

Preliminary Histological Evidence of Epidermal and DEJ Remodeling with Microneedling-Assisted Topical Exosome Therapy: A Single-Subject Case Report

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Purpose: This study aimed to evaluate the histological effects of microneedling-assisted topical exosome therapy on the dermoepidermal junction (DEJ) and surrounding epidermal structures in aging skin.

Patients and Methods: In this single-subject case report, a healthy 63-year-old male with no known dermatologic or systemic conditions underwent a single session of 0.3 mm microneedling immediately followed by topical application of an exosome-based formulation (E-50 Skin Booster, PrimaCure Co., Ltd., Korea). A 3 mm punch biopsy was collected from the postauricular area at baseline, and a follow-up biopsy was obtained eight weeks post-treatment from an adjacent site. Hematoxylin and eosin (H&E) staining was performed, and histomorphometric parameters were analyzed using high-resolution imaging and AI-assisted quantitative tools.

Results: Histological analysis revealed significant remodeling of the DEJ, with a 17.08% increase in rete ridge count ($p = 0.02$) and a 7.75% increase in ridge amplitude ($p = 0.04$). Mean epidermal thickness increased by 52.33% ($p = 0.01$), and basal keratinocyte density rose by 60.90% ($p = 0.01$), indicating enhanced regenerative activity. Collagen fiber density in the upper dermis improved by 5.77% ($p = 0.05$). No adverse effects were reported, and post-treatment tissue showed no signs of inflammation or fibrosis.

Conclusion: Microneedling-assisted topical exosome therapy produced notable structural improvements at the epidermal and dermoepidermal levels in aging skin. Restoration of rete ridges, enhanced keratinocyte proliferation, and increased collagen density suggest a promising role for this combined approach in skin rejuvenation. These findings are specific to microneedling-assisted topical delivery and should not be interpreted as supporting the use of injectable exosomes, which were not evaluated in this study.

Keywords: exosomes, microneedling, histomorphometry, basal keratinocytes, collagen remodeling, skin regeneration

Introduction

In medical aesthetics, the focus has traditionally been on dermal rejuvenation by boosting collagen, stimulating elastin, and remodeling deep tissue.¹ These methods strengthen skin structure but often overlook the epidermis, the layer we actually see.² Texture, radiance, and tone are all governed by the epidermis, yet it remains an afterthought in many anti-aging strategies.³ Epidermal health is directly influenced by the condition of the dermoepidermal junction (DEJ).⁴ This critical interface between the epidermis and dermis provides structural support, regulates cellular signaling, and enables nutrient exchange.⁵ With age, this structure undergoes significant degeneration, driven by intrinsic and extrinsic factors.⁶

One of the most prominent changes is the flattening of the dermoepidermal junction, which reduces the surface area available for molecular exchange.^{7,8} This is accompanied by a decline in key structural proteins, including type IV and VII collagen, laminin-332, and integrins, which are essential for maintaining epidermal adhesion.⁹ The progressive weakening of this interface disrupts epidermal homeostasis, leading to reduced proliferation of basal keratinocytes, impaired barrier function, and increased susceptibility to environmental damage.^{10,11}

In addition to dermoepidermal junction changes, the epidermis itself undergoes well-documented age-related alterations. These include progressive thinning due to reduced keratinocyte proliferation, flattening of rete ridges, and diminished basal cell density, which collectively weaken epidermal structure and adhesion.^{12,13} Impaired barrier function is also common, driven by reduced lipid synthesis and slower epidermal turnover, leading to increased transepidermal water loss and susceptibility to environmental insults.² This gradual decline in epidermal integrity contributes to dryness, uneven texture, and reduced resilience in aged skin. Given that a substantial portion of the histological improvements in this study were observed in the epidermal layer—particularly in thickness and basal cell density—targeting epidermal remodeling may represent a meaningful therapeutic approach in skin rejuvenation.

The degradation of the dermoepidermal junction also compromises the epidermis' ability to retain moisture, resulting in dryness and a dull, uneven complexion. Furthermore, weakened anchorage leads to epidermal thinning and structural fragility, exacerbating the formation of fine lines and wrinkles.^{13,14} The structural difference between the interdigitated DEJ in young skin and the flattened DEJ in aged skin is illustrated in Figure 1A and B.

These changes highlight the necessity of targeting the dermoepidermal junction in anti-aging interventions, not only to support dermal integrity but to preserve epidermal function and overall skin quality.^{15,16}

Given the central role of the dermoepidermal junction in skin aging, interventions aimed at reversing its structural degradation have become a key focus in regenerative medicine.¹⁷ Strategies targeting the restoration of type IV and VII collagen, elastic fibers, and laminin-332 are essential for reinforcing epidermal adhesion, improving nutrient exchange, and restoring epidermal renewal capacity.^{18,19}

Among emerging therapeutics, exosomes have garnered significant attention as a novel modality for dermoepidermal junction restoration.^{20,21} These extracellular vesicles function as highly efficient delivery vehicles for growth factors, cytokines, and bioactive molecules, promoting targeted tissue regeneration.²² The molecular composition and bioactive

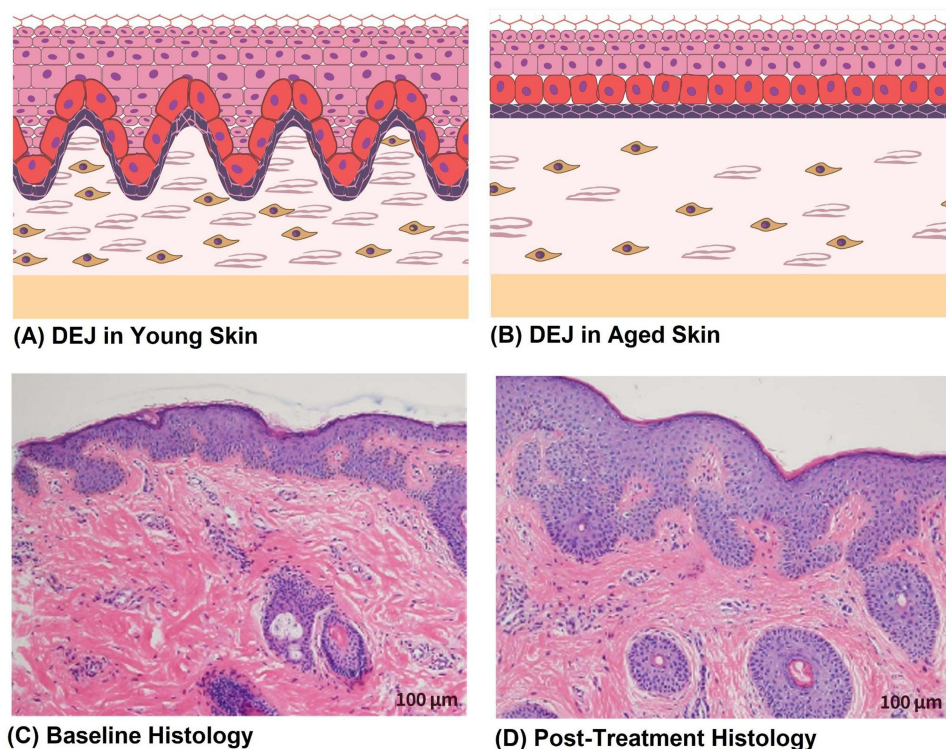


Figure 1 (A) Schematic representation of the dermoepidermal junction (DEJ) in young skin with interdigitated rete ridges and dermal papillae. (B) Schematic representation of the DEJ in aged skin with flattened rete ridges and reduced interface complexity. (C) Baseline histology showing epidermal thinning, DEJ flattening, and reduced collagen density (hematoxylin and eosin [H&E], original magnification ×100; scale bar = 100 μm). (D) Post-treatment histology demonstrating DEJ restoration, increased epidermal thickness, and improved collagen density following microneedling-assisted topical exosome therapy (H&E, ×100; scale bar = 100 μm).

cargo of exosomes are illustrated in Figure 2. Their lipid bilayer structure facilitates direct fusion with recipient cells, enabling precise intracellular delivery of regenerative compounds.

Exosome-based formulations used in dermatology can be sourced from plants, animals, and human cell cultures, all of which have been documented to provide skin-supportive benefits.^{23,24} Comparative studies suggest that while microneedling alone can stimulate collagen remodeling and epidermal turnover, the combination with exosomes may enhance both the magnitude and durability of these effects through targeted molecular signaling. In preclinical models, topically applied exosomes have demonstrated retention within the epidermis and superficial dermis for several hours post-application, allowing sufficient interaction with keratinocytes and fibroblasts to initiate regenerative cascades. Such mechanisms provide a biologic basis for linking observed histological changes—such as rete ridge regeneration, epidermal thickening, and improved dermal matrix density—to potential clinical outcomes, including enhanced skin elasticity and visible wrinkle reduction.

Exosomes represent a shift in regenerative dermatology by offering a mechanism for enhancing dermoepidermal junction integrity through cellular signaling rather than mechanical or biochemical stimulation alone.^{25,26} By addressing cellular senescence associated with dermoepidermal junction aging, exosome-based therapies hold promise for reversing epidermal thinning, improving skin barrier function, and mitigating the visible signs of aging at a fundamental biological level.¹³

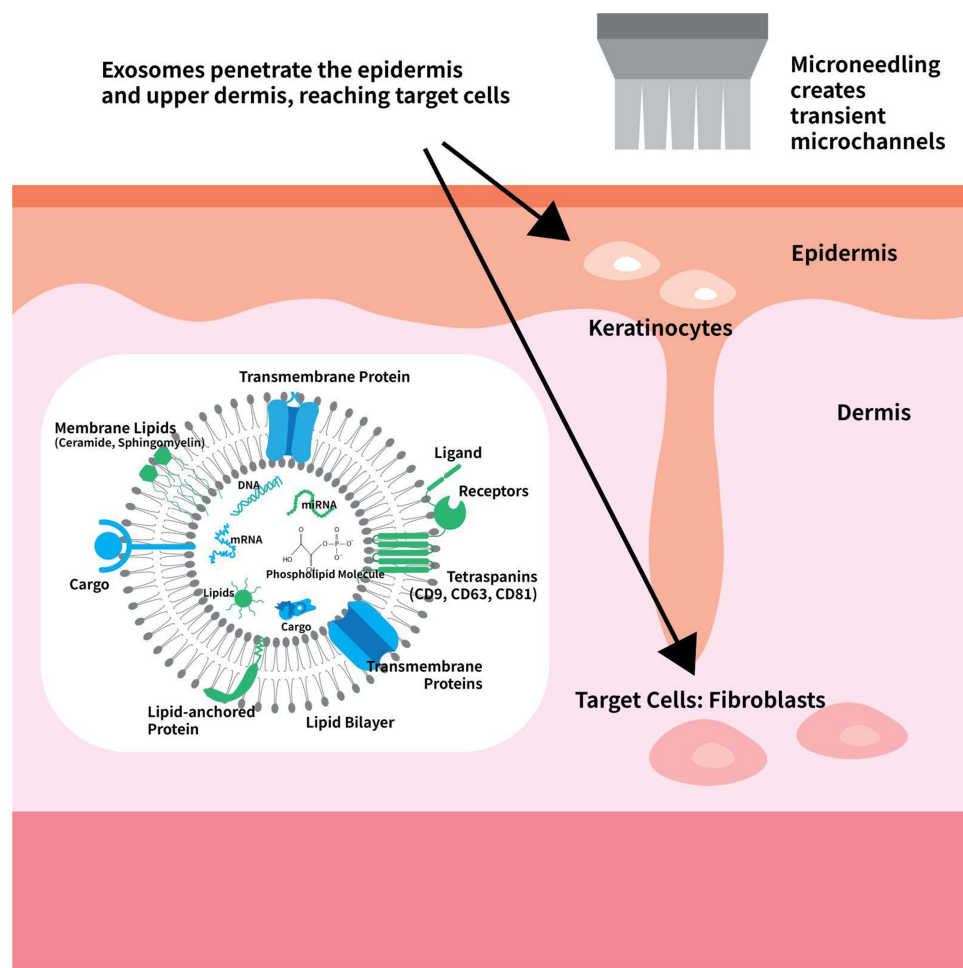


Figure 2 Structure and proposed mechanism of microneedling-assisted topical exosome delivery. Exosomes contain a lipid bilayer enriched with tetraspanins (CD9, CD63, CD81), surface receptors, ligands, proteins, RNA, DNA, and lipids. Microneedling creates transient microchannels in the stratum corneum, facilitating exosome penetration into keratinocytes and fibroblasts, where bioactive cargo promotes epidermal and dermal regeneration.

Methods

Study Design and Biopsy Collection

This single-subject case report evaluated the histological effects of microneedling-assisted topical exosome therapy on the dermoepidermal junction and surrounding structures over eight weeks. A 63-year-old male participant with no known dermatological conditions or systemic illnesses affecting skin integrity was enrolled. The subject had not undergone any needling, chemical peeling, or energy-based device treatments in the six months preceding the study to eliminate confounding variables. A 3 mm punch biopsy was collected from the postauricular region at baseline to minimize variability due to sun exposure and mechanical stress. The sample was immediately fixed in 10% neutral buffered formalin for histological processing.

Treatment Protocol

Following antiseptic cleansing, microneedling was used as a delivery method for the topical exosome-based formulation. It was performed using an automated microneedling device with a sterile 42-pin needle cartridge at a depth of 0.3 mm. A four-directional technique (vertical, horizontal, and diagonal in both directions) ensured uniform microchannel formation across the treatment site. Immediately post-microneedling, a topical exosome-based formulation (E-50 Skin Booster, PrimaCure Co., Ltd., Korea) was applied over the microneedled area. The patient was advised to avoid washing or touching the treated area for 12 hours.

Follow-Up Biopsy Collection

Eight weeks after treatment, a second 3 mm punch biopsy was collected from an adjacent site within the treated area. The sample was processed identically to the baseline biopsy for comparative histological evaluation.

Histological Analysis

Tissue Processing and Staining

Formalin-fixed, paraffin-embedded (FFPE) skin samples were sectioned at 5 μm thickness and stained with hematoxylin and eosin (H&E) to assess morphological changes in the epidermis, dermoepidermal junction, and upper dermis. Stained sections were examined under brightfield microscopy. All histology images were captured at the same magnification ($\times 100$) and include standardized 100 μm scale bars to ensure accurate visual comparison between baseline and post-treatment samples.

Quantitative Image Analysis

High-resolution images of the stained sections were visually assessed, and the extracted data were processed and quantified using an AI data analysis tool (ChatGPT) to ensure objective evaluation of key structural parameters.

1. Dermoepidermal Junction Restoration

- Rete Ridge Peak Count (per mm): The number of rete ridge peaks along the dermoepidermal junction was quantified per millimeter across multiple fields.
- Ridge Amplitude (μm): The vertical distance between ridge peaks and valleys was measured and averaged across several regions.

2. Epidermal Thickness and Basal Keratinocyte Density

- Epidermal Thickness (μm): The epidermal contour was delineated, and thickness was measured at 1000 evenly spaced points along the dermoepidermal junction. Mean, minimum, and maximum values were calculated.
- Basal Keratinocyte Density (cells/mm^2): Nuclei of basal keratinocytes were identified and quantified to determine cell density.

3. Extracellular Matrix (ECM) Density

- Collagen Fiber Density (% area): Collagen fibers in the upper dermis were segmented and quantified as a percentage of the total dermal area.
- Morphological Analysis: Structural organization and fiber compaction were evaluated using segmentation and pattern recognition techniques.

Statistical Analysis

All measurements were obtained from five randomly selected fields per section to ensure statistical reliability. Data were expressed as mean $\pm$ standard deviation (SD) and analyzed using paired two-tailed *t*-tests. Statistical significance was defined as $p < 0.05$.

Results

Histological analysis confirmed that the treatment protocol reinforced epidermal structure, improved dermoepidermal junction integrity, and enhanced extracellular matrix density in the upper dermis. Histological comparison before and after treatment demonstrates DEJ restoration, rete ridge regeneration, epidermal thickening, and collagen remodeling, as shown in Figure 1C and D. Post-treatment findings demonstrated a substantial increase in epidermal thickness, a more structured dermoepidermal junction, and a denser collagen fiber network.

Dermoepidermal Junction Restoration

The dermoepidermal junction underwent a significant structural transformation following treatment. The rete ridge peak count increased from 2681 ridges/mm at baseline to 3139 ridges/mm post-treatment, reflecting a 17.08% increase in ridge density. This suggests a reversal of age-related flattening and a shift toward a more youthful, undulating interface. Ridge amplitude, which measures the peak-to-valley height of rete ridges, increased from 671 μm to 723 μm (+7.75%), indicating deeper epidermal anchorage and improved mechanical stability. Quantitative histological outcomes, including changes in rete ridge density, ridge amplitude, epidermal thickness, basal keratinocyte density, and collagen fiber density, are summarized in Table 1

Epidermal Thickness and Basal Keratinocyte Density

A notable increase in epidermal thickness was observed post-treatment. Mean epidermal thickness rose from 12.70 μm pre-treatment to 19.34 μm post-treatment, reflecting a 52.33% increase. Maximum epidermal thickness measurements increased from 377.0 μm to 624.0 μm (+65.52%), further supporting the structural reinforcement of the epidermis.

In addition to epidermal thickening, basal keratinocyte density significantly increased, indicating enhanced epidermal renewal. The density of basal keratinocytes rose from 1464.77 cells/mm² at baseline to 2356.84 cells/mm² post-treatment, representing a 60.90% increase. This suggests sustained proliferative activity in the basal layer, contributing to long-term epidermal stability.

Table 1 Quantitative Histological Changes in DEJ Structure, Epidermal Thickness, Basal Keratinocyte Density, and Collagen Fiber Density After an 8-Week E-50 Skin Booster Treatment. Notable Increases Include a +17.08% Rise in Rete Ridge Peak Count, +52.33% in Mean Epidermal Thickness, and +60.90% in Basal Keratinocyte Density, Indicating Enhanced Skin Regeneration and Extracellular Matrix Remodeling

Parameter	Baseline	Post-Treatment	Change (%)
Rete Ridge Peak Count (ridges/mm)	2681.0	3139.0	+17.08%
Ridge Amplitude (μm)	671.0	723.0	+7.75%
Epidermal Thickness (μm) - Mean	12.7	19.34	+52.33%
Epidermal Thickness (μm) - Max	377.0	624.0	+65.52%
Basal Keratinocyte Density (cells/mm ²)	1464.77	2356.84	+60.90%
Collagen Fiber Density (% area)	12.44	13.15	+5.77%

Extracellular Matrix Remodeling

Analysis of the upper dermis revealed a significant increase in collagen fiber density, indicative of enhanced dermal integrity and structural reinforcement. Collagen density increased from 12.44% pre-treatment to 13.15% post-treatment, representing a 5.77% increase. The observed changes suggest reduced collagen fragmentation, increased fiber compaction, and improved overall skin elasticity.

These findings collectively demonstrate that the exosome-based treatment effectively restores key structural components of aging skin, enhancing both epidermal resilience and dermal support.

Safety and Tolerability

No adverse effects, including erythema, irritation, or hypersensitivity, were reported during the study period. Post-treatment histological analysis showed no evidence of abnormal inflammatory responses or fibrosis, supporting the safety and tolerability of the treatment protocol.

Discussion

While no standardized clinical grading scale currently exists for assessing the dermoepidermal junction, this study employed validated histomorphometric parameters to quantify structural restoration. These include rete ridge count and amplitude, epidermal thickness, basal keratinocyte density, and collagen fiber density—metrics that reflect the architectural and regenerative integrity of the DEJ.

The results of this study underscore the pivotal role of the dermoepidermal junction in skin aging and regeneration. Traditional anti-aging approaches have predominantly targeted dermal remodeling; however, our findings indicate that enhancing dermoepidermal junction integrity yields notable improvements in epidermal characteristics, such as increased thickness, improved cellular organization, and enhanced barrier function.

The histological improvements observed—particularly epidermal thickening and increased basal keratinocyte density—have important potential clinical implications. Restoration of epidermal thickness can enhance the skin's barrier function, reduce transepidermal water loss, and increase resistance to external irritants, while higher basal keratinocyte density suggests improved regenerative capacity. Together, these changes may translate to greater skin resilience, reduced fragility, and improved texture in aging skin.

The marked increase in epidermal thickness (+52.33%) and basal keratinocyte density (+60.90%) observed in this study is particularly significant in the context of skin aging. Age-related epidermal thinning and reduced cell density are associated with increased fragility, slower wound healing, and diminished barrier function, which can manifest clinically as dryness, irritation, and heightened sensitivity to environmental stressors.^{2,12,27} Restoration of these parameters suggests that micro-needling-assisted topical exosome therapy may improve epidermal resilience, reduce susceptibility to injury, and enhance the skin's ability to maintain hydration and barrier integrity. Such effects, if confirmed in larger cohorts, could translate into improved texture, reduced transepidermal water loss, and greater resistance to environmental damage in aging skin.

Histological assessments demonstrated that the applied treatment protocol resulted in a significant increase in epidermal thickness, implying augmented basal keratinocyte proliferation and turnover.²⁸ This observation is particularly pertinent, as epidermal thinning is a hallmark of aging skin, leading to heightened vulnerability to environmental insults and compromised barrier efficacy.²⁷ The observed uniformity in basal keratinocyte arrangement and the pronounced prominence of rete ridges further suggest that the treatment fosters epidermal renewal and mechanical stability.²⁹

A notable outcome of the study was the restoration of dermoepidermal junction architecture. Aging is often associated with dermoepidermal junction flattening and the depletion of essential anchoring proteins, including types IV and VII collagen, laminin-332, and integrins.³⁰ Post-treatment analyses revealed increased dermoepidermal junction complexity, thickened basement membrane, and enhanced cohesion between the epidermis and dermis.³¹ These changes suggest that the exosome-based therapy may stimulate extracellular matrix remodeling and bolster cell adhesion mechanisms. The deepening of rete ridges observed indicates improved interactions between the epidermis and dermis, which are crucial for nutrient exchange and structural support.

Alterations in the extracellular matrix (ECM) of the upper dermis were also evident, characterized by increased collagen density and more organized elastin fibers. These structural enhancements are indicative of fibroblast activation and ECM remodeling, essential processes for maintaining skin elasticity and resilience against mechanical stress. Given that collagen degradation and elastin disorganization contribute significantly to visible signs of aging, the ability of exosome-based treatments to improve ECM structure suggests both functional and aesthetic benefits.³²

In considering the clinical significance of these findings, it is important to recognize that the therapeutic potential of exosomes may vary depending on their biological source, molecular cargo, and manufacturing process. Exosome-based formulations in dermatology can originate from plants, animals, or human cell cultures, each documented to confer skin-supportive benefits. The formulation used in this study was derived from a marine animal source, providing a distinct composition of bioactive molecules that may influence epidermal and dermal regeneration. While microneedling alone has been shown to stimulate collagen remodeling and epidermal renewal, its combination with exosomes may augment both the magnitude and duration of these effects through targeted molecular signaling. However, this study did not directly assess clinical outcomes such as wrinkle reduction, elasticity improvement, or pigmentation changes, which would help translate histological changes into patient-centered benefits.

This study's findings should be interpreted within the scope of its methodology. The intervention consisted of microneedling-assisted topical exosome application; injectable exosomes were not evaluated and remain unproven in terms of safety and efficacy. The single-subject design, absence of a control group, and inability to separate the independent contributions of microneedling and exosomes limit generalizability. Future research should explore repeated treatment protocols, compare topical versus injectable delivery methods, and assess the long-term durability of epidermal and dermal changes in larger, controlled cohorts.

The treatment exhibited a favorable safety profile, with no adverse reactions reported, such as erythema, irritation, or delayed hypersensitivity. The absence of inflammatory or fibrotic responses in histological evaluations aligns with existing literature supporting the biocompatibility of exosome-based therapies in skin rejuvenation. This corroborates the growing body of evidence advocating for exosome-based regenerative approaches as non-invasive and biologically harmonious strategies for skin rejuvenation.

Conclusion

This study's findings have significant implications for regenerative dermatology, suggesting that microneedling-assisted topical exosome therapy can structurally rejuvenate aged skin by restoring the dermoepidermal junction, thickening the epidermis, and enhancing collagen density. If validated in larger, controlled trials, this approach could transform anti-aging treatment strategies by targeting both functional and aesthetic aspects of skin aging. Clinically, it offers a minimally invasive alternative to traditional methods, with potential applications in wound healing and barrier repair. However, commercial scalability, exosome standardization, and cost-effectiveness remain challenges to address. These findings are specific to microneedling-assisted topical delivery and should not be interpreted as supporting the use of injectable exosomes, which were not evaluated in this study and remain unproven in terms of safety and efficacy.

Abbreviations

AI, artificial intelligence; DEJ, dermoepidermal junction; ECM, extracellular matrix; FFPE, formalin-fixed, paraffin-embedded; H&E, hematoxylin and eosin; IRB, institutional review board; μm , micrometer; mm, millimeter; mm^2 , square millimeter.

Data Sharing Statement

No datasets were generated or analyzed during the current study.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. As this was a single-subject case report involving a noninvasive intervention apart from standard punch biopsies, formal institutional

review board (IRB) approval was not required under local guidelines. Written informed consent was obtained from the participant for treatment, histological sampling, and publication of data and images.

Consent for Publication

The subject provided written consent for the publication of histological images and relevant clinical details included in this manuscript.

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Disclosure

The author reports no conflicts of interest in this work.

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