

Original Article





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OPEN ACCESS

Received: Dec 4, 2024 Revised: Jan 21, 2025 Accepted: Feb 17, 2025 Published online: Mar 18, 2025

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ABSTRACT

Background: Skin rejuvenation has become an increasingly popular noninvasive approach to address age-related changes such as sagging, wrinkles, and skin laxity. Energy-based devices (EBDs) and injectables are widely used, but their application requires careful customization based on individual patient characteristics to optimize outcomes and minimize potential adverse effects. **Objective:** This study aimed to explore clinical practice patterns among board-certified dermatologists in South Korea, focusing on their strategies for tailoring skin rejuvenation treatments to individual patients, including the integration of EBDs, injectables, and senotherapeutics. **Methods:** A structured survey comprising 10 questions was administered to 13 experienced dermatologists specializing in skin rejuvenation. The survey covered treatment strategies for patients with varying facial fat volumes, pain management approaches, and the use of EBDs, injectables and senotherapeutics.

Results: High-intensity focused ultrasound (HIFU) and radiofrequency (RF) were the most employed EBDs, often combined with injectables for enhanced outcomes. For patients with higher facial fat, HIFU and deoxycholic acid injections were preferred for contouring and tightening. For those with lower facial fat, biostimulatory agents such as poly-D, L-lactic acid and microneedle RF were favored to restore volume and elasticity. Pain management strategies included topical



anesthetics and stepwise protocols. Although less commonly used, senotherapeutics were occasionally prescribed for specific conditions, such as melasma and extensive photoaging.

Conclusion: Dermatologists in South Korea employ a variety of patient-specific strategies for skin rejuvenation, combining various EBDs, injectables, and senotherapeutics. These findings highlight the importance of personalized treatment protocols and the need for further research to optimize treatment efficacy and safety.

Keywords: Aging; Rejuvenation; Respondents; Skin; Surveys and questionnaires

INTRODUCTION

Skin rejuvenation, which seeks to reverse the signs of aging, has garnered increasing interest from both patients and practitioners¹. Aging affects the skin through various mechanisms, including collagen breakdown, alterations in the dermal matrix, and loss of facial fat. These factors contribute to sagging, fine lines, wrinkles and pigmentation. Intrinsic changes are often worsened by extrinsic factors such as ultraviolet exposure, pollution, and lifestyle habits like smoking². In response to these age-related changes, a variety of invasive and noninvasive treatments have been developed. The global demand for cosmetic interventions continues to grow, with the market for aesthetic treatments projected to experience significant expansion in the coming decades¹.

Among the available options, noninvasive skin rejuvenation techniques using energy-based devices (EBDs), such as lasers, high-intensity focused ultrasound (HIFU), and radiofrequency (RF), have gained significant popularity. These technologies are favored for their minimal downtime and proven efficacy in tightening the skin and stimulating collagen production. EBDs have shown great potential in enhancing skin elasticity, improving facial contours, and achieving rejuvenation without the need for surgical intervention^{1,3}. However, the success of these treatments depends on several patient-specific factors, such as facial fat volume, skin type, age, degree of skin laxity, and underlying medical conditions. The selection of treatment protocols typically involves a personalized approach, often combining EBDs with injectables and senotherapeutics.

Senotherapeutics have emerged as a promising strategy for addressing cellular and tissue aging by targeting cellular senescence. Senescent cells, though metabolically active, lose their ability to proliferate and exhibit harmful characteristics by secreting inflammatory cytokines, growth factors, and proteases, collectively known as the Senescence-Associated Secretory Phenotype (SASP)⁴⁻⁶. These factors disrupt tissue homeostasis, impair regenerative capacity, and degrade the extracellular matrix (ECM), leading to signs of skin aging such as rhytids, pigmentation, atrophy, and substructural deterioration⁷. While the removal or rejuvenation of senescent cells holds significant potential as an

effective alternative to traditional anti-aging treatments, its clinical application remains in the early stages. Therefore, we tried to investigate how clinicians are utilizing senotherapeutics in clinical practice.

The objective of this study is to examine how board-certified dermatologists in South Korea customize skin rejuvenation procedures based on patient-specific factors, use injectables in combination with other noninvasive techniques, and apply senotherapeutics in their practice. By conducting a survey of experienced dermatologists, this study provides valuable insights into the realworld implementation of anti-aging therapies and contributes to the existing literature on noninvasive aesthetic procedures.

MATERIALS AND METHODS

A survey on skin rejuvenation treatment patterns was conducted under the supervision of the Korean Society of Dermatologic Laser Surgery. The survey involved 13 board-certified dermatologists (with 7 to over 20 years of experience) in South Korea, all of whom specialize in skin rejuvenation procedures. The questionnaire comprised 10 items, each designed to gather detailed insights into their clinical practices. Topics covered in the questions included treatment strategies for patients with high or low facial fat, pain management during EBDs or injectable procedures, the use of oral senotherapeutics, and the application of various injectables in treatments. Responses varied across individuals, and the results will be presented in a narrative format. The questionnaire items are as follows:

- 1. Please share your expertise on rejuvenation for patients with high facial fat.
- 2. Please share your expertise on rejuvenation for patients with low facial fat.
- 3. How do you typically manage pain during EBD or injectable treatments?
- 4. Do you prescribe oral senotherapeutics (e.g., metformin, quercetin) for skin rejuvenation? If so, which medications do you use?



- 5. Please share your experience with polynucleotide (PN) products (e.g., Rejuran®; PharmaResearch Inc., Seoul, Korea), including their main indications and the EBDs you commonly combine with them.
- 6. Please share your expertise with poly-D, and L-lactic acid (PDL-LA) (e.g., Juvelook®; VAIM Co. LTD., Seoul, Korea) including their main indications and EBDs you commonly combine.
- 7. Please share your expertise with the combination solution containing glutathione, vitamin C, hyaluronic acid (HA), tranexamic acid and niacinamide (Lorient Element®; Joonghun Pharmaceutical, Seoul, Korea), including its main indications and EBDs you commonly combine.
- 8. Please share your experience with deoxycholic acid (e.g., V-olet®; Daewoong Pharmaceutical, Seoul, Korea) including its main indications and EBDs you commonly combine.
- 9. Please share your preferred EBDs and senotherapeutics (oral, injectable, or topical).
- 10. Have you encountered any side effects after using EBDs or senotherapeutics (e.g., skin boosters or exosomes)? If so, what were the side effects?

RESULTS

Treatment strategies for patients with higher facial fat volume

The survey responses revealed that dermatologists use a variety of treatment strategies for patients with higher facial fat volume, aiming to address skin laxity and achieve facial rejuvenation. A consistent approach among respondents was the prominent use of HIFU, with 61.5% of participants reporting high shot counts, typically exceeding 450-600 shots, directed at the face, particularly focusing on the jowl and submental areas. Additionally, 46.2% of respondents employ RF treatments including monopolar, bipolar and microneedle RF devices. Multipolar RF systems, such as InMode® (Inmode Inc, Irvine, CA, USA), were often mentioned in combination with microneedle RF, highlighting the preference for multi-modal approaches that target skin tightening and fat deposits. Notably, 36.4% of respondents combine HIFU with injectables, such as deoxycholic acid (marketed as V-olet[®]), to dissolve localized fat in areas like the zygoma, inferior jowl, and submental regions. This synergistic approach was noted to enhance both contouring and skin tightening effects. One respondent also emphasized the importance of intradermal botulinum toxin injections for treating conditions like double chin and sagging jawlines, especially in cases where skin laxity and muscle hyperactivity coexist.

Treatment strategies for patients with lower facial fat volume

For patients with lower facial fat volume, clinicians typically adopt a more conservative approach to avoid further fat loss, focusing on skin tightening and volume restoration. Low-power RF treatments were commonly used by 46.2% of respondents, with monopolar RF devices occasionally employed for midface enhancement to induce adipogenesis. This approach was aimed to reinforce the midface structure without compromising the limited fat reserves. Additionally, 30.8% of respondents preferred microneedle RF due to its precision in treating skin laxity without reducing fat. HIFU with a superficial transducer to stimulate musculoaponeurotic system (SMAS) was also cited as a necessary treatment for achieving optimal lifting without over-reducing fat. In this group, 30.8% of respondents reported using a lower energy level and fewer lines (around 300–350 shots) of HIFU compared to the higher facial fat volume group.

Biostimulatory injectable treatments were heavily favored in this patient population, with 23% of respondents utilizing Poly-L-lactic acid (PLLA) and PDLLA to restore volume and promote collagen synthesis. These biostimulators were often combined with HIFU and RF (monopolar, bipolar or microneedle RF) to achieve a comprehensive rejuvenation effect. Furthermore, 7.7% of respondents preferred 1,064 nm long-pulse or quasi-long pulse lasers to raise the skin's temperature and induce collagen remodeling for skin tightening.

Pain management strategies for EBD and injectable procedures

Pain management during EBD treatments and injectable procedures is a critical concern for many dermatologists. The most used anesthetic is topical cream, specifically 2.5% lidocaine and 2.5% prilocaine (known as the eutectic mixture of local anesthetics, or EMLA® cream [Aspen Pharmacare, Södertälje, Sweden]). In addition to this, one practitioner also reported using vibratory devices during injections to alleviate discomfort, alongside nerve blocks for sensitive areas such as the jawline.

For more invasive or painful treatments, like HIFU and RF, some dermatologists take a stepwise approach to pain management. They typically begin with the basic topical EMLA application. If pain relief is inadequate, they introduce non-steroidal anti-inflammatory drugs, benzodiazepines, opioids. In some cases, sleep anesthesia may also be considered, depending on the severity of the pain. A notable 15.4% of respondents reported applied topical EMLA after procedures like cold plasma or Er:YAG fractional laser treatments. This post-procedure application enhances the absorption of the cream, thus improving pain control.



Additionally, some clinicians highlighted the importance of setting patient expectations prior to treatment. Specifically, they emphasize that some degree of discomfort is a necessary part of achieving effective results with HIFU treatment. To ensure the desired tissue response, nerve blocks are avoided during HIFU procedures. Similarly, during RF treatments, the use of cold air is also avoided as it can interfere with the intended tissue heating patterns.

The use of oral senotherapeutics in skin rejuvenation

The survey also addressed the use of oral senotherapeutics in skin rejuvenation treatments. Although most respondents (69.2%) do not routinely prescribe these agents for facial rejuvenation, 30.8% of respondents indicated their use in patients with concomitant melasma or extensive photoaging. 23% of respondents use vitamin-based senotherapeutics, particularly Vitamin D, Vitamin C, and isoquercetin, for their antioxidant and reparative properties in aging skin. One respondent prescribed nicotinamide (vitamin B3) to patients with actinic keratosis, chronic actinic dermatitis, or dermatoheliosis, with treatment courses lasting up to one year. The 15.4% of respondents reported having clinical experience with prescribing metformin.

Application of PN

PN injectables, such as Rejuran®, were widely used for wound healing, anti-inflammation, and skin rejuvenation. For general skin rejuvenation, 53.8% of respondents used PN to address issues like fine lines, wrinkles, enlarged pores, and dry skin. Additionally, 30.8% of respondents frequently used PN to treat depressed scars, including acne scars. Rejuran S® (A Rejuran product which contains twice the concentration of PN compared to the original Rejuran Healer), which is particularly affective for treating atrophic scars, was often combined with ablative or non-ablative fractional lasers to enhance the treatment outcomes.

The 15.4% of respondents used PN after laser treatments to promote skin regeneration and reduce the risk of post-inflammatory hyperpigmentation. The anti-inflammatory effects of PN were also noted, making it a popular choice for sensitive skin conditions, such as patients with rosacea, stable acne, and other forms of dermatitis. Practitioners reported using PN both as a standalone treatment and in combination with various EBDs like RF, HIFU, triple wavelength laser (TWL), and ablative $\rm CO_2$ fractional lasers to enhance recovery and stimulate collagen production.

Application of PDLLA

PDLLA, marketed as Juvelook®, emerged as a widely used biostimulatory agent for general skin rejuvenation. 53.8% of respondents reported using PDLLA to improve skin texture, pore size, overall surface smoothness, wrinkles and photoaging. Juvelook volume® was particularly noted for its ability to address laxity and restore

volume in aging skin, especially in areas such as the neck and hands. Dermatologists frequently combined PDLLA with various EBDs like HIFU, RF and TWL. Furthermore, 46.2% of respondents highlighted that PDLLA's collagen-inducing properties made it useful for treating atrophic scars and acne scars. PDLLA can be used alone or in combination with microneedle RF for this patient population.

Application of Lorient Element®

Lorient Element®, a topical solution designed to address hyperpigmentation, was another agent frequently used by dermatologists. The 15.4% of respondents noted that it was either used alone or combined with modalities which target melasma, lentigo, and dark and uneven skin tone. Lorient Element® was particularly favored for its ability to treat post-inflammatory hyperpigmentation and background dyschromia which may be difficult to address using traditional EBDs alone. Practitioners paired Lorient Element® with fractional lasers or plasma-assisted delivery systems to enhance penetration and effectiveness. Microneedle RF was also mentioned as a valuable device for improving drug absorption.

Application of deoxycholic acid

Deoxycholic acid (commercially available as V-olet® in South Korea) is primarily used for patients seeking permanent adipocytolysis in areas of stubborn fat accumulation. In our survey, 30.8% of respondents reported using V-olet®. For facial rejuvenation, V-olet® is commonly applied to the submental, jowl, and zygomatic areas to permanently dissolve fat. Beyond the face, it can be also used on areas such as the upper arms, periumbilical region, bra fat, abdomen and above the knees. Respondents often combine V-olet® with HIFU or TWL to enhance results, particularly for facial and body contouring.

The most preferred EBDs and injectables

When asked about their preferred choice of EBDs and injectables, expert dermatologists provided a diverse range of responses, highlighting the flexibility involved in skin rejuvenation treatments. The survey results are summarized in **Table 1**.

Adverse events associated with EBDs, injectables and senotherapeutics

The most reported adverse event for HIFU treatments was lipoatrophy, with occasional occurrences of welt formation and perioral asymmetry. RF treatments were occasionally linked to burns, swelling, and, in a few cases, infection. Among injectables, including biostimulators, skin boosters, and deoxycholic acid, PLLA was most frequently associated with the formation of nodules. Vascular ischemia was a potential complication associated with HA microdroplet injectables when administered near major facial arteries. Regarding oral senotherapeutics, one respondent who had used metformin reported discontinuing it due to dizziness.



Table 1. Most preferred energy-based devices and injectables among Korean dermatologists who expertise on skin rejuvenation

Expert	Energy-based devices	Injectables
1	1,927 nm fractional laser (LaseMD)	PN+HA (Rejuran HB)
	Plasma (Helium/Nitrogen/Argon, Plazmagik, Pladuo)	PDLLA (Juvelook, Juvelook volume)
	RF+injector (DoubleTite)	
	Hyperbaric needless jet injector (Curejet)	
2	HIFU (Ulthera)	Skin booster-PDLLA (Juvelook), PN (Rejuran), HA (Skinvive)
	RF (Thermage)	Biostimulator–Juvelook Volume, CaHA (Radiesse)
	TWL (Titanium)	
3	RF+injector (DoubleTite)	PN (Rejuran)
4	RF (Corage)	
5	Fractional laser	PN (Rejuran)
6	Monopolar RF	PN (Rejuran)
7	Mono/bipolar RF (Density)	PN (Rejuran)
8	Microwave, needless injector	PDLLA (juvelook)
9	Microneedle RF (Virtue)	
10	IPL, monopolar RF	PN (Rejuran)
11	Microneedle RF (Secret)	PDLLA (Juvelook)
12	HIFU (Ulthera)	PDRN (Placentex)
13		Botulinum toxin

RF: radiofrequency, HIFU: high-intensity focused ultrasound, TWL: triple wavelength laser, IPL: intense pulsed light, PN: polynucleotide, HA: hyaluronic acid, PDRN: polydeoxyribonucleotide, PDLLA: poly-D, L-lactic acid, CaHA: calcium hydroxylapatite.

DISCUSSION

The survey findings reveal several important trends in facial skin rejuvenation treatments, particularly emphasizing the customization of procedures based on patient characteristics. For patients with higher facial fat, practitioners generally prefer a more aggressive approach, often combining HIFU and RF with injectables such as deoxycholic acid to target localized fat deposits, particularly in areas like the jowls and submentum. These treatments are typically applied using high-energy settings and large treatment zones to maximize skin tightening and fat reduction, in line with global trends in noninvasive aesthetic procedures^{1,3}.

In contrast, for patients with lower facial fat, clinicians favor less aggressive methods, focusing more on tissue tightening while avoiding significant fat reduction. Monopolar RF and microneedle RF are commonly used, often in combination with biostimulators like PDLLA and PLLA to restore volume and stimulate collagen production. This reflects a broader trend toward volume restoration as a key aspect of facial rejuvenation in individuals with lower subcutaneous fat.

HIFU and RF are both widely used EBDs for skin rejuvenation, but they work through different mechanisms⁸. HIFU targets the SMAS and deep dermal layers by creating thermal coagulation zones that stimulate collagen regeneration and skin lifting. It is particularly effective for lifting and tightening sagging skin, as well as treating moderate to severe skin laxity and wrinkles, especially in the jowls and neck, without damaging the epidermis. However, while HIFU is effective, it can cause temporary discomfort during the procedure, due to the thermal energy reaching deeper skin structures^{8,9}.

RF, by contrast, generates heat by passing electromagnetic energy passing through tissue resistance, stimulating collagen contraction and remodeling across various skin depths, including the dermis and subcutaneous layers. It is commonly used to improve skin texture, reduce fine lines, and treat wrinkles^{3,8,10}. There are three main types of RF systems: monopolar, bipolar, and fractional RF, each with different penetration depths and applications. Monopolar RF provides deeper penetration and is effective for treating deeper wrinkles and skin laxity, while bipolar RF delivers more controlled, superficial heating for fine lines and moderate laxity1042. Fractional RF, which combines micro-needling with RF energy, is particularly effective for treating acne scars and skin texture irregularities¹³. The choice between HIFU and RF depends on patient-specific factors such as skin laxity and fat distribution. HIFU is favored for lifting and tightening deeper structures, while RF is more versatile, targeting different skin layers and offering benefits for both wrinkle reduction and collagen stimulation^{14,15}. In many cases, combining HIFU and RF can enhance overall treatment outcomes by addressing both deep tissue and surface skin concerns, resulting in a more comprehensive rejuvenation effect.

Minimally invasive injectable procedures have revolutionized facial rejuvenation treatments and have become one of the most sought-after procedures in modern cosmetic dermatology. Initially focused on addressing fine lines and wrinkles, the application of traditional HA fillers has expanded to include restoring volume and enhancing facial contours in aging skin. However, these treatments can sometimes result in adverse events, such as vascular complications, allergic reactions, and foreign body reactions¹⁶⁴⁸. To mitigate these risks, a technique known as hydrolifting has



gained popularity. This approach involves injecting small amounts of skin boosters across larger areas (e.g., the entire face), offering not only subtle volumizing effects but also promoting more comprehensive d skin rejuvenation¹⁹. Current skin boosters include non-cross linked HA, DNA fragments, biodegradable collagen stimulators, and nonbiodegradable products²⁰.

Polydeoxyribonucleotide (PDRN) is a tissue regeneration activator composed of low molecular weight DNA fragments, derived from the sperm DNA of *Oncorhynchus mykiss* (Salmon trout) or *Oncorhynchus keta* (Chum Salmon). PDRN activates adenosine A2A receptors, which promote angiogenesis and enhance fibroblast activity²¹. It is particularly effective for wound healing and improving skin health in patients with damaged or compromised skin. Additionally, PDRN has anti-inflammatory properties that help reduce redness and swelling, thus accelerating recovery after procedures^{20,22-24}.

In contrast, PN, extracted from gonads of salmon or trout, consists of high molecular weight DNA fragments, providing significant viscoelasticity^{23,24}. This structure retains water molecules and undergoes gradual enzymatic degradation, releasing oligonucleotide fragments and water molecules over time. As PN breaks down, it supplies the extracellular environment with essential nucleotides, nucleosides, and nitrogen bases, which are critical substrates for cellular functions. This controlled breakdown helps maintain hydration and structural support, making PN particularly effective for skin rejuvenation^{25,26}.

PN forms a 3-dimensional matrix in the dermis, which makes it especially useful for treating fine lines, uneven texture, and dry skin. Additionally, PN is often combined with EBDs like HIFU and RF to enhance results by reducing post-treatment dryness and inflammation, while accelerating recovery. When used in conjunction with RF or HIFU, PDRN can improve skin tightening effects and promote faster recovery by supporting cellular repair and collagen synthesis. Adverse effects of PDRN and PN are generally minimal, with most side effects being mild and transient, such as swelling or bruising²⁴.

PDLLA and PLLA are biodegradable polymers widely used in aesthetic treatments for their ability to stimulate collagen production. PDLLA is an amorphous, biocompatible material known to promote tissue regeneration by boosting collagen production and enhancing the ECM. This makes it particularly effective for addressing fine lines, wrinkles, and skin laxity. Studies have shown that PDLLA aids in volume restoration by forming a supportive matrix within the skin, leading to gradual tissue thickening and skin rejuvenation over time^{20,27}. PLLA, while similar to PDLLA, has a more crystalline structure and is known for its longer-lasting effects. It is often used for deep dermal volumization, particularly in patients experiencing significant volume loss²⁸. Both PDLLA and PLLA are frequently combined with other treatments, such as RF

or microneedle fractional RF, to enhance overall skin texture and reduce acne scars. Adverse effects are generally mild. Some cases of nodules or granulomas, particularly with PLLA, have been reported, but these are typically manageable and resolved over time.

The discovery of senotherapeutics is relatively recent, and their beneficial effects have been well-documented in an increasing number of preclinical and clinical studies²⁹⁻³². However, much remains to be understood about their role in skin aging and their clinical application, which is not yet widely established. Some experts in our survey reported prescribing isoquercetin, a glycosylated form of quercetin that enhances its water-solubility and bioavailability. Quercetin, a natural plant flavonoid, targets the BCL-2 and PI3K/AKT pathways to eliminate senescent cells³³. The senolytic effects of both dasatinib and quercetin have been shown to reduce the burden of senescent cells and inflammation, particularly in radiation-induced ulcers and age-related skin changes³⁴. Metformin also shows promise in skin rejuvenation through its senomorphic properties which involve reducing senescence-associated β-galactosidase activity and SASP expression. Additionally, metformin has been shown to promote cellular proliferation and to enhance the function of dermal fibroblasts and stem cells^{35,36}. Nicotinamide (also known as niacinamide), a form of vitamin B3, is not formally classified as a senotherapeutic, but it exhibits properties that overlap with those with senotherapeutics, particularly in managing oxidative stress, DNA repair, and inflammation³⁷. Similarly, while vitamin C is not classified as a senotherapeutic, it shares senomorphic-like characteristics by addressing oxidative stress, DNA repair, collagen synthesis and inflammation³⁸. For senotherapeutics to become a standard treatment for skin rejuvenation, further studies are needed to identify optimal senotherapeutic compounds, determine effective treatment regimens, and evaluate the safety of long-term use.

In conclusion, this survey provides valuable insights into the clinical nuances of skin rejuvenation practices among dermatologists in South Korea, highlighting the importance of tailoring treatment plans to individual patient characteristics. While global trends increasingly favor noninvasive approaches to skin rejuvenation, this study emphasizes the need for further research to optimize treatment protocols and effectively manage associated adverse effects. The ongoing development of senotherapeutics and pain management strategies will be crucial for improving patient outcomes in this rapidly evolving field.

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FUNDING SOURCE

None.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

DATA SHARING STATEMENT

Data of this article is available from the corresponding author upon reasonable request.

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