



CASE REPORT

Regenerative Skin Remodeling through Exosome-Based Therapy: A Case Study Demonstrating 21-Month Sustained Outcomes in Pore Size, Erythema, and Hyperpigmentation

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Received: June 16, 2025 / Accepted: July 15, 2025
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ABSTRACT

Introduction: Visible signs of skin aging, including enlarged pores, rosacea, and melasma, are often difficult to treat due to their multifactorial etiology. Most conventional therapies offer only temporary improvement and require ongoing maintenance. Exosome-based treatments present a regenerative approach that targets key biological dysfunctions associated with aging skin.

Case report: A healthy female in her late 40s with Grade 3 pore enlargement, Subtype I rosacea, and epidermal-type melasma (MASI score 10) underwent two sessions of topical exosome application following superficial microneedling at 0.3 mm depth, performed on Day 1 and Day 21. Clinical progress was documented at baseline, 3 weeks, 5.5 months, and 21 months using standardized photography, AI-assisted 3D imaging, and validated scales (MASI, CEA, GAIS). Progressive, multidimensional improvements were observed: pore size reduced by up to 41%, erythema by 42%, and melanin deposition by

31% at 5.5 months. These effects were largely sustained at 21 months. Surface roughness metrics (Ra, Rq, Rmax, Rz, Rp, Rv) also improved significantly.

Discussion: The results indicate that topical exosome therapy combined with superficial microneedling promotes lasting improvements in key clinical markers of skin aging. The sustained effects over 21 months suggest biological remodeling rather than transient cosmetic correction. No adverse events occurred throughout the follow-up period, confirming the safety and tolerability of the protocol.

Conclusion: A short protocol of topical exosomes with superficial microneedling achieved durable improvements in pore size, redness, and pigmentation that persisted for nearly two years without retreatment. These findings support its potential as a low-risk, regenerative modality for long-term facial rejuvenation.

PLAIN LANGUAGE SUMMARY

Many people struggle with visible signs of facial aging, such as enlarged pores, persistent redness, and uneven pigmentation. These changes are often difficult to treat, and available options may require multiple sessions or produce only short-term effects. In this case study, we explored

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the use of a topical exosome-based therapy combined with microneedling to improve these concerns. The subject received just two treatment sessions, spaced 21 days apart, and was followed for nearly 2 years. We monitored outcomes using high-resolution 3D imaging, clinical photography, and validated scoring systems to measure pore size, skin redness, and pigmentation levels over time. The results showed significant improvement in all parameters, with changes visible as early as 3 weeks and sustained through the 21-month follow-up. Objective measurements confirmed smoother skin texture, reduced erythema, and decreased hyperpigmentation. No adverse events were reported, and no additional treatments were needed during the follow-up period. These findings suggest that a short course of exosome-based therapy may offer safe, long-lasting results for age-related skin concerns.

Keywords: Exosome therapy; Superficial microneedling; Pore reduction; Facial erythema; Melasma; Skin rejuvenation; Long-term outcomes

Key Summary Points

Exosome-based therapies offer a regenerative strategy for age-related skin conditions, targeting biological dysfunction rather than providing temporary cosmetic relief.

This case involved a healthy female patient with visible signs of aging—enlarged pores, erythema, and melasma—who underwent only two sessions of topical exosome application with superficial microneedling.

Objective measurements showed sustained improvements: pore size reduction of up to 41%, erythema reduction of 42%, and melanin reduction of 31% at 5.5 months, with effects largely maintained at 21 months.

Surface roughness parameters, Melasma Area and Severity Index (MASI), Clinician's Erythema Assessment (CEA), and Global Aesthetic Improvement Scale (GAIS) scores all improved significantly, with no adverse events reported throughout the study period.

These findings suggest that short-course exosome therapy may induce long-term dermal remodeling and pigmentation normalization with minimal intervention and excellent safety.

INTRODUCTION

As skin ages, it undergoes progressive deterioration in structural integrity, cellular function, and regenerative capacity. These changes are driven by both intrinsic mechanisms—such as hormonal decline and genetic programming—and extrinsic factors, including ultraviolet (UV) radiation, pollution, and oxidative stress [1]. A central contributor to this process is cellular senescence [2], a state in which cells lose their ability to divide and begin secreting pro-inflammatory cytokines and matrix-degrading enzymes. The accumulation of senescent cells disrupts tissue homeostasis and accelerates visible signs of aging. [3–5]

Common manifestations of cutaneous aging—such as enlarged pores, rosacea, and melasma—are directly associated with these biological changes. Enlarged pores result from dermal thinning, collagen loss, and increased sebaceous activity [6, 7]. Rosacea, a chronic inflammatory disorder, is exacerbated by impaired vascular regulation and immune dysregulation in aging skin [8, 9]. Melasma is influenced by hormonal shifts and UV exposure, but its persistence and recurrence are linked to slowed cellular turnover and dysregulated melanogenesis—both hallmarks of senescent skin [10, 11].

Conventional therapies, including topical agents, chemical peels, and energy-based devices, are frequently used to manage these conditions. However, they largely provide symptomatic relief without addressing the underlying

biological dysfunction. Topicals such as retinoids and depigmenting agents require long-term use and often yield inconsistent results [12]. Chemical peels [13–15] and laser treatments may produce more immediate effects but are associated with downtime, irritation, and the risk of rebound pigmentation [16, 17]. Across all categories, sustained improvements are limited, and repeated maintenance is typically required.

In contrast, regenerative therapies aim to restore the skin's intrinsic repair mechanisms by targeting the biological processes disrupted by aging. Among these, exosome-based treatments have emerged as a promising modality. Exosomes are nanoscale extracellular vesicles that facilitate intercellular communication and tissue regeneration. They are rich in growth factors, cytokines, and other bioactive molecules capable of modulating inflammation, stimulating extracellular matrix production, and supporting cellular turnover—making them a rational therapeutic option for reversing age-related skin changes [18, 19].

Exosomes are commonly administered in conjunction with superficial microneedling, a technique increasingly used in dermatologic practice to enhance the transdermal delivery of topically applied products. Superficial microneedling creates transient microchannels in the stratum corneum, allowing for improved penetration into the viable layers of the epidermis and superficial dermis. This approach is preferred over deeper microneedling due to its minimal inflammatory response, reduced risk of complications, and suitability for use in sensitive or pigment-prone skin types [20].

In this study, exosomes were applied topically following superficial microneedling at a standardized depth of 0.3 mm. This depth was selected to optimize delivery to target cells while minimizing dermal injury. The treatment protocol consisted of two sessions only, with no further intervention during the 21-month follow-up period. The study aimed to assess long-term improvements in pore size, erythema, and pigmentation in patients presenting with age-related skin concerns.

MATERIALS AND METHODS

This was a prospective single-subject case study conducted in a clinical setting to assess the long-term clinical efficacy of a topical exosome-based treatment in a healthy female subject presenting with visible signs of skin aging. The subject, in her late 40s, exhibited three primary dermatological features: enlarged pores, erythematotelangiectatic rosacea, and facial hyperpigmentation consistent with melasma. Pore visibility was most pronounced on the nasal, forehead, and malar regions, corresponding to grade 3 on the Quantitative Pore Grading Scale (QPGS), reflecting dilated pilosebaceous units under ambient lighting. Rosacea presented as persistent centrofacial erythema and episodic flushing, with no inflammatory lesions, and was classified as subtype I according to the National Rosacea Society criteria. Facial hyperpigmentation involved bilateral brown macules across the malar and forehead areas, consistent with epidermal-type melasma, with a baseline Melasma Area and Severity Index (MASI) score of 10, indicating moderate severity [21].

Validated clinical scales were used to support outcome evaluation throughout the study, including the Clinician's Erythema Assessment (CEA) [22] for rosacea, the Melasma Area and Severity Index (MASI) [21] for pigmentation, and the Global Aesthetic Improvement Scale (GAIS) [23] for both physician- and patient-reported results.

The subject had no other known dermatologic disease, systemic illness, or recent exposure (within 90 days) to cosmetic procedures such as microneedling, lasers, chemical peels, or injectables. The treatment protocol consisted of two sessions administered on day 1 and day 21, with no additional intervention during the 21-month follow-up period. Clinical progress was monitored at four timepoints: baseline, 3 weeks, 5.5 months, and 21 months.

Microneedling was performed using the Auto-DN Smart device (Skin Care Master by Auto-MTS), which features adjustable speed control from level 1.0 to 6.0 and a maximum of 8700 revolutions per min (RPM) across three operational modes. A

single sterile 42-pin needle cartridge was used per session to cover the entire face.

The topical exosome product used was E-50 Skin Booster (PrimaCure Co., Ltd., Republic of Korea), composed of purified exosomes derived from salmon tissue. The formulation contains bioactive components including signaling proteins, growth factors, and microRNAs known to support tissue regeneration.

A total of 5 mL of exosome solution was used per session. The solution was drawn into a 5 cc Luer lock syringe fitted with a 23-gauge needle and gently dropped onto each treatment zone. The solution was microneedled over each section using the Auto-DN device. No massage or occlusive dressing was applied. Residual product was left on the skin to absorb naturally, with no cleansing or additional topical applied for at least 6 h post-treatment.

Clinical photography was paired with 3D imaging using the QuantifiCare LifeViz® Mini, which provided reproducible high-resolution surface mapping and colorimetric data. These images were further analyzed using an artificial intelligence (AI)-assisted model (ChatGPT) to quantify changes in pore size, erythema, and melanin concentration. ChatGPT (OpenAI, San Francisco, CA) was also used to assist in manuscript writing. This layered methodology enabled objective, image-based tracking of skin response over time, beyond subjective observation.

Safety monitoring was conducted throughout the study period. The subject was regularly assessed for any adverse reactions, including erythema, pruritus, irritation, or delayed hypersensitivity.

Written informed consent was obtained from the subject for treatment, clinical photography, and publication of identifying images and case details.

RESULTS

The subject demonstrated sustained, multidimensional skin improvements following two sessions of topical exosome-based treatment, administered on day 1 and day 21. Clinical photographs revealed visible refinement in

skin texture and tone beginning at the 3-week mark, with continued progression over the next several months. By 3 weeks, a reduction in visible pore size and improved uniformity of the skin's surface were clearly observable, particularly across the cheeks and nose. At 5.5 months, these improvements had deepened further, and remarkably, they persisted at the 21-month follow-up despite no additional treatment after the initial two sessions (Fig. 1).

Quantitative imaging using the QuantifiCare LifeViz® Mini further validated these clinical changes. High-resolution, color-calibrated photos were analyzed using AI-assisted algorithms to evaluate key parameters: pore size, facial redness (erythema), and melanin concentration. Pore size showed a progressive decrease from baseline, with a 22% reduction noted at 3 weeks, increasing to 35% at 5.5 months, and peaking at 41% by 5.5 months. By 21 months, a 38% reduction was maintained, indicating lasting improvement in pilosebaceous unit visibility (Fig. 2). Redness analysis revealed a 27% reduction in erythema at 3 weeks, particularly in the centrofacial zone, with a 42% reduction at 5.5 months and a sustained 35% decrease at 21 months—suggesting stable vascular modulation and resolution of rosacea-related flushing (Fig. 3). Similarly, melanin mapping demonstrated a 19% reduction in hyperpigmentation at 3 weeks, progressing to 31% by 5.5 months and remaining at 29% below baseline at 21 months, indicating durable correction of pigment irregularities associated with melasma (Fig. 4).

In parallel with visual and chromatic improvements, objective surface roughness parameters corroborated the textural changes. Average roughness (Ra) decreased from 0.05 to 0.01, and RMS roughness (Rq) was reduced by more than 50%. Quantitative changes in skin surface topography were confirmed using profilometry (Table 1). Peak-to-valley measurements, including Rmax, Rz, and R3z, all showed marked declines, indicating smoother surface topography. Both maximum peak height (Rp) and valley depth (Rv) also diminished significantly, pointing to a more uniform skin contour with fewer pronounced textural disruptions.



Fig. 1 Pore Size Reduction and Skin Texture Improvement. Standardized clinical photography captured at four timepoints showed progressive tightening of pores and refinement of skin texture. By 3 weeks, pore visibility had

noticeably decreased, particularly on the cheeks and nasal area. These improvements continued at 5.5 months and were maintained at the 21-month follow-up, despite no further treatment



Fig. 2 Rosacea and Redness Reduction. Red fluorescence mapping from the QuantifiCare LifeViz® Mini revealed a visible decrease in facial erythema, particularly across the central cheeks and forehead. A marked improvement was observed by 3 weeks, with further normalization at

5.5 months and long-term vascular stability evident at 21 months. The absence of flushing or rebound redness suggests a sustained modulation of inflammatory vascular responses

Objective surface profilometry using Ra, Rq, Rmax, Rz, R3z, Rp, and Rv values confirmed the subjective improvements seen in photographs and imaging.

Average roughness (Ra) declined from 0.05 at baseline to 0.01 at 21 months, while RMS roughness (Rq) was halved. Max peak-to-valley height (Rmax) dropped from 0.53 to 0.19, and all remaining peak and valley metrics (Rz, R3z, Rp, Rv) showed proportional

improvements—demonstrating substantial smoothing of the skin surface.

These findings align with the visual smoothing seen in topographical overlays and cross-polarized light images.

Importantly, no adverse events were recorded throughout the study. The subject tolerated both sessions without erythema, pruritus, irritation, or delayed hypersensitivity. There were no signs of rebound pigmentation or postinflammatory hyperpigmentation during the 21-month



Fig. 3 Melasma and Hyperpigmentation Improvement. UV-pigment mapping demonstrated gradual fading of melanin deposits consistent with melasma. A reduction in pigmentation was already noticeable at 3 weeks.

By 5.5 months, the hyperpigmented regions had largely resolved, and by 21 months, no rebound pigmentation was observed—indicating persistent correction of pigment dysregulation



Fig. 4 Surface Roughness Improvement. Cross-polarized light imaging paired with topographical overlay showed a steady smoothing of the skin surface. At 3 weeks, early reduction in uneven texture was observed in the forehead

and malar zones. This effect deepened by 5.5 months and remained consistent through the 21-month follow-up, signifying long-term dermal remodeling

follow-up, underscoring the safety and long-term efficacy of the exosome-based protocol administered with superficial microneedling. Together, the clinical, imaging, and topographical data demonstrate that just two sessions of E50 Skin Booster can yield profound and lasting improvements in signs of aging, including pore size, vascular sensitivity, pigmentation, and surface

roughness. Clinical outcome scores using validated scales are presented in Table 2. Progressive changes in MASI and CEA scores were observed at each timepoint, with clear reductions in pigmentation and erythema. Subjective improvements were confirmed using the GAIS scale from both clinician and patient perspectives.

Table 1 Surface roughness parameters at baseline and 21 months

Parameter	Description	Baseline (2022)	Month 21 (2024)
Ra	Average roughness	0.05	0.01
Rq	RMS roughness	0.23	0.11
Rmax	Max peak-to-valley height	0.53	0.19
Rz	Average max height	0.53	0.19
R3z	Top 3 peak-valley average	0.49	0.17
Rp	Max peak height	0.21	0.13
Rv	Max valley depth	0.32	0.06

DISCUSSION

This case study demonstrates that two sessions of topical exosome application following superficial microneedling can produce profound and durable improvements in visible signs of skin aging, including pore size, erythema associated with rosacea, melasma, and overall surface roughness. Notably, clinical improvements were not only observed within weeks, but continued to progress for several months after treatment and were sustained for nearly 2 years without any additional intervention.

The use of a consistent sterile microneedle cartridge and precision delivery via the Auto-DN Smart device helped ensure uniform treatment across sessions, supporting the reproducibility of the protocol.

The findings align with the regenerative paradigm that addresses the biological underpinnings of skin aging rather than merely providing symptomatic correction. The durable tightening of pores suggests a restoration of dermal structural integrity, likely mediated by enhanced extracellular matrix production and improved cellular signaling triggered by exosome-derived growth factors and cytokines. [24] Reduction in facial erythema points toward a normalization of vascular reactivity and inflammation, consistent with the antiinflammatory and immunomodulatory potential of exosomal cargo [25]. Similarly, the progressive fading of melasma without rebound suggests a reprogramming of melanogenic activity, likely through modulation of melanocyte homeostasis and keratinocyte-melanocyte interactions [26].

The use of superficial microneedling at a 0.3 mm depth was critical to the success of the protocol. [27] This depth was sufficient to enhance epidermal and superficial dermal delivery while minimizing unnecessary dermal trauma, inflammation, and the associated risks of pigmentary complications, especially in Fitzpatrick skin types III–V where postinflammatory hyperpigmentation is a significant concern [28].

Objective topographic data reinforced the visual and colorimetric findings. Significant reductions across all roughness parameters (Ra, Rq, Rmax, Rz, R3z, Rp, and Rv) demonstrate tangible remodeling of the skin’s surface architecture. Such smoothing is unlikely to occur through temporary cosmetic effects and strongly suggests biological repair and tissue regeneration at the cellular level [29].

Table 2 Clinical outcome scores over time

Timepoint	MASI score	CEA score	GAIS (clinician)	GAIS (patient)
Baseline	10.0	3.0	Not applicable	Not applicable
Week 3	8.1	2.2	2, Improved	2, Improved
Month 5.5	6.9	1.7	1, Much Improved	1, Much Improved
Month 21	7.1	1.9	1, Much Improved	1, Much Improved

Importantly, the absence of adverse events, including no delayed hypersensitivity, postinflammatory hyperpigmentation, or rebound melasma, [30] underscores the safety and tolerability of this exosome-based approach when applied under a controlled delivery method.

While the results are promising, several limitations must be acknowledged. This study was based on a single-subject design without a placebo or control arm, which limits generalizability. [31] Environmental factors, lifestyle habits, or intrinsic skin cycling could have contributed in part to the observed outcomes, although the magnitude and duration of improvements argue strongly for a true therapeutic effect. Future studies with larger sample sizes, randomized controls, and histological confirmation would further strengthen these preliminary findings. [32]

Nonetheless, the exceptional durability of results following only two sessions suggests that exosome-based therapies, when correctly administered, may fundamentally reset biological dysfunctions associated with aging skin, rather than simply offering temporary cosmetic benefits [33].

CONCLUSIONS

In this case study, two sessions of topical exosome application combined with superficial microneedling resulted in sustained clinical improvements across multiple markers of cutaneous aging, including pore size, rosacea-associated erythema, melasma, and surface texture. Objective imaging and surface profilometry confirmed long-term regenerative effects, maintained for up to 21 months after treatment without additional intervention.

These findings support the use of exosome-based therapies as a biologically driven, low-risk approach for achieving profound and lasting rejuvenation of the aging skin. By targeting fundamental mechanisms of cellular senescence, inflammation, and pigment dysregulation, exosome treatments may offer a new paradigm in esthetic dermatology focused on

true skin restoration rather than symptomatic management.

Further controlled studies are warranted to validate these results and optimize protocols for broader clinical application.

ACKNOWLEDGEMENTS

We thank the participant of the study.

Medical Writing/Editorial Assistance. The author received editorial assistance with English language editing to improve grammar and clarity, as the author is not a native English speaker. This support was limited to language review and did not affect the scientific content of the manuscript.

Author Contributions. The author conceptualized the case design, conducted treatment, supervised data collection, and reviewed the manuscript for critical intellectual content. He approved the final version and is accountable for the integrity of the work.

Funding. No funding or sponsorship was received for this study or publication of this article. The Rapid Service Fee was funded by the authors.

Data Availability. The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of Interest. Young Seob Lee has nothing to disclose.

Ethical Approval. Written informed consent was obtained from the subject for treatment, clinical photography, and publication of identifying images and case details. The study was conducted in accordance with the principles of the Declaration of Helsinki. No formal IRB approval was required as this was a single-subject

case report involving noninvasive treatment within the scope of routine clinical care.

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REFERENCES

- Shin SH, Lee YH, Rho NK, Park KY. Skin aging from mechanisms to interventions: focusing on dermal aging. *Front Physiol.* 2023;14:1195272. <https://doi.org/10.3389/fphys.2023.1195272>.
- Chin T, Lee XE, Ng PY, Lee Y, Dreesen O. The role of cellular senescence in skin aging and age-related skin pathologies. *Front Physiol.* 2023;14:1297637. <https://doi.org/10.3389/fphys.2023.1297637>.
- Rinnerthaler M, Bischof J, Streubel MK, Trost A, Richter K. Oxidative stress in aging human skin. *Biomolecules.* 2015;5(2):545–89. <https://doi.org/10.3390/biom5020545>.
- Childs BG, Durik M, Baker DJ, van Deursen JM. Cellular senescence in aging and age-related disease: from mechanisms to therapy. *Nat Med.* 2015;21(12):1424–35. <https://doi.org/10.1038/nm.4000>.
- Parrado C, Mercado-Saenz S, Perez-Davo A, Gilberte Y, Gonzalez S, Juarranz A. Environmental stressors on skin aging: mechanistic insights. *Front Pharmacol.* 2019;10:759. <https://doi.org/10.3389/fphar.2019.00759>.
- De Tollenaere M, Meunier M, Durduret A, et al. Facial pore refining by targeting dermal and epidermal functions: assessment across age and gender. *J Cosmet Dermatol.* 2024;23(10):3395–408.
- Hameed A, Akhtar N, Khan HMS, Asrar M. Skin sebum and skin elasticity: major influencing factors for facial pores. *J Cosmet Dermatol.* 2019;18(6):1968–74.
- Del Rosso JQ. Advances in understanding and managing rosacea: part 1. *J Clin Aesthet Dermatol.* 2012;5(3):16–25.
- Liu Y, Zhou Y, Chu C, Jiang X. The role of macrophages in rosacea: implications for targeted therapies. *Front Immunol.* 2023;14:1211953.
- Hughes BK, Bishop CL. Current understanding of the role of senescent melanocytes in skin ageing. *Biomedicines.* 2022;10(12):3111. <https://doi.org/10.3390/biomedicines10123111>.
- Kang HY, Lee JW, Papaccio F, Bellei B, Picardo M. Alterations of the pigmentation system in the aging process. *Pigment Cell Melanoma Res.* 2021;34(4):800–13.
- Kafi R, Kwak HSR, Schumacher WE, et al. Improvement of naturally aged skin with vitamin A (retinol). *Arch Dermatol.* 2007;143(5):606–12.
- Măgerusan SE, Hancu G, Mircia E. Considerations on the use of organic substances in chemical peels: a systematic review. *Acta Marisiensis Ser Med.* 2020;66(2):50–55. <https://doi.org/10.2478/amma-2020-0010>.
- Sarkar R, Katoch S. Chemical peels in treatment of melasma. *Dermatol Clin.* 2024;42(1):21–32.
- Jiang X, Li X. Chemical peels for skin rejuvenation. In: *Skin Photoaging*. 2nd ed. IOP Publishing; 2024:6-1
- Kheirieh A, Mahdavi Z, Halvani AM, et al. Energy-based methods and nanocarrier-based approaches for melasma treatment. *Adv Pharm Bull.* 2024;14(4):749.
- Chen A, Choi J, Balazic E, et al. Review of laser and energy-based devices to treat rosacea in skin of color. *J Cosmet Laser Ther.* 2024;26(1–4):43–53.
- Hajjaliasgari Najafabadi A, Soheilifar MH, Masoudi-Khoram N. Exosomes in skin photoaging: biological functions and therapeutic opportunity. *Cell Commun Signal.* 2024;22(1):32. <https://doi.org/10.1186/s12964-023-01451-3>.
- Tienda-Vázquez MA, Hanel JM, Márquez-Arteaga EM, et al. Exosomes: a promising strategy for repair, regeneration and treatment of skin

- disorders. *Cells*. 2023;12(12):1625. <https://doi.org/10.3390/cells12121625>.
20. Nainggolan ADC, Anjani QK, Hartrianti P, et al. Microneedle-mediated transdermal delivery of genetic materials, stem cells, and secretome: an update and progression. *Pharmaceutics*. 2023;15(12):2767. <https://doi.org/10.3390/pharmaceutics15122767>.
 21. Pandya AG, Hynan LS, Bhole R, et al. Reliability assessment and validation of the Melasma Area and Severity Index (MASI) and a new modified MASI scoring method. *J Am Acad Dermatol*. 2011;64(1):78-83.e1-2. <https://doi.org/10.1016/j.jaad.2009.10.051>.
 22. Tan J, Liu H, Leyden JJ, Leoni MJ. Reliability of clinician erythema assessment grading scale. *J Am Acad Dermatol*. 2014;71(4):760-3. <https://doi.org/10.1016/j.jaad.2014.05.044>.
 23. Callan P, Goodman GJ, Carlisle I, et al. Efficacy and safety of a hyaluronic acid filler in subjects treated for correction of midface volume deficiency: a 24-month study. *Clin Cosmet Investig Dermatol*. 2013;6:81-9. <https://doi.org/10.2147/CCID.S40581>.
 24. Weiliang Z, Lili G. Research advances in the application of adipose-derived stem cells derived exosomes in cutaneous wound healing. *Ann Dermatol*. 2021;33(4):309-17. <https://doi.org/10.5021/ad.2021.33.4.309>.
 25. Ha DH, Kim HK, Lee J, et al. Mesenchymal stem/stromal cell-derived exosomes for immunomodulatory therapeutics and skin regeneration. *Cells*. 2020;9(5):1157. <https://doi.org/10.3390/cells9051157>.
 26. Cho BS, Lee J, Won Y, et al. Skin brightening efficacy of exosomes derived from human adipose tissue-derived stem/stromal cells: a prospective, split-face, randomized placebo-controlled study. *Cosmetics*. 2020;7(4):90. <https://doi.org/10.3390/cosmetics7040090>.
 27. Chu S, et al. Safety profile for microneedling: a systematic review. *Dermatol Surg*. 2021;47(9):1249-54.
 28. El-Domyati M, et al. Microneedling in skin of color: a review of uses and efficacy. *J Am Acad Dermatol*. 2015;73(5):849-57.
 29. Zhang Z, et al. Estimation of skin surface roughness in vivo based on optical coherence tomography combined with convolutional neural network. *Front Med*. 2024;11:1453405.
 30. Proietti I, Battilotti C, Svara F, et al. Efficacy and tolerability of a microneedling device plus exosomes for treating melasma. *Appl Sci*. 2024;14:7252. <https://doi.org/10.3390/app14167252>.
 31. Smith JD. Single-case experimental designs: a systematic review of published research and current standards. *Psychol Methods*. 2012;17(4):510-50. <https://doi.org/10.1037/a0029312>.
 32. Walker SG, Carr JE. Generality of findings from single-case designs: it's not all about the "N." *Behav Anal Pract*. 2021;14(4):991-5. <https://doi.org/10.1007/s40617-020-00547-3>.
 33. Wu JY, Wu SN, Zhang LP, et al. Stem cell-derived exosomes: a new method for reversing skin aging. *Tissue Eng Regen Med*. 2022;19(5):961-8. <https://doi.org/10.1007/s13770-022-00461-5>.

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