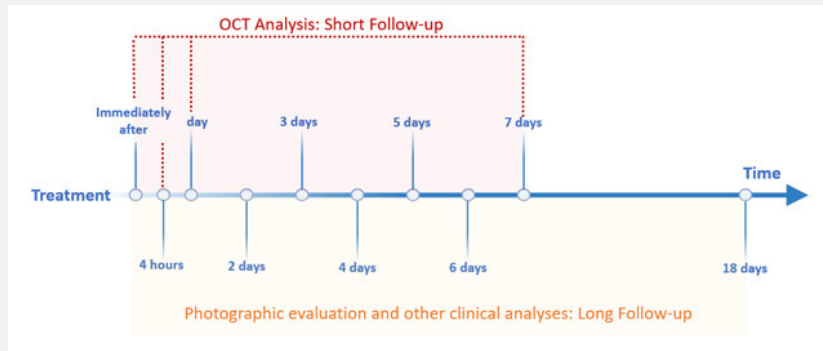


Figure 1: Study evaluation Timelines.

A written informed consent was obtained by subjects involved in this study.

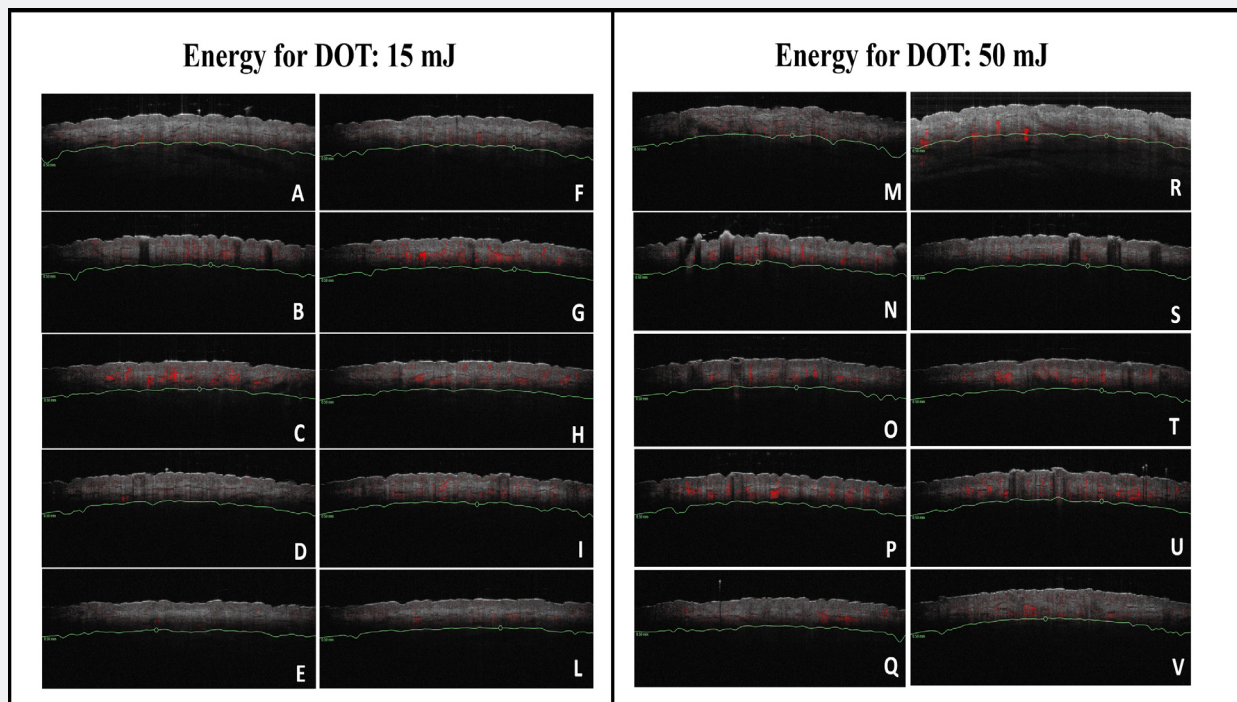


Figure 2: OCT images of vascular network of frontal plane of areas treated with CO₂ laser alone (A-E; M-Q) and with CO₂ laser and skin collagen booster (F-L; R-V) with minimum (left panel) and maximum energies for DOT (right panel) at different follow-ups: before (A;F;M;R); immediately after treatment (B;G;N;S); 4 hours after treatment (C;H;O;T), 1 day after treatment (D;I;P;U) and 7 days after treatment (E;L;Q;V).

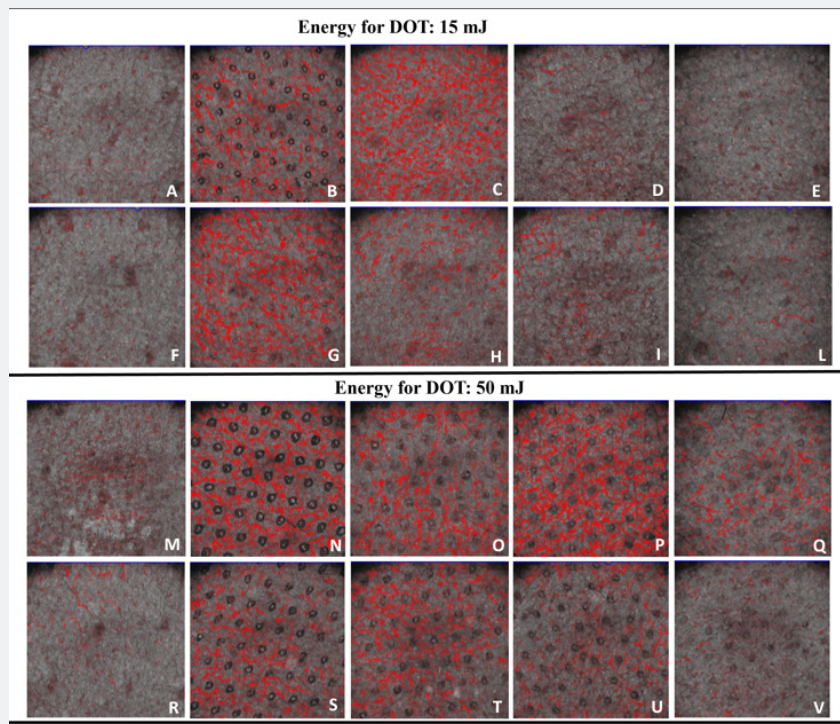


Figure 3: OCT images of vascular network at 300 μm of depth of areas treated with CO_2 laser alone (A-E; M-Q) and with CO_2 laser and skin collagen booster (F-L; R-V) with minimum (top panel) and maximum (bottom panel) energies for DOT at different follow-ups: before (A;F;M;R); immediately after treatment (B;G;N;S); 4 hours after treatment (C;H;O;T), 1 day after treatment (D;I;P;U) and 7 days after treatment (E;L;Q;V).

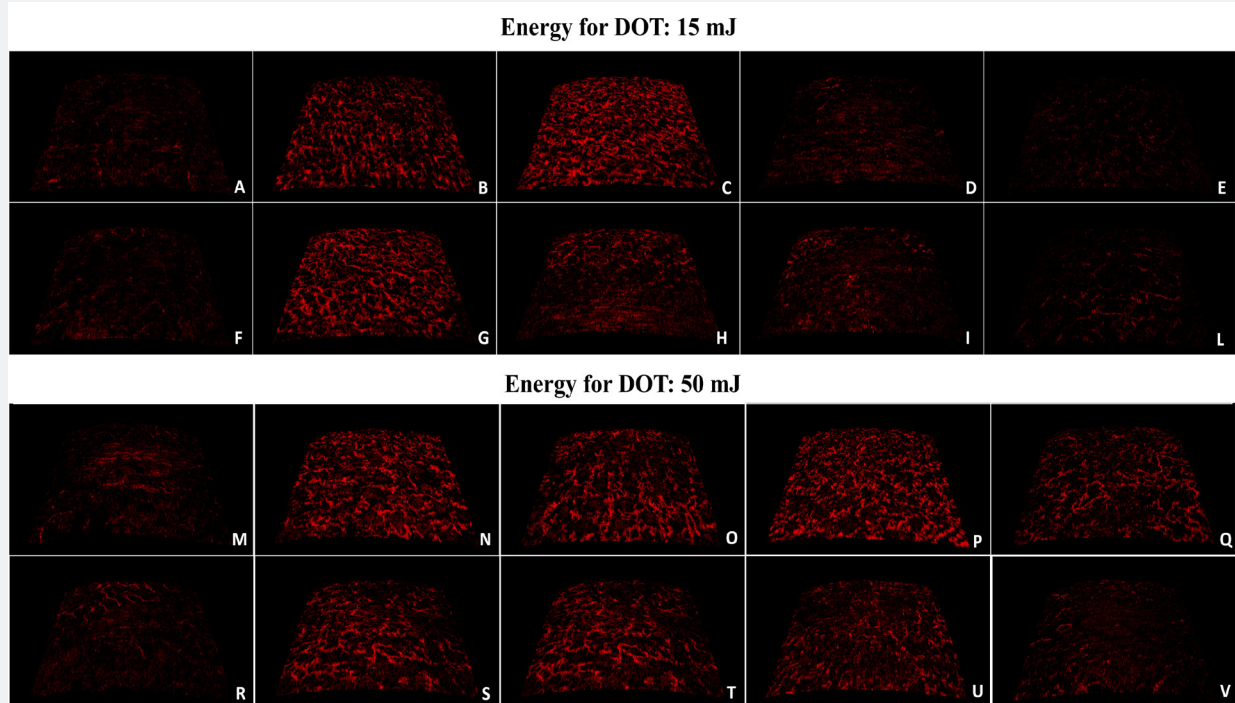


Figure 4: OCT images of 3D vascular network of area treated with CO_2 laser alone (A-E; M-Q) and with CO_2 laser and skin collagen booster (F-L; R-V) with minimum (top panel) and maximum (bottom panel) energies for DOT at different follow-ups: before (A;F;M;R); immediately after treatment (B;G;N;S); 4 hours after treatment (C;H;O;T), 1 day after treatment (D;I;P;U) and 7 days after treatment (E;L;Q;V).

Results

From the OCT analysis, it was possible to extrapolate frontal plane (Figure 2), transverse plane (Figures 3) and 3D reconstructions (Figures 4) of the vascular component of the treated areas. For all energies used, an increase in the vascular component can be seen in both types of treatment, which resolves almost completely at 7-day follow-up. However, making a comparative analysis between the two treatments, it can be seen that the areas treated with the CO₂ laser and the skin collagen booster show a reduced vascularisation compared to that obtained with CO₂ laser alone, thus highlighting the soothing action of the skin collagen booster on the post-laser inflammation.

From the OCT images it was possible to extrapolate quantitative data that confirmed the qualitative data shown previously. In the graph (Figure 5), in fact, the trend of the vascular component at the various follow-ups for the two types of treatment is shown and the difference between the two is evident, especially immediately after, 4 hours after and 1 day after treatment. The

photographic documentation for CO₂ laser protocol with DOT PRO scanner and 50 mJ of energy for DOT (Figure 6) revealed that the combination of CO₂ laser with skin collagen booster-containing exosomes accelerates crust expulsion as compared to CO₂ treatment alone. Furthermore, post-treatment redness and dryness also tended to be milder on sides treated with CO₂ laser combined with skin collagen booster compared to sides treated with CO₂ laser alone. These preclinical data are confirmed by the quantitative assessment of the percentage of crust disappearance as shown in the Figure 7. Additionally, the skin healing time was monitored in relation with energy for DOT for both CO₂ scanners (DOT PRO AND SCAR 3 PRO scanner) as represented in Figure 8 showing a greater acceleration of skin healing process with the synergy between skin collagen booster and SCAR 3 PRO fractional treatment. Furthermore, calculating the percentage difference in the days needed for complete expulsion of fibrin plugs between the two types of treatment and at different energies for DOT, gives a maximum percentage difference of approximately 23%.

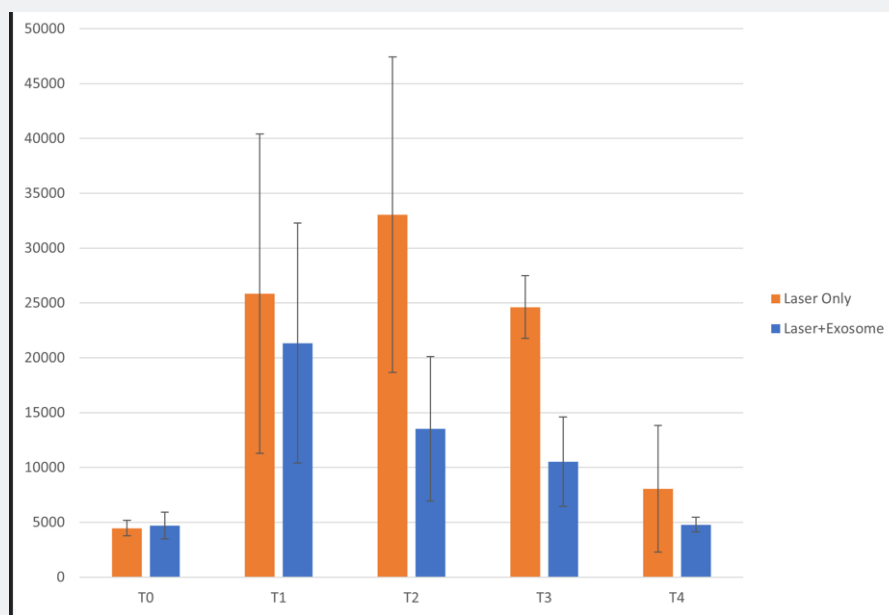


Figure 5: Graph showing mean and standard deviation of vascular network at different follow-ups: before (T0), immediately after treatment (T1), 4 hours after treatment (T2), 1 day after treatment (T3) and 7 days after treatment (T4).

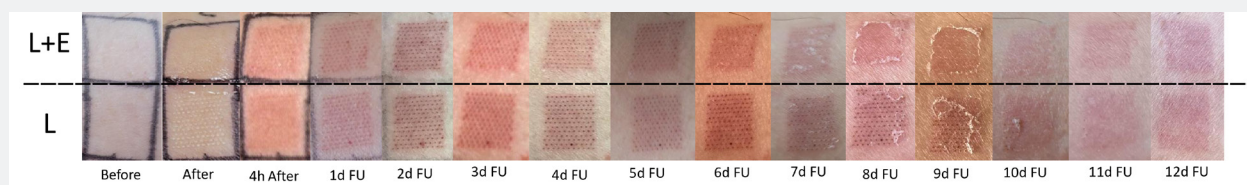


Figure 6: Photographic documentation of skin healing process before and up to 12 days follow up (FU) with CO₂ laser combined with skin collagen booster-containing exosomes (L+E) and with CO₂ laser alone (L) with an energy for DOT of 50 mJ and with the use of DOT PRO scanner.

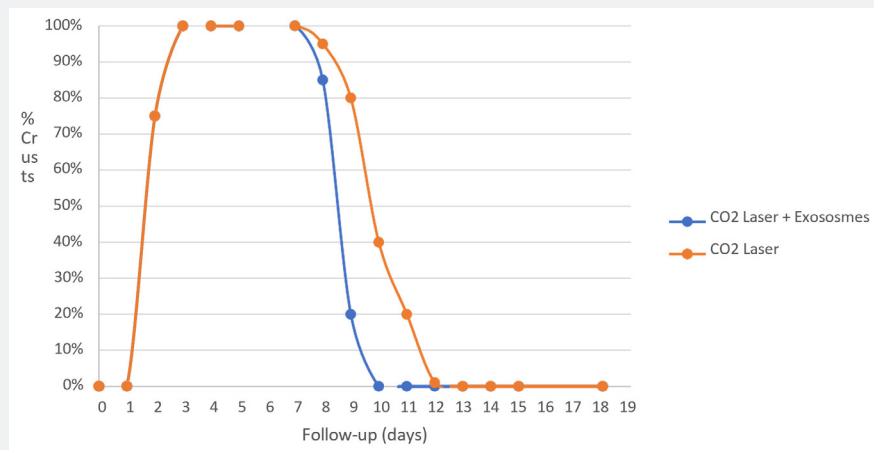


Figure 7: Graphical illustration showing the percentage of crusts expelled up to 18 days with CO₂ laser combined with skin collagen booster-containing exosomes (blue line) and CO₂ laser alone (orange line) for and energy for DOT of 50 mJ and the use of DOT PRO scanner.

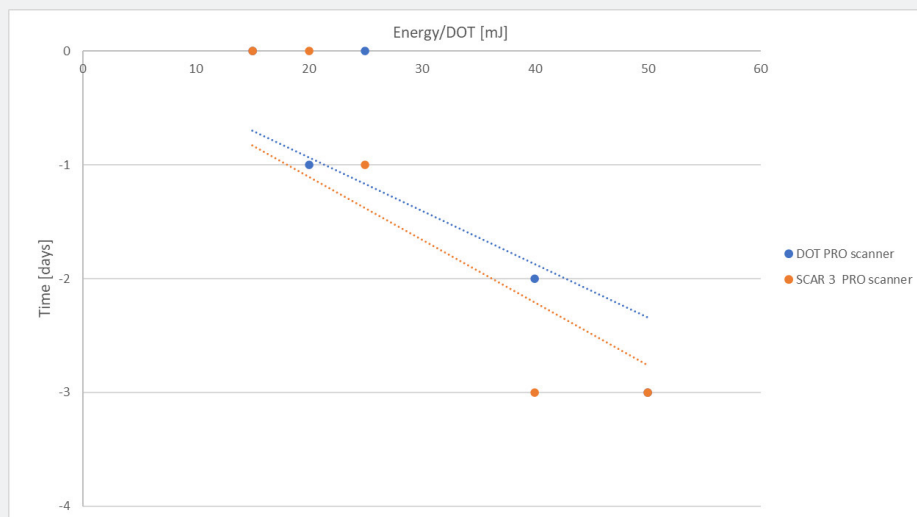


Figure 8: Graphical illustration showing the difference healing process (expressed in days) between CO₂ laser alone and combination of CO₂ laser and collagen booster for two different scanners and at different energies for DOT. The trend lines between the two scanners show that the healing process with the SCAR3 PRO scanner is faster than that achieved with the DOT PRO Scanner. This is even more evident at high energy for DOT values.

Discussion

Skin regeneration is one of the fields where exosomes have demonstrated their efficacy [2]. Preclinical studies have shown that exosomes promote wound healing in vitro, and they can represent a therapeutic avenue for hair growth and regeneration [16-19]. The recent study of Li et al. highlights the significant clinical promise of stem cells and their derivatives, including exosomes and noncoding RNAs, in rejuvenating aging skin and mitigating

the effects of photoaging [20]. Furthermore, existing literature reported promising results on the efficacy of the combined application of exosomes and CO₂ laser for skin remodelling [21]. In this regard, our preclinical qualitative and quantitative data showed that the combined treatment of exosomes and CO₂ laser afforded more favourable responses and a shorter skin recovery time. Therefore, co-treatment with this novel material with CO₂ resurfacing device may provide synergistic effects on both efficacy and safety for skin resurfacing treatments. These promising results

were further validated by using OCT system which represents a promise real-time imaging technology of skin microstructure that offers subsurface images of the microstructure of the skin with a significantly higher resolution compared to that of magnetic resonance imaging (MRI) or high frequency ultrasound [22]. Indeed, OCT is used as a significant tool in pre- and post-treatment decision-making to determine the appropriate laser therapy parameters. Specifically, in our study the selected parameters are those that are typically used for skin rejuvenation treatments.

This laser scanning technology that provides images of the vascular network obtained at different depths, has shown an increase in the vascular component for all energies used, in both types of treatment, which resolves almost completely at the 7-day follow-up. However, it can be noted that the areas treated with the CO₂ laser and the skin collagen booster show a reduced vascularization compared to that obtained with the CO₂ laser alone, thus highlighting the soothing action of the skin collagen booster on post-laser inflammation.

These pre-clinical tests were conducted on the anterior portion of the forearm (areas with fewer hair follicles) which, being a peripheral area of human body, has a slower healing process in comparison to the face area. We specifically selected this anatomical site since it allows us to better monitor this process. Considering the pre-clinical data published by Scarcella et al. [15] and the percentage difference obtained with our data, we can assume a decrease in healing time from 9-5 days (CO₂ laser only) to 7-4 days (CO₂ laser and skin collagen booster) for facial treatments. In summary, as the energy increases, the depth of penetration of the CO₂ laser increases, which allows the active ingredients necessary for tissue repair to be brought directly into our skin and, therefore, to speed up the healing process. The next step will be to collect clinical data in order to support our preclinical investigation, by comparing these different forms of treatment (also combining exosomes with other types of lasers) and monitoring the results for a longer follow up.

Conclusion

In conclusion exosomes are on the horizon as an exciting adjuvant therapeutic approach (or future pharmaceutical drug delivery vehicle) for laser application in aging skin management.

Acknowledgements

Author Contributions: Conceptualization, IF,TZ, FM, CC, SA, MEG, GR, EZ, PB, SN; methodology, TZ, FM, CC, SA, GR, SN; software, IF, TZ, FM, CC, SA, GR, SN; validation, IF, TZ, FM, CC, SA, MEG, GR, EZ, PB, SN; formal analysis, IF, TZ, FM, CC, SA, GR, EZ, PB, SN; investigation, IF, TZ, FM, CC, SA, GR, EZ, PB, SN; resources, IF, TZ, FM, CC, SA, GR, EZ, PB, SN; data curation,; writing-original draft preparation, IF, TZ, FM, CC; writing-review and editing, IF, TZ, FM, CC, SA, MEG, GR, EZ, PB, SN; visualization, IF, TZ, FM, CC, SA, MEG, GR, EZ, PB, SN; supervision, IF, TZ, FM, CC, SA, MEG, GR, EZ, PB, SN; project administration, TZ, SN; funding acquisition, TZ, SN. All authors have read and agreed to the published version of

the manuscript.

Institutional Review Board Statement: The article is in accordance with the Declaration of Helsinki on Ethical Principles for Medical Research involving human subjects. Ethical approval is not necessary as the study device is already CE marked since 2024.

Data Availability Statement: Data available on request from the authors.

Conflicts of Interest

Authors TZ, FM and IF were employed by El. En. Group. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Y KH, Winayanuwattikun W, K SY, Wan J, Vachatanont V et al. (2024) Skin boosters: Definitions and varied classifications. *Skin Res Technol* 30(3): e13627.
2. Yang GH, Lee YB, D Kang, Choi E, Nam Y et al. (2021) Overcome the barriers of the skin: exosome therapy. *Biomater Res* 25(1): 22.
3. Olumesi KR, Goldberg DJ (2023) A review of exosomes and their application in cutaneous medical aesthetics. *J Cosmet Dermatol* 22(10): 2628-2634.
4. Xiong M, Zhang Q, Hu W, Zhao C, Lvet W et al. (2021) The novel mechanisms and applications of exosomes in dermatology and cutaneous medical aesthetics. *Pharmacol Res* 166: 105490.
5. Raik S, Kumar A, Bhattacharyya S (2017) Insights into cell-free therapeutic approach: Role of stem cell "soup-ernatant". *Biotechnol Appl Biochem* 65: 104-118.
6. Ha DH, Kim SD, Lee J, Kwon HH, Park G-H et al. (2020) Toxicological evaluation of exosomes derived from human adipose tissue-derived mesenchymal stem/stromal cells. *Regul Toxicol Pharmacol* 115: 104686.
7. Bian D, Wu Y, Song G, Azizi R, Zamani A (2022) The application of mesenchymal stromal cells (MSCs) and their derivative exosome in skin wound healing: A comprehensive review. *Stem Cell Res Ther* 13(1):24.
8. Ha DH, Kim HK, 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.
9. Adriano B, Cotto NM, Chauhan N, Jaggi M, Chauhan SC, et al. (2021) Milk exosomes: Nature's abundant nanoplateform for theranostic applications. *Bioact Mater* 6(8): 2479-2490.
10. Lai RC, Arslan F, Lee MM, Choo A, Chen TS et al. (2010) Exosome secreted by MSC reduces myocardial ischemia/reperfusion injury. *Stem Cell Res* 4(3): 214-22.
11. Yousefian F, Espinoza L, Yadlapati S, Lorenc ZP, Gold M (2024) A comprehensive review of the medical and cosmetic applications of exosomes in dermatology. *J Cosmet Dermatol* 23(4): 1224-1228.
12. Zhang B, Gong J, He L, Khan A, Xiong T, et al. (2022) Exosomes based advancements for application in medical aesthetics. *Front Bioeng Biotechnol* 10: 1083640.
13. Lueangarun S, Cho BS, Tempark T (2024) Hair repigmentation of poliosis circumscripta in androgenetic alopecia patient treated with exosomes and fractional picosecond laser. *J Cosmet Dermatol* 23(6): 2307-2311.

14. Piccolo D, Zingoni T, Fusco I, Madeddu F, Conforti C (2024) faster CO2 fractional scanner system mode for skin rejuvenation. A clinical study. *Skin Res Technol* 30(8): e13843.
15. Scarcella G, Pieri L, Fusco I (2022) Skin Fractional Scar Treatment with a New Carbon Dioxide Scanner: Histological and Clinical Evaluation. *Photobiomodul Photomed Laser Surg* 40(6): 424-432.
16. Prasai A, Jay JW, Jupiter D, Wolf SE, Ayadi AEI (2022) Role of Exosomes in Dermal Wound Healing: A Systematic Review. *Journal of Investigative Dermatology* 142: 662-678.e8.
17. Bian D, Wu Y, Song G, Azizi R, Zamani A (2022) The application of mesenchymal stromal cells (MSCs) and their derivative exosome in skin wound healing: a comprehensive review. *Stem Cell Res Ther* 13(1): 24.
18. Paiewonsky B, Heinen N, Bellefeuille G et al (2022) Exosome therapy for scalp hair growth—a review of the in vivo and in vitro evidence. *J Am Acad Dermatol* 87(3): AB167.
19. Park B-S, Choi H-I, Huh G, Kim W-S et al. (2022) Effects of exosome from adipose-derived stem cell on hair loss: A retrospective analysis of 39 patients. *J Cosmet Dermatol* 21(5): 2282-2284.
20. Li KJ, Zhou PJ, Guo YN, Xu T-X, Lin S-F et al. (2023) Recent advances in exosomal non-coding RNA-based therapeutic approaches for photoaging. *Skin Res Technol* 29(9): e13463.
21. 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 CO2 Laser for Acne Scars: A 12-week Prospective, Double-blind, Randomized, Split-face Study. *Acta Derm Venereol* 100(18): adv00310.
22. Abrouk, C Gianatasio, Y Li, Holmes J, Dong J et al. (2022) An Atlas of Optical Coherence Tomography (OCT): Elucidating In Vivo Differences of Scar Types Using OCT in Order to Guide Laser Treatment Parameters. *J Clin Aesthet Dermatol* 15(9): 30-39.



This work is licensed under Creative Commons Attribution 4.0 License
DOI: [10.19080/JOJDC.2025.06.555694](https://doi.org/10.19080/JOJDC.2025.06.555694)

**Your next submission with Juniper Publishers
will reach you the below assets**

- Quality Editorial service
- Swift Peer Review
- Reprints availability
- E-prints Service
- Manuscript Podcast for convenient understanding
- Global attainment for your research
- Manuscript accessibility in different formats
(Pdf, E-pub, Full Text, Audio)
- Unceasing customer service

Track the below URL for one-step submission
<https://juniperpublishers.com/online-submission.php>