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Original Article

Bio-skin-gineering: a novel method to focus cutaneous aging treatment on each individual layer of the skin specifically and precisely

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Abstract
Facial cutaneous aging changes are clinically visible to both the patient and the physician as progressing wrinkles, cutaneous sagging, textural and tone changes as well as an overall lack of radiance of the skin. Histologically the aging changes are seen within each layer from epidermis, dermo-epidermal junction, papillary dermis, reticular dermis and through to the subdermal layer. In order to effectively treat the entire spectrum of cutaneous aging changes, physicians need to understand that each layer requires therapy and merely single depths of treatment may not recover the pathology in all the layers. The concept of Bio-Skin-Gineering focuses on treating each layer individually with precision of depth and with suitable agents. This article describes the precise injection techniques of reaching each layer of the skin to ensure safe and effective results are obtained when treating cutaneous aging changes.

Keywords
Skin aging, skin quality, hyaluronic acid fillers, mesotherapy

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Introduction

Techniques of skin rejuvenation most commonly remain the ablative and exfoliative types of treatments such as peelings, lasers and micro-dermabrasions[1]. In contrast, the revitalizing treatments focus on replenishment and nourishment to reverse the cutaneous aging signs. This concept, unique to the technique of skin rejuvenation mesotherapy or revitalization, focuses on replacement and nourishment of the vital components of the skin with mostly poly-vitamin solutions and especially non-cross-linked hyaluronic acid.

Also, soft tissue filler injections have evolved to unique formulations adapted to various depths of injections by altering the rheology of the hyaluronic acid (HA) fillers with various concentrations, cross-linking degree and chain lengths to adapt product injection to unique depths and indications[2].

HA fillers are being used for skin rejuvenation purposes by utilizing the low density, low cross-linked HA products suited for dermal injections and not purely sub-dermal as with past and traditional HA fillers used mostly for contouring and volumizing.

Many doctors will perform skin rejuvenation with either fine line filler products (minimal cross-linked HA) placed dermally or just sub-dermal by manual or device injection or some may prefer to treat with poly-vitamin products with mesotherapy techniques of injection. Only recently have we realized the importance of combining both techniques for optimal results.

The technique, which I have named "Bio-skin-gineering", focuses on treating each individual layer of the skin, with knowledge of exact depths and angle of injection with various products according to the suitability of the product for the specific layer. The rationale behind this concept is that each layer from epidermal, DEJ, dermal to subdermal needs to be treated individually in order to reduce aging changes in the layers individually and to optimize results.

Indications

This protocol is a natural, safe and effective therapeutic intervention to improve the external cutaneous signs of solar elastosis and photo-aging of the face, neck, décolleté region and for the hands.

Patient profile

The protocol is especially suitable for patients with:

- Thin or dehydrated skin
- Fine wrinkling (crepe paper appearance)
- Superficial lines or skin coarseness
- Textural skin aging (due to solar elastosis or poor lifestyle habits)
- Need for preventative intervention

The specific indications that can benefit from this treatment includes:

- Peri-orbital loose skin and wrinkling
- Peri-oral wrinkles
- Cheek wrinkles
- Forehead lines
- Neck and décolleté skin aging
- Skin aging on hands

Treatment rationale

The proposed protocol focuses on replenishment of the decrease in HA (free HA) within the layers; supplementation of the necessary anti-oxidants, vitamins, minerals and agents that will stimulate cell renewal and reduce oxidative aging process; and lastly to replace lost volume within the deep dermal and sub-dermal layers with minimally cross-linked HA to obtain a cushioning effect. The bio-skin-gineering technique opinion aims to emphasize the importance of knowledge of the precise depths of each layer of the skin and how to accurately reach each layer to optimize treatment outcomes.

Methods

Treatment techniques

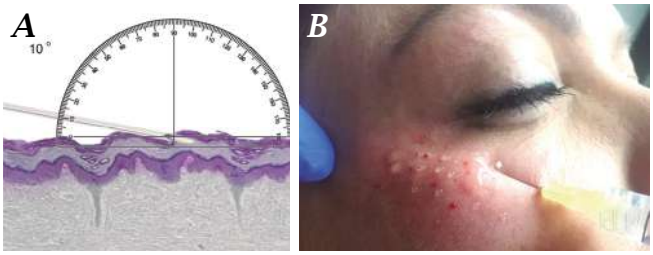
The technique is performed in 4 steps, all done in the same treatment session.

1. Epidermal rejuvenation (0.05 - 0.1mm thick on face to décolleté) [8]

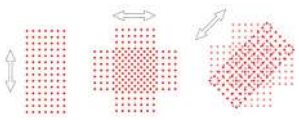
The epidermis is avascular and not too sensitive. The techniques used can be either with the epidermal needle technique or with epidermal skin needling. The epidermic technique, as described in mesotherapy practice, is performed with a 30G needle of 12mm length at an angle of 10° or less to the skin, with only the bevel entering this superficial layer[9-13] (*Figures 1A and B*). The movement is rapid and almost 'tremor - like' to ensure that the needle does not enter too deep. Soft pressure on the syringe plunger will ensure droplets of the product are deposited on the surface and reach the epidermis.

Alternatively, the technique of epidermal skin needling with a device containing short 0.5mm - 1.0mm needles and very slight pressure (minimal bleeding) can be used to rejuvenate the epidermis. The product is applied to the skin before and during the rolling technique on the skin (*Figures 1C and D*). Rejuvenation of the epidermis is performed using a sterile injectable poly-vitamin solution with only free hyaluronic acid (not cross-linked at all) that is suitable for epidermal level of injection or needling. An example of a suitable product for this technique is NCTF135HA®, due to its optimal suitability within the epidermis and dermis, and due to the numerous scientific safety and efficacy data.

Role of epidermal technique: enhance cell turnover, improve moisture balance, nourishment of the avascular epidermis and intense cutaneous stimulation. The epidermic technique contributes greatly to the radiance that patients notice from the 1st session.

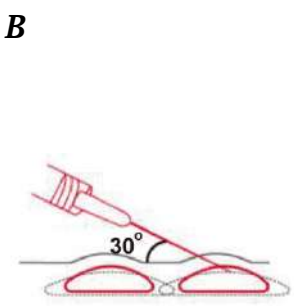


***Figures 1A and B** - Epidermal technique: 30G needle at a <10° angle to the skin.*



Figures 1C and D *- Epidermal technique with a skin-needling roller in 3 directions with soft pressure with minimal to no bleeding, which confirms epidermal depth.*

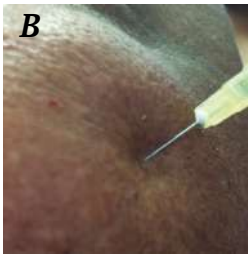
2. Dermo-epidermal Junction (DEJ) Rejuvenation (±0.5mm)
This technique has been described in mesotherapy practice as the papule technique[13]. This layer can only be reached with a manual injection with a 30G - 32G needle of about 4mm length. Separating the epidermis from the dermis, with a papule forming, is the aim of the technique. A typical wheel or papule has to be visible during injection, avoiding too deep injection as this will reach deeper dermis or subdermal level.
The technique is focused on problem areas such as inside wrinkles, scars, eyelid skin or areas where maximal lifting is required. The same product as mentioned in epidermal technique and not at all with a cross-linked HA, as the papule will remain. Product choice is essential and should be water soluble, neutral pH and sterile for injection purposes to minimize pain and complications.
Role of papule technique in DEJ: optimizes transfer of nutrients, enhanced microcirculation and improvement of the upper part of the papillary dermis (DEJ).

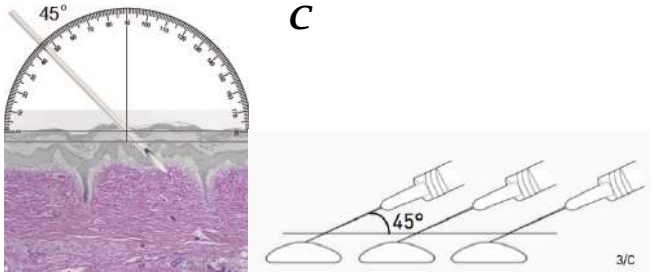


Figures 2A and B *- Showing the technique of "papules"*

3. Dermal Rejuvenation (±0.5mm - 1mm)
The dermis is most often treated with aesthetic treatments. Low viscosity and minimal cross-linked HA fillers have become popular for dermal injection to enhance collagen quality and quantity[14].
Non cross-linked HA solutions are often used for intra-dermal injection. The purpose of dermal injections: enhancing collagen content and quality, extracellular matrix enhancement and also improvement of fibroblast and elastin quality[14-18].

The objective is to nourish the dermis and the fibroblasts with essential vitamins and minerals, to replace free HA within the dermis and to create multiple punctures into the dermis for microcirculatory improvement, growth factor release and to create a favorable environment for dermal fibroblast cell function[21]. A quality product containing an ideal combination of essential nutrients, vitamins, minerals, anti-oxidants and free HA will further ensure the bio-revitalising effect of the treatment[16,17].
The technique used is referred to as a multi-puncture technique (*Figures 3A, B and C*). Ideally performed with a 30G or 32G needle of 4 - 6mm length at an angle of 45° to the skin. Multiple, fast and repetitive punctures into the dermis is used. Free (non cross-linked) HA integrates in the dermis and will not cause any complications of long-term nodules or 'Tyndell effect'. This will replenish the ECM, induce deep hydration and stimulate fibroblast activity to increase production of the scaffolding components within the ECM[16,17].





Figures 3A, B and C *- Multipuncture or "nappage" technique with free HA containing product.*

Dermal rejuvenation with cross-linked HA fillers (low degree cross-linking) are done with a different technique to avoid nodules and other possible complications. Very small amounts of product should be injected per point. The techniques that I have found to cause the least amount of side effects for the patients are not papules, but rather very fine 'worms' or lines of product in a mesh/grid pattern. Alternatively a micro-cannula (25 - 27G) can be used intradermal or immediately sub-dermal which is associated with more resistance due to the density of the dermis and more pain compared to sub-dermal.
Role of cross-linked HA in dermis: maximizes collagen stimulation, support and enhancement of a thin and dehydrated dermis.

4. Subdermal rejuvenation (1.0 - 1.5mm)
The deepest injection of this protocol could either be performed last or one could also start with this layer, especially when using a product that has lidocaine incorporated within the product. This would minimize the discomfort of the previous techniques in a sensitive patient. The sub-dermal layer, which is the superficial fat pad directly below the dermis, forms a 'cushioning' effect to plump a thin and fragile skin. The depth ranges from 1 - 1.5 mm in facial skin and is reached with at least 45° angle of injection.
Use a product containing low degree cross-linked HA and also with free HA that is suitable for superficial injection and should not leave nodule formation or uneven lumps or bumps.
The use of low viscosity hyaluronic acid fillers as a cushioning effect and enhancement of the superficial fat pads under the dermis have increased in popularity over the past few years (*Figure 4A*).

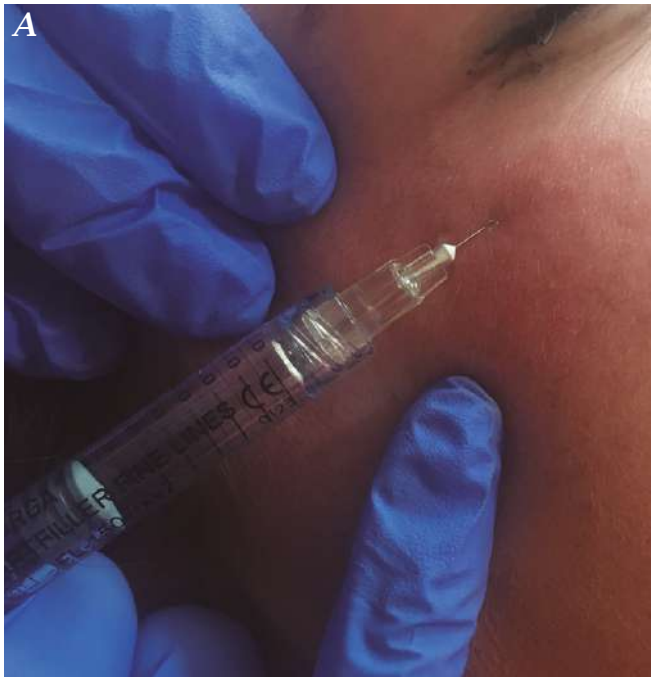
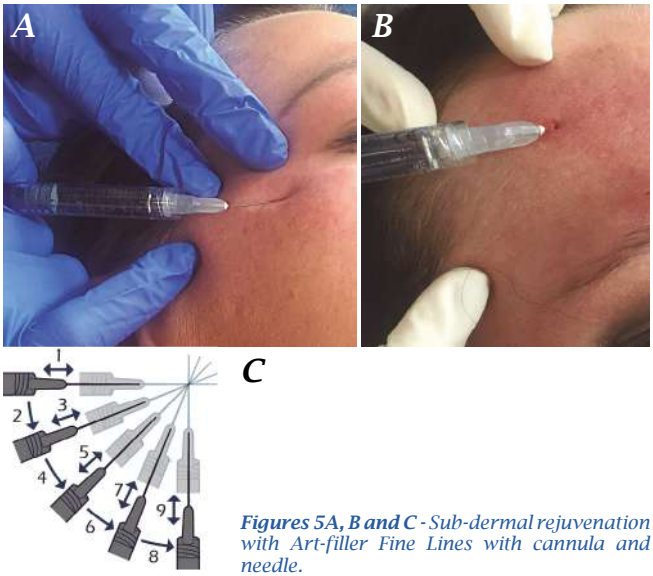


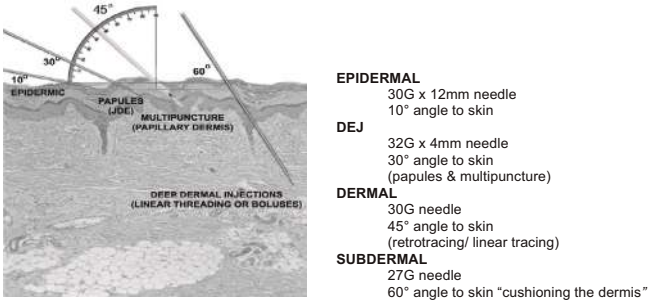
***Figure 4A** - Intradermal placement of low viscosity hyaluronic acid filler with a 30G needle.*

This technique is ideal to use in patients with loss of sub-dermal fat pads and a skinny or skeletal face. The loss of superficial as well as deep fat pads leads to more excessive wrinkling and dehydration of the skin and dermis.
Subdermal cross-linked HA injections will give an instant plumping of wrinkling, as well as continued stimulation of collagen and elastin production[14,18]. Though, the revitalizing, hydrating and long-term improvement of the dermis and epidermis is only seen when combined with the prior techniques. The technique used can be either with a micro-cannula (27G or 30G) with a fanned technique (less bruising and reduced risk for vascular placement) or with sub-dermal multipuncture technique with needles (*Figures 5A, B and C*). The technique choice varies according to the physician's comfort in skills and according to the product used (*Figure 6*).

In high-risk regions such as peri-orbital and forehead region, the use of a 25G cannula is vital to reduce the risk of intravascular placement. When using a needle technique, it is recommended to perform aspiration on the syringe before injection of a cross-linked HA filler.
Most side effects are transient, mild and technique dependent. These may include mild erythema, bruising and swelling[17]. Using exclusively HA soft tissue fillers for this directly subdermal level will ensure safety, reversibility and reduced lumpiness, especially with a very low viscosity product.



***Figures 5A, B and C** - Sub-dermal rejuvenation with Art-filler Fine Lines with cannula and needle.*



***Figures 6** - Summary of the combined injection techniques in the Bio-skin-gineering protocol.*

Clinical notes

- Prior treatment with anaesthetic cream improves patient comfort
- In practice, I sometimes start from the deepest technique and end with the most superficial technique. This reduces pain for sensitive patients because the fine line filler contains lidocaine, which then makes the following techniques almost pain free.
- Finish the treatment with an intensive massage with a suitable post procedure product.

The bio-skin-gineering technique can be scheduled in a course of treatments ranging from 2 - 3 treatments depending on the severity of cutaneous aging of the patient. The treatments can be spaced apart from 4 - 6 weeks apart with ideally 3 sessions per year.

Results

Clinical results are visible from the first session, which includes improved hydration, smoothness and plumpness (*Figures 7A and B*).

Continued improvement from 6 weeks to 6 months includes wrinkle reduction and firmness, this can be explained by understanding the wound healing phases of neocollagenesis starting from 4 to 6 weeks only (*Figures 8A, B and C*).

In a clinical practice it is not possible for physicians to confirm histological improvement on each of our patients following procedures, but we can rely on the studies performed by the manufacturers for efficacy and safety. In general we understand from clinical data that HA soft tissue fillers have a good safety profile, especially when performed with quality products and meticulously safe and sterile techniques[18].

Various manufacturers of HA fillers have further shown the improvement of collagen quality and quantity following sub- and intra-dermal placement[14,18]. Gathering from these studies, we understand that this protocol will therefore improve collagen quantity and quality.

Injectable polyrevitalizing solutions used with good mesotherapy techniques have also clinically proven the benefits of treatment with quality products on skin hydration, glow, evenness and further collagen stimulation[11-13,15-17].

Therefore, we could assume that the combined technique would give us the combined the histological improvement within the skin.

Results are most visible in patients with dehydrated, wrinkled or dull skin requiring an intensive boost. Results are specifically evident on areas with thinner skin such as peri-orbital, neck and décolleté regions.

Before *Immediately after* *1 week after*

Figures 7A and B *- Before and immediately after the treatment of epidermal technique, papules, multipuncture and subdermal injection. The images show that many patients will require no recovery period.*

Figures 8A, B and C *- Results of Bio-skin-gineering protocol on the forehead of a patient (8A) and the full face (8B and C). The results shown are following 1 treatment session and both images are taken with frontalis muscle contraction.*

Discussion

Revision of aging changes within the individual skin layers

Each layer has specific purposes of functionality and contributing towards the skin's external appearance (*Tables 1 and 2*).

Histological Changes seen in Skin Photoaging or solar elastosis.

The importance of Hyaluronic acid (HA)

The use of injectable HA to rejuvenate the skin, rehydrate the dermis and reduce wrinkles are based of the role it plays within the human skin.

Some of the functions of HA within human skin:

- Cushioning and plumping effect (anti-wrinkle)
- Hydrating (retaining water)
- Keeps collagen and elastin moist – youthful skin
- Optimizing wound healing
- Immune function
- UV radiation protection
- Improves collagen synthesis and normal skin function
- Indispensable for the visco-elastic balance of epidermis and dermis
- Role player in keratinization in epidermis

Conclusion

The BIO-SKIN-GINEERING protocol is a combination of techniques to ensure rejuvenation from the deepest layer to the most superficial layer to improve the total rejuvenation of the skin and long-term patient satisfaction.

Ideal for wrinkled, dehydrated or dull skin requiring an intensive boost. The protocol is most suitable for peri-orbital, peri-oral, neck and décolleté, or other areas.

Side effects may include some small bruises depending on technique, but other than this no significant risks are involved when using high quality products.

The benefits for the patients include instant radiance and hydration with textural improvement from 4 weeks following the treatment is visible, especially when using high quality products with supporting data. This technique aims to improve the total rejuvenation of the skin and long-term patient satisfaction.

Physicians should be familiar with the techniques to reach each layer separately and have knowledge of the average depth of the layers in facial skin especially. High quality polyrevitalising solution with non-crosslinked hyaluronic acid is used for the epidermal, DEJ and dermal layers. Low degree crosslinking HA fillers are used for the deep dermal injections and sub-dermal placement. Ensure that products used for this technique has sufficient safety and efficacy data. The combined techniques and products ensure combined histological benefits and combined clinically evident benefits for both the patient and the physician.

Although scientific data exists for the use of low viscosity HA fillers and also for the use of certain mesotherapy or revitalizing solutions, this combined technique shows promising results and more research in the combination of these techniques and products would be beneficial.

SKIN LAYER	FUNCTION	AESTHETIC IMPORTANCE
Epidermis	Barrier function (protection from injury, microbial and UV) Water repellant	Keeps skin smooth, soft, supple and prevents water loss.
Dermo-epidermal junction	Nutrient and moisture transfer from vascular dermis to avascular epidermis.	Flattening of DEJ results in skin fragility and dull appearance.
Dermis	Skin quality and strength: fibroblasts producing extracellular matrix glycoaminoglycans (GAGs), collagen, elastin, hyaluronic acid.	Reduced quality and quantity of GAGs leads to dehydration and wrinkle formation.
Hypodermis/ Subcutis	Adipocytes and collagen fibers for support of dermis and allows dynamic movement.	Gives youthful and plump appearance. Atrophy and gravitational changes contributes to wrinkles and sagging in face.

***Table 1** – Summary of the role of each layer in its functionality and aesthetic importance [3-6].*

Skin Layer	*Aging changes*	*Symptoms/ Signs*
EPIDERMIS	Slow cell turnover Atrophy Barrier dysfunction Poor moisture balance Atypical keratinocytes and stratum basale Irregular distribution of melanocytes	Dehydrated surface Rough texture Sensitivity/ Fragility Pigmentary changes
DEJ	Flattening of DEJ Reduced nutrient transfer form vascular dermis to avascular epidermis	Reduced radiance Fine lines Skin fragility
DERMIS	ECM health and moisture balance reduces Dermal elastosis Fibroblast dysfunction Reduced collagen and elastin network Disorderly arranged network	Wrinkles Sagging skin Loss of elasticity Crepe-paper appearance
SUBCUTIS	Atrophy and irregularity of superficial fat pads Reduced support of dermis	Thin, wrinkled skin Loss of volume/ plumpness of skin

***Table 2** – Summary of the aging changes in the various layers of the skin [4-6].*

REFERENCES

1. Ramose da Silva, da Silva Carneiro SC. Elderly skin and its rejuvenation: products and procedures for the aging skin. *J Cosmet Dermatol.* 2007; 6(1):40-50.

2. Born T. Hyaluronic acids. *Clin Plast Surg.* 2006; 33(4):525–38.

3. Waterston K, Naysmith L, Rees LJ. Variation in skin thickness may explain some of the within-person variation in ultraviolet radiation-induced erythema at different body sites. *J Invest Dermatol.* 2005; 124(5):1078-1078.

4. Elias P, Feingold KR. Lipids and the epidermal waterbarrier: metabolism, regulation, and pathophysiology. *Semin Dermatol.* 1992; 11(2):176-82.

5. Baumann L. Skin ageing and its treatment. *J Pathol.* 2007; 211(2):241-251.

6. Varani J. Fibroblast aging: intrinsic and extrinsic factors. *Drug Discov Today Ther Strateg.* 2010; 7(3-4):65-70.

7. Prikhnenko S. Polycomponent mesotherapy formulations for the treatment of skin aging and improvement of skin quality. *Clinical Cosmetic Investig Dermatol.* 2015; 8:151-157.

8. Ha RY, Nojima K, Adams WP Jr, Brown SA. Analysis of facial skin thickness: defining the relative thickness index. *Plastic Reconstr Surg.* 2005; 115(6):1769-1773.

9. Madhere, S. Aesthetic Mesotherapy and Injection Lipolysis in Clinical Practice. Informa Healthcare UK Ltd 2007.

10. Rohrich RJ. Mesotherapy: what is it? Does it work? *Plast Reconstr Surg.* 2005; 115(5):1425.

11. Pistor M. What is mesotherapy? *Chir Dent Fr.* 1976; 46(288):59-60.

12. Amin S, Phelps RG, Goldberg DJ. Mesotherapy for facial skin rejuvenation: a clinical, histologic, and electron microscopic evaluation. *Dermatol Surg.* 2006; 32(12):1467-72.

13. Petit P. Prevention and treatment of skin aging and wrinkles with mesotherapy. *MIMS Handbook of Aesthetic Medicine including Wound Care.* 2013.

14. Wang F, Garza LA, Kang S, et al. In vivo stimulation of de novo collagen production caused by cross-linked hyaluronic acid dermal filler injections in photodamaged human skin. *Arch Dermatol.* 2007; 143(2):155-163.

15. Prikhnenko S. Polycomponent mesotherapy formulations for the treatment of skin aging and improvement of skin quality. *Clin Cosmet Investig Dermatol.* 2015; 8:151-7.

16. Sparavigna A, Tenconi B, De Ponti I. Antiaging, photoprotective and brightening activity in biorevitalization: a new solution for aging skin. *Clin Cosmet Investig Dermatol.* 2015; 8:57-65.

17. Tedeschi A, Lacarrubba F, Micali G. Mesotherapy with an intradermal hyaluronic acid formulation for skin rejuvenation: an intrapatient, placebo-controlled, long-term trial using high-frequency ultrasound. *Aesthetic Plast Surg.* 2015; 39(1):129-33.

18. Wollina U, Goldman A. Hyaluronic acid dermal fillers: safety and ef cacy for the treatment of wrinkles, aging skin, body sculpturing and medical conditions. *Clin Med Rev Ther.* 2011; 3:107-121.