



Exosomal Liquid Laser (EXOLASER): Development of a Laser-Free Regenerative Skin Remodeling Methodology and Initial Clinical Experience in More Than 500 Patients

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Abstract

Background: Skin resurfacing remains one of the cornerstones of aesthetic dermatology for the treatment of photoaging, dyschromia, acne scarring and overall skin quality. Although ablative and fractional laser technologies provide clinically meaningful outcomes, their use may be associated with prolonged recovery, persistent erythema, post-inflammatory pigmentary alterations, patient discomfort and seasonal limitations. These limitations have prompted interest in regenerative methods that enhance structural remodeling through biological signaling while reducing tissue injury.

Objective: To describe the development, scientific rationale and initial clinical experience of **Exosomal Liquid Laser**, a laser-free regenerative skin remodeling methodology designed to promote tissue regeneration through controlled superficial stimulation and regenerative biological signaling.

Methods: Exosomal Liquid Laser was developed through progressive clinical refinement beginning in 2006 and subsequently standardized in 2021. The methodology combines controlled chemical resurfacing using a microencapsulated priming strategy, ultra-superficial nanochanneling (0.25 mm), neutralization of resurfacing agents and topical application of bovine colostrum-derived secretomes. This manuscript describes the scientific rationale underlying the methodology and summarizes the author's observational clinical experience in more than 500 treated patients, including representative VISIA-documented clinical cases and long-term follow-up.

Results: In the author's clinical experience, clinically meaningful improvement was observed following a single treatment in representative cases, while a treatment series of three or more procedures performed at six- to eight-week intervals produced progressive structural skin remodeling. Standardized clinical photographs and VISIA analyses demonstrated improvements in wrinkle appearance, skin texture, pigmentation, diffuse erythema, post-acne remodeling and overall skin quality. Clinical recovery was typically completed within approximately five days. Among more than 500 treated patients, one transient case of post-inflammatory hyperpigmentation resolved completely within one month. No cases of scarring, infection or prolonged erythema were observed in the author's clinical experience. Longitudinal follow-up suggested continued improvement in selected patients for several months following completion of treatment.

Conclusions: Exosomal Liquid Laser introduces a regenerative treatment philosophy centered on biological signaling optimization with minimal tissue injury. The clinical observations establish a reproducible laser-free regenerative skin remodeling methodology and provide a foundation for future prospective clinical studies evaluating efficacy, biological mechanisms, and long-term structural remodeling using standardized imaging, histological assessment, and controlled comparative investigations.

Keywords: Regenerative Aesthetics; Regenerative Dermatology; Regenerative Skin Remodeling; Laser-Free Skin Resurfacing; Chemical Resurfacing; Nanochanneling; Exosomes; Bovine Colostrum Secretome; VISIA Skin Analysis; Photoaging.

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INTRODUCTION

The Evolving Landscape of Regenerative Skin Remodeling

Skin aging is a multifactorial biological process characterized by progressive deterioration of the epidermis, extracellular matrix (ECM), dermal architecture, vascular function, and skin barrier integrity.[11–20,63,64] Intrinsic aging, cumulative ultraviolet radiation, environmental pollution, oxidative stress, hormonal changes, and chronic low-grade inflammation (“inflammaging”) collectively contribute to collagen degradation, elastin fragmentation, reduced fibroblast activity, impaired extracellular matrix turnover, and diminished regenerative capacity.[11–20,65–69] Clinically, these biological alterations manifest as wrinkles, skin laxity, dyschromia, enlarged pores, diffuse erythema, rough skin texture, reduced elasticity, impaired wound healing, and progressive loss of structural support.[11–20]

As patient expectations evolve, aesthetic medicine has shifted toward regenerative strategies that restore tissue quality and support long-term skin health. Regenerative dermatology now emphasizes restoration of tissue function over isolated correction of visible aging signs. [44–53,70–72]

Current Approaches to Skin Resurfacing

A wide range of technologies has been developed to stimulate skin remodeling, including ablative carbon dioxide (CO₂) laser resurfacing, erbium:YAG laser systems, fractional photothermolysis, radiofrequency microneedling, conventional microneedling, medium-depth chemical peels, and combination resurfacing techniques.[21–28] These modalities have demonstrated clinical efficacy in the management of photoaging, acne scarring, pigmentary disorders, and overall skin rejuvenation.[21–28]

Despite their effectiveness, many resurfacing procedures rely primarily on controlled tissue injury to activate wound-healing pathways and induce collagen and extracellular matrix remodeling.[1–10,21–28] Greater tissue injury may enhance outcomes but can also prolong recovery, increase discomfort, cause persistent erythema, elevate the risk of post-inflammatory pigmentation, and limit options for darker skin phototypes or patients seeking minimal downtime.[21–28]

A Shift toward Regenerative Treatment Philosophy

Recent advances show that successful skin remodeling depends not only on the magnitude of tissue injury but on the signaling network that orchestrates healing.[1–10] Growth factors, extracellular vesicles, cytokines, chemokines, fibroblasts, keratinocytes, immune cells, endothelial cells, and extracellular matrix components interact through coordinated signaling pathways that regulate inflammation, cellular proliferation, angiogenesis, matrix remodeling, and restoration of tissue homeostasis.[7–10,33–53,65–69]

Newer therapeutic approaches therefore seek to optimize the biological environment for regeneration through controlled stimulation, rather than relying on maximal tissue injury. [44–53,70–72]

This paradigm provides a foundation for the development of Exosomal Liquid Laser.

Development of Exosomal Liquid Laser

The methodology described in this manuscript, Exosomal Liquid Laser (**EXOLASER**), is a clinical methodology developed by the author through progressive clinical refinement beginning in 2006. Throughout this manuscript, the term Exosomal Liquid Laser refers exclusively to this standardized treatment methodology and should not be interpreted as laser-assisted exosome delivery.

The methodology originated from a fundamental clinical question:

Can structural skin remodeling comparable to that achieved with established resurfacing procedures be promoted through optimized regenerative biological signaling while minimizing unnecessary tissue injury and reducing patient recovery time?

To explore this, the author progressively developed a standardized methodology integrating controlled chemical resurfacing with a microencapsulated priming strategy, ultra-superficial nanochanneling at a depth of 0.25 mm, neutralization of resurfacing agents, and topical application of a bovine colostrum-derived extracellular vesicle-rich secretome.

Unlike laser-based resurfacing, which primarily induces remodeling through controlled thermal injury,[21–24] EXOLASER was designed to promote regenerative biological signaling while maintaining controlled superficial stimulation, rapid recovery, and high patient tolerability.

Maximize biological regeneration while minimizing unnecessary tissue injury.

Purpose of the Present Study

The purpose of this manuscript is to describe the development, scientific rationale, biological principles, standardized methodology, and initial clinical experience associated with EXOLASER. Rather than attempting to establish definitive comparative efficacy with existing resurfacing technologies, this paper introduces a novel regenerative clinical methodology, summarizes observational clinical experience from more than 500 treated patients, and proposes biologically plausible hypotheses to guide future prospective clinical, mechanistic, and translational research.

HISTORICAL DEVELOPMENT OF THE EXOLASER METHODOLOGY

EXOLASER evolved over nearly two decades of clinical

refinement aimed at improving regenerative skin remodeling while reducing tissue injury and recovery time. The methodology developed through continuous observation and iterative optimization of treatment parameters.

The initial concept originated in 2006, when the author began investigating the possibility of combining chemical resurfacing with microneedling to enhance skin regeneration and improve post-acne scar remodeling. The motivation for this work arose from personal clinical experience. Following an unsuccessful attempt to combine aggressive chemical resurfacing with microneedling, the author experienced a severe facial chemical burn that required several months of recovery.

Rather than abandoning the concept, this experience fundamentally changed the direction of future development. It highlighted that successful regenerative skin remodeling should not depend exclusively on increasing tissue injury, but should instead focus on determining how controlled superficial stimulation could activate endogenous repair mechanisms while preserving tissue integrity. This developmental principle is consistent with contemporary understanding of the importance of coordinated wound-healing signaling and extracellular matrix remodeling. [1–10]

Over the following years, numerous treatment variables were progressively refined, including chemical resurfacing strategies, penetration depth, delivery techniques, treatment sequencing, patient recovery, and long-term clinical outcomes. Particular attention was directed toward identifying the minimum level of tissue stimulation capable of producing clinically meaningful structural remodeling.

A significant milestone occurred in 2015, when the author introduced the original Liquid Laser concept to the international aesthetic community. The methodology combined controlled chemical resurfacing with ultra-superficial microneedling at a depth of approximately 0.25 mm. Clinical observations suggested that limiting penetration to the superficial epidermal compartment improved patient comfort while maintaining clinically meaningful improvements in skin texture, pigmentation, and wrinkle appearance. These observations challenged the assumption that deeper mechanical injury is necessarily required to achieve superior regenerative outcomes. The broader scientific rationale for ultra-superficial channel formation as a delivery strategy is supported by research on microneedle-assisted transdermal delivery.[29–32]

Continued clinical refinement eventually led to the development of a more comprehensive regenerative strategy. Following integration of a microencapsulated chemical priming system and a bovine colostrum-derived extracellular vesicle-rich secretome, the methodology evolved into Exosomal Liquid Laser (EXOLASER) in 2021.

The incorporation of microencapsulated technology represented an important conceptual advance. Rather than relying exclusively on acid penetration, microencapsulated active ingredients including pigment-regulating agents, antioxidants, retinoids, peptides, and additional biologically active compounds—were delivered within controlled-release carriers intended to enhance tissue availability while maintaining a favorable safety profile. Because the exact priming formulation and delivery characteristics are proprietary to the methodology, these statements describe the design rationale rather than comparative evidence established in the present study.

At the same time, the role of mechanical stimulation was deliberately reconsidered. Instead of increasing needle depth, the author adopted ultra-superficial nanochanneling at a depth of 0.25 mm to facilitate topical delivery while minimizing unnecessary tissue injury. Microneedle-based approaches are recognized as capable of transiently increasing epidermal permeability and facilitating transdermal delivery, although the optimal depth and clinical contribution of nanochanneling within EXOLASER require direct investigation.[29–32] In the author's clinical experience, this approach enhanced topical distribution without requiring deeper dermal injury or substantial disruption of tissue integrity.

The final stage of the methodology incorporated topical application of a bovine colostrum-derived extracellular vesicle-rich secretome following complete neutralization of the resurfacing procedure. This sequence was intentionally designed to terminate acid activity before application of the regenerative preparation, based on the hypothesis that separating the chemical activation and regenerative-support phases may help preserve the biological activity of extracellular vesicles and associated signaling components. Extracellular vesicles are involved in intercellular communication and have been investigated for potential roles in wound healing and cutaneous regeneration.[33–49]

Through continued refinement across more than 500 clinical treatments, EXOLASER gradually evolved from a resurfacing procedure into a comprehensive regenerative clinical methodology. Rather than focusing solely on controlled injury, the methodology integrates chemical stimulation, controlled superficial nanochanneling, optimized topical delivery, and regenerative biological support into a standardized treatment sequence.

The objective of regenerative skin remodeling is not to maximize tissue injury, but to maximize the biological response to precisely controlled superficial stimulation.

This principle has guided the subsequent development of the EXOLASER methodology and provides the conceptual foundation for the biological mechanisms discussed in the following sections.

BIOLOGICAL RATIONALE

Biological Rationale for the Development of EXOLASER

As outlined in the Introduction, conventional resurfacing relies on controlled tissue injury as the primary stimulus for remodeling. The biological rationale for EXOLASER rests on the premise that the quality and coordination of post-stimulation signaling may be equally important. [9,10,33–53,67–72] The development of Exosomal Liquid Laser (EXOLASER) originated from a fundamental clinical and biological question:

Can clinically meaningful structural skin remodeling be achieved by optimizing regenerative biological signaling rather than by increasing the magnitude of tissue injury?

This question emerged from the author's clinical observations beginning in 2006, following an unsuccessful attempt to combine aggressive chemical resurfacing with microneedling that resulted in prolonged recovery. Rather than abandoning the concept, this experience shifted the developmental focus toward identifying the minimum degree of controlled superficial stimulation required to activate regenerative processes while preserving tissue integrity and improving patient recovery.

Through continuous clinical refinement over nearly two decades, the author consistently observed that carefully controlled superficial stimulation could produce progressive improvements in skin quality without requiring extensive epidermal or dermal injury. These observations ultimately led to the development of the EXOLASER methodology, which was intentionally designed to optimize biological signaling through a precisely sequenced combination of microencapsulated chemical priming, ultra-superficial nanochanneling (0.25 mm), neutralization of resurfacing agents, and topical application of a bovine colostrum-derived extracellular vesicle-rich secretome.

Within this methodology, each component performs a specific biological function. Chemical priming prepares the tissue for controlled stimulation, nanochanneling transiently enhances topical delivery while minimizing mechanical trauma, neutralization terminates ongoing acid activity before regenerative biologics are introduced, and the bovine colostrum-derived secretome provides a complex biological environment rich in extracellular vesicles and soluble signaling molecules intended to support tissue repair and coordinated regeneration. [33–53]

Unlike conventional resurfacing procedures, in which tissue injury itself represents the principal therapeutic mechanism, EXOLASER proposes a regenerative treatment philosophy centered on optimization of the biological response to controlled superficial stimulation. The methodology

therefore views tissue injury not as the therapeutic objective, but as a carefully regulated biological trigger that initiates regenerative signaling while preserving the structural integrity of healthy tissue.

The central hypothesis underlying the EXOLASER methodology can therefore be summarized as follows:

The long-term quality of skin regeneration may depend less on the magnitude of tissue injury and more on the precision with which regenerative biological signaling is initiated, coordinated, and supported throughout the healing process.

Why Microencapsulated Chemical Priming?

A defining characteristic of the EXOLASER methodology is the use of microencapsulated chemical priming before ultra-superficial nanochanneling. The methodology employs chemical priming as the initial step in preparing the biological environment for subsequent regenerative stimulation. [21–24]

The rationale for this approach originated from long-term clinical observations demonstrating that the sequence of treatment components is as important as the individual components themselves. Rather than applying regenerative biologics directly onto untreated skin or relying solely on deeper mechanical penetration, the methodology first establishes a controlled biochemical environment intended to optimize the skin's regenerative response.

The priming formulation is based on a carboxymethylcellulose (CMC) vehicle containing multiple microencapsulated bioactive ingredients. Although the precise formulation may vary according to individual clinical indications, the microencapsulation strategy enables gradual release of biologically active compounds while facilitating more uniform distribution across the treated surface. Microencapsulation has been widely investigated as a controlled-delivery strategy capable of improving stability, regulating release kinetics, and enhancing local bioavailability of active compounds. [21–24]

The author hypothesizes that this initial priming phase serves several complementary biological functions.

First, the CMC-based formulation creates a homogeneous protective interface over the epidermal surface before the introduction of trichloroacetic acid (TCA). In the author's clinical experience, this controlled priming contributes to a more predictable resurfacing response while reducing unnecessary focal tissue injury.

Second, microencapsulation enables simultaneous delivery of multiple biologically active ingredients, including pigment-regulating agents, antioxidants, peptides, retinoids, and additional regenerative compounds. Rather than producing rapid diffusion immediately after application, the encapsulated delivery system is intended to provide

gradual release within the superficial skin layers, potentially extending biological activity beyond the initial treatment procedure. [21–24]

Third, the subsequent combination of the priming formulation with TCA creates a controlled resurfacing environment in which the effective concentration of free acid is substantially reduced while maintaining sufficient biological stimulation to initiate epidermal renewal. Within the standardized EXOLASER protocol, the approximate one-to-one mixture of the priming formulation and 35% TCA produces an effective working concentration below the original TCA concentration while preserving the desired clinical response.

The objective of chemical priming is not to maximize acid penetration but to establish a favorable biological environment before nanochanneling, distinguishing the approach from conventional peeling strategies.[21–24]

Based on the author's long-term clinical observations, this staged approach may contribute to improved patient comfort, rapid recovery, and consistent clinical outcomes while reducing the likelihood of excessive inflammatory responses. Although the precise molecular mechanisms remain to be elucidated, the observed clinical behavior supports the hypothesis that controlled biochemical preparation of the skin may influence the quality of subsequent regenerative signaling.

Within the overall EXOLASER methodology, microencapsulated chemical priming should therefore be viewed not simply as a peeling step but as the biological foundation upon which the remaining phases of the regenerative protocol are built. By preparing the tissue before mechanical stimulation and regenerative biologic application, this stage establishes the conditions necessary for the coordinated sequence of events that follows.

Why Ultra-Superficial Nanochanneling?

Ultra-superficial nanochanneling represents one of the defining technical characteristics of the EXOLASER methodology. In contrast to conventional microneedling protocols, which frequently employ penetration depths ranging from 0.5 mm to more than 2.0 mm depending on the anatomical region and clinical indication, the EXOLASER methodology standardizes mechanical stimulation at an approximate depth of 0.25 mm. [25–32]

This depth emerged from extended clinical refinement aimed at identifying the minimum mechanical stimulation needed to facilitate regenerative signaling with acceptable recovery.

Conventional microneedling has been extensively investigated as a method for stimulating collagen production through controlled mechanical injury. In addition to initiating wound-healing responses, microneedles create transient microchannels that increase epidermal permeability and enhance transdermal delivery of topically applied

compounds. [25–32] The extent of biological response depends on multiple factors, including needle depth, density, treatment pattern, and the biological characteristics of the applied therapeutic agents. [25–32]

Within the EXOLASER methodology, however, nanochanneling serves a fundamentally different purpose. Rather than maximizing collagen induction through deeper dermal injury, ultra-superficial nanochanneling is intended primarily to facilitate uniform distribution of regenerative biologics following controlled chemical priming while preserving the structural integrity of the deeper dermis.

The author hypothesizes that limiting penetration to approximately 0.25 mm provides several potential biological advantages.

First, superficial nanochannels temporarily increase epidermal permeability, allowing improved contact between the topically applied bovine colostrum-derived secretome and the biologically active superficial skin layers without creating extensive mechanical disruption. [29–32]

Second, because penetration remains confined to the superficial epidermal compartment, tissue trauma is substantially reduced compared with conventional microneedling protocols employing greater needle depths. In the author's clinical experience, this contributes to rapid recovery, minimal discomfort, and a favorable safety profile.

Third, minimizing unnecessary mechanical injury may reduce excessive inflammatory signaling while preserving the coordinated regenerative environment established during the preceding chemical priming phase. Rather than functioning as an independent collagen-induction procedure, nanochanneling within the EXOLASER methodology acts as a controlled delivery platform integrated into a sequential regenerative protocol.

The selection of a 0.25-mm penetration depth therefore reflects the central biological philosophy of EXOLASER: **the objective is not to maximize tissue injury, but to maximize the biological response to precisely controlled superficial stimulation.**

Clinical observations accumulated over more than 500 treatments suggest that this ultra-superficial approach is capable of producing progressive improvements in skin texture, pigmentation, wrinkle appearance, and overall skin quality while maintaining a relatively short recovery period. Although the specific mechanisms responsible for these observations require further investigation, the findings support the hypothesis that deeper mechanical injury may not always be necessary to achieve clinically meaningful regenerative remodeling.

Within the EXOLASER methodology, nanochanneling functions as an integrated delivery strategy rather than a standalone collagen-induction procedure.[29–32]

Why Neutralization before Regenerative Biologic Application?

An essential component of the EXOLASER methodology is the complete neutralization of the resurfacing procedure before application of the bovine colostrum-derived extracellular vesicle-rich secretome. Beyond terminating acid activity, neutralization in EXOLASER intentionally separates the stimulation phase from the regenerative support phase. [21–24]

The rationale for this sequence originated from the author's progressive clinical refinement of the protocol. Early clinical observations suggested that regenerative biologics should not be applied while residual chemical activity remains present on the skin surface. Consequently, complete neutralization became an integral component of the standardized methodology before introduction of the secretome preparation.

The author hypothesizes that this sequence may provide several biological advantages.

First, neutralization terminates ongoing acid activity, thereby limiting continued chemical injury and establishing a more physiologically favorable environment before application of regenerative biologics. [21–24]

Second, separating the resurfacing phase from the regenerative phase may help preserve the biological integrity of extracellular vesicles and associated soluble signaling molecules contained within the bovine colostrum-derived secretome. Extracellular vesicles participate in intercellular communication through complex membrane-associated structures and biologically active cargo, and maintenance of their structural integrity is considered important for their biological function. [33–40,50–53]

Third, completion of the chemical stimulation phase before regenerative biologic application allows each stage of the protocol to perform a distinct biological role. Within the EXOLASER methodology, controlled chemical resurfacing serves as the initiating stimulus, whereas the subsequent secretome application is intended to support the coordinated regenerative processes activated by that stimulation rather than contribute additional chemical injury.

This sequence coordinates interventions in a biologically logical order: each phase prepares the tissue for the next, creating a sequential regenerative environment.

From a clinical perspective, the author has consistently observed favorable recovery following implementation of this staged protocol. Although the specific molecular mechanisms underlying these observations remain to be established, the clinical experience accumulated during development of the methodology supports the hypothesis that complete neutralization before regenerative biologic application contributes to the reproducibility, safety, and favorable recovery profile observed with EXOLASER.

Neutralization thus represents a biological transition between controlled stimulation and regenerative support. [33–53]

Biological Role of the Bovine Colostrum-Derived Secretome in Regenerative Skin Repair

The final biological component of the EXOLASER methodology is the topical application of a **bovine colostrum-derived extracellular vesicle-rich secretome** following completion of chemical resurfacing, ultra-superficial nanochanneling, and complete neutralization. Unlike conventional resurfacing procedures, in which tissue remodeling depends primarily on the endogenous wound-healing response, EXOLASER incorporates a regenerative biologic during the early post-stimulation period to support physiological tissue repair signaling. [33–53]

The bovine colostrum-derived secretome selected for the EXOLASER methodology (Purasomes®, Dermoaroma, Italy) was chosen because, according to the manufacturer's technical documentation, each 5-mL vial contains approximately 20 billion extracellular vesicles (reported as exosomes), a standardized complex of 20 growth factors (200 mg), 70 mg of polynucleotides, amino acids, vitamins, minerals, cytokines, and additional low-molecular-weight regenerative mediators. [80] This biologically active composition was considered particularly suitable for supporting regenerative signaling following controlled superficial stimulation.

Extracellular vesicles are increasingly recognized as important mediators of intercellular communication. Rather than functioning as living cells, they transport biologically active molecules between neighboring cells and may influence inflammation, angiogenesis, extracellular matrix remodeling, fibroblast activity, keratinocyte proliferation, and tissue regeneration. Growing experimental and clinical evidence suggests that extracellular vesicle-based therapies may represent an important direction in regenerative medicine and cutaneous repair. [33–53]

Growth factors contained within regenerative secretomes play complementary roles in coordinating tissue repair. They regulate multiple biological processes, including cellular proliferation, migration, angiogenesis, extracellular matrix synthesis, and remodeling of damaged tissue. Similarly, cytokines and other soluble signaling molecules contribute to the complex communication network that orchestrates the sequential phases of wound healing. [9,10,33–53]

In addition to extracellular vesicles and growth factors, the selected secretome contains polynucleotides, which have attracted increasing interest in regenerative dermatology because of their potential role in supporting tissue repair, fibroblast activity, dermal hydration, and extracellular matrix homeostasis. Although the precise contribution of polynucleotides within combination regenerative protocols has not yet been fully elucidated, they may provide additional

biological support during the regenerative phase following controlled superficial stimulation. [73–78]

The formulation also provides amino acids, vitamins, minerals, and additional low-molecular-weight biologically active mediators that may contribute to maintaining a favorable biochemical environment during tissue repair. Because these components are delivered simultaneously within a standardized secretome preparation, the methodology is intended to support multiple regenerative signaling pathways rather than relying on a single isolated biological mechanism. [50–53,80]

An additional biological consideration underlying the EXOLASER methodology involves the potential contribution of **dermal white adipose tissue (DWAT)** to regenerative skin remodeling. Increasing evidence indicates that DWAT functions as an active biological compartment involved in wound healing, immune regulation, extracellular matrix homeostasis, hair follicle biology, and communication with dermal fibroblasts. Rather than serving solely as an energy reservoir, dermal adipocytes participate in complex signaling processes that influence tissue repair and skin homeostasis. [54–62]

Based on the author's clinical observations, one proposed mechanism underlying the sustained improvement observed following EXOLASER is that optimization of the regenerative microenvironment may extend beyond the epidermis and superficial dermis to influence deeper structural compartments involved in long-term tissue remodeling. Although this hypothesis remains to be confirmed through histological and molecular investigations, the prolonged improvements observed in skin quality, elasticity, facial contour, and objective imaging suggest that regenerative remodeling may continue long after complete epidermal recovery.

Importantly, the EXOLASER methodology does not rely on the secretome as an isolated therapeutic intervention. Instead, the regenerative biologic represents the final phase of a carefully coordinated sequence that includes controlled chemical priming, ultra-superficial nanochanneling, complete neutralization, and optimized topical delivery. The author hypothesizes that the biological activity of the secretome is enhanced by this sequential treatment design, in which each preceding step prepares the tissue for the next phase of regeneration.

Accordingly, within the EXOLASER methodology, the bovine colostrum-derived secretome should be viewed not simply as a topical product but as an integral component of a comprehensive regenerative strategy designed to optimize biological signaling during the early phases of tissue repair. While the individual contribution of each component requires further investigation, the overall treatment philosophy is based on the hypothesis that coordinated modulation of

the regenerative environment may produce more sustained structural remodeling than reliance on controlled tissue injury alone. [33–53,54–62]

Proposed Biological Cascade of Regenerative Remodeling

The EXOLASER methodology integrates multiple treatment phases to establish and maintain a favorable regenerative microenvironment, rather than relying solely on tissue injury. [1–10,33–53]

The proposed biological cascade begins with **microencapsulated chemical priming**, which prepares the skin through controlled superficial stimulation while creating a more uniform biochemical environment for the subsequent stages of treatment. Rather than functioning solely as a conventional chemical peel, this phase initiates the regenerative process while minimizing excessive tissue disruption. [21–24]

The second phase consists of **ultra-superficial nanochanneling (0.25 mm)**, which transiently increases epidermal permeability and facilitates homogeneous distribution of the regenerative biologic across the treated surface. Because the penetration depth remains limited to the superficial epidermal compartment, unnecessary mechanical injury is minimized while topical delivery is enhanced. [25–32]

Following completion of the resurfacing phase, **complete neutralization** terminates ongoing acid activity before introduction of the regenerative biologic. This transition intentionally separates controlled chemical stimulation from regenerative support, creating conditions that may better preserve the biological activity of extracellular vesicles and associated signaling molecules. [21–24,33–53]

The final therapeutic phase involves topical application of the **bovine colostrum-derived extracellular vesicle-rich secretome**, which provides a complex network of extracellular vesicles, growth factors, cytokines, polynucleotides, amino acids, vitamins, minerals, and additional biologically active mediators intended to support the physiological processes of tissue repair. [33–53,73–80]

Based on the author's clinical observations, these sequential treatment stages may collectively promote a coordinated regenerative response involving several interconnected biological processes. The proposed cascade includes modulation of the early inflammatory response, restoration of skin barrier function, activation of fibroblasts, stimulation of extracellular matrix remodeling, angiogenic support, improvement of epidermal renewal, and progressive restoration of overall tissue homeostasis. [1–10,9,10,33–53,63–69]

An additional component of the proposed biological model is the potential participation of **dermal white adipose tissue**

(DWAT). Contemporary research has demonstrated that dermal adipocytes actively participate in wound healing, extracellular matrix regulation, immune responses, and communication with dermal fibroblasts. [54–62] Based on the sustained clinical improvements observed following EXOLASER, the author hypothesizes that optimization of the regenerative microenvironment may extend beyond superficial epidermal repair and contribute to progressive remodeling within deeper structural compartments, including the dermis and DWAT. This hypothesis remains speculative and requires confirmation through future histological, molecular, and mechanistic investigations.

Importantly, the proposed biological cascade should be regarded as a working mechanistic model derived from current understanding of wound healing biology, regenerative medicine, extracellular vesicle research, and the author's long-term clinical observations. Although each individual component is supported by established biological principles, the integrated sequence proposed for EXOLASER has not yet been directly validated through mechanistic experimental studies. Accordingly, the cascade presented here should be interpreted as a biologically plausible framework intended to guide future translational research rather than as definitive proof of mechanism.

Within this conceptual framework, EXOLASER represents a shift from an injury-centered model of skin resurfacing toward a **regeneration-centered treatment philosophy**, in which carefully controlled superficial stimulation is used to initiate endogenous repair mechanisms while subsequent treatment phases are designed to optimize the biological environment supporting tissue regeneration. The author hypothesizes that this coordinated sequence may contribute to the sustained clinical improvements observed in skin quality, texture, pigmentation, elasticity, and overall structural remodeling following treatment. [1–10,33–53,54–69]

Clinical Translation of the Proposed Regenerative Concept

The biological principles described above provide the theoretical framework for the EXOLASER methodology. However, the clinical relevance of any proposed regenerative mechanism ultimately depends on reproducible patient outcomes, objective assessment, long-term follow-up, and a favorable safety profile. The clinical observations presented in this manuscript therefore serve as the practical translation of the proposed biological concept into routine aesthetic practice.

Between 2006 and the preparation of this manuscript, the EXOLASER methodology was progressively refined through continuous clinical application and standardized treatment protocols. Since introduction of the current protocol in 2021, more than **500 patients** have undergone treatment in clinical practice. The majority were treated for facial photoaging,

skin laxity, fine wrinkles, dyschromia, enlarged pores, diffuse erythema, post-inflammatory pigmentation, acne scarring, and overall deterioration of skin quality. Clinical observations presented in this manuscript are derived from this cumulative experience.

Unlike conventional resurfacing procedures that frequently require prolonged recovery, the standardized EXOLASER protocol was designed to achieve clinically meaningful regenerative remodeling while maintaining a relatively short recovery period. In the majority of treated patients, visible re-epithelialization occurred within approximately **5–6 days**, although individual recovery varied according to baseline skin condition, treatment intensity, and patient-specific biological factors. In selected patients with more advanced photodamage or impaired regenerative capacity, complete epidermal renewal required an additional **2–3 days**, while maintaining an overall favorable healing profile.

Clinical improvement was evaluated using a combination of standardized photography, serial **VISIA® Complexion Analysis System** examinations, and longitudinal clinical follow-up. Objective assessment included wrinkle analysis, pigmentation, pore characteristics, skin texture, erythema, ultraviolet damage, porphyrins, brown spots, red areas, and **TruSkin Age®** estimation, providing reproducible documentation of structural skin changes over time. [79]

Across the representative clinical cases presented in this manuscript, objective imaging consistently demonstrated progressive improvement in multiple skin-quality parameters following treatment. These findings included reductions in wrinkle severity, improvement in overall skin texture, decreased pigmentation irregularities, reduction in diffuse erythema, normalization of pore appearance, and improvement in estimated TruSkin Age®. Particularly noteworthy was the observation that several patients continued to demonstrate progressive structural improvement for many months after completion of treatment, despite the absence of additional procedures during the observation period. Although the biological mechanisms responsible for these sustained improvements remain to be fully elucidated, these longitudinal observations support the hypothesis that regenerative remodeling may continue well beyond complete epidermal recovery.

One of the most notable clinical observations throughout the development of the methodology has been the apparent dissociation between the degree of visible tissue injury and the magnitude of subsequent clinical improvement. In numerous patients, substantial long-term improvement in skin quality was observed despite relatively rapid recovery and limited visible post-procedural inflammation. These observations support the central hypothesis of the EXOLASER methodology: that optimization of regenerative biological signaling may play a more important role in long-term tissue remodeling than the magnitude of tissue injury itself.

The safety profile observed throughout the author's clinical experience has also been favorable. No permanent scarring, persistent infection, or long-term adverse tissue remodeling attributable to the standardized EXOLASER protocol was observed within the clinical cohort described in this manuscript. The most frequently encountered treatment response consisted of expected transient erythema and controlled superficial exfoliation during the normal recovery period. Isolated cases of prolonged desquamation and a single case of post-inflammatory hyperpigmentation resolved with conservative management, without permanent sequelae. These findings are discussed in greater detail in the Results section.

Importantly, the clinical observations presented in this manuscript should be interpreted within the context of an observational case series rather than a controlled comparative clinical trial. The absence of randomization, untreated controls, histological confirmation, and standardized mechanistic investigations limits definitive conclusions regarding the precise biological mechanisms responsible for the observed clinical outcomes. Nevertheless, the combination of objective imaging, long-term follow-up, standardized treatment methodology, and consistent clinical observations across a large cumulative patient population provides a strong foundation for future prospective clinical trials and translational research.

Collectively, these clinical observations demonstrate that the proposed regenerative treatment philosophy underlying EXOLASER is not only biologically plausible but also clinically applicable. While additional mechanistic studies are required to validate the proposed biological cascade, the clinical experience accumulated to date supports continued investigation of regenerative strategies that prioritize optimization of biological signaling rather than progressive escalation of tissue injury. [1–10,33–53,79]

CLINICAL EVALUATION OF THE EXOLASER METHODOLOGY

Study Design and Patient Population

This manuscript presents the methodological development and initial clinical experience with the EXOLASER methodology, a regenerative skin remodeling protocol progressively refined by the author and standardized in 2021.

A retrospective observational analysis was performed on more than **500 consecutive patients** treated in routine clinical practice for various aesthetic indications, including photoaging, wrinkles, skin laxity, dyschromia, post-acne scarring, enlarged pores, and overall skin rejuvenation. Patients ranged in age from **15 to 78 years**, with the majority representing **Fitzpatrick skin phototypes I–IV**.

The primary objective of this study was to describe the

standardized EXOLASER methodology, evaluate its safety profile, and present representative clinical outcomes supported by standardized photography, **VISIA® Complexion Analysis System** evaluation, and long-term clinical follow-up. [79]

EXOLASER Treatment Protocol

The following protocol represents the **standardized EXOLASER methodology** used throughout the clinical observations presented in this manuscript. All treatments were performed according to the same sequential protocol described below.

The EXOLASER methodology is performed as a standardized **five-phase sequence** designed to prepare the skin, establish controlled chemical activation, enhance superficial delivery through nanochanneling, terminate acid activity, and support regenerative signaling. The sequence of these phases is considered a fundamental component of the methodology and reflects the biological rationale described in the preceding section.

Phase I – Biological Priming

Following cleansing and pre-peeling preparation, a proprietary **microencapsulated carboxymethylcellulose (CMC)-based priming formulation** containing multiple biologically active compounds was applied uniformly to the treatment area. [21–24]

The formulation was actively massaged into the skin to establish homogeneous surface coverage and prepare the epidermis for the subsequent controlled resurfacing phase. This initial priming step was performed **without** the TCA-containing boost formulation.

Phase II – Priming-Boost Chemical Activation

After completion of biological priming, the same CMC-based priming formulation was freshly combined with a TCA-containing boost formulation in an approximately **1:1 ratio**. [21–24]

The resulting mixture was applied as the first layer of a standardized **sandwich technique**. This phase was intended to provide controlled superficial chemical stimulation within the biologically prepared tissue environment while minimizing unnecessary tissue injury.

Phase III – Nanochanneling-Assisted Sandwich Completion

Immediately after application of the first priming-boost layer, **ultra-superficial nanochanneling** was performed at a standardized depth of **0.25 mm** using a sterile single-use roller device. [25–32]

Nanochanneling was performed sequentially across the treatment area to create a high density of transient superficial

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channels while avoiding significant dermal trauma or bleeding. Residual formulation present on the skin was gently incorporated during treatment to facilitate uniform distribution and topical delivery. [29–32]

After completion of nanochanneling, the remaining priming–boost mixture was applied as the second layer of the sandwich technique and actively massaged into the treated skin. This sequence - **first chemical layer, ultra-superficial nanochanneling, followed by the second chemical layer** represents a defining technical component of the standardized EXOLASER methodology.

The treatment endpoint was assessed clinically according to the standardized protocol before proceeding to neutralization.

Phase IV – Neutralization

Following completion of controlled chemical activation and nanochanneling, residual acid activity was terminated using a standardized neutralization procedure. The treated skin was subsequently cleansed until patient discomfort had resolved and no clinically significant burning sensation remained. [21–24]

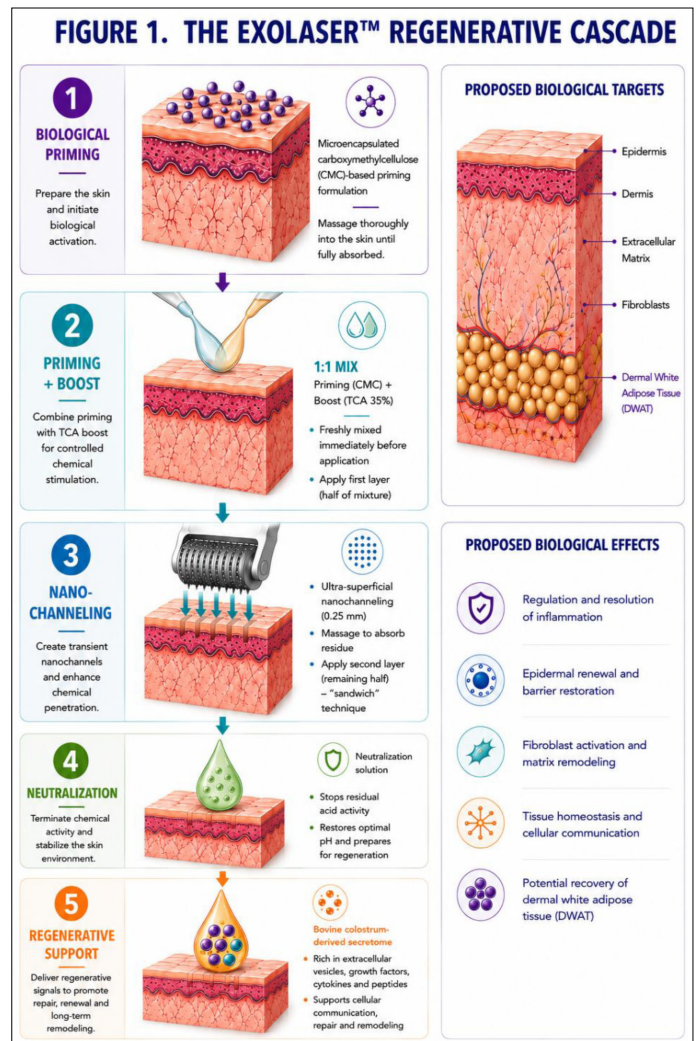
Neutralization established the transition from the resurfacing phase to the regenerative phase and was completed before application of the regenerative biologic. This sequence was intentionally designed to separate controlled chemical stimulation from subsequent regenerative support. [33–53]

Phase V – Regenerative Support

Immediately after neutralization, a **bovine colostrum-derived extracellular vesicle-rich secretome** (Purasomes®, Dermoaroma, Italy) was applied uniformly to the treated skin according to the standardized EXOLASER protocol. According to the manufacturer's technical documentation, the preparation contains extracellular vesicles (reported as approximately 20 billion exosomes), a standardized complex of 20 growth factors (200 mg), 70 mg of polynucleotides, amino acids, vitamins, minerals, cytokines, and additional biologically active regenerative mediators. [33–53,73–80]

All patients received standardized post-treatment instructions together with a regenerative home-care regimen intended to support epidermal barrier recovery and physiological healing during the early post-treatment period. [63,64]

Although individual treatment parameters may be modified according to patient characteristics and specific clinical indications, **preservation of the treatment sequence represents a fundamental principle of the EXOLASER methodology**, ensuring that each biological phase is performed under conditions intended to optimize the subsequent regenerative response.



CLINICAL OUTCOMES AND RESULTS

Patient Population and Clinical Experience

Since its introduction in 2021, the standardized **EXOLASER (Exosomal Liquid Laser)** methodology has been applied in more than **500 patients** across multiple international clinical settings as part of routine aesthetic practice. The present manuscript summarizes the author's initial clinical experience with the standardized methodology and presents representative clinical outcomes supported by objective skin imaging and long-term clinical follow-up.

The standardized EXOLASER methodology evolved from the previously developed **Liquid Laser** protocol following incorporation of a **bovine colostrum-derived extracellular vesicle-rich secretome** in 2021. The methodology was subsequently implemented in routine clinical practice across multiple international locations while maintaining the same standardized biological treatment sequence described in this manuscript.

Patients ranged in age from **15 to 78 years**, with the majority representing **Fitzpatrick skin phototypes I–IV**. Approximately **80%** of treated patients were female and **20%** were male. The most common clinical indications included facial photoaging, fine and moderate wrinkles,

diffuse erythema, dyschromia, enlarged pores, post-acne skin remodeling, and overall improvement of skin quality.

Most patients underwent treatment of the face, while selected cases also included the neck and décolletage according to individual clinical indications. Although visible clinical improvement was frequently observed after a single treatment session, a treatment course consisting of **three or more sessions** performed at **6- to 8-week intervals** was generally recommended to maximize progressive regenerative remodeling.

Clinical outcomes were documented using standardized clinical photography, objective skin analysis with the **VISIA® Complexion Analysis System** whenever available, physician assessment, and longitudinal clinical follow-up extending up to **24 months** in selected patients. [79]

Representative clinical cases presented in this manuscript were selected to illustrate the spectrum of clinical applications of the EXOLASER methodology, including facial rejuvenation, post-acne remodeling, improvement of dyschromia, reduction of diffuse facial erythema, and long-term structural skin remodeling. Together, these representative cases demonstrate both the early clinical response and the progressive regenerative changes observed during extended follow-up.

Safety and Recovery

The standardized **EXOLASER** methodology was generally well tolerated throughout the author's clinical experience. Treatment-related skin responses consisted primarily of transient erythema followed by controlled superficial exfoliation, representing the expected physiological healing

response after controlled superficial chemical activation and ultra-superficial nanochanneling. [1–10,21–32]

The typical recovery period was approximately **5–6 days**, during which progressive resolution of erythema and superficial desquamation was observed. Most patients were able to resume normal daily and professional activities shortly after treatment, with complete restoration of the epidermal barrier generally occurring during the first week of healing. [1–10,63,64]

Among more than **500 patients** treated with the standardized EXOLASER methodology, **no cases of permanent scarring, infection, prolonged erythema, or delayed wound healing** were observed during routine clinical follow-up.

One patient developed **transient post-inflammatory hyperpigmentation**, which resolved completely within **one month** following conservative management. Five patients experienced superficial exfoliation lasting **2–3 days longer** than the typical recovery period. No permanent adverse skin changes were documented.

Overall, the favorable safety profile observed throughout the author's clinical experience supports the concept that **controlled superficial biological activation**, when combined with a standardized regenerative support protocol, may provide effective skin remodeling while minimizing the complications commonly associated with more aggressive resurfacing procedures. Although the present study was not designed to directly compare safety outcomes with other resurfacing modalities, the consistently favorable recovery profile observed across the clinical cohort supports further prospective investigation of this regenerative treatment approach. [1–10,21–32]

Table 1. Summary of Safety Outcomes Following EXOLASER Treatment

Parameter	Clinical Observation
Total treated patients	>500
Typical recovery period	Approximately 5–6 days
Initial response	Transient erythema
Expected healing	Mild superficial exfoliation
Infection	None observed
Permanent scarring	None observed
Prolonged erythema	None observed
Delayed wound healing	None observed
Post-inflammatory hyperpigmentation	One transient case; resolved within one month
Extended exfoliation	Five patients (additional 2–3 days)

Clinical Effectiveness

Clinical improvement was consistently observed following treatment with the standardized **EXOLASER** methodology across multiple aesthetic indications. The degree of improvement varied according to baseline skin condition, patient age, and treatment objectives; however, favorable changes in overall skin quality were observed in the majority

of treated patients during routine clinical follow-up.

Visible improvement was frequently evident after a **single treatment session**, particularly with respect to skin radiance, texture, diffuse erythema, and overall skin appearance. Progressive enhancement of clinical outcomes was observed following additional treatment sessions, with a treatment series consisting of **three or more procedures** performed

at **6- to 8-week intervals** generally producing the most pronounced regenerative remodeling.

Across the clinical population, the most frequently observed improvements included:

- reduction in the appearance of fine and moderate wrinkles;
- improvement in overall skin texture and smoothness;
- increased skin firmness and elasticity;
- reduction of diffuse facial erythema;
- improvement in dyschromia and uneven pigmentation;
- decreased visibility of enlarged pores;
- improvement in post-acne skin quality and scar appearance;
- enhanced skin radiance and overall complexion.

One of the most notable clinical observations throughout long-term follow-up was the continued progression of skin improvement beyond the initial healing period. In many patients, improvements in skin quality appeared to continue for several months after complete epidermal recovery, suggesting that tissue remodeling extended beyond the visible wound-healing phase. Similar prolonged remodeling has been described in studies evaluating extracellular matrix remodeling and regenerative wound-healing processes following cutaneous interventions. [1–10,33–53,67–69]

Although the present study was not designed to investigate the precise biological mechanisms responsible for these observations, the longitudinal clinical findings support the hypothesis that regenerative signaling initiated by the **EXOLASER** methodology may contribute to sustained structural remodeling of the skin that continues beyond the immediate post-procedural recovery period. This hypothesis forms the basis for future prospective mechanistic, histological, and controlled clinical investigations. [1–10,33–53]

Multimodal Clinical Outcome Assessment

Clinical outcomes were evaluated using a **multimodal assessment strategy** combining standardized clinical photography, objective computerized skin imaging, physician assessment, and longitudinal clinical follow-up. The objective of this evaluation was not only to document immediate post-treatment improvement but also to characterize the progression, durability, and long-term evolution of tissue remodeling following treatment with the standardized **EXOLASER** methodology.

Standardized Clinical Photography

Standardized digital photographs were obtained before treatment and during follow-up using identical camera settings, patient positioning, facial expression, lighting

conditions, and image acquisition protocols whenever possible. Images were reviewed side by side to evaluate changes in overall facial appearance, skin texture, wrinkle severity, pigmentation, diffuse erythema, pore visibility, skin laxity, and facial contours.

Because one of the central biological hypotheses underlying the EXOLASER methodology is that regenerative remodeling continues beyond complete epidermal healing, photographic documentation extended well beyond the immediate recovery period whenever long-term follow-up was available.

Objective Skin Analysis

Objective skin analysis was performed using the **VISIA® Complexion Analysis System** (Canfield Scientific, Fairfield, NJ, USA), which provides standardized quantitative assessment of multiple skin-quality parameters using multispectral facial imaging and automated image analysis. [79]

Representative VISIA® examinations were used to evaluate changes in:

- wrinkle count and severity;
- skin texture;
- pore appearance;
- pigmentation;
- ultraviolet and brown spot distribution;
- vascular features, including red areas;
- porphyrins; and
- calculated TruSkin Age®. [79]

Whenever available, identical imaging conditions and standardized patient positioning were maintained throughout follow-up examinations to improve longitudinal comparability and minimize technical variability. [79]

Clinical Assessment

Clinical evaluation was performed by the treating physician during routine follow-up visits. Particular attention was directed toward parameters reflecting **overall tissue quality**, rather than isolated wrinkle reduction.

The following clinical characteristics were systematically assessed:

- skin texture and smoothness;
- elasticity and firmness;
- facial contour and structural support;
- skin hydration and radiance;
- pigmentation uniformity;
- diffuse erythema;

- pore visibility;
- overall skin quality; and
- the duration and progression of clinical improvement over time.

Because the EXOLASER methodology proposes a regenerative rather than purely resurfacing mechanism, particular emphasis was placed on identifying **progressive clinical improvements occurring after complete epidermal healing**. Longitudinal observations extending for several months following treatment were therefore considered especially relevant to the biological hypothesis proposed in this manuscript.

Safety Assessment

Safety evaluation included documentation of treatment tolerance, recovery time, duration of erythema, superficial exfoliation, patient-reported discomfort, and all adverse events observed during routine follow-up.

Particular attention was directed toward identifying clinically significant complications, including infection, prolonged erythema, persistent edema, scarring, delayed wound healing, and post-inflammatory pigmentary alterations.

Long-Term Follow-up

Whenever possible, patients underwent longitudinal follow-up ranging from several weeks to **24 months** after treatment.

The rationale for prolonged observation was based on the central hypothesis of the EXOLASER methodology that structural regenerative remodeling may continue well beyond the initial wound-healing phase. Consequently, long-term follow-up was considered essential for evaluating not only the **persistence** but also the **progression** of clinical improvement over time. Although the present study was observational in nature, these longitudinal assessments provided important clinical evidence supporting the hypothesis that regenerative tissue remodeling may continue after complete restoration of the epidermal barrier. [1–10,33–53,79]

Objective Skin Analysis Using the VISIA® Complexion Analysis System

Objective clinical outcomes were assessed using the **VISIA® Complexion Analysis System** (Canfield Scientific, Fairfield, NJ, USA), a standardized multispectral facial imaging platform that provides quantitative evaluation of multiple skin-quality parameters under reproducible imaging conditions. Representative longitudinal VISIA® examinations were available for patients who underwent standardized photographic follow-up after treatment with the EXOLASER methodology. [79]

VISIA® analysis was used to objectively evaluate changes in:

- wrinkle appearance;
- skin texture;
- pore appearance;
- pigmentation-related parameters;
- red areas;
- ultraviolet spots;
- porphyrins; and
- calculated TruSkin Age®. [79]

These objective measurements complemented routine clinical evaluation and enabled standardized longitudinal comparison of skin quality over time.

Across the representative VISIA® examinations included in this study, objective improvement was consistently observed in multiple parameters of skin quality following treatment with the standardized **EXOLASER** methodology. The most reproducible improvements involved wrinkle appearance, skin texture, overall spot distribution, pore appearance, and calculated **TruSkin Age®**. Improvement in vascular and pigmentation-related parameters varied according to baseline skin characteristics and individual treatment goals, reflecting the heterogeneous nature of photoaging and regenerative skin remodeling.

In several representative patients, calculated **TruSkin Age®** demonstrated measurable reductions of **up to 12 years** during follow-up, accompanied by parallel improvement in wrinkle percentile, skin texture, pore appearance, and overall facial skin quality. Longitudinal analysis further demonstrated that objective improvement frequently continued during extended follow-up after complete clinical recovery, supporting the hypothesis that regenerative remodeling may continue beyond the initial wound-healing phase. Although these findings originate from representative observational cases rather than a controlled clinical trial, they provide objective support for the sustained clinical improvements documented throughout this manuscript. [1–10,33–53,79]

Overall, the objective VISIA® findings were consistent with routine clinical observations throughout the author's clinical experience and supported the reproducibility of the standardized **EXOLASER** methodology across patients presenting with different baseline skin characteristics and aesthetic indications.

A summary of the principal objective VISIA® findings is presented in **Table 2**, while representative clinical cases demonstrating **single-treatment rejuvenation, serial regenerative treatment, post-acne remodeling, and long-term structural skin regeneration** are presented in **Figures 4–7**.

Table 2. Summary of Representative VISIA® Findings Following EXOLASER Treatment

VISIA® Parameter	Overall Observation
Wrinkle appearance	Consistent improvement observed in representative cases
Skin texture	Consistent improvement observed
Overall spot distribution	Frequently improved
Pore appearance	Frequently improved
Calculated TruSkin Age®	Reduced in representative patients
Diffuse erythema	Improvement observed in selected patients
Pigmentation-related parameters	Consistent improvement
Overall skin quality	Progressive improvement documented during follow-up
Long-term remodeling	Objective improvement documented beyond the initial recovery period

Representative Clinical Cases

To further illustrate the clinical application and regenerative potential of the standardized **EXOLASER** methodology, four representative clinical cases were selected from the author's cumulative clinical experience. These cases were chosen to demonstrate the diversity of clinical indications, the reproducibility of treatment outcomes, and the progressive nature of regenerative remodeling documented through standardized clinical photography, objective **VISIA®** analysis when available, and extended longitudinal follow-up.

Rather than representing exceptional or isolated outcomes, the selected cases illustrate different aspects of the regenerative response observed following treatment with EXOLASER, including single-treatment facial rejuvenation, serial regenerative remodeling, post-acne skin regeneration, and long-term structural improvement documented over extended observation periods.

Whenever available, objective assessment was performed using the **VISIA® Complexion Analysis System**, including evaluation of wrinkle appearance, skin texture, pore characteristics, pigmentation-related parameters, red areas, and calculated **TruSkin Age®**. Standardized photography and physician assessment complemented the objective imaging findings to provide a comprehensive evaluation of clinical outcomes. [79]

Particular emphasis was placed on documenting **long-term follow-up**, as one of the central hypotheses underlying the EXOLASER methodology is that regenerative tissue remodeling continues beyond complete epidermal recovery. Accordingly, the presented cases include follow-up periods extending from several months to two years, demonstrating not only the persistence but, in several patients, the continued progression of clinical improvement over time. Although these observations originate from an observational clinical series and cannot establish causality, they provide clinically relevant examples supporting the proposed regenerative concept described in this manuscript. [1–10,33–53]

The four representative cases presented below demonstrate the broad clinical applicability of the EXOLASER methodology

across different aesthetic indications while illustrating the integration of subjective clinical assessment, objective skin imaging, and prolonged follow-up in evaluating regenerative skin remodeling.

Representative Case 1 – Progressive Facial Rejuvenation Following Serial EXOLASER Treatment

Clinical Presentation

A 56-year-old female presented with clinical signs of facial photoaging, including fine wrinkles, uneven skin texture, diffuse facial erythema, enlarged pores, and overall deterioration in skin quality. Treatment outcomes were documented using standardized clinical photography and serial VISIA® Complexion Analysis.

Treatment Course

The patient underwent **three standardized EXOLASER treatments** according to the protocol described in this manuscript.

Clinical improvement became visible following the **first treatment**, with reduction in diffuse erythema, improvement in skin texture, and increased skin radiance observed on standardized photography. Progressive structural improvement continued throughout the treatment series and was objectively documented at long-term follow-up using VISIA® analysis.

Objective VISIA® Findings

Serial VISIA® analysis demonstrated progressive improvement in multiple objective skin quality parameters following the three-treatment course. The most pronounced improvements were observed in wrinkle appearance, overall spot distribution, skin texture, pore appearance, and calculated TruSkin Age®.

The patient's calculated **TruSkin Age® decreased from 65 years at baseline to 53 years following completion of the treatment series**, representing a **12-year reduction** despite the chronological age remaining unchanged during the observation period.

Objective improvement was accompanied by increased

wrinkle percentile (30th to 66th percentile), improvement in overall spot percentile (29th to 65th percentile), enhancement of skin texture (32nd to 51st percentile), improvement in pore appearance (68th to 93rd percentile), and visible reduction in diffuse facial erythema.

Clinical Interpretation

This representative case illustrates both the **early clinical**

Table 3. Objective VISIA® Findings – Representative Case 1

Parameter	Baseline	After 3 Treatments	Change
Chronological Age	56 years	56 years	—
TruSkin Age®	65 years	53 years	–12 years
Spots	29th percentile	65th percentile	+36 percentile points
Wrinkles	30th percentile	66th percentile	+36 percentile points
Texture	32nd percentile	51st percentile	+19 percentile points
Pores	68th percentile	93rd percentile	+25 percentile points

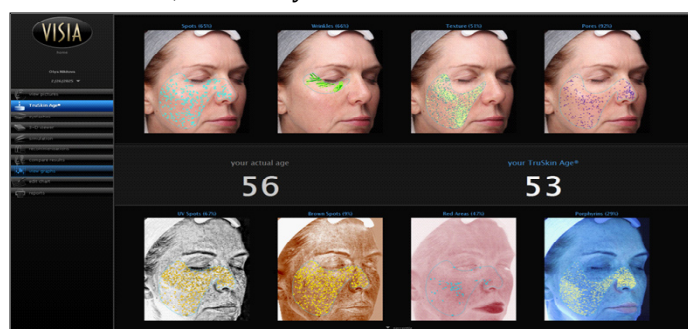
Figure 2. Representative Case 1. Progressive facial rejuvenation following serial EXOLASER™ treatment.



(A) Baseline clinical appearance before treatment.



(B) Standardized clinical photograph following a **single EXOLASER treatment**, demonstrating early improvement in skin texture, diffuse erythema and overall skin radiance.



response following a single EXOLASER treatment and the **progressive structural remodeling** observed after completion of a three-treatment protocol. The sequential improvement documented by standardized photography and objective VISIA® analysis supports the concept that regenerative skin remodeling continues beyond the initial recovery phase, with cumulative enhancement of overall skin quality during serial treatment.

(C) and (D) Objective VISIA® analysis following completion of **three EXOLASER treatments**, demonstrating progressive improvement in multiple skin quality parameters, including a reduction in calculated **TruSkin Age® from 65 to 53 years**, accompanied by improvement in wrinkle appearance, skin texture, pore quality, and overall facial skin appearance.

Representative Case 2 – Progressive Skin Rejuvenation Following a Single EXOLASER Treatment

Clinical Presentation

A 49-year-old female presented with clinical signs of facial photoaging, including uneven skin tone, fine periorbital rhytides, enlarged pores, and reduced overall skin quality. Standardized clinical photography and VISIA® Complexion Analysis were performed before treatment and at follow-up.

Treatment Course

The patient underwent a **single standardized EXOLASER treatment** according to the protocol described in this manuscript.

Clinical recovery was completed within the expected postoperative period of approximately **5–6 days**. Follow-up evaluation demonstrated visible improvement in overall skin appearance, with increased skin luminosity, smoother texture, and reduction in fine wrinkles.

Objective VISIA® Findings

Objective VISIA® analysis demonstrated measurable improvement across multiple skin quality parameters following a single treatment.

The calculated **TruSkin Age® decreased from 52 years to 47 years**, representing a **5-year reduction** following one EXOLASER session.

Objective improvement was also observed in:

- Overall spots (29th → 55th percentile)
- Wrinkle percentile (39th → 86th percentile)

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• Pore percentile (90th → 93rd percentile)

The texture parameter remained stable (9th percentile), while improvement in vascular and pigmentation-related parameters was also observed clinically.

Standardized photography demonstrated visible reduction in fine periorbital wrinkles, improvement in skin smoothness, enhanced skin radiance, and more homogeneous skin tone.

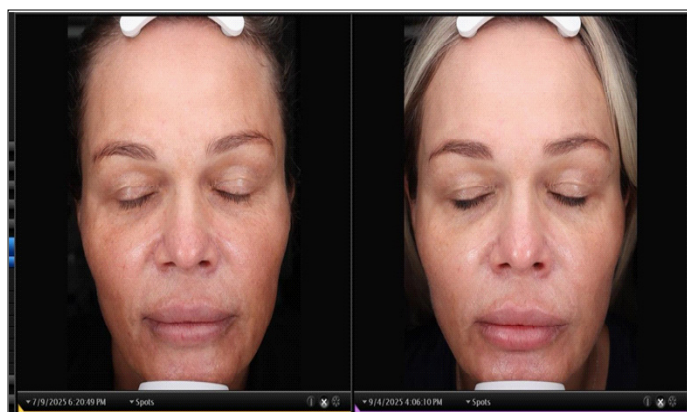
Clinical Interpretation

This case demonstrates that clinically meaningful

Table 4. Objective VISIA® Findings – Representative Case 2

VISIA® Parameter	Baseline	Follow-up	Change
Chronological Age	49 years	49 years	—
TruSkin Age®	52 years	47 years	–5 years
Spots	29th percentile	55th percentile	+26 percentile points
Wrinkles	39th percentile	86th percentile	+47 percentile points
Texture	9th percentile	9th percentile	Stable
Pores	90th percentile	93rd percentile	+3 percentile points
Red Areas	Qualitative improvement	Qualitative improvement	Improved

Figure 3. Representative Case 2. Single-session facial rejuvenation following EXOLASER treatment.



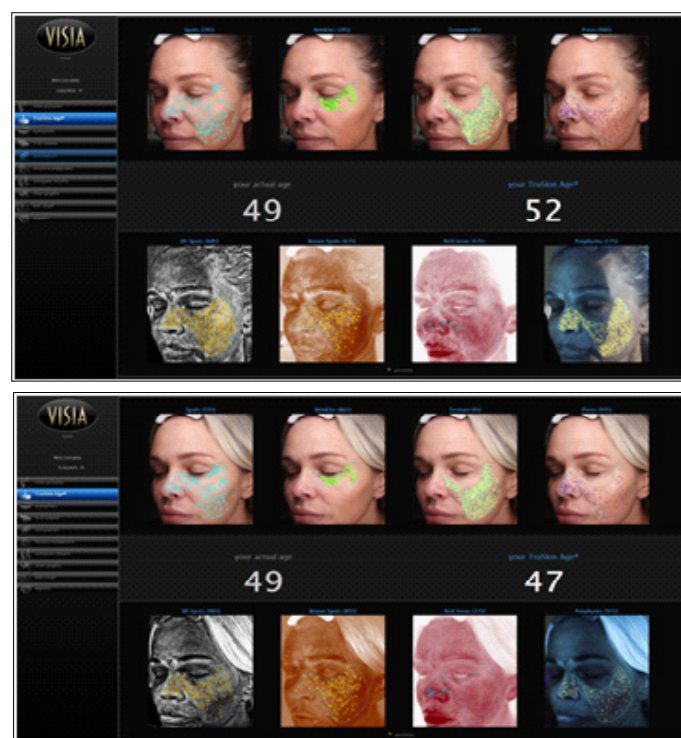
(A) Baseline standardized facial photographs before treatment.



(B) Follow-up photographs after a single EXOLASER treatment demonstrating smoother skin texture, reduction of fine periorbital wrinkles, improved skin tone uniformity, and enhanced skin radiance.

improvement may be achieved following a **single EXOLASER treatment**. The objective VISIA® findings paralleled the visible clinical improvement observed on standardized photography, supporting the ability of the methodology to induce measurable skin rejuvenation with minimal recovery time.

The reduction in calculated TruSkin Age®, together with improvement in wrinkle appearance and overall skin quality, illustrates the potential of EXOLASER to promote early regenerative remodeling after a single treatment session.



(C) & (D) Objective VISIA® analysis documenting improvement in multiple skin quality parameters, including a reduction in calculated **TruSkin Age® from 52 to 47 years** and increased wrinkle and spot percentiles.

Representative Case 3 - Progressive Remodeling of Post-Acne Scarring During Long-Term Follow-up

A young male patient with inflammatory acne, post-inflammatory erythema, and early atrophic acne scarring underwent treatment with the standardized EXOLASER methodology. Standardized clinical photographs were

obtained before treatment, approximately four months after the first treatment session, one month following the second treatment, and nine months after the second treatment, without additional regenerative procedures during the final observation period.

Clinical improvement was progressive throughout the follow-up. Four months after the initial treatment, a marked reduction in inflammatory lesions and post-inflammatory erythema was accompanied by visible improvement in skin texture and scar appearance. One month after the second treatment, further smoothing of the skin surface and softening of atrophic scars were observed. Importantly, additional improvement remained evident nine months after the second treatment despite the absence of further procedures, suggesting continued tissue remodeling beyond the active treatment phase.

Objective VISIA® analysis supported these clinical observations. Texture percentile increased from **19% at baseline to 56% at the final follow-up**, indicating substantial improvement in overall skin surface quality. Spots percentile improved from **15% to 95%**, while pore analysis increased from **83% to 96%**. TruSkin Age® decreased from **19 years to 17 years** despite the patient's young chronological age. Wrinkle percentile remained essentially unchanged, as expected for this age group.

Collectively, the serial clinical photographs and objective VISIA® measurements demonstrated progressive improvement in skin quality, reduction of post-inflammatory changes, and gradual remodeling of early atrophic acne scars throughout long-term follow-up.



Table 5. Objective VISIA® Changes in Representative Case 3

VISIA® Parameter	Baseline	Final Follow-up	Change
TruSkin Age®	19	17	–2 years
Texture	19%	56%	+37
Spots	15%	95%	+80
Pores	83%	96%	+13
Wrinkles	67%	69%	Stable



Representative Case 4 – Long-Term Structural Skin Remodeling Following Serial EXOLASER Treatments

Clinical Presentation

A 47-year-old female presented with facial photoaging characterized by diffuse erythema, uneven skin tone and texture, visible pores, fine periorbital rhytides, and reduced overall skin quality. Baseline assessment was performed on April 23, 2024, using standardized clinical photography and the VISIA® Complexion Analysis System.

In accordance with the patient's preference and publication consent, only cropped photographs of the treated facial regions are presented. These images permit evaluation of the cheek, forehead, and periorbital areas without displaying the patient's complete facial identity.

Treatment Course and Follow-up

The patient underwent a course of **six standardized EXOLASER treatments** during the approximately 22-month observation period. Treatments were performed according to the protocol described in this manuscript, with intervals selected to allow complete clinical recovery and continued tissue remodeling between sessions.

Follow-up assessment on March 2, 2026, demonstrated sustained and progressive improvement in the appearance

of the cheek, forehead, and periorbital regions. The patient's chronological age increased from 47 to 49 years during the observation period, permitting evaluation of treatment-associated changes against the expected progression of intrinsic aging.

Clinical Findings

Comparison of standardized cropped photographs demonstrated visible improvement in multiple aspects of facial skin quality. The cheek showed reduced diffuse erythema, more homogeneous coloration, smoother surface texture, and decreased pore visibility. The periorbital region demonstrated softening of fine rhytides and improvement in overall tissue smoothness. The forehead appeared more uniform in texture and tone at final follow-up.

The improvement remained evident nearly two years after baseline assessment and was not limited to a transient post-procedural effect. The serial images instead demonstrated a progressive pattern of skin-quality enhancement throughout the treatment course and long-term observation period.

Objective VISIA® Findings

Objective VISIA® assessment demonstrated improvement across several independent skin-quality parameters.

Calculated **TruSkin Age® decreased from 50 years at baseline to 44 years at final follow-up**, representing a six-year absolute reduction. Because the patient's chronological age increased from 47 to 49 years during the same interval, the difference between chronological age and calculated skin age shifted from the skin appearing three years older than chronological age at baseline to five years younger at final assessment. This corresponds to an **eight-year favorable change relative to chronological aging**.

Table 6. Objective VISIA® Findings in Representative Case 4

VISIA® Parameter	Baseline: April 23, 2024	Final follow-up: March 2, 2026	Change
Chronological age	47 years	49 years	+2 years
TruSkin Age®	50 years	44 years	-6 years
Difference between TruSkin Age® and chronological age	+3 years	-5 years	8-year favorable shift
Texture percentile	19	78	+59 points
Wrinkle percentile	33	69	+36 points
Spots percentile	68	91	+23 points
Pores percentile	15	46	+31 points
Red Areas percentile	9	18	+9 points
Brown Spots percentile	88	87	-1 point; stable
UV Spots percentile	84	61	-23 points
Porphyrins percentile	12	11	-1 point; stable

Percentile changes are reported as generated by the VISIA® system. Higher percentile values were interpreted as favorable only for parameters for which the longitudinal findings were consistent with the corresponding clinical images. No formal statistical inference was performed for this individual case.

Texture percentile increased from **19 to 78**, representing an improvement of 59 percentile points. Wrinkle percentile increased from **33 to 69**, while spots improved from **68 to 91** and pores from **15 to 46**. Red Areas increased from the 9th to the 18th percentile.

Brown Spots remained essentially stable, changing from the 88th to the 87th percentile. UV Spots decreased from the 84th to the 61st percentile, and Porphyrins remained stable at approximately the 12th and 11th percentiles, respectively. These parameters were not interpreted as treatment improvements because their direction and magnitude may be affected by environmental exposure, imaging conditions, baseline distribution, and factors unrelated to structural remodeling.

Clinical Interpretation

This case demonstrates progressive and durable improvement in facial skin quality following serial EXOLASER treatments over approximately 22 months. The photographic changes were supported by objective improvement in calculated TruSkin Age®, texture, wrinkles, spots, pores, and red-area percentiles.

The marked improvement in texture - from the 19th to the 78th percentile - was particularly consistent with the visible smoothing and greater homogeneity of the treated skin. Importantly, these changes occurred despite the patient becoming two chronological years older during follow-up.

Although the present observational case cannot establish the biological mechanism responsible for the result, the persistence and progression of improvement are consistent with prolonged structural skin remodeling extending beyond the immediate epidermal recovery period.

Figure 5. Representative Case 4: Long-term structural skin remodeling following serial EXOLASER treatments

Cropped standardized clinical photographs obtained at baseline on April 23, 2024, and at final follow-up on March 2, 2026, after a course of six EXOLASER treatments.



(A) Cheek comparison demonstrating reduced diffuse erythema, more uniform skin tone, smoother texture, and decreased pore visibility.



(B) Periorbital comparison demonstrating softening of fine rhytides and improvement in skin smoothness.



(C) Forehead and upper periorbital comparison demonstrating improved texture and greater uniformity of the skin surface.

Overall Clinical Results

Across the observational cohort of more than 500 patients treated with the standardized EXOLASER protocol, consistent improvements in overall skin quality were observed clinically, with representative cases presented to illustrate the range of

treatment responses. The clinical findings were supported by standardized VISIA® imaging in patients for whom objective analysis was available.

The most reproducible improvements included enhanced skin texture, reduction in the appearance of fine wrinkles, more homogeneous pigmentation, decreased facial erythema, improved pore appearance, and an overall healthier skin surface. Patients frequently demonstrated progressive enhancement in skin quality over time rather than an isolated early response following treatment.

Representative VISIA® analyses documented objective improvements across multiple independent skin-quality parameters. Among the presented cases, texture percentile increased by as much as 59 percentile points, wrinkle percentile more than doubled, and substantial improvements were observed in pigmentation- and pore-related parameters. In patients undergoing serial assessment, calculated TruSkin Age® demonstrated reductions ranging from **5 to 12 years**, despite the natural progression of chronological aging during the observation period.

Long-term follow-up extending to nearly two years demonstrated persistence of clinical improvement following completion of the treatment course. In several patients, skin quality continued to improve months after the final procedure, suggesting that tissue remodeling extended well beyond the immediate epidermal recovery phase. These longitudinal observations were consistent with sustained biological remodeling rather than a transient cosmetic effect.

The presented representative cases further demonstrated that the protocol was applicable across multiple clinical indications, including facial photoaging, uneven pigmentation, erythema, reduction in skin quality associated with intrinsic aging, and post-acne skin remodeling. Although the magnitude of response varied among individuals, improvement was consistently observed in both clinical photography and objective imaging when available.

Throughout the observational cohort, the treatment protocol demonstrated a favorable safety profile. Most patients experienced the expected transient recovery period characterized by superficial desquamation lasting approximately five to six days. A small number of patients experienced prolonged exfoliation for an additional two to three days, which resolved without intervention. One patient developed post-inflammatory hyperpigmentation that resolved completely within one month following appropriate topical management. No infections, permanent pigmentary alterations, hypertrophic scarring, or other serious adverse events were observed during follow-up.

Taken together, these findings suggest that the standardized EXOLASER protocol was associated with reproducible improvements in multiple objective and clinical indicators of skin quality while maintaining a favorable safety profile

across a broad spectrum of patients treated in routine clinical practice.

DISCUSSION

EXOLASER: A Regenerative Rather Than Destructive Approach to Skin Remodeling

The standardized **EXOLASER** methodology was developed from a different conceptual perspective. Rather than maximizing chemical injury, the protocol aims to optimize the biological environment in which regeneration occurs. The methodology combines controlled superficial chemical stimulation with biological priming, ultra-superficial nanochanneling, and topical application of a biologically active **bovine colostrum-derived extracellular vesicle-rich secretome** to support physiological tissue repair while minimizing unnecessary structural damage. [21–24,25–32,33–53]

A key characteristic of the protocol is the use of **ultra-superficial nanochanneling (0.25 mm)**, which preserves the integrity of the deeper dermis while facilitating uniform distribution of the biologically active formulation. Combined with a proprietary microencapsulated priming system and controlled application of trichloroacetic acid, this approach is designed to initiate a regenerative cascade without the extensive tissue destruction typically associated with more aggressive resurfacing techniques. [21–32]

Unlike conventional ablative procedures, the clinical objective of EXOLASER is not simply epidermal renewal but progressive restoration of overall skin quality. The representative clinical cases presented in this study demonstrated objective improvements in skin texture, wrinkle appearance, pigmentation homogeneity, pore appearance, and calculated **TruSkin Age®**, while long-term follow-up suggested that improvement frequently continued beyond the initial recovery period. Although the biological mechanisms responsible for these prolonged changes require further investigation, the clinical observations support the hypothesis that regenerative remodeling extends beyond immediate wound healing. [79]

The philosophy underlying EXOLASER therefore differs from traditional resurfacing approaches by emphasizing **controlled biological stimulation rather than maximal tissue injury**, with the goal of promoting progressive structural skin remodeling while maintaining a favorable recovery profile. This regenerative treatment philosophy aligns with the growing emphasis in regenerative medicine on optimizing endogenous repair mechanisms rather than increasing procedural aggressiveness. [50–53,70–72]

Proposed Biological Mechanisms Underlying EXOLASER-Induced Skin Remodeling

The precise biological mechanisms responsible for the clinical improvements observed following the

standardized **EXOLASER** methodology have not been experimentally confirmed.

Nevertheless, the consistent clinical outcomes, objective **VISIA®** findings, and prolonged improvement documented during long-term follow-up support the hypothesis that the protocol initiates a coordinated regenerative response extending beyond the initial wound-healing phase. [79]

Unlike conventional resurfacing procedures that rely primarily on controlled tissue injury, the EXOLASER methodology combines several complementary biological stimuli designed to optimize the regenerative microenvironment. These include superficial chemical stimulation, biological priming, ultra-superficial nanochanneling, and topical application of a biologically active **bovine colostrum-derived extracellular vesicle-rich secretome**. Rather than acting independently, these components are hypothesized to function synergistically throughout the different phases of tissue repair. [21–24,25–32,33–53]

Controlled superficial chemical stimulation represents the initial trigger for activation of the wound-healing cascade. Early inflammatory signaling is followed by cellular recruitment, extracellular matrix turnover, fibroblast activation, angiogenic responses, and progressive remodeling of dermal architecture. These biological processes are well recognized as essential components of physiological skin repair and provide the biological foundation upon which regenerative interventions may act. [1–10,67–69]

The proprietary biological priming stage is proposed to enhance the uniformity of superficial chemical stimulation while creating favorable conditions for subsequent regenerative signaling. Ultra-superficial nanochanneling performed at a depth of approximately **0.25 mm** may facilitate homogeneous distribution of biologically active molecules throughout the superficial skin layers while preserving the integrity of deeper dermal structures. Limiting mechanical injury to this superficial depth may contribute to the favorable recovery profile observed clinically while maintaining activation of endogenous repair mechanisms. [25–32]

An additional distinguishing feature of the EXOLASER methodology is the topical application of a **bovine colostrum-derived extracellular vesicle-rich secretome** immediately following nanochanneling. The selected preparation (**Purasomes®**, Dermoaroma, Italy) was incorporated into the protocol because, according to the manufacturer's technical documentation, it contains approximately 20 billion extracellular vesicles (reported as exosomes), a standardized complex of 20 growth factors (200 mg), 70 mg of polynucleotides, amino acids, vitamins, minerals, cytokines, and additional biologically active regenerative mediators. These components participate in intercellular communication during tissue repair and may influence

fibroblast activity, extracellular matrix organization, angiogenesis, inflammatory modulation, and coordinated tissue regeneration. [9,10,33–53,73–80]

One of the most interesting observations arising from the present clinical experience was the continued improvement documented **months after completion of treatment**. Representative patients demonstrated progressive enhancement of skin texture, reduction in wrinkle appearance, improvement in pigmentation homogeneity, and sustained improvement in calculated **TruSkin Age®** during extended follow-up, including prolonged periods without additional procedures. Such continued improvement appears unlikely to be explained solely by transient epidermal renewal and instead suggests progressive remodeling of deeper skin structures. [79]

Although the present study did not include histological evaluation or molecular analyses, one possible explanation for these prolonged clinical observations is progressive remodeling of the extracellular matrix together with restoration of normal dermal architecture. In addition, based on emerging evidence regarding the biological role of **dermal white adipose tissue (DWAT)** in cutaneous homeostasis, wound healing, immune regulation, and fibroblast communication, it is reasonable to hypothesize that regenerative interventions capable of optimizing the dermal microenvironment may also influence the functional recovery of this specialized adipose compartment. This possibility remains speculative and requires dedicated experimental investigation but represents an important direction for future translational research. [54–62,67–69]

Collectively, the biological rationale proposed for **EXOLASER** extends beyond conventional concepts of resurfacing. Rather than viewing the procedure as a method of controlled epidermal injury alone, the methodology is conceived as a coordinated regenerative strategy that combines superficial tissue stimulation with biological support to promote progressive structural remodeling of the skin. The sustained clinical improvements documented throughout long-term follow-up are consistent with this regenerative concept and provide the foundation for future mechanistic, histological, and prospective controlled clinical studies. [1–10,33–53,54–72]

Integration of a Standardized Bovine Colostrum-Derived Secretome into the EXOLASER Regenerative Protocol

The incorporation of this standardized secretome into clinical practice in 2021 was based on the author's objective of enhancing regenerative signaling during post-procedural recovery. Following its introduction, consistent clinical observations suggested faster tissue recovery together with progressive improvement in long-term treatment outcomes compared with previous clinical experience using the original Liquid Laser protocol. Although the present observational

study was not designed to directly compare outcomes before and after integration of the secretome, these observations contributed to development of the current standardized EXOLASER methodology and support future prospective investigations evaluating the contribution of secretome-based regenerative support to skin remodeling.

The present clinical observations further support the concept that regenerative medicine may benefit not only from controlled tissue stimulation but also from optimization of the biological microenvironment during the early phases of wound healing. Future mechanistic investigations including histological, molecular, immunohistochemical, and biomarker-based studies will be important to further clarify the individual contribution of secretome-based regenerative support within the overall EXOLASER treatment protocol. [1–10,33–53,50–53,70–72]

Clinical Implications and Potential Applications of the EXOLASER Methodology

The clinical observations presented in this study suggest that the standardized **EXOLASER** methodology may represent a versatile regenerative approach applicable across a broad spectrum of aesthetic indications. Rather than targeting a single manifestation of skin aging, the protocol is designed to improve overall skin quality through controlled superficial stimulation combined with biologically guided regenerative support. [1–10,33–53,70–72]

Within the present observational experience, consistent clinical improvement was observed in patients presenting with facial photoaging, uneven skin texture, fine rhytides, enlarged pores, diffuse erythema, dyschromia, and post-acne skin remodeling. Representative clinical cases further demonstrated that objective improvement was not restricted to a single **VISIA®** parameter but frequently involved simultaneous enhancement of multiple indicators of skin quality, including skin texture, wrinkle appearance, pigmentation homogeneity, pore appearance, and calculated **TruSkin Age®**. [79]

One of the most clinically relevant observations was the apparent durability of treatment outcomes. In several representative patients, progressive improvement continued during extended follow-up despite the absence of additional procedures. Although the mechanisms responsible for these prolonged clinical changes remain to be established, this pattern suggests that regenerative remodeling may continue after completion of the initial epidermal healing phase. [1–10,33–53]

The favorable recovery profile observed throughout the clinical series further supports the potential utility of the methodology in routine clinical practice. Most patients completed visible recovery within approximately **5–6 days** while demonstrating progressive improvement in overall skin quality during subsequent follow-up. This balance between clinically meaningful improvement and

relatively short recovery time may represent an important practical advantage for appropriately selected patients.

The biological concept underlying **EXOLASER** also supports potential integration with other regenerative treatment strategies. Because the methodology emphasizes optimization of the tissue microenvironment rather than aggressive tissue destruction, future investigation may evaluate its role in combination with additional evidence-based regenerative interventions, including cell-free biologics, energy-based technologies, and other minimally invasive skin remodeling procedures. Such combination strategies, however, require formal prospective evaluation before clinical recommendations can be established. [33–53,70–72]

Collectively, the findings presented in this study support the concept that regenerative skin treatment may benefit from combining controlled superficial stimulation with biologically guided tissue support. Although further controlled clinical studies are required, the present observations suggest that the standardized **EXOLASER** methodology may represent a promising addition to the expanding field of regenerative dermatology and aesthetic medicine.

Study Limitations

The present study has several limitations that should be considered when interpreting the findings. First, the clinical observations are based on a large observational experience rather than a randomized controlled clinical trial. Although more than **500 patients** were treated using the standardized **EXOLASER** methodology, the present manuscript focuses primarily on representative clinical cases and objective longitudinal **VISIA®** analyses rather than formal statistical evaluation of the entire clinical cohort. [79]

Second, the current study was conducted within a single clinical practice using one standardized treatment protocol. Although this approach ensured procedural consistency, multicenter investigations involving independent investigators will be important to further evaluate the reproducibility and generalizability of the reported clinical outcomes.

Third, while standardized **VISIA®** imaging provided objective assessment of multiple skin-quality parameters, the present study did not include histological analysis, molecular profiling, high-frequency ultrasound, optical coherence tomography (**OCT**), or other tissue-based investigations capable of directly evaluating extracellular matrix remodeling or changes within deeper skin compartments. Consequently, the biological mechanisms proposed throughout the Discussion should be regarded as scientifically plausible hypotheses derived from current knowledge of wound healing and regenerative biology rather than experimentally confirmed mechanisms specific to the **EXOLASER** methodology. [1–10,33–53,54–69]

An additional limitation is the absence of direct comparative evaluation against other established resurfacing techniques or alternative regenerative protocols. Comparative prospective studies will be necessary to determine the relative efficacy, recovery profile, durability, and cost-effectiveness of **EXOLASER** within contemporary aesthetic practice.

Finally, although long-term follow-up extending to nearly **two years** was available for selected representative patients, not all treated individuals underwent standardized objective imaging at identical follow-up intervals. Future prospective investigations using predefined imaging schedules and standardized outcome measures will further strengthen the evidence supporting this methodology.

Despite these limitations, the combination of a standardized treatment methodology, objective **VISIA®** assessment, representative long-term follow-up, and consistent clinical observations provides a strong foundation for future controlled investigations. The present study should therefore be regarded as an important step in the clinical development and scientific evaluation of the **EXOLASER** regenerative methodology rather than its final validation.

Future Directions

The clinical findings presented in this study provide a foundation for further investigation of the **EXOLASER** methodology using prospective, controlled, and mechanistically oriented study designs. Future research should focus not only on confirming clinical efficacy but also on identifying the biological processes responsible for the progressive and prolonged skin remodeling observed during longitudinal follow-up.

A primary research priority should be prospective controlled clinical trials using predefined treatment schedules, standardized follow-up intervals, and validated objective outcome measures. Randomized comparison with established resurfacing modalities including conventional chemical peeling, microneedling, and selected energy-based procedures would help determine the relative efficacy, recovery profile, durability, and safety of the **EXOLASER** methodology. Multicenter studies involving independent investigators and diverse patient populations would additionally establish the reproducibility and generalizability of the protocol. [21–32]

Future studies should also incorporate advanced quantitative imaging. In addition to standardized **VISIA®** analysis, high-frequency ultrasound, optical coherence tomography (**OCT**), three-dimensional surface imaging, and objective assessment of skin biomechanics could provide complementary information regarding changes in dermal thickness, surface topography, elasticity, and tissue architecture. Serial measurements obtained at baseline and at predefined intervals extending beyond **12 months** would be particularly valuable for determining whether the progressive clinical

improvement observed in the present study corresponds to measurable structural changes within the skin. [79]

Histological and molecular investigation represents another important priority. Serial skin biopsies could be used to evaluate changes in epidermal architecture, collagen organization, elastin networks, extracellular matrix composition, vascular structures, and fibroblast activity. Immunohistochemical and molecular analyses of relevant remodeling and inflammatory pathways could further clarify whether the prolonged clinical response reflects persistent biological activity after completion of the initial wound-healing phase. [1–10,67–69]

Of particular interest is the potential involvement of **dermal white adipose tissue (DWAT)**. Emerging evidence increasingly recognizes DWAT as a metabolically and biologically active component of the skin that participates in wound healing, immune regulation, extracellular matrix homeostasis, hair follicle biology, and communication with dermal fibroblasts. Dedicated histological and molecular studies will be required to determine whether the prolonged volumetric and structural changes observed clinically following **EXOLASER** treatment are accompanied by measurable alterations within this compartment. At present, involvement of DWAT remains a hypothesis and should be investigated directly. [54–62]

The individual contribution of the **bovine colostrum-derived extracellular vesicle-rich secretome** represents another important area for investigation. Controlled studies comparing the complete **EXOLASER** protocol with otherwise identical protocols performed without secretome application could help distinguish the effects of controlled chemical stimulation and nanochanneling from those potentially associated with regenerative biological support. Molecular studies could additionally examine changes in inflammatory signaling, fibroblast activity, extracellular matrix turnover, and related regenerative pathways. [33–53,73–80]

Future investigations should also evaluate whether the **0.25-mm nanochanneling depth** represents an optimal balance between biological delivery and minimization of mechanical injury. Comparative studies using different channeling depths could determine whether deeper penetration provides additional clinical benefit or whether preservation of deeper dermal architecture is advantageous within this particular regenerative sequence. [25–32]

Long-term clinical studies should extend beyond conventional three- or six-month aesthetic endpoints. The continued improvement documented in selected patients months after their final **EXOLASER** treatment raises an important question regarding the temporal dynamics of regenerative remodeling. Serial objective assessment at **1, 3, 6, 12, 18, and 24 months** could characterize when maximal improvement occurs, how long it persists, and whether different skin parameters follow distinct remodeling trajectories.

Finally, incorporation of validated patient-reported outcome measures, blinded investigator assessments, standardized adverse-event reporting, quantitative statistical analysis, and artificial intelligence-assisted image analysis may further strengthen future investigations by enabling objective longitudinal quantification of wrinkles, erythema, pigmentation, texture, and additional skin-quality parameters across large clinical datasets.

Collectively, these investigations could determine whether the prolonged clinical improvements observed following **EXOLASER** treatment reflect measurable structural and molecular regeneration and clarify the relative contribution of each component of the protocol. Such research may also contribute more broadly to an emerging paradigm in aesthetic medicine in which treatment strategies evolve beyond controlled tissue destruction toward precisely regulated biological stimulation combined with optimization of the regenerative tissue microenvironment. [1–10,33–53,54–72]

CONCLUSION

The standardized **EXOLASER** methodology represents a novel **laser-free regenerative skin remodeling approach** that combines controlled superficial chemical stimulation, biological priming, ultra-superficial nanochanneling, and topical application of a standardized **bovine colostrum-derived extracellular vesicle-rich secretome** within a sequential treatment protocol. [21–53]

Across an observational clinical experience involving more than **500 treated patients**, the methodology demonstrated a favorable safety profile together with reproducible improvements in overall skin quality. Representative clinical cases supported by standardized **VISIA® Complexion Analysis System** evaluation documented objective improvement in skin texture, wrinkle appearance, pigmentation homogeneity, pore appearance, and calculated **TruSkin Age®**. Recovery was typically completed within **5–6 days**, while several patients demonstrated continued clinical improvement during extended follow-up extending from several months to nearly **two years**. [79]

One of the most notable observations arising from the present study was the apparent persistence of progressive skin remodeling beyond the immediate healing period. Although the biological mechanisms responsible for these prolonged clinical improvements remain to be fully elucidated, the findings are consistent with the concept that regenerative skin therapies may continue to influence tissue remodeling after visible epidermal recovery has been completed. [1–10,33–53,54–69]

Rather than viewing skin resurfacing primarily as a process of controlled tissue destruction, the **EXOLASER** methodology proposes an alternative regenerative philosophy in which

carefully regulated superficial stimulation is combined with optimization of the biological environment supporting physiological tissue repair. This concept may represent an important evolution in contemporary regenerative dermatology and aesthetic medicine and is consistent with the broader transition toward biologically guided regenerative therapies. [50–53,70–72]

The present study should be regarded as an initial clinical and scientific foundation for future investigation rather than definitive validation of the methodology. Prospective randomized clinical trials, multicenter validation studies, histological analyses, molecular investigations, advanced imaging techniques, and mechanistic research will be essential to further define the biological mechanisms, long-term efficacy, safety profile, and broader clinical applications of the standardized EXOLASER methodology.

The future of regenerative aesthetics may lie not in creating greater tissue injury, but in creating a more favorable biological environment for tissue regeneration.

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