The 3-D Approach to Cosmetic Dermatology

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ABSTRACT

The demand for evidence-based cosmetic treatments against visible signs of skin aging is growing. Nonsurgical procedures in particular are becoming more and more popular. Although until recently the primary aim in cosmetic dermatology was softening of facial lines and wrinkles, replacement of volume loss and facial contouring is now rapidly catching up. However, modern cosmetic dermatology takes into consideration all three key areas of skin aging ("3-D" approach): (1) wrinkles and lines, (2), loss of volume and contour, and (3), skin surface and texture impairment. A "holistic" approach accessing the entire face, and combining different treatment modalities, achieves best aesthetic results.

This article presents minimal-invasive treatment modalities to address all three key areas of facial skin aging. In addition novel treatment modalities and combinations are discussed. Overall aesthetic results are now aimed to be more "natural" appearing, achieving a harmonious look, and should include evaluation and treatment of extra-facial, exposed skin such as the neck, décolletage, and hands.

Keywords: Cosmetic Dermatology, Aesthetic Dermatology, 3-D, holistic, wrinkles, volume, texture

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INTRODUCTION

The skin is not only the largest organ of the human body and immensely important for nonverbal communication but also the only organ where aging processes are directly visible. Life expectancy has steadily increased throughout the past decades and with this the demand for effective and evidence-based treatments against visible signs of aging has increased. Nonsurgical cosmetic dermatology procedures in particular are becoming more and more popular. Until recently it was custom to concentrate on isolated problem areas of the face, primarily aiming to reduce lines and wrinkles. However, it is now appreciated that a more "holistic" approach accessing the entire face as well as extra-facial exposed skin areas, and combining different treatment modalities, achieves much better and more natural-appearing aesthetic results. To develop an individual treatment plan for each patient, the skin's aging mechanisms have to be understood.

INTRINSIC AND EXTRINSIC SKIN AGING

Scientific research into mechanisms of skin aging has vastly increased during the last few decades.[1–3] An important scientific step was the differentiation between intrinsic (chronological aging) and extrinsic (premature aging) skin aging and their underlying causes and mechanisms. Chronological aging and premature aging share important molecular characteristics, such as altered signal transduction pathways that promote matrix metalloproteinase (MMP) expression, decreased collagen biosynthesis, and connective tissue damage. However, extrinsic skin aging is not simply an acceleration of intrinsic skin aging and both can be readily distinguished clinically and histologically.[4–8] Comparably pure forms of intrinsic skin aging can be found in constantly covered body parts such as the buttocks of elderly persons. Typical features of extrinsic skin aging can be observed in chronically exposed skin areas such as the face, nape of the neck, and the hands of, for example, people working outdoors.

While intrinsic skin aging is determined by genetic influences and endogenous factors such as hormones and pro-oxidative cell metabolism ("biological clock"), extrinsic skin aging can be caused by a variety of environmental factors including chronic UV exposure and smoking. Due to the fact that up to 80% or 90% of visible skin aging is thought to be related to chronic UV exposure, premature aging is often referred to as "photoaging." UV irradiation leads to a variety of molecular chain reactions, including activation of skin surface receptors, which leads to intracellular signaling through mitogen-activated protein kinases, and ultimately results in nuclear transcription of activator protein-1 (AP-1).[9,10] AP-1 induction leads to decreased synthesis of collagen I and III as well as upregulation of dermal MMPs.[9–11] The result of the latter is degradation and damage of collagen, elastin, and other extracellular matrix components such as proteoglycans. Chronic UV exposure leads to repeated dermal insults with progressively more imperfect attempts to repair the induced damage. Cumulative changes in the dermal layer include collagen degradation and disorganization, cross-linking of dermal proteins, accumulation of abnormal elastotic material, and overall disruption of skin structure and support.[1,4,5,9,11] It is thought that about half of UV-induced skin damage is caused by formation of free radicals.[10] UV A irradiation (320–400 nm) penetrates deeper into the skin and is the main causative wavelength for solar elastosis. Besides elastosis, biological effects of UV irradiation in

the skin also include nuclear and mitochondrial DNA damage, inflammation, immunosuppression, and carcinogenesis.[12,13]

Smoking in another well-recognized cause for premature skin aging.[14,15] Apart from well-established epidemiological data, tobacco smoke has also been shown to impair collagen biosynthesis in fibroblasts and induce MMPs,[14,15] both contributing to extracellular matrix impairment. Although UV irradiation and smoking currently seem to be the most important environmental stressors leading to premature skin aging, numerous other factors are also thought to contribute, including infrared irradiation, visible light, and pollution.[4,5,16–26] Furthermore, there are several additional factors contributing to aging in general, including lifestyle factors such as sleep deprevation, stress, lack of physical exercise, unbalanced and/or high-glycaemic index diet, and obesity.[27–30] However, some of these factors remain a topic of controversy.

CLINICAL CHARACTERISTICS OF AGING SKIN

Intrinsic and extrinsic aging have recognized differences in clinical appearance, although in practice mixed forms with predominance of either one or the other are often the case. Intrinsic aging characteristically displays a marked loss of hydration and elasticity with atrophic crinkling and predominantly fine criss-cross pattern wrinkles. It remains without pigment irregularities, but appears very thin and "transparent," with visible underlying vascular structures. Chronologically aged skin is also less resistant to shearing forces, is more easily injured, and suffers from impaired wound healing.

Photoaged skin is typically characterized by a leather-like thickening and coarseness, yellowish hue, and generally deeper wrinkles and furrows. Photoaged skin is also frequently blemished with irregular pigmentation including solar/senile lentigines next to focal areas of hypopigmentation. In advanced cases, extrinsically aged skin may display teleangiectasias, purpura, senile comedones, and actinic keratoses.

Loss of elasticity, formation of wrinkles, and irregular pigmentation are all well-known features of aged skin (Table 1). However, one of the most characteristic features in the appearance of older individuals is a loss of volume (subcutaneous fat tissue, but also underlying facial structures including skeletal changes) especially in the mid-third of the face.[31] With volume loss and decrease of the underlying craniofacial support, the overlying skin and soft tissue tends to sag under the effects of gravity.[32,33] This volume loss is something that is gaining increasing attention recently and has important implications for cosmetic dermatology.

Table 1. Clinical Characteristics of Extrinsic and Intrinsic Skin Aging

Intrinsic Skin Aging	Extrinsic Skin Aging
➢ Very thin skin	➢ Leather-like, thickened appearance
➢ Transparent-appearing skin with visible underlying vascular structures	➢ Yellowish discoloration
➢ Fine lines and atrophic crinkling	➢ Deep wrinkles, folds, and furrows
➢ Markedly reduced elasticity and firmness	➢ Reduced elasticity
➢ No pigment changes	➢ Various pigment irregularities
➢ Reduced resilience against shearing forces, increased tendency for injuries/lacerations, compromised wound healing	➢ Potentially teleangiectasias, purpura, spider nevi
➢ Benign neoplasms such as seborrhoeic keratoses and cherry angiomas	➢ In some cases solar comedones (open or closed)
	➢ Higher risk of precancerous (e.g., AKs) or malignant skin lesions (e.g., BCC, SCC)
➢ Reduced sebaceous and sweat gland activity	
➢ Impaired epidermal barrier function with tendency for xerosis increases skin surface roughness and senile pruritus	
➢ Tendency for irritation and erythema	
➢ Decrease in sensory perception of the skin	
➢ Reduced volume of subcutaneous fat tissue	

THE "3-D" APPROACH TO COSMETIC DERMATOLOGY

In cosmetic dermatology, there are three main area of clinical aging which all have to be accessed when planning a holistic facial rejuvenation: (1) lines and wrinkles (i.e., dynamic wrinkles, static wrinkles, and wrinkle folds), (2) volume loss and loss of facial contour (e.g., loss of subcutaneous fat in mid-face, with subsequent gravitational folds), and (3) skin surface and textural changes (pigmentation changes, impaired skin firmness and elasticity, atrophic crinkling, crepe-like textural changes, etc.). Only if all three key areas are addressed, a successful and natural appearing rejuvenation can be achieved (Table 2). This requires an ongoing relationship with cosmetic patients with planning of a combination of different treatment modalities.

Lines and Wrinkles

For dynamic/hyperkinetic facial lines, caused by repeated contraction of underlying mimic muscles, botulinum toxin, which can transiently and reversibly relax target muscles, remains an effective treatment with very good benefit/risk ratio and patient satisfaction, in particular when used in the upper third of the face.[34–37] Indications in the upper face include glabella lines, "crow's feet," and horizontal forehead lines.[36,37] As injector confidence has grown, indications in the mid- and lower-face as well as jaw line and neck have been added.[36,39,40] Botulinum toxin is now also used to restore symmetry and for facial sculpting and contouring.[36,41] In the upper face, botulinum toxin can achieve eye brow elevation and widening of the eyes.[38,39,42] In the lower face it can reshape the mandibular angle and change the shape of the jawline with reduction of muscle bulk.[36,43,44] Botulinum toxin is also increasingly used in conjunction with other minimal invasive cosmetic procedures and has been shown to be able to enhance and prolong the effects of soft tissue augmentation and improve the outcome of light- and laser-based treatments.[45–49]

In addition to classic intramuscular injections, microinjection techniques ("meso botox") with intradermal injections are now increasingly performed and evaluated.[49–52] In an investigator-blinded, split-face study, Chang et al.[50] found a significant wrinkle reduction after intradermal botulinum toxin

Table 2. Three Columns of Cosmetic Dermatology

Three Key Areas of Skin Aging Lines and Wrinkles	Volume and Contour	Skin Surface and Texture
- Dynamic lines and wrinkles, caused by mimic muscles - Static lines and wrinkles - Deep wrinkle folds and furrows	- Loss of volume (subcutaneous fat, bone structure etc.), e.g., in mid-face - Loss of volume + gravity = skin sagging ("pseudoptosis") ⇒ gravitational furrows - Age-related remodeling of facial contours	- Pigmentary changes (e.g., lentigines solares/seniles) - Nonpigmentary or mixed dyschromias (e.g., facial teleangiectasias, poikiloderma of civatte, etc.) - Loss of skin firmness and elasticity - Atrophic crinkling and crepe-like textural changes
Three Columns of Cosmetic Dermatology Treatment Modalities		
- Relaxing of mimic muscles with botulinum toxin - Injectable soft-tissue implants/dermal fillers - Tissue stimulators	- Volumetric restauration/augmentation with injectable soft-tissue implants/volumizers - Facial contouring/sculpting - Tissue stimulators	- Laser- and light-based treatments - Chemical peels - Medical skin needling/"Gel needling lift" - HA skin revitalization - (Micro-)dermabrasion - Tretinoin or cosmeceutical skincare regimes

injections in the mid- and lower-face, but no lifting effect. Petchngaovilai[51] on the other hand did confirm lifting effects to the mid-face after intradermal botulinum toxin. There is also some preliminary data suggesting that intradermal botulinum toxin injections might be able to reduce sebum production and facial pore size.[53]

A number of products containing botulinum neurotoxin type A are now licensed for cosmetic use (e.g., Vistabel®, Azzalure®, Bocouture®). The latest generation botulinum toxin A, Xeomin/Bocouture®, seems to have a slightly quicker onset of action and is free of complexing proteins, which some believe might reduce the risk of sensitization and development of neutralizing antibodies.[36,54,55] Botulinum toxin type B (Neurobloc/Myobloc) does not currently have approval for cosmetic use.

For static facial wrinkles, injectable soft-tissue implants remain an important tool in the armamentarium of the cosmetic dermatologist. The available number of products and types of materials is rapidly growing, in particular in Europe, and can be roughly divided into (1) temporary (e.g., hyaluronic acid and collagen), (2) long-lasting/semi-permanent (e.g., calcium hydroxylapatite, carboxymethylcellulose/polyethylene oxide), (3) permanent (e.g., certain acryl-derivatives, silicone oil), and (4) mixed products (e.g., collagen plus polymethyl/methacrylate microspheres). Injection depth (dermal, subcutaneous, supraperiosteal) and possible unwanted effects/complications differ in nature depending on injection technique, location, and type of injectable material used. In addition to typical needle-related risks such as hematomas, risk of infection, swelling and erythema, there is also a potential risk of migration of material, delayed inflammatory reactions, development of granulomas, and tissue necrosis, depending on a combination of parameters. Biodegradable hyaluronic acid (HA) fillers are regarded as one of the safest agents to date, whereas complications are more frequently seen with semipermanent or nondegradable fillers.[56–61] Permanent fillers also have the additional drawbacks that a misplaced or disliked product cannot easily be removed and that the aesthetic result might not seem optimal anymore with physiological, age-related changes of the face over time. Augmentation with HA gels on the other hand can be easily reversed using injectable hyaluronidase.[60,62]

Apart from filling individual lines and folds with immediately visible effects, "tissue stimulators" (e.g., tri-calcium phosphate, poly-lactic-acic) may cause a stimulation of collagen neosynthesis in the dermis, thus gradually bringing about correction and volume over time.[63,64] Some of these products may contain a mix of a tissue-stimulating material with a traditional static filling material to offer an instantly visible improvement while waiting for gradual collagen induction. Interestingly however, studies suggest that besides its mechanical filling properties, even HA has some fibroblast-stimulating effects.[65,66]

Overall, there is a movement away from filling individual wrinkles and depressions to more of sculpting and contouring of the entire face ("liquid face lift"). Full-face correction with multiple syringes of filler material has been shown by Taub et al. to reduce the perceived age by 6–9 years.[67] The volumetric restoration of a more youthful roundness of the aging face is discussed in more detail below (see Section "Loss of Volume").

Another trend is the addition of local anaesthetic to injectable soft-tissue implants. Dermal fillers containing lidocaine have been shown to reduce procedural pain while maintaining effectiveness and longevity.[68,69] However, they require a change of injection technique for the patient to fully benefit from the numbing effect.

Loss of Volume

While it remains important to reduce the appearance of lines and wrinkles, research and clinical experience have shown

that one of the most aging features of the face is a loss of volume. Fat compartments in the deep medial cheeks are among the first to go and this is now appreciated to contribute substantially to the aged appearance of a person.[31] Volume loss also leads to an excess in skin envelope with subsequently more prominent nasolabial folds because of effects of gravity—"pseudoptosis."[32] Replacing deep supporting structures does not only increase anterior projection but also repositions overlying tissue and reduces depth of nasolabial folds.[32,33] Restoration of volume loss with volumetric augmentation and facial contouring have now been recognized as being fundamental for any holistic facial rejuvenation treatment. Products used are, for example, more viscous HA products with ability to restore larger volume with improved longevity, autologous fat, calcium hydroxylapatite, poly-L-lactic acid, and a variety of polymers.[63,70–74]

Newer indications of facial contouring include nonsurgical nose shaping, chin augmentation, brow shaping, filling of hollowed temples, and correction of deep tear troughs. It is also possible to restore or augment volume on body areas such as breasts, calves, and buttocks nonsurgically with larger amounts of a larger particle size, stabilized HA gel.[75]

Skin Surface and Textural Changes

The third, but by no means less important, column of cosmetic dermatology is addressing skin surface and textural changes. An evenly colored, firm, and smooth-appearing skin surface is crucial for an attractive looking face. Interestingly, Matt and coworkers have demonstrated that an even skin color does not only correlate with perceived youthfulness and attractiveness, but also with perceived healthiness.[76,77] The improvement of skin surface and texture is arguably the quintessential area of expertise of cosmetic dermatologists.

Typical extrinsic aging–related epidermal changes are diffuse mottled hyperpigmentation and lentigines solares/seniles. Apart from cryotherapy, chemical peels, and topical treatment (e.g., with azelaic acid, hydroquinone/retinoic acid/topical steroid = Kligman's formulation, or tyrosinase-inhibiting cosmeceutical ingredients such as Kojic Acid), there is a large variety of laser- and light-based devices on offer to treat different types of pigmentation problems.[78–80] Facial dyschromia caused by vascular lesions or mixed forms such as Poikiloderma Civatte can also be treated with selective photothermolysis with certain types of laser and light devices.[81–83]

With regard to improving cutaneous texture with crepe-like skin appearance and atrophic crinkling, up until recently one of the few ways to exert significant effects in the dermis was resurfacing via complete ablation of epidermal and upper dermal layers of the skin.[84,85] This can be achieved with certain lasers such as Erbium-YAG and CO_2 laser, dermabrasion, or deep chemical peels.[84,86–88] Although the results can be very good, these procedures inherit significant risks of morbidity and adverse effects such as infection, dyspigmentation, and scaring, as well as a protracted recovery time.[85] Although nonablative resurfacing procedures such as intense pulsed light and radiofrequency, which induce thermal injury in the dermis while preserving the epidermis, are not able to reproduce the same results, there are newer technologies available, which are able to target collagen metabolism effectively without having to denude large areas of the epidermis.[84,89] After initially we saw nonablative fractionated devices, there are now fractionated, ablative laser technologies available.[90,91] These create distinct columns of thermal damage in epidermis and dermis in regularly spaced intervals over a fraction of the full skin surface.

Medical needling is a procedure that is currently experiencing a strong revival, especially in Europe, with good clinical results (Figure 1). "Collagen induction therapy" with fine needles of 1–3 mm lengths partly mimics the effects of fractionated laser technologies, although mechanically, by creating defined, microscopic columns of injury down to the dermis without the need to fully denude the epidermis. The micro-punctures in the skin surface close up quickly, thus reducing risks and down-time, whereas dermal multi-micro-injuries induce a controlled wound healing response with induction of growth hormones, attraction of fibroblasts, and neosynthesis of extracellular matrix components such as collagen.[92–95]

An alternative method of improving skin texture and surface is cutaneous "revitalization" with micro-droplet injections of active ingredients over large skin areas ("mesotherapy"). Traditional mesotherapy solutions contain variable, often nonstandardized mixtures of vitamins, minerals, low-dose native HA, natural plant extracts, homeopathic agents, and/or other bioactive substances.[96] The solution is usually administered into the superficial dermis through means of countless injections, often using a "meso-gun." Treatment sessions have to be repeated frequently to achieve clinical results. Convincing, controlled, double-blind clinical studies distinguishing pure needling effects from active ingredient–related effects of mesotherapy are outstanding.[96,97] In a study by Amin and coworkers, skin biopsies taken after mesotherapy for skin rejuvenation revealed no significant differences in routine histology, mucin, and elastin stains.[97]

However, a scientifically better investigated variation of traditional mesotherapy is skin "revitalization" with micro-droplet HA gel injections. In HA skin "revitalization," small aliquots

Figure 1. Medical needling procedure with 1.5-mm micro-needle roller.

Figure 2. Skin revitalization procedure with micro-droplet injections of hyaluronic acid gel through semiautomatic injector pen.

of HA are injected into large areas of the dermis (e.g., covering both cheeks or the entire face) in intervals of 2–6 weeks. This method has been shown to improve cutaneous hydration with enhancement of tissue turgor, increase skin elasticity, and induce collagen neosynthesis, thus gradually rejuvenating the skin.[66,98–101] Interestingly, we were able to show in a clinical and bioengineering study that stabilized HA achieves superior results to "native," nonstabilized HA.[101] A new development are disposable, semiautomatic HA injector pens, allowing deposition of standardized amounts of HA (Figure 2). It is also possible to combine this treatment with a medical micro-needling procedure ("gel needling lift"), which achieves superior results to either treatment alone, for both skin aging and acne scaring reduction (unpublished data).

In addition to any in-clinic procedure, the long-term benefits of effective cosmeceuticals must not be underestimated and an individualized skin care regimen should accompany cosmetic dermatology procedures. In the morning, this should include a high-grade antioxidant product containing, for example, high-dose L-ascorbic acid plus tocopherol and ferulic acid, followed by broad-spectrum UV protection all year around.[102–104] In the evening, a collagen-inducing "repair" cream containing tretinoin or nonprescription alternatives such as retinaldehyde, retinol, or retinyl retinoate have been shown to be of benefit.[105,106] In addition, the 3-D cosmetic dermatology approach should be completed with professional advice on lifestyle factors such as sun exposure, smoking, nutrition, stress, and exercise.

CHANGING IDEALS IN COSMETIC DERMATOLOGY

Aesthetic ideals change over time and with it the goals of cosmetic dermatology treatments. While aesthetic treatments aimed to achieve a more "dramatic" effect in the past, cosmetic patients and practitioners now value a "natural" and "relaxed" look.[37,107] Cosmetic dermatology has come to embrace rejuvenation treatment results, where all facial features still work in harmony and balance. The trend goes toward not trying to make patients look artificially *younger*, but to aim for making them look *good* for their age. This also includes the recognition that problem areas should not be treated in isolation, but as part of a general treatment plan.

EXTRA-FACIAL SKIN

In addition to addressing the three key aging features of the face, it is also becoming more recognized to include extra-facial skin in treatment planning. There is good scientific evidence to show that the skin on extra-facial, exposed areas such as hands, neck, and décolletage contribute significantly to the overall age appearance of the person.[108–110] With regard to the hands, a thinning of epidermis, dermis, and subcutaneous fat tissue will lead to a "skeletal" appearance with prominent veins and extensor tendons.[111] Bains et al.[108] demonstrated that digital removal of dorsal hand veins on images of older hands led to a younger perceived age. Lentigines and irregular pigmentation are also proven signs of ageing hands.[108]

Laser, intense pulsed light devices and peels are popular therapeutic approaches for hand rejuvenation. However, they mainly address skin surface and textural changes and should be combined with procedures to replace loss of volumen on the back of the hands. The loss of volume and skin elasticity on the dorsal hands can be addressed effectively with, for example, large-area, micro-droplet injections with HA (Figure 3) or bolus injections of calcium hydroxylapatite.[101,112] Hand rejuvenation with micro-droplet HA injections has been shown to mask bulging veins effectively, often rendering sclerotherapy of dorsal hand unnecessary.[101] At the same time this treatment maintains the natural shape of the back of the hands with preserved visible movement of dorsal hand structures. For natural-appearing hand rejuvenation, a "cushion"-like appearance of the dorsal hand, which sometimes accompanies injections with more viscous or stimulatory materials and fat grafting, should be avoided. In addition to replacing the loss of volume on the dorsal hands, laser and light devices, peels, medical needling, topical treatment regimes and others can help to improve skin surface quality and remove pigment lesions.

The neck and décolletage can be treated with a similar combination approach.[110]

CONCLUSIONS

In summary, modern cosmetic dermatology has come to embrace a holistic evaluation of the cosmetic patient with the aim to achieve a natural-appearing, balanced look. The 3-D approach to cosmetic dermatology takes into consideration all three key areas of skin ageing: (1) wrinkles and lines, (2) loss of volume and contour, and (3) impairment of skin surface and texture. Combining different cosmetic treatment modalities has been shown to improve aesthetic outcome and patient satisfaction. An essential aspect is thus development of an

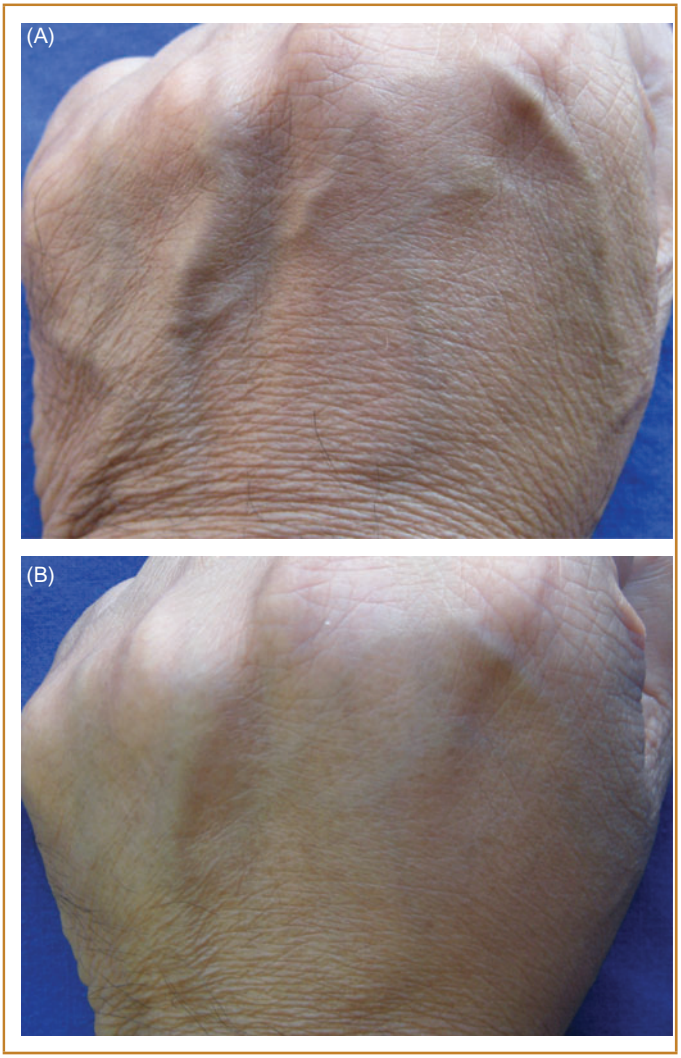

Figure 3. Male hands before (A) and after (B) three treatment session with injectable hyaluronic acid revitalization.

individually tailored treatment plan for each patient, which needs to be reassessed on an ongoing basis and modified, if need be. This treatment plan should also include consideration of extra-facial, exposed skin such as décolletage, neck, and hands. Finally, a thorough pretreatment patient assessment to identify risks and contraindications should be a cornerstone of each consultation.

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