A SUPPLEMENT TO

JOURNAL OF DRUGS IN DERMATOLOGY

JDD

DRUGS • DEVICES • METHODS

Noninvasive Rejuvenation for Graceful Aging

ISSN: 1545 9616

June 2017 • Volume 16 • Issue 6 (Supplement)

JO0617

Disclosure of Commercial Support
This supplement to the *Journal of Drugs in Dermatology* is supported by L'Oréal.

L'ORÉAL

Research & Innovation

Noninvasive Rejuvenation for Graceful Aging

INTRODUCTION

ORIGINAL ARTICLES

ORIGINAL ARTICLES (CONTD)

Aging Gracefully

Heidi A. Waldorf MD

At the Annual Meeting of the American Academy of Dermatology in 2016, I directed the symposium entitled 'Aging Gracefully' for the second time. The symposium's primary learning objective was to give the audience a framework for managing aesthetic patients. In the last decade, there has been a significant increase in the options for and availability of noninvasive and minimally invasive rejuvenation. With that has been an associated surge in interest by physicians and patients. And, as the number of procedures across the globe increases, so too do the number of aesthetically poor outcomes. Most come from practitioners doing paint-by-numbers treatment. As experts in skin biology and treatment, dermatologists should practice the highest-level cosmetic as well as general dermatology. The faculty presented information to aid practitioners how best to approach patients and formulate a cosmetic plan. The faculty discussed important considerations based on patient gender, age, and skin type. Updated information on the science of cosmeceuticals and the benefits of early noninvasive intervention was presented as were next generation devices and alternatives to standard therapies. The faculty have kindly condensed their AAD presentations for this supplement. I thank L'Oréal and the *Journal of Drugs in Dermatology* for giving us the opportunity to present this information to a wider audience in this e-supplement.

Heidi A. Waldorf MD

Director of Laser & Cosmetic Dermatology, The Mount Sinai Hospital, New York, NY
Icahn School of Medicine of Mount Sinai, New York, NY
Waldorf Dermatology Aesthetics, Nanuet, NY

The Benjamin Button Effect: Recognizable Rejuvenation

Heidi A. Waldorf MD
Director of Laser & Cosmetic Dermatology, The Mount Sinai Hospital, New York, NY
Icahn School of Medicine at Mount Sinai, New York, NY
Waldorf Dermatology Aesthetics, Nanuet, NY

ABSTRACT

The "Benjamin Button" effect inspired by the popular motion picture, is used to describe the goal of achieving a clearly younger and more attractive, yet still natural appearance utilizing noninvasive and minimally invasive therapies and procedures. Due to high patient demand for enhancement and rejuvenation of the face and body with minimal downtime, there is an ever-increasing number of companies developing products and devices, variety of indications, and field of practitioners offering them. Each option, including topicals, injectables, and devices, promises near magical results. Despite that, a brief review of online discussions and media resources reveals both patients complaining of inadequate results and celebrities with extreme appearances. For clinical practitioners, it is critical to understand the art, science, and economics of noninvasive rejuvenation in order to properly evaluate potential patients, set appropriate expectations, develop, and provide an effective noninvasive rejuvenation plan to achieve a true "Benjamin Button" effect for patients.

J Drugs Dermatol. 2017;16(6 Suppl):s74-76.

INTRODUCTION

Traditionally, improving the appearance of the aging patient focused on skin laxity: surgery to remove excess skin. That meant waiting until this sign of aging was sufficient to warrant cosmetic surgery. This was effective but could result in a sudden and unnatural change in appearance that was not always natural. Deep chemical peels, dermabrasion, and even early lasers improved texture and color significantly but often with difficult recoveries and resultant permanent loss of normal pigmentation. Early injectable fillers provided short term reduction in wrinkles or enhancement of lips and did nothing to slow the appearance of aging.

A turning point in treating the skin signs of aging was the recognition that a significant portion is due to volume depletion or 'deflation', not laxity or gravity.[1] In fact, cadaver studies have shown the presence of distinct fat pads that are lost in a fairly consistent pattern with age.[2] Skeletal changes are also foreseeable.[3] At the same time, new products for soft tissue augmentation were developed to maximize rheologic properties for different areas and uses; the use of botulinum toxin became to change the position of anatomic landmarks, not just to paralyze muscle; and improved energy based devices allowed visible resurfacing or tightening without significant downtime.[4,5] It became a realistic aesthetic goal to improve a patient's appearance over time. And, in fact, if started early enough, these interventions have been seen to slow the aging process.[6]

"Benjamin Button" is a short story by F. Scott Fitzgerald and later a movie with Brad Pitt in which a man ages backward. The phrase has been used in popular culture to describe people who look as if they haven't aged or became younger but don't have obvious signs of intervention. In Dermatology, it describes our patients who, with a combination of cosmeceuticals and rejuvenation procedures, look more attractive and youthful after years or decades than when they first presented. The improvement is clearly recognizable but not identifiable as from a particular procedure. That is the "Benjamin Button effect".

Achieving Recognizable Rejuvenation from Consult to Practice

There will always be patients who want or need more significant changes. A patient presenting to a plastic or facial plastic surgeon likely expects to be offered a surgical procedure that will make a significant difference quickly, like a rhitidectomy or rhinoplasty. However, even surgeons have seen an upsurge in patients wanting alternatives to surgery. According to the American Society of Plastic Surgeons 2016 National Plastic Surgery Statistics, the number of cosmetic surgical procedures decreased by 6% between 2000 and 2016 while the number of cosmetic minimally-invasive procedures increased by 180% over the same period.[7] Because surgical procedures can result in extreme changes, patients often express concern about 'not looking like me'. In contrast, after some minimally invasive cosmetic procedures, patients complain that they cannot see a significant improvement and that 'no one noticed' and complimented the change.

By self-selection, most patients presenting to a cosmetic dermatologic surgeon do so specifically to avoid surgery. They express concern about making extreme changes, becoming a caricature, or just 'not looking like me'. At the same time, patients want assurance that there will be enough improvement

to be noticeable. Those with the best outcomes report compliments from close friends and family and exclamations of 'you look younger every time I see you' at reunions. Patients particularly concerned about remaining recognizable may be more likely to seek advice first from a dermatologist instead of a surgeon. They want natural-appearing, recognizable rejuvenation.

The process begins with the cosmetic consultation. After reviewing the patient's pertinent history and aesthetic concerns and performing a physical exam, it is helpful to review the pertinent areas with the patient sitting or standing in front of a mirror or monitor that provides front and side views. Ask what the patient sees. Educate patients about the process of aging, describe how it relates to their face and how those issues can be improved. Prioritize treatment of color, texture, laxity, volume, and proportion: the order will depend on what the physician sees combined with the patient's top concerns, budget, ability for downtime, and time frame.

This holistic cosmetic evaluation is based on the recognition that the characteristics of what we call beautiful and handsome are fairly consistent cross culturally.[8] For women, that means a heart or upside-down egg shape face – wider on the top than the bottom. It is no accident that every Disney princess, regardless of race, looks the same. For men, a more angular face with a strong jaw represents masculinity, while a softer rounder face is considered boyish. In both men and women, prominent open eyes are signs of youthful attractiveness.[9] As both men and women age, volume depletion or 'deflation' causes the youthful triangle, wider upper than lower face, to invert. The facial framing of the eyes disappears. On exam, the observer's gaze is drawn down to the lower face and jowls. Tear troughs created by deep medial volume loss and downturned angles of the mouth from lack of lower face support give an appearance of fatigue and sadness.

Clinical evaluation of facial proportions to plan treatment can be done by eye, using anatomic guidelines like Hinderer's lines, or mathematically modeled calipers based on Phi, the golden number. The face must be reviewed from all sides; photos taken from the front at rest and with movement and bilaterally at 45 and 90 degrees are helpful. Areas of depletion or excess, the position of pertinent anatomic structures like the brows, and the distances between structures like the nose and the lips should be noted. Evaluation of skin quality includes color, texture, tone, and laxity. These changes in the aging face occur from the interplay of skin, bone, fat, muscle, and ligaments. Consideration of the relative contributions of each layer will determine which therapies will be most helpful.[10]

Recommendations must include not only specific treatments, but a realistic schedule. For the older patient new to cosmetic treatment, achieving the desired therapeutic goal noninvasively will likely require a combination of treatments that can be done over days, months, or years depending on health, social, emotional, or budget limitations. This patient needs to understand that a so-called 'tipping point' must be reached for the changes to make a significant difference. The younger patient may begin with topicals and perhaps a neurotoxin or peel depending on a history of acne or photoexposure. The physician can change or add procedures as necessary as this patient ages. With experience, most of these changes can be anticipated based on the science of aging; surprising shifts like a sudden reduction in volume should be investigated to rule out any underlying medical condition.

All patients must have realistic expectations: a combination of therapies at one time or over decades is necessary to achieve results. When patients ask which treatment to choose, the analogy of buying an outfit is helpful: an outfit is made up of a top, bottom, shoes, and accessories, none of which will provide acceptable attire alone. Ultimately, both older and younger patients can settle into a comfortable pattern of maintenance and improvement with their cosmetic dermatologist. Coco Chanel said, 'Simplicity is the keynote of all true elegance' and 'Before you leave the house, look in the mirror and take one thing off.' In other words, make beauty look effortless. That should be the goal not only of fashion but also of cosmetic dermatology.

CONCLUSION

Everyone ages and our patients need both our skills and advice to do it well. Guiding them requires a solid understanding of the anatomy and physiology of aging, knowledge of cosmeceuticals, and expertise in minimally and noninvasive rejuvenation. However, that is not enough. Cosmetic dermatologists must have 'expert eyes' in addition to 'good hands'. Only then can we create and maintain a naturally youthful aesthetic appearance for our patients. Only then can we truly continue to get older while looking younger with them.

DISCLOSURES

Dr. Waldorf has no conflicts of interest to declare.

REFERENCES

1. Lambros V. Commentary on: The Role of Gravity in Periorbital and Midfacial Aging. *Aesthet Surg J.* 2014;34(6):823-4.
2. Rohrich RJ, Pessa JE, Ristow B. The youthful cheek and the deep medial fat compartment. *Plast Reconstr Surg.* 2008;121(6);2107-12.
3. Rohrich RJ, Pessa JE. Discussion. Aging of the facial skeleton: aesthetic implications and rejuvenation strategies. *Plast Reconstr Surg.* 2011;127(1);384-5.
4. Gilbert E, Hui A, Waldorf HA. The basic science of dermal fillers: past and present Part I: background and mechanisms of action. *J Drugs Dermatol.* 2012;11(9):1059-68.
5. Jacono AA, Malone MH, Lavin TJ. Nonsurgical facial rejuvenation procedures in patients under 50 undergoing facelift: habits, costs and results. *Aesthet Surg J.* 2017;37(4):448-453.
6. Hamilton HK, Arndt KA. When is "too early" too early to start cosmetic procedures? *JAMA Dermatol* 2013;149(11):1271.
7. https://www.plasticsurgery.org/news/plastic-surgery-statistics
8. Steven Dayan. *Subliminally Exposed,* Morgan James Publishing, NY 2013.

9. Vernon RJ, Sutherland CA, Young AW, Hartley T. Modeling first impressions from highly variable facial images. *Proc Natl Acad Sci USA*. 2014;111(32);E3353-61.
10. Cotofana S, Fratila AA, Schenck TL, Redka-Swoboda W, Zilinsky I, Pavicic T. The Anatomy of the Aging Face: A Review. *Facial Plast Surg*. 2016;32(3):253-60.

AUTHOR CORRESPONDENCE

Heidi A. Waldorf MD
E-mail:..... drheidi@waldorfderm.com

Ethnicity and Aging Skin

Andrew F. Alexis MD MPH[a,b] and Jasmine O. Obioha MD[c]
[a]Department of Dermatology, Mount Sinai St. Luke's and Mount Sinai West, New York, NY
[b]Icahn School of Medicine at Mount Sinai, New York, NY
[c]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY

ABSTRACT

Aging is a complex process influenced by both extrinsic and intrinsic factors. Premature signs of aging due to cumulative UV exposure represent a major concern of the cosmetic patient. Skin of color is less susceptible to photodamage and thus signs of aging are less pronounced and occur later than in Caucasians. Understanding structural and functional differences among different racial/ethnic groups is important to achieve favorable treatment outcomes when addressing aging concerns.

J Drugs Dermatol. 2017;16(6 Suppl):s77-80.

INTRODUCTION

Skin aging is a complex phenomenon influenced by extrinsic and intrinsic factors. Variations in age of onset, severity, and specific concerns are observed across the spectrum of racial/ethnic populations. According to the US Census Bureau Projections, by 2044 more than half of the United States (US) is projected to belong to a non-white racial and ethnic group.[1] As the minority population continues to grow, minorities represent an expanding cohort seeking cosmetic procedures. As such, understanding structural and functional differences of the skin and aging process in different skin types is of increasing importance.

Structural and Functional Differences

Darkly pigmented skin is characterized by larger, more numerous melanosomes that contain more melanin and are more singly dispersed throughout the epidermis compared to lightly pigmented skin. The increased melanin content and widely dispersed melanosomes in darker skin provide photoprotection.[2] In a 1979 study by Kaidbey et al using cadaveric skin, the mean protective factor from Ultraviolet (UV) B radiation in black skin was found to be 13.4 compared to 3.4 for white skin; and the mean rate of UVB transmission into the dermis was 5.7% in black skin compared to 29.4% in white skin.[3] While increased melanin is advantageous in delaying the onset and/or reducing the severity of photoaging in darker skin, labile melanocyte responses contribute to a greater risk of pigment alteration - a feature of both photoaging and a common sequela of inflammation and injury.[4]

There are also structural differences in the dermis and epidermis that can potentially influence variations in aging. Notwithstanding inherent limitations of limited studies with small sample sizes, the stratum corneum in black skin (compared to white skin) has been reported to have more layers that are arranged more compactly.[2,5] Additionally, fibroblasts have been reported to be larger, more numerous, and more frequently binucleated or multinucleated in black skin vs white skin, generating compact collagen bundles that are arranged more parallel to the epidermis.[2,5] The heightened fibroblast activity is thought to contribute to the lower incidence of facial rhytides, but increased risk of keloids in black skin and other darker skin types.

Aging

In general, signs of aging occur at a later age and are less pronounced in ethnic skin. Facial wrinkles and fine lines appear later in African Americans than in Caucasians and may not appear until late in the fifth or sixth decade.[4] In a multinational, cross-sectional, web-based survey study assessing ten facial features of aging across different racial/ethnic groups and Fitzpatrick types, white women self-reported more signs of moderate and severe facial aging than Asian and Hispanic women beginning in the fourth decade.[6] In more than 30% of study participants aged 40-49, white individuals reported to have forehead lines, glabellar lines, crow's feet, nasolabial folds, and puffiness under the eyes, in contrast to the presence of nasolabial folds and puffiness reported by Asian women and nasolabial folds in Hispanic women.[6] In this study, black women did not describe signs of facial aging until the fifth decade and these were limited to nasolabial folds and forehead lines.[6] When comparing the severity of facial features against photonumeric rating scales, the mean severity of crow's feet lines were most severe in Fitzpatrick skin type I and least severe in Fitzpatrick skin types IV and V.[6]

Hyperpigmentation and uneven skin tone are of greater concern in individuals with skin of color compared to patients with lighter skin types, among whom fine lines and wrinkles are more frequent concerns. Patients with skin of color are additionally more prone to develop and become preoccupied with the ac-

quisition of benign facial neoplasms, textural irregularities, and intrinsic structural changes. Moreover, there are facial structural differences among different ethnic groups that influence the aging process. In Figures 1a and 1b, Alexis and Alam highlight the differences in facial architecture of aged Caucasian, African American, Latino, and Asian women from frontal and lateral views.[7] While wide individual variability within populations is expected and broad generalizations about specific population groups should be used with caution, nuances in facial anatomic structure and manifestations of skin aging have been described in published studies.

African Americans and Aging

Skin aging among African Americans tends to be most striking in the midface. Published descriptions of common facial anatomic features among African Americans include a hypoplastic malar eminence, increased soft tissue in the midface, and more ocular proptosis.[7,8] With aging, the malar fat pads descend toward the nasolabial folds resulting in lengthening of the lower eyelids, more pronounced nasolabial folds, and accentuated nasal jugal folds (Figure 2).[7,8] These changes ultimately lead to a double convexity of the midface. Additionally, dermatochalasis of the upper lid is often seen, which can be attributed to pseudoherniation of the medial orbital fat pad into an eyelid space that is on average smaller in African Americans than Caucasians. Mattory and colleagues found that the distance between the upper eyelid crease and lid margin is 6 to 8 mm in African Americans compared to 8 to 10 mm in Caucasians.[9] These anatomic differences in combination with increased ocular proptosis also contribute to the presence of infraorbital shadowing.[8]

Perioral rhytides and loss of lip volume are prominent changes with aging seen in Caucasians that are less common, of lower severity, and delayed in onset among African Americans.

Dermatosis papulosa nigra (DPN) is a common facial neoplasm and sign of aging in black individuals. Lesions are 1- to 3-mm flat or pedunculated papules. Although benign, they represent a frequent cosmetic concern in black patients.

Asians and Aging

Cutaneous manifestations of photoaging in the Asian population are well documented in the literature. In East and Southeast Asians, pigmentary changes predominate. These changes include actinic lentigines, pigmented seborrheic keratoses, and

FIGURE 1. Features of facial aging in Caucasian, African American, Latino, and Asian women, from left to right. (A) frontal view (B) lateral view.
Reproduced with permission from Alexis AF, Alam M. Racial and ethnic differences in skin aging: implication for treatment with soft tissue fillers. *J Drugs Dermatol.* 2012;11(suppl 8):s30-s32.

FIGURE 2. A 74-year-old African American woman with characteristic signs of facial aging.
Reproduced with permission from Alexis AF, Alam M. Racial and ethnic differences in skin aging: implication for treatment with soft tissue fillers. *J Drugs Dermatol.* 2012;11(suppl 8):s30-s32.

mottled hyperpigmentation. In a study comparing Chinese and French age-matched women, wrinkle onset was delayed by 10 years in Chinese women compared to French women, however Chinese subjects were found to have an increased frequency of pigmented spots on the face and hands.[10]

In Koreans, the development of lentigines increases with age and is more common in women. Conversely, the appearance of seborrheic keratoses (SKs) increases with age and is more common in Korean men.[11,12] In a study by Kwon et al, pigmented seborrheic keratoses were greater number and larger in size in chronically sun exposed skin compared to sun protected or intermittently sun exposed skin.[11]

Although many authors suggest that pigment alterations are the most prominent signs of aging in Asians, skin wrinkling remains a significant but late feature. Skin wrinkling may not become visibly apparent in Asians until age 50, however, using an author developed 7-point photographic wrinkle scale in Koreans, Chung concluded that Asians have coarser, thicker, and deeper rhytides on the forehead, perioral, and Crow's feet.[12] In contrast, Caucasians tend to have fine rhytides on the cheeks and Crow's feet area. The mechanism of these differences is unknown.

Hispanic and Aging

Aging in Hispanics and/or Latinos is not well characterized; generalizations are confounded by the broad range of skin types and ancestry in this population. Skin mottling, jowl formation, infraorbital hollowness, and shadowing have been described as leading concerns in this population.[9,13]

While great diversity exists, common anatomic features among Hispanic/Latino populations that have been described in the published literature include a broad face, prominent malar eminence, and small nose with overlying thick skin.[14] They are described to have more sebaceous skin than Caucasian women and heavy eyelids.[14] With aging, these features become more pronounced. The midface becomes thicker and heavier with fat pad accumulation contributing to more pronounced nasolabial folds.[7,14] Additionally, eyebrows droop (especially laterally), eyelid hooding becomes more prominent and the lower lid fat pad herniates.[14] And similar to the midface, the skin in the neck area appears thick, heavy, and loose.[14]

Approach to Cosmetic Procedures in Aging Ethnic Skin

The goal of cosmetic procedures in skin of color is to achieve maximal results while minimizing epidermal and dermal injury. The risk of post inflammatory pigment alteration and scarring should be considered when performing any procedure on darker skin types.

Botulinum toxin is the leading nonsurgical cosmetic procedure performed in the United States. To date, the studies on botulinum toxin in different ethnic groups have established botulinum toxin to be both safe and effective for the correction of facial rhytides. Although it is most frequently used for the correction of facial rhytides, there are ethnic variations in aesthetic concerns that influence its' use. In East Asian populations, especially Koreans, botulinum toxin is a popular procedure to contour the jaw. Benign hypertrophy of the masseter muscle is common in East Asians, which contributes to a wider lower third of the face compared to Caucasians. The square jaw appearance is often undesirable in this population, leading to a high demand for correction. Using ultrasonography in a sample of 121 Korean patients, Kim et al demonstrated that botulinum toxin is effective in the reducing the thickness of the masseter muscle.[15]

Attention to anatomical differences and nuances in aesthetic concerns is also important in the use of soft tissue filler. In Asian patients, the approach to dermal fillers to correct age-related structural defects requires understanding of this ethnic group's desire for an oval facial shape. The bizygomatic distance in most Asians is wider than that of whites, thus it is important to avoid the volumization of the lateral maxilla and zygoma as one would consider in other racial groups in order to avoid further widening of the midface.[16] Volumization of the medial half of the maxilla and alar base can achieve anterior projection of the central third of the face and reduce infraorbital and perialar shadowing.[16] The practice of combining dermal fillers to midface and neuromodulators to the masseter muscle can achieve fullness in the upper half of the face and a narrow lower face, effectively reshaping an undesirable square shape into a preferred ovoid shape.[16]

In African Americans, soft tissue augmentation is unique with respect to the goal of correcting structural age-related changes that are specific to this population. Histologically, there is less thinning of collagen bundles and elastic tissue in black skin. Thus in contrast to the need to treat superficial creases common in photoaged Caucasian skin, volume restoration in African Americans focuses largely on correcting the previously described prominent midfacial fat atrophy and soft tissue redistribution.[17] Authors Burgess and Awosika suggest that stimulatory fillers that produce ongoing reactions that contribute to volumizing (calcium hydroxylapatite and poly-L-lactic acid) may be more effective in this population.[17] While there are few randomized controlled studies evaluating the safety and efficacy of dermal fillers in skin of color, the literature to date supports their use in darker skin types. In a study by Taylor et al, variable-particle hyaluronic acid dermal fillers were shown to be well tolerated and 93% effective in the correction of nasolabial folds at 12 weeks in 150 patients with Fitzpatrick skin types IV, V, and VI.[18]

However, as with any cosmetic procedure performed in skin of color, it is important to consider the risk of post inflammatory hyperpigmentation and scarring. Taylor et al reported the most common adverse effect after the injection of variable particle hyaluronic acid fillers was mild or moderate hyperpigmentation (17 of 150 patients), which resolved within 12 weeks for all but 3 patients wherein the pigmentation persisted for greater than 12 weeks.[18] The majority of cases of hyperpigmentation were associated with multiple puncture techniques (13%) compared to linear threading (2%).[18] As such, in darker skin types, the threading and fanning technique may be preferred over multiple punctures to decrease the risk of hyperpigmentation.

CONCLUSION

The population seeking anti-aging cosmetic procedures is becoming increasingly diverse. For safety reasons, more conservative approaches are generally recommended for darker skin types. Pre- and post-treatment precautions should be considered, such as prophylactic use of bleaching agents, post-procedure topical steroids, sunscreen, and sun avoidance. Lastly, achieving optimal treatment outcomes requires an individualized approach tailored to each patient. Understanding individual variations in anatomy, treatment expectations, and risks is paramount to achieving successful outcomes.

DISCLOSURES

Dr. Obioha has no relevant financial relationships or potential conflicts of interests. Dr. Alexis has served as an advisory board member for L'Oréal, Allergan, and Galderma.

REFERENCES

1. https://www.census.gov/content/dam/Census/library/publications/2015/demo/p25-1143.pdf
2. Taylor SC. Skin of color: biology, structure, function, and implications for dermatologic disease. *J Am Acad Dermatol.* 2002;46(2 Suppl Understanding):S41–S62.
3. Kaidbey KH, Agin PP, Sayre RM, et al 1979 Photoprotection by melanin – a comparison of black and Caucasian skin. *J Am Acad Dermatol.* 1979;1(3):249–260.
4. Rawlings AV. Ethnic skin types: are there differences in skin structure and function? *Int J Cosmet Sci.* 2006;28:79-93.
5. Montagna W, Prota G, Kenney J. The structure of black skin. In: Montagna W, Prota G, Kenney J, eds. Black Skin Structure and Function. Gulf Professional Publishing; 1993.
6. Grimes P, Boyd C, Alexis A, Downie J, Kolodziejczyk J, Gallagher C. Self-reported characteristics associated with the signs of facial aging by race/ethnic group and Fitzpatrick skin type among a diverse, multinational sample. 74th Annual Meeting of the American Academy of Dermatology; 2016 Mar 4-8; Washington, DC
7. Alexis AF, Alam M. Racial and ethnic differences in skin aging: implication for treatment with soft tissue fillers. *J Drugs Dermatol.* 2012;11(suppl 8):s30-s32.
8. Brissett AE, Zevallos JP. Rejuvenation of the aging African face. In: Trustwell WH, ed. Surgical Facial Rejuvenation; a Road Map to Safe and Reliable Outcomes. New York, NY:Thieme Medical Publishers; 2009:146–152.
9. Matory WE. Skin care. In: Matory WE, ed. *Ethnic Considerations in Facial Aesthetic Surgery.* Philadelphia, PA: Lippincott-Raven; 1998:100.
10. Nouveau-Richard, S., Yang, Z., Mac-Mary, S. et al. Skin aging: a comparison between Chinese and European populations. A pilot study. *J Dermatol Sci.* 2005;40(3):187–193.
11. Kwon OS, Hwang EJ, Bae JH et al. Seborrheic keratosis in Korean males: causative role of sunlight. *Photodermatol Photoimmunol Photomed.* 2003;19:73–80.
12. Chung JH. Photoaging in Asians. *Photodermatol Photoimmunol Photomed.* 2003;19:109–121.
13. Talakoub L, Wesley NO. Differences in perceptions of beauty and cosmetic procedures performed in ethnic patients. *Semin Cutan Med Surg.* 2009;28(2):115–129.
14. Cobo R, Garcia CA. Aesthetic surgery for the Mesitzo/Hispanic patient: special considerations. *Facial Plast Surg.* 2010;26(2):164-173.
15. Kim NH, Park RH, Park JB 2010 Botulinum toxin type A for the treatment of hypertrophy of the masseter muscle. *Plast Reconstr Surg.* 2010;125(6):1693–1705.
16. Liew S. Ethnic and gender considerations in the use of facial injectables: Asian patients. *Plast Reconstr Surg.* 2015;136(5 Suppl):22S-27S.
17. Burgess C, Awosika O. Ethnic and gender considerations in the use of facial injectables: African-American patients. *Plast Reconstr Surg.* 2015;136(5 Suppl):28S-31S.
18. Taylor SC, Burgess CM, Callender VD. Efficacy of variable-particle hyaluronic acid dermal fillers in patients with skin of color: a randomized, evaluator-blinded comparative trial. *Dermatol Surg.* 2010;36:741-749.

AUTHOR CORRESPONDENCE

Andrew F. Alexis MD MPH

E-mail:..... alexisderm@yahoo.com

Treating the Young Aesthetic Patient: Evidence-Based Recommendations

Lauren Meshkov Bonati MD[a] and Sabrina Guillen Fabi MD[b]
[a]Icahn School of Medicine at Mount Sinai, New York, NY
[b]Cosmetic Laser Dermatology, San Diego, CA

ABSTRACT

Background: There is growing demand for cosmetic treatments in the younger population, yet counseling and treating this age group can be difficult to justify.
Objective: Chronologic changes that cause noticeable signs of aging are discussed within each age group. Age-appropriate cosmetic preventions and interventions are therefore recommended.
Methods: A PubMed search was performed for high quality trials and evidence based reviews on the basic science of aging, as well as on cosmetic modalities and their histological, biochemical, and clinical effects.
Results and Conclusion: Specific age-related changes occur with each decade of life. A complete understanding of when these physiologic changes occur helps determine age-appropriate cosmetic counseling, preventions, and interventions.

J Drugs Dermatol. 2017;16(6 Suppl):s81-83.

INTRODUCTION

Recent speculation has indicated that it is rarely too early to begin aesthetic treatments.[1] The growing demand for anti-aging in younger populations requires thoughtful and age-appropriate counseling for delivering preventions and interventions. The physiologic, age-related changes that occur with each decade of life may serve as a blueprint for when to start cosmetic treatments.

Under 20

Photoprotection

Photodamage begins with childhood exposure to Ultraviolet radiation (UVR). Between the 1st and 9th decade of life, staining for type I and type III collagen has been shown to reduce from 82.5% and 80.4% to 53.2% and 44.1%, respectively, in sun-exposed skin when compared to photoprotected skin (P=0.0004 and P=0.0008).[2] Daily UV filters that contain zinc oxide and titanium dioxide are less irritating and recommended for anyone over 6 months old.

Alpha-Hydroxy Acids

Alpha-hydroxy acid (AHA) cleansers reduce photodamage, wrinkling, roughness, dyschromia, and additionally improve acne that may affect this age group. After months of daily use, histologic benefits include a thickened epidermis, increased papillary mucopolysaccharides, improved elastic fiber quality, and increased collagen density.[3]

Retinoids

Topical retinoids are a mainstay of anti-aging and a first-line treatment for those with acne. Multiple studies have demonstrated the beneficial effects of tretinoin on overall appearance, surface roughness, fine and coarse wrinkling, mottled pigmentation, uneven skin tone, and sallowness. Histologically, tretinoin has been shown to increase anchoring fibrils and collagen in the papillary dermis, and to normalize overall structure.[4]

During the 20s

Daily exposure to UVR, smoking, and pollution causes cumulative damage that results in dyschromia, loss of collagen, reduced elastic recoil, and premature aging. Collagen decline beginning in the 20s reduces from 70% to 50% by age seventy.[5] A similar decline in bony volume starts in the mid to late 20s, resulting in poor resting tone of the mimetic musculature that originates on bone, and results in static rhytides.[6] A stepwise increase in rhytides has been reported by age 33,[7] warranting preventative treatment in younger patients with noticeable fine lines and wrinkles.

Topicals

Antioxidants

Topical antioxidants compensate for the declining endogenous response to oxidative photodamage that begins in the 20s.[8] A double-blinded, split-face study of 10 patients who used a daily antioxidant blend found increased Grenz zone collagen and type I collagen mRNA when compared to vehicle control (P=0.01).[9]

Growth Factors

Topical growth factors may help reduce photodamage and wrinkles. Twelve subjects who used twice daily human growth factors for 6 months reported 33% and 25% average improvement in periorbital and perioral wrinkles, respectively.[10] Histological

analyses showed moderate change in epidermal thickness, increased fibroblast density, and new collagen formation on electron microscopy.

Injectables

Neuromodulators

Botulinum toxin A (BoNTA) blocks acetylcholine release at the neuromuscular junction and is FDA approved for the treatment of rhytides in those over age 18. The superiority of BoNTA versus placebo has been well documented in many randomized, controlled trials with higher satisfaction and increased responder rates seen in younger populations.[11]

BoNTA-induced neocollagenesis improves skin pliability, elasticity, and dermal architecture, softening static lines. Resultant muscle atrophy inhibits muscles of negative expression, slowing future wrinkle development. A multi-center, retrospective study of 207 BoNTA patients followed over 9.1 years reported a drop in perceived age by 6.9 years in 89.7% of patients.[12] Identical twin studies have corroborated the cumulative and preventative effects of BoNTA over a 19-year period.[13]

Lasers and Light

Intense Pulsed Light

Photodamage, dyschromia, telangiectasias, freckling, and acne in this age group may be treated with intense pulsed light (IPL). Neocollagenesis and elastic fiber proliferation are known benefits, with conversion to a younger pattern of RNA expression after 3 treatments.[14]

Lasers

Acne scars in any age group are effectively treated with resurfacing lasers that offer additional anti-aging benefit. Fractional photothermolysis via ablative (AFL) and nonablative (NAFL) devices are effective alone or in combination for the treatment of rhytides.[15]

Body Contouring

Cryolipolysis

Cryolipolysis triggers adipocyte apoptosis and is FDA approved in patients over 18 with unwanted fat in the abdominal, flank, thigh, and submental regions. Average fat reduction has been reported between 10.3-25.5%[16] with the additional benefit of improved skin texture, laxity, and cellulite. Younger patients are more likely to have localized fat bulges in the setting of normal body weight, which makes them ideal candidates.

High Intensity Focused Ultrasound

High Intensity Focused Ultrasound (HIFU) ablates subcutaneous adipose tissue and is FDA approved for the waistline. A 2.0 cm reduction in waist circumference was reported in a muticenter, randomized, sham-controlled, single-blinded trial of 180 patients after one HIFU treatment.[17]

Deoxycholic Acid

Submental fullness may occur in all age groups and can be treated with Deoxycholic acid injection, an FDA approved method that triggers adipocyte lysis and cell membrane disruption. In two multi-center, randomized, controlled, double-blinded trials of over 500 patients who received up to 6 deoxycholic acid treatments, 70.0% and 66.5% of subjects saw a 1-grade improvement on the submental fullness score when rated by clinician and subject, respectively (P<0.001).[18] An 8-fold improvement was seen on magnetic resonance imaging (MRI) when compared to placebo (P<0.001).

Cellulite Devices

Cellulite at any age may be treated by destroying fibrous septae that bind down herniating adipose tissue. A multi-center study of 55 women who underwent 1 treatment with the FDA-approved vacuum-assisted controlled tissue release system, saw 93% improvement of buttock and thigh cellulite in 47 subjects (P<0.001).[19] There was 96% improvement after 1 year, 98% after 2 years, and 94% satisfaction rate. Another study of 15 females with thigh and buttock cellulite who underwent Nd:YAG 1,440-nm laser treatment, reported improved contour in 66% of patients and reduced dimple depth by 49% at 6 months.[20]

30s and 40s

Signs of aging worsen with accumulated photodamage, continued collagen decline, and significant bony loss in the 30s and 40s, making dyschromia, laxity, rhytides, and accentuated skin folds of particular concern.

Topicals

Hydroquinone

Dyschromia and mottled hyperpigmentation may be treated with topical hydroquinone (HQ) or a HQ-free formulation used nightly after a topical retinoid. After 12 weeks of HQ or HQ-free lightener, a study of 36 females reported significantly reduced scores on the Mottled Pigmentation Area and Severity Index and improved sallowness.[21]

Injectables

Fillers

Injectable fillers restore youthful contour and reposition ligaments and vectors when bony volume loss and facial fat pad descent begins in the mid-30s. A 10-degree reduction in the maxillary angle between age 30 and 60 further results in mid-cheek volume loss, sunken hollows, and poor bony projection that may be compensated with soft tissue fillers.[22] Hyaluronic acid (HA) injection was shown to decrease perceived age in 10 patients by 6.1-7.3 years and 7.8-9 years as judged by dermatologists and subjects, respectively.[23]

Injectable fillers are known to stimulate neocollagenesis, resulting in less frequency of treatments needed over time. Persistent

volume was seen in 63 patients at 21.6 months post-HA injection and 2.5 years after calcium hydroxylapatite injection.[24-25] Poly-L-Lactic acid stimulates long-term neocollagenesis beginning 3-6 months post treatment and lasting up to 2 years or more.

Energy Devices

Lasers

Skin laxity in this age group may be treated with various fractionated and non-fractionated, ablative and nonablative laser types. Although ablative lasers are known to be most efficacious,[26] laser choice depends on patient budget and tolerance of downtime.

Microfocused Ultrasound

Skin laxity on the face, neck, chest, and arms may be treated with microfocused ultrasound (MFU), which causes thermal coagulation and neocollagenesis. In a retrospective study of 45 patients, face and neck laxity improved after MFU treatment in 75% and 77.8% of subjects, respectively, at 90 and 180-day follow-up, as per subject reporting.[27]

Radiofrequency

Monopolar radiofrequency (MRF) causes thermal damage via high-frequency electric current and stimulates neocollagenesis. It is FDA approved for body laxity, facial lines, and cellulite. Upper eyelid tightening and reduced hooding was seen in 88% and 86% of patients, respectively, in a study of 63 subjects who underwent MRF treatment.[28]

CONCLUSION

The aging process is chronologically predictable, with outward manifestations beginning in the late 20's and progressing with each decade. Appropriate cosmetic counseling, preventions, and interventions for younger populations are justified based on standard physiologic aging and individual concerns.

DISCLOSURES

Sabrina Guillen Fabi is an Investigator, Consultant, and Advisor for Galderma, Valeant, Allergan, and Merz. Dr Fabi serves on the Speakers bureau for Galderma, Allergan, Merz, Lumenis, and Coolsculpting. Lauren Meshkov Bonati has no conflicts of interest to declare.

REFERENCES

1. Hamilton HK, Arndt KA. When is "too early" too early to start cosmetic procedures? *JAMA Dermatol*. 2013;149(11):1271.
2. El-Domyati M, Attia S, Saleh F, et al. Intrinsic aging vs. photoaging: a comparative histopathological, immunohistochemical, and ultrastructural study of skin. *Exp Dermatol*. 2002;11(5):398-405.
3. Ditre CM, Griffin TD, Murphy GF, et al. Effects of alpha-hydroxy acids on photo aged skin: a pilot clinical, histologic, and ultrastructural study. *J Am Acad Dermatol*. 1996;34(2 Pt 1):187-95.
4. Griffiths CE, Russman AN, Majmudar G et al. Restoration of collagen formation in photodamaged human skin by tretinoin (retinoic acid). *N Engl J Med*. 1993;329:530–5.
5. Luebberding S, Krueger N, Kerscher M. Mechanical properties of human skin in vivo: a comparative evaluation in 300 men and women. *Skin Res Technol*. 2014;20(2):127-135.
6. Vleggaar D, Fitzgerald R. Dermatological implications of skeletal aging: a focus on supraperiosteal volumization for perioral rejuvenation. *J Drugs Dermatol*. 2008;7(3):209-90.
7. Kuwazuru O, Miyamoto K, Yoshikawa N, et al. Skin wrinkling morphology changes suddenly in the early 30s. *Skin Res Technol*. 2012;18:495-503.
8. Kimball AB, Multi-Decade and Ethnicity Study. Presented at 23rd World Congress of Dermatology, Vancouver, Canada, June 2015.
9. Fitzpatrick RE, Rostan EF. Double-blind, half-face study comparing topical vitamin C and vehicle for rejuvenation of photodamage. *Dermatol Surg*. 2002;28(3):231-6.
10. Hussain M, Phelps R, Goldberg DJ. Clinical, histologic, and ultra-structural changes after use of human growth factor and cytokine skin cream for the treatment of skin rejuvenation. *J Cosmet Laser Ther*. 2008;10:104–109.
11. Carruthers A, Bruce S, de Coninck A et al. Efficacy and safety of onabotulinumtoxinA for the treatment of crow's feet lines: a multicenter, randomized, controlled trial. *Dermatol Surg*. 2014;4011:1181-1190.
12. Trindade de Almeida A, Carruthers J, Cox SE, et al. Patient satisfaction and safety with aesthetic onabotulinumtoxinA after at least 5 years: a retrospective cross-sectional analysis of 4,402 glabellar treatments. *Dermatol Surg*. 2015;41:S19-S28.
13. Binder WJ, Rivken A. Long-term effects of onabotulinumtoxinA on facial lines: a 19-year experience of identical twins. *Dermatol Surg*. 2015;41:S64-S66.
14. Chang AL, Bitter PH Jr, Qu K, et al. Rejuvenation of gene expression pattern of aged human skin by broadband light treatment: a pilot study. *J Invest Dermatol*. 2013;133(2):394-402.
15. Cohen JL, Ross EV. Combined fractional ablative and nonablative laser resurfacing treatment: a split-face comparative study. *J Drugs Dermatol*. 2013;12(2):175-8.
16. Ingargiola MJ, Motakef S, Chung MT, et al. Cryolipolysis for fat reduction and body contouring: safety and efficacy of current treatment paradigms. *Plast Recontr Surg*. 2015;135(6):1581-90.
17. Jewell ML, Baxter RA, Cox SE, et al. Randomized sham-controlled trial to evaluate the safety and effectiveness of a high-intensity focused ultrasound device for noninvasive body sculpting. *Plast Reconstr Surg*. 2011;128(1):253contr
18. Jones DH, Carruthers J, Joseph JH, et al. REFINE-1, a multicenter, randomized, double-blind, placebo-controlled, phase 3 trial with ATX-101, an injectable drug for sub mental fat reduction. *Dermatol Surg*. 2016;42(1):38-49.
19. Kaminer MS, Coleman WP 3rd, Weiss RA, et al. Multicenter pivotal study of vacuum-assisted precise tissue release for the treatment of cellulite. *Dermatol Surg*. 2015;41(3):336-7.
20. Katz B. Quantitative and qualitative evaluation of the efficacy of a 1440 nm Nd:YAG laser with novel bi-directional optical fiber in the treatment of cellulite as measured by 3-dimensional surface imaging. *J Drugs Dermatol*. 2013;12(11):1224-30.
21. Fabi SG, Goldman MP. Comparative study of hydroquinone-free and hydroquinone-based hyperpigmentation regimens in treating facial hyperpigmentation and photoaging. *J Drugs Dermatol*. 2013;12(3):S32-7.
22. Mendelson BC, Hartley W, Scott M, et al. Age-related changes of the orbit and midcheek and the implications for facial rejuvenation. *Aesthetic Plast Surg*. 2007;31:419–423.
23. Taub AF, Sarnoff D, Gold M, et al. Effect of multisyringe hyaluronic acid facial rejuvenation on perceived age. *Dermatol Surg*. 2010;36(3):322-8.
24. Mashiko T, Mori H, Kato H, et al. Semipermanent volumization by an absorbable filler: onlay injection technique to the bone. *Plast Reconstr Surg Glob Open*. 2013;1(1).
25. Pavicic T. Complete biodegradable nature of calcium hydroxylapatite after injection for malar enhancement: an MRI study. *Clin Cosmet Investig Dermatol*. 2015;8:19-25.
26. Park SH, Kim DW, Jeong T. Skin-tightening effect of fractional lasers: comparison of non-ablative and ablative fractional lasers in animal models. *J Plast Recontr Aesthet Surg*. 2012;65(10):1305-11.
27. Fabi SG, Goldman MP. Retrospective evaluation of micro-focused ultrasound for lifting and tightening the face and neck. *Dermatol Surg*. 2014;40(5):569-75.
28. Biesman BS, Baker SS, Carruthers J, et al. Monopolar radiofrequency treatment of human eyelids: a prospective, multi center, efficacy trial. *Lasers Surg Med*. 2006;38(10):890-8.

AUTHOR CORRESPONDENCE

Lauren Meshkov Bonati MD

E-mail:..... lauren.bonati@gmail.com

Approach to the Mature Cosmetic Patient: Aging Gracefully

Susan Weinkle MD[a,b] and Michael Saco MD[a]
[a]University of South Florida Department of Dermatology & Cutaneous Surgery, Tampa, FL
[b]Cosmetic Dermatologist and Mohs Surgeon, Bradenton, FL

ABSTRACT

Aging gracefully has taken on a whole new meaning over the past few decades as new aesthetic treatments have been developed and are becoming more sophisticated by the day. The aging process, which is exacerbated by chronic UV exposure, results in dyspigmentation, loss of skin laxity, precancerous and cancerous skin lesions, fat loss and redistribution, and bone resorption. Laser and light devices can be used to treat dyspigmentation, while neuromodulators and soft tissue fillers can be used for rhytides and revolumization. Newer procedures include using resorbable polyglycolide/L-lactide suspension sutures with bidirectional cones for mid face revolumization, deoxycholic acid injections for submental fat reduction, and radiofrequency energy. Certain over-the-counter products can increase the risk of postprocedure bruising, while arnica and bromelain may help decrease this risk. Dermatologists continue to be at the forefront of aesthetic treatments, ready and willing to help the aging population look and feel their best.

J Drugs Dermatol. 2017;16(6 Suppl):s84-86.

Our population is aging and has accumulated a significant amount of UV exposure, resulting in sun damage, wrinkles, textural changes, and skin cancer.[1,2] These complications affect the economy as a whole, with skin care representing an ever-expanding $80 billion industry.[3] Women ages 35 and older look at their face, on average, about 5 times per day, equivalent to approximately once every 3 waking hours. Forty-five million American women (60%) were likely to worry about "looking old and wrinkled," and 60% of women think men would rather kiss a woman with a beautiful face. Our mature patients desire safe and effective techniques to "turn back the clock," with most women preferring dermal injectables over surgery. Women on average would prefer to look about 13 years younger than their actual age, and 75% of women want their skin to look and feel new. As the aging population increases, dermatologists continue to be at the forefront of aesthetic treatments.[4]

Aging skin is a cumulative process that is a consequence of genetically programmed decreases in functional capacity and loss of the ability to repair damage. Fat redistribution and loss from facial fat compartments contribute to multiple changes in the aging face, including the increased prominence of nasojugal creases, nasolabial folds, marionette lines, and jowls.[5] Patients in their fifties have usually already started or will start menopause, as well as start to develop changes in facial contour, reduced skin elasticity, and more brittle hair and nails. When patients reach their sixties, dyschromias become more prominent, as do seborrheic keratoses, actinic keratoses, dilated pores, lusterless hair, and vascular erythema. Past age 70, volume loss becomes more apparent, as lipoatrophy begins and bone resorption progresses. Skin laxity increases even further, as does easy bruising and hair thinning or loss.[5-8]

When a patient presents for a cosmetic consultation, the best way to start the conversation is by asking the patient what bothers them and then discussing what aspects can be improved. Asymmetry and other notable features can be documented with pretreatment photographs, which can then be compared to posttreatment photographs to show patients how their appearance has been improved. A wide variety of aesthetic treatment options are available to patients. Laser and light treatments can treat pigmentary alterations and telangiectasias, as well as help with evening skin tone.[9] In contrast, neuromodulators and soft tissue fillers are essential tools for improving rhytides and volume loss. Men can also benefit from aesthetic procedures, although they typically require greater amounts of neuromodulator to be injected than that needed to achieve the same result in women.

Tear troughs that have undergone lipoatrophy can give the eyes a sunken, tired appearance. Injecting hyaluronic acid into this region using a blunt-tipped cannula can take years off the face in a way that decreases the chance of running into vessels in this highly vascular area (Figure 1). Cannulas are an excellent way to inject filler into other highly vascular areas, such as the mid face, to minimize the risk of bruising and other vascular complications related to intravascular filler injections. However, cannulas are not suitable for revolumizing the temples since this procedure requires injection down to the level of periosteum. Cannulas are not appropriate for revolumizing thin ear lobules either, which is a simple procedure in which filler is injected into the ear lobules to give them a more plump, youthful appearance to counteract the sagging and thinning that results from years of wearing heavy earrings.

With age, there is an overall loss of lip volume and structure. The upper lip becomes thin and elongated, Cupid's bow

FIGURE 1. Before (left) and after (right) hyaluronic acid injections into the tear troughs using a blunt-tipped cannula, giving the eyes less of a sunken, tired appearance.

FIGURE 2. Before (left) and after (right) hyaluronic acid injections into the lips to revolumize the lips and recreate Cupid's bow.

FIGURE 3. Before (left) one week after (right) calcium hydroxylapatite injections to soften marionette lines and pre-jowl sulci.

becomes effaced and flattened, and the philtral columns lose definition.[10] Lip augmentation needs to be performed correctly, recreating Cupid's bow and adding volume to the lips without giving them a sausage appearance (Figure 2). Upper cutaneous lip rejuvenation using neuromodulators and fillers can soften perioral rhytides and redefine the philtral columns.

Sagging cheeks can result from fat and bone loss in the mid face. The cheek can be resculpted by either injecting filler or by using resorbable polyglycolide/L-lactide (PLGA) suspension sutures with bidirectional cones that reposition the tissue and stimulate collagen formation to add back volume. Repositioning the cheeks can also improve the appearance of the lower face, thus minimizing the interventions that will need to be performed in this area.

Marionette lines and more prominent pre-jowl sulci result from volume loss in the lower third of the face and can give the appearance of a frown. Injection of fillers, such as calcium hydroxylapatite, can replace lost volume, soften these lines, and be used to turn the corners of the mouth upward, giving patients their smiles back (Figure 3).

The mandibular sweep can also be recreated to hide sagging jowls by injecting filler, such as calcium hydroxylapatite, along the angle of the jaw and in front of the jowl. In contrast, platysmal bands, as well as horizontal neck lines, which have started to appear in even younger people as a result of looking down at one's phone while texting, are best treated using neuromodulators.

Even if patients have aesthetic procedures to improve their facial appearance, their hands, which can appear skeletonized due to volume loss if left untreated, can provide a clue to their true age. Injecting calcium hydroxylapatite using a blunt-tipped cannula can reshape a skeletonized hand and give the hands a more youthful appearance (Figure 4).

Newer innovations, including the aforementioned PLGA suspension sutures, have allowed dermatologists to expand their aesthetic repertoire. Deoxycholic acid injections can be used to reduce submental fat and sharpen the cervicomental angle (Figures 5 and 6). Radiofrequency energy can be used for a variety of applications, since heat from the injectable cannula can stimulate collagen production beneath the skin, as well as shrink fibrous septae and melt fat at higher target temperatures.

FIGURE 4. Calcium hydroxylapatite has been injected into patient's right hand using a blunt-tipped cannula; patient's revolumized right hand appears more youthful compared to patient's untreated left hand.

FIGURE 5. Before (left) and after (right) submental deoxycholic acid injections with noticeably reduced submental fat and sharper cervicomental angle.

FIGURE 6. Before (left) and after (right) submental deoxycholic acid injections with noticeably reduced submental fat and sharper cervicomental angle.

Ultimately, any procedure where insertion of a needle or cannula is required can result in bruising. Patients using over-the-counter products like glycerin, evening primrose, and vitamin C can have a greater risk of bruising. In contrast, arnica and bromelain can help decrease the likelihood of postprocedure bruising.[11,12]

Overall, as our population continues to age, the demand for minimally invasive aesthetic procedures continues to increase. Various changes happen as people age, which can be combatted using laser and light devices, neuromodulators, soft tissue fillers, and some of the newer treatment modalities, including PLGA suspension sutures, deoxycholic acid, and radiofrequency energy devices. Ultimately, it is up to dermatologists to master these and future aesthetic procedures in order to give a whole new meaning to aging gracefully.

DISCLOSURES

Dr. Weinkle is a Medical Consultant, Allergan; Clinical Investigator, Allergan; Medical Consultant, DermAvance; Clinical Investigator, DermAvance; Medical Consultant, Galderma; Clinical Investigator, Galderma; Medical Consultant, Merz; Medical Consultant, Procter and Gamble; Medical Consultant, Kythera; Clinical Investigator, Kythera; Medical Consultant, Myoscience; Medical Consultant, Teoxane; Clinical Investigator, Teoxane; Medical Consultant, Sinclair; Clinical Investigator, Alphaeon. Dr. Saco has no conflicts of interest to declare.

REFERENCES

1. Mayoral FA, Kenner JR, Draelos ZD. The skin health and beauty pyramid: a clinically based guide to selecting topical skincare products. *J Drugs Dermatol.* 2014;13:414-421.
2. Lupo M, Jacob L. Cosmeceuticals used in conjunction with laser resurfacing. *Semin Cutan Med Surg.* 2011;30:156-162.
3. Weiss RA, Weiss MA. Evaluation of a novel anti-aging topical formulation containing cycloastragenol, growth factors, peptides, and antioxidants. *J Drugs Dermatol.* 2014;13:1135-1139.
4. Wisniewski JD, Ellis DL, Lupo MP. Facial rejuvenation: combining cosmeceuticals with cosmetic procedures. *Cutis.* 2014;94:122-126.
5. Rohrich RJ, Pessa JE. The fat compartments of the face: anatomy and clinical implications for cosmetic surgery. *Plast Reconstr Surg.* 2007;119:2219-2227; discussion 2228-2231.
6. Fenske NA, Lober CW. Structural and functional changes of normal aging skin. *J Am Acad Dermatol.* 1986;15:571-585.
7. Weinkle S. Facial assessments: identifying the suitable pathway to facial rejuvenation. *J Eur Acad Dermatol Venereol.* 2006;20 Suppl 1:7-11.
8. Levin J, Momin SB. How much do we really know about our favorite cosmeceutical ingredients? *J Clin Aesthet Dermatol.* 2010;3:22-41.
9. Sadick NS. Device-assisted transepidermal delivery of cosmeceuticals: a new way to enhance aesthetic procedures? *Aesthetic Plast Surg.* 2013;37:973-974.
10. Wollina U. Perioral rejuvenation: restoration of attractiveness in aging females by minimally invasive procedures. *Clin Interv Aging.* 2013;8:1149-1155.
11. Broughton G, 2nd, Crosby MA, Coleman J, Rohrich RJ. Use of herbal supplements and vitamins in plastic surgery: a practical review. *Plast Reconstr Surg.* 2007;119:48e-66e.
12. Rowe DJ, Baker AC. Perioperative risks and benefits of herbal supplements in aesthetic surgery. *Aesthet Surg J.* 2009;29:150-157.

AUTHOR CORRESPONDENCE

Michael Saco MD
E-mail:..... ms20142018@aol.com

Neurotoxins: Evidence for Prevention

Shannon Humphrey MD
Carruthers & Humphrey Cosmetic Dermatology, Vancouver, BC Canada
Department of Dermatology, University of British Columbia, Vancouver, BC Canada

ABSTRACT

Onabotulinum Toxin A is the gold standard treatment for temporary dynamic rhytid reduction. Clinicians have observed a long-term and preventive benefit for patients beyond muscle relaxation particularly in patients who receive repeated treatments over time. These changes include progressive reduction of rhytides, prevention of dynamic rhytides, and improvements in skin quality. In this brief paper, we review basic science, clinical, and anecdotal evidence that explores a long-term and potential preventive effect of Onabotulinum Toxin A injections.

J Drugs Dermatol. 2017;16(6 Suppl):s87-90.

INTRODUCTION

Since its introduction for the treatment of glabellar rhytides over two decades ago, botulinum toxin type A (BoNTA) has since become the most frequently performed cosmetic procedure in the United States[1] and is considered the gold standard treatment for dynamic facial wrinkles. BoNTA injections block the release of acetylcholine required for muscle contraction, causing temporary paralysis of the treated muscle.[2] However, there is evidence that regular, repeated treatments provide aesthetic benefit independent of muscular chemodenervation.[3-6] Although the exact mechanism of action is unknown, limited clinical studies, case studies, and personal experience cumulatively suggest that long-term use of BoNTA not only prevents the formation of new wrinkles but also leads to progressive improvements in skin quality and the appearance of established rhytides.

Long-term Effects: Review of the Evidence

Studies evaluating the long-term efficacy and safety of BoNTA injections beyond a year are scarce, and there are few reports evaluating the clinical benefits of repeated treatments over the course of many years. In the early nineties, Binder began documenting the facial changes over time in two identical twins living in different countries in what would become a 19-year case-report demonstrating that prophylactic use of BoNTA over a long period of time can prevent the formation of static.[4,6] One twin (based in Los Angeles) received BoNTA in the forehead and glabella regularly every 4 to 6 months for 19 years. For the last 8 years, she received additional treatment in the periorbital region. The other twin (based in Munich, Germany) received a total of four treatment sessions in the forehead, glabella, and crow's feet over the entire study. Photographs reveal a striking contrast between the two women. The treated twin displays no evidence of forehead or glabellar lines at rest, while the sporadically treated twin has visible static forehead rhytides. Similarly, the treated twin exhibits mild dynamic crow's feet; deeper lines are evident in the sporadically treated twin. Interestingly, skin texture also improved in the treated twin, while the skin of the sporadically treated twin shows signs of aging, with greater number of wrinkles and visible pores. Of note, neither twin used any topical retinoid preparation or received any other cosmetic treatments.

The long-term effects may go beyond the prevention of new wrinkles. Bowler published a case series of two individuals (one male, one female) who received 21 to 24 treatment sessions over a 7-year period every 3 to 6 months for glabellar, forehead, and periorbital rhytides.[3] Post-treatment skin quality significantly improved compared to pre-treatment in terms of wrinkles reduction and skin smoothness, with eventual effacement of non-reducible forehead lines. Similarly, Dailey demonstrated a cumulative reduction in wrinkle severity in 50 women who received 20 U BoNTA for glabellar rhytides in repeated treatment cycles (every 4 months) over a 20-month period.[5] Progressive improvement from baseline in facial wrinkles continued up to 6 months after treatment ended. Given the downward trend in wrinkle severity, the author suggests that further wrinkle effacement could be achieved with continued treatment beyond 2 years. Moreover, it may be possible to widen the treatment interval between sessions without losing aesthetic benefit, an important consideration for patient satisfaction.

Mechanism of Action: Theoretic Possibilities

There are several theories to explain the progressive reduction in wrinkle severity and improvements in skin quality observed after repeated treatments over a long period of time. First: the theory of learned response, in which patients learn to avoid using facial muscles that lead to wrinkle formation. There is also evidence of long-term physiologic change in the muscle itself (ie, atrophy) of up to 12 months after a single, low dose of BoNTA.[7] It is obvious that wrinkle formation stops after muscle

motion is inhibited, at least until the effects of the toxin begin to wane. Less clear, however, is why established rhytides appear to fade with repeated treatment sessions. Some evidence points to a direct effect on the skin at the histologic level that is not due to local inflammation.[7]

Human skin has three key biomechanical features: strength, pliability (ability to stretch), and elasticity (ability to recoil).[7] These biomechanical properties change as we age; skin elasticity, in particular, undergoes a progressive decline over time that accelerates with ultraviolet (UV) exposure.[9] Recent evidence suggests that the use of BoNTA also results in alteration in skin elasticity and pliability, producing characteristics consistent with youthful skin.[8,10] A prospective cohort study of 48 BoNTA-naïve women examined elastic recoil and pliability of the skin after only one treatment session using low doses in the glabella, forehead, and lateral orbit.[10] Elasticity and pliability was assessed at 2 weeks, 2 months, 3 months, and 4 months after treatment using a Cutometer. Mean pliability significantly increased from baseline at 2 and 3 months post-treatment across all sites. Significant improvements in elastic recoil were noted at 2 months for all sites, but only in the glabella for months 3 and 4, which correlates to the clinical observation that treatment in the glabella typically lasts longer than in the forehead or lateral orbit. The authors highlight that the biomechanical changes induced by BoNTA are the opposite of those that develop with aging and suggest the results may reflect a change in the organization of collagen network in the dermis.

The dermal extracellular matrix (ECM) is composed mainly of collagen (types I and II) in addition to glycosaminoglycans and elastic fibers.[11] Collagen is the most abundant protein in human skin and responsible for maintaining structural integrity and proper functioning within the ECM. In aged skin, disorganization of this collagen network contributes to skin laxity and wrinkle formation.[12] El-Domyati and colleagues obtained skin biopsy specimens from 16 volunteers with moderate-to-severe wrinkles before and 3 months after a single injection of BoNTA in the periorbital region.[13] Immunohistochemical changes failed to show a difference in collagen or elastin levels. However, treatment led to a significant increase in wrinkle width and granular layer thickness, and the collagen bundles became more organized and compact around the wrinkles, with the appearance of regular and smooth fibers, compared to the disorganized, enhanced breakdown of collagen seen on baseline biopsy. These findings may explain the extended improvements observed after repeated BoNTA injections: perhaps results are not solely due to ongoing denervation of facial muscles but can also be attributed to potential dermal remodeling.

Certainly, this theory has been suggested elsewhere in the literature. Some physicians have noted a face-lifting effect after intradermal injection of BoNTa, attributed, in part, to increased collagen synthesis.[14-15] However, it has also been argued that percutaneous injury with needles initiates the wound-healing cascade that eventually results in collagen production, rather than any direct influence on fibroblasts.[16,17] To weigh in on this controversy, Oh and colleagues investigated the effect of BoNTA on cultured human dermal fibroblasts in vitro.[18] Fibroblasts secrete the precursors of collagen, procollagen types I and II. Dermal remodeling requires activation of fibroblasts and is an essential aspect of facial rejuvenation. Fibroblasts treated with BoNTA showed increased production of procollagen type I carboxy-terminal peptide (PIP), which indirectly reflects overall collagen I levels, and reduced expression of two matrix metalloproteases (MMPs), the enzymes

FIGURE 1. 52-year-old male before (A) and after (B) 10 years and 18 treatments of onabotulinumtoxin A to the glabella, forehead, and lateral canthal region.

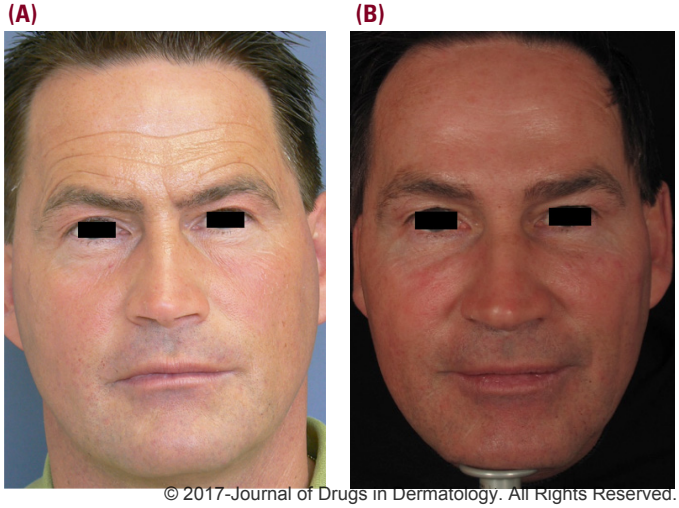


FIGURE 2. 48-year-old woman before (A) and after (B) 10 years and 20 treatments with onabotulinumtoxin A to the glabella and lateral canthal region.

FIGURE 3. 54-year-old female over a 7-year period (A-G) during which she received 23 treatments with onabotulinumtoxin A to the glabella.

responsible for the degradation of collagen and other components of the ECM.[18] Levels of two pro-alpha collagen chains—alpha-1, the major component of type I collagen, and alpha-2—were also higher after treatment. These results provide further evidence that BoNTA promotes fibroblast activity and has the potential to stimulate dermal remodeling.

Anecdotal Evidence

Evidence-based medicine is the optimal approach for patient care. As individual clinicians, however, we are heavily influenced by clinical observation and patient feedback. Clinical practice yields certain observation: first, regular, sustained injections of BoNTA lead to consistent, ongoing improvements in wrinkles—initial treatment leads to softening of wrinkles that often fill in over time with repeated injections; second, long-term treatment leads to an intangible improvement in skin quality, with improved light reflection for skin that is more luminous and radiant (Figures 1-3). Patient satisfaction is higher for men and women who receive regular injections over several years compared to those who receive only sporadic treatment, and this makes sense: a regular treatment regimen means that muscles do not regain function, the skin is not repeatedly creased by dynamic musculature, and the collagen network is able to reorganize cohesively in a way that prevents the formation of new wrinkles for a more youthful appearance and better clinical results.

CONCLUSION

Over the past two decades, BoNTA has become an indispensible part of aesthetic medicine and the most popular non-invasive option for facial rejuvenation. However, evidence suggests that injections do more than temporarily stay wrinkle formation. Data show that BoNTA alters biomechanical properties of the skin and may enable dermal remodeling for improvements in elasticity, pliability, and radiance. Although clinical evidence for the prophylactic use of BoNTA may be limited, anecdotal evidence and case studies tell us what we have yet to prove

via controlled trials: repeated treatment cycles with BoNTA for facial rhytides over a long period of time not only prevent new wrinkle development but also improve skin texture and appearance and lead to progressive wrinkle reduction of established rhytides. Clinically, these reports and observations translate to better aesthetic outcomes and much higher levels of patient satisfaction.

DISCLOSURES

The author has not disclosed any conflicts of interest.

REFERENCES

1. American Society of Plastic Surgeons (2015). 2014 Plastic Surgery Statistics Report. Available at: www.plasticsurgery.org. Accessed September 7, 2016.
2. Carruthers A, Carruthers J. Botulinum toxin type A: History and current cosmetic use in the upper face. *Semin Cutan Med Surg*. 2001;20:71-84.
3. Bowler PJ. Dermal and epidermal remodeling using botulinum toxin type A for facial, non reducible, hyperkinetic lines: Two case studies. *J Cosmet Dermatol*. 2008;7:241-4.
4. Binder WJ. Long-term effects of botulinum toxin type A (Botox) on facial lines: A comparison in identical twins. *Arch Facial Plast Surg*. 2006;8:426–31.
5. Dailey RA, Philip A, Tardie G. Long-term treatment of glabellar rhytides using onabotulinumtoxina. *Dermatol Surg*. 2011;37:918-28.
6. Rivkin A, Binder WJ. Long-term effects of onabotulinumtoxinA on facial lines: a 19-year experience of identical twins. *Dermatol Surg*. 2015;41 Suppl 1:S64-6.
7. Koerte IK, Schroeder AS, Fietzek UM, Borggraefe I, et al. Muscle atrophy beyond the clinical effect after a single dose of OnabotulinumtoxinA injected in the procerus muscle: a study with magnetic resonance imaging. *Dermatol Surg*. 2013;39:761-5.
8. Bonaparte JP, Ellis D. Skin biomechanical changes after injection of onabotulinum toxin A: Prospective assessment of elasticity and pliability. *Otolaryngol Head Neck Surg*. 2014;150:949-55.
9. Luebberding S, Krueger N, Kerscher M. Mechanical properties of human skin in vivo: a comparative evaluation in 300 men and women. *Skin Res Technol*. 2014;20:127-35.
10. Bonaparte JP, Ellis D. Alterations in the elasticity, pliability, and viscoelastic properties of facial skin after injection of onabotulinum toxin A. *JAMA Facial Plast Surg*. 2015;17:256-63.
11. Uitto J. Molecular pathology of collagen in cutaneous diseases. *Adv Dermatol*. 1991;6:265–86.
12. Kim KH, Geronemus RG. Non-ablative laser and light therapies for skin rejuvenation. *Arch Facial Plast Surg*. 2004;6:398–409.
13. El-Domyati M, Attia SK, El-Sawy AE, Moftah NH, et al. The use of Botulinum toxin-a injection for facial wrinkles: A histological and immunohistochemical evaluation. *J Cosmet Dermatol*. 2015;14:140-4.
14. Chang SP, Tsai HH, Chen WY, Lee WR, et al. The wrinkles soothing effect on the middle and lower face by intradermal injection of botulinum toxin type A. *Int J Dermatol*. 2008;47:1287–94.
15. Shah AR. Use of intradermal botulinum toxin to reduce sebum production and facial pore size. *J Drugs Dermatol*. 2008;7:847–50.
16. Fernandes D, Signorini M. Combating photoaging with percutaneous collagen induction. *Clin Dermatol*. 2008;26:192–9.
17. Kapoor R, Shome D, Jain V, et al. Facial rejuvenation after intradermal botulinum toxin: Is it really the botulinum toxin or is it the pricks? *Dermatol Surg*. 2010;36(Suppl 4):2098–105.
18. Oh S, Lee Y, Seo YJ, et al. The potential effect of botulinum toxin Type A on human dermal fibroblasts: An in vitro study *Dermatol Surg*. 2012; 38:1689–1694.

AUTHOR CORRESPONDENCE

Shannon Humphrey MD
E-mail:..... shannon@carruthers-humphrey.com

"Man-some": A Review of Male Facial Aging and Beauty

Terrence Colin Keaney MD
George Washington University, Washington, DC

ABSTRACT

Gender plays a significant role in determining facial anatomy and behavior, both of which are key factors in the aging process. Understanding the pattern of male facial aging is critical when planning aesthetic treatments on men. Men develop more severe rhytides in a unique pattern, show increased periocular aging changes, and are more prone to hair loss. What also needs to be considered when planning a treatment is what makes men beautiful or "man-some". Male beauty strikes a balance between masculine and feminine facial features. A hypermasculine face can have negative associations. Men also exhibit different cosmetic concerns. Men tend to focus on three areas of the face – hairline, periocular area, and jawline. A comprehensive understanding of the male patient including anatomy, facial aging, cosmetic concerns, and beauty are needed for successful cosmetic outcomes.

J Drugs Dermatol. 2017;16(6 Suppl):s91-93.

INTRODUCTION

Facial aging results from progressive changes to the skin, soft tissue, and skeletal structure. The changes associated with aging are produced by both intrinsic and extrinsic factors.[1] Intrinsic aging refers to the role of one's genes and hormones in the aging process. Extrinsic factors are environmental insults, such as smoking and sun exposure, which accelerate facial aging. Although the factors influencing aging are well understood, the rate and pattern of aging is unique to each individual due to the combination of behavioral, genetic, and anatomical differences. Gender is a key determinant in the aging process because of the genetic and behavioral differences between men and women. The importance of recognizing male facial aging is critical when planning an aesthetic treatment on men. What is less understood is the aesthetic goal when treating the aging male face. What is the male aesthetic ideal? What makes men beautiful or "man-some"? Since beauty is in the eye of the beholder, it is important to understand the male aesthetic ideal when planning aesthetic treatments. Ultimately, an aesthetic treatment is successful if the results align with the patient goals. Men exhibit a different set of motivations, goals, and concerns about aging than women. With increasing aesthetic interest among male patients, an understanding of anatomy and aging is not enough. This article will review facial aging and beauty ideals in men in order to provide a framework for physicians to plan successful aesthetic treatments in men.

Male Facial Aging

Men tend to age more poorly due to their susceptibility to intrinsic and extrinsic factors.[2] Men have reduced innate antioxidant capacity and are more prone to greater UV-induced immunosuppression.[3] Men are also more likely to participate in high risk health behaviors that accelerate aging. Men are more likely to smoke and are less likely to adopt sun protective behaviors.[4] Men use sunscreen less frequently, are more likely to develop a sunburn, and have demonstrated less knowledge regarding sun safety and skin cancer formation than women. Rhytides tend to be more severe and develop earlier in men starting on the forehead.[5] The male wrinkle pattern is unique due to differences in facial muscle movement and cutaneous appendages. Men lack substantial perioral rhytides. The downward fan lateral canthal wrinkle pattern and "U" glabellar wrinkle pattern are more common in men. A steady atrophy of facial soft tissue occurs in men as opposed to the rapid decline found in perimenopausal women.[6] Male volume loss is more pronounced in the periocular area with men developing more severe lower eyelid sagging.[7] Men are also more susceptible to hair loss, with 50 % of Caucasian men showing at least some signs of hair loss by age 50. Hair loss is associated with the loss of youth and can make men appear older than their stated age.[8]

While the pattern and rate of facial aging differs between genders, the underlying facial anatomy differs as well. Testosterone plays a critical role in secondary sexual characteristics including skeletal shape, subcutaneous fat distribution, and cutaneous physiology. A "masculine" youthful face is not only larger but exhibits a different shape. The male face is wider at all levels including the forehead, cheeks, and jawline. Men exhibit less subcutaneous soft tissue that is distributed more evenly with less anterior medial projection and more lateral projection in the midface. Men have more prominent supraorbital ridges and a wider and larger chin with forward prominence. These features contribute to the "square" and "angular" contour of the masculine, male face.

"Man-some": Male Beauty

Aesthetic procedures are elective procedures designed to make patients look and feel better. In order to provide a successful outcome, aesthetic providers must understand what makes men look and feel better. Most research on beauty has invariably focused on women. Across ethnicities, feminine features ("inverted triangle of youth") are considered attractive.[9] The positive effect of feminized features on attractiveness has been shown in multiple studies measuring facial features of photographs and manipulating facial features.[10] It is thought that estrogen dependent female facial characteristics (full mid face, tapered lower face) correlate with youth, health, and reproductive fitness). The link between sexual dimorphism and attractiveness is not as evident in men. Male faces are thought to be more attractive if they are more masculine than the average male face.[11] However, conflicting studies have shown that male faces with feminine features are also preferred.[12] Enhanced masculine facial characteristics increased both perceived dominance and negative attributions (eg, coldness or dishonesty).[13] Extreme masculinized male faces indicate high testosterone levels, which are associated with more troubled relationships including increased infidelity, violence, and divorce.[14] Male facial attractiveness is likely a balancing act between feminity and masculinity. From an evolutionary standpoint, this may reflect, on the one hand, masculine characteristics that are associated with dominance and an effective immune system. On the other hand, this also reflects characteristics that are related to minimal paternal investment and poor relationships. In clinical practice, a careful assessment of the masculine features (supraorbital ridge, jawline, etc) of the male face should be performed. Treatment should be focused on averaging the male face (eg, feminizing a hypermasculine face). This "regression to the mean" approach with men can be challenging and requires a thorough understanding of male facial anatomy in order to decide which approach, feminizing and masculinizing, is appropriate for the patient.

Understanding what makes men attractive to the opposite gender is important, but in clinical practice the treating physician must satisfy the male patient. What are men's aesthetic concerns and goals? A recent survey study examined male aesthetic motivators. The primary motivating factors for considering a facial aesthetic injectable treatment were to "look good for my age" and to "look more youthful".[15] The male aesthetic motivators are more internally driven as opposed to external factors such as workplace competition or attracting a mate. Men also exhibit different cosmetic concerns. The survey study found that men prioritize three facial areas – hairline, periorbital area, and jawline. Hair loss is the number one cosmetic concern in men. The periorbital area is another area of focus among men with crow's feet lines and tear troughs as treatment priorities. Lastly, maintaining a masculine jawline through treatment of the submental fullness and chin is also desired.

CONCLUSION

Men represent a small segment of most cosmetic practices, historically representing approximately 10% of cosmetic procedures.[16] Despite their small piece of the medical aesthetic industry, male interest in cosmetic procedures is increasing. A survey of 25,000 men found that over 40% of men were interested in having a cosmetic surgical procedure.[17] Other industries reflect men's increasing interest in their appearance. Men's grooming is the fastest growing segment in the skincare market. Men's luxury fashion accounts for 40% of the market and is growing faster than the female market. In order to capitalize on the increase in male aesthetic interest, physicians have to develop a comprehensive approach to their male patients. A thorough understanding of anatomy, facial aging, cosmetic concerns, and beauty are needed when treating male patients. A complete understanding of the gender differences will allow physicians to tailor cosmetic treatments for their male patients.

DISCLOSURES

Dr. Keaney is a Consultant and Advisory Board Member for Allergan.

REFERENCES

1. Friedman, O. Changes associated with the aging face. *Facial Plast Surg Clin North Am.* 2005;13:371–80.
2. Keaney TC. Aging in the Male Face: Intrinsic and Extrinsic Factors. *Dermatol Surg.* 2016; 42(7):797-803.
3. Damian DL, Patterson CR, Stapelberg M, Park J, Barnetson RS, Halliday GM. UV radiation-induced immunosuppression is greater in men and prevented by topical nicotinamide. *J Invest Dermatol.* 2008;128:447–54.
4. Sattler U, Thellier S, Sibaud V, et al. Factors associated with sun protection compliance: results from a nationwide cross-sectional evaluation of 2215 patients from a dermatological consultation. *Br J Dermatol.* 2014;170(6):1327-35
5. Luebberding S, Krueger N, Kerscher M. Quantification of age related facial wrinkles in men and women using a three-dimensional fringe projection-method and validated assessment scales. *Dermatol Surg.* 2014;40(1):22-32.
6. Wysong A, Kim D, Joseph T, et al. Quantifying soft tissue loss in the aging male face using magnetic resonance imaging. *Dermatol Surg.* 2014;40(7):786-93.
7. Ezure T, Yagi E, Kunizawa N, Hirao T, et al. Comparison of sagging at the cheek and lower eyelid between male and female faces. *Skin Res Technol.* 2011;17(4):510-5.
8. Cash TF. The psychosocial consequences of androgenetic alopecia: a review of the research literature. *Br J Dermatol.* 1999;141(3):398-405.
9. Cunningham MR, Roberts AR, Wu CH, et al. Their ideas of beauty are, on the whole, the same as ours": consistency and variability in the cross-cultural perception of female physical attractiveness. *J Pers Soc Psychol.* 1995;68:261–79.
10. Rhodes G, Hickford C, Jeffery L. Sex-typicality and attractiveness: Are supermale and superfemale faces super attractive? *Br J Med Psycho.* 2000;91:125–40.
11. Johnston VS, Hagel R, Franklin M, et al. Male facial attractiveness: Evidence for hormone-mediated adaptive design. Evolution and Human Behavior. 2001; 22, 251–267.
12. Little AC, Hancock PB. The role of masculinity and distinctiveness in judgments of human male facial attractiveness. *Br J Med Psycho.* 2002;93:451–464.
13. Perrett DI, Lee KJ, Penton-Voak I, et al. Effects of sexual dimorphism on facial attractiveness. *Nature.* 1998; 394(6696):884-7.
14. Booth A, Dabbs JM. Testosterone and men's marriages. *Social Forces.* 1993;72:463-77.
15. Jagdeo J, Keaney T, Narurkar V, et al. Facial Treatment Preferences Among Aesthetically Oriented Men. *Dermatol Surg.* 2016;42(10):1155-63.

16. American Society for Plastic Surgery 2012 statistics. Available at http://www.plasticsurgery.org/news-and-resources/2012-plastic-surgery-statistics.html. Accessed June 1, 2013.
17. Frederick DA, Lever J, Peplau LA. Interest in cosmetic surgery and body image: views of men and women across the lifespan. *Plast Reconstr Surg.* 2007;120:1407–15.

AUTHOR CORRESPONDENCE

Terrence Colin Keaney MD
E-mail:..... drterrencekeaney@gmail.com

The Rationale of Anti-Aging Cosmetic Ingredients

Michèle Verschoore MD[a,b] and Marion Nielsen PharmD[a]
[a]L'Oréal Research & Innovation, Clichy, France
[b]Hopital Saint Louis, Centre Sabouraud, Paris, France

ABSTRACT

Anti-aging cosmetics are a mainstay in the skin care regimen irrespective of gender or human ethnics. Skin aging involves functional slowdown combined with environmental induced alterations. This paper focuses on cosmetic ingredients that aim at alleviating the signs of skin aging, with proven/controlled results of efficacy. Anti-aging skin care widely benefits from new ingredients and modern evaluation methods that can substantiate the effects of innovative products in a perceivable and sensitive manner. Our approach in controlling skin aging consists of following steps: 1) Developing novel testing methods; 2) Preventing photo-aging by sunscreens that protect from UV damage; 3) Protecting and restoring skin from damage induced by environmental exposure through active ingredients; 4) Boosting the cell metabolism and cell renewal to restore skin mechanical properties and improved appearance.

J Drugs Dermatol. 2017;16(6 Suppl):s94-97.

INTRODUCTION

Skin aging is a multifactorial process resulting from both intrinsic and external factors. Intrinsic functional alterations resulting from metabolic slowdown that cumulates with age is a major factor resulting in skin aging. External environmental factors include: exposures to solar rays, pollutants such as ozone, smog or particulate matter or lifestyle factors (smoking, alcohol consumption etc). A combination of all these factors leads to a premature skin aging leading to the perception (self-perceived or perceived by others) of an older look than the true chronological age of the skin

The major extrinsic factor of skin aging is UV rays, as evidenced by the clearly altered condition of naturally uncovered skin areas such as the face and dorsum of hands. Extensive studies have demonstrated the damaging effects of acute and chronic solar UVB rays[1] on epidermal cells including DNA damage, mainly on Caucasian skin. However, the last two decades have emphasized the insidious effects of the far more abundant and common (no zenithal hours) UVA rays that penetrate much deeper into skin and that, unlike UVB, are not associated with warning signs such as erythema/sunburn. UVA's are indeed strong inducers of oxidative stress through generating reactive oxygen species (ROS) and of early signs of skin aging through dermal damage[2] and pigmentation disorders. Facial wrinkles, mottled uneven pigmentation, pigmented spots, laxity, and sagging are usual UV-related photo-aging signs.[1] Recently, specific signs of skin aging according to skin color have been identified.[3]

Other extrinsic factors are tobacco and pollutants, as highlighted by recent studies. Tobacco smoking reduces elastin and collagen I-III synthesis resulting in older skin appearance and dull complexion.[4] The skin of subjects who live in highly polluted cities presents higher oxidative stress, higher lactic acid content, and a lower hydration level, as compared to those living in less polluted areas.[5-8]

Developed or fast emerging societies express an overall growing concern for a younger look. Accordingly, there is a strong demand for rejuvenating cosmetic products, treatments, and techniques to reduce wrinkle appearance, restore skin texture, smoothness, radiance, even pigmentation, and to lighten aging spots, etc. This article focuses on cosmetic ingredients that aim at alleviating the signs of both chronological and environmental skin aging, with proven/controlled results of efficacy.

1. Development of Novel Testing Methods

The first requirement for developing a skin anti-aging cosmetic ingredient lies in developing reliable instruments for objective measurements of changes occurring in aged condition and appearance of skin. Visual grading methods for affording quantitative support to clinical evaluation or self-appraisal of subjects are now available together with instrumental/objective methods of skin properties, or imaging the skin surface relief or the ultra-structure of skin at various depths as well as determining the location and amount of various biological molecules of interest, such as melanin, collagen, and elastin.[9]

Photographic charts for grading signs of aging in Caucasian, Asian, dark-skinned subjects have been published.[3] Evaluation scores can be determined by trained individuals at baseline and different time-points of product application or follow up post treatment or sessions.

The palette of techniques[9] used for assessing age-related skin properties and effect of treatment, which include high-frequency ultrasound, laser confocal microscopy, optical coherence

FIGURE 1. Skin aging induced by pollution: clinical signs and biological mechanisms.

Dryness	↓	Desquamation
Increased visibility of pores	↓	Hydration
Uneven skin texture	↑	SC Lipids and proteins peroxidation, decreased barrier function
Increased sebum flow		Aryl carbon receptors activation
Increased lentigines	↑	Inflammation

tomography (epidermis and dermis thickness), fringe projection (wrinkles), colorimetry (skin color, pigmentation evenness), devices for measuring visco-elastic properties, surface texture, and hydration (SkinChip™), have been published.[10-12]

2. Prevention from UV Damage

First line of defense against UV induced skin damage is daily application of photo-stable sunscreens with high UVA protection index. Even short term exposures over long periods of time can add to cumulative damage to the dermal and epidermal structures and functions. The harmful effects of skin exposure to sun (and simulated solar UVA's) including sub-erythemal doses and the efficient prevention of damage afforded by broad spectrum sunscreens have been thoroughly documented albeit mainly on subjects with light skins of phototypes I-III, ie, the most concerned people. Interestingly, a recent study on an ethnically diverse subject cohort treated for 8 weeks with either a SPF 30/UVA PF 20 or SPF 60/UVA PF 20 product showed a significant decrease in lightening of pre-existing face and hand pigmentary abnormalities and the overall lightening of facial skin in subjects with skin of color.[13] No difference was found between the two sunscreens, suggesting the relevance of high UVA protection to prevent hyperpigmentation disorders of sun exposed skin areas, a sign of perceived age in dark-skinned subjects.

Prevention of skin aging can also be obtained by using highly photo-protective products that combine effective UVB and UVA sunscreens, in all skin color phenotypes. The efficiency of combinations of antioxidants (Vit C, Vit E) in alleviating the signs of skin aging has also been extensively studied.

3. Protection and Restoring Skin

Topical antioxidants are among the most adequate complementary products to sunscreens as they protect cells from oxidative stress and UVA-induced ROS that are highly involved in skin photo-aging process. Hydrophilic vitamin C (Vit C) and lipophilic vitamin E (Vit E) are the gold standards for this purpose. Topically applied Vit C enhances the mRNA levels of collagen I and III and epidermal turnover, which improves skin surface condition.[14] Combining vitamins C and E provides an interactive, synergistic pair of antioxidants in tissues, Vit C regenerating and Vit E involved in neutralization of ROS.[14] Stabilized by the plant antioxidant ferulic acid, the combination turned out to efficiently supplement the protection against UV-induced cell damage.[15]

Many reported studies show that extrinsic aging is at least partially reversible and may be retarded or corrected by some cosmetic ingredients. One of the most investigated ingredient has been vitamin A (Retinol), and its derivatives, where a number of clinical trials have proven its benefits. Collagen

FIGURE 2. Quantification and evaluation methods for skin aging.

FIGURE 3. Skin aging in different skin color types.

Caucasian

Aging: Fine wrinkles, deep wrinkles in men too.

Asian

Aging: Long lasting pigmented spots UV induced.

African-American

Aging: Long lasting pigmented spots UV induced.

synthesis becomes stimulated, together with an enhanced regulation of epidermal cell proliferation and differentiation. Among others, two 6-month clinical studies on a retinol lotion vs vehicle[16] and on a retinol-sunscreen combination[17] in elderly and 45-60-year-old cohorts led to a significant reduction of wrinkles, as compared to their respective vehicles.

Another successful anti-aging agent is dehydrojasmonic acid, a derivative of a plant stress hormone that possesses various activities. It favors a gentle desquamation of the upper layers of the stratum corneum (SC) thus restoring a "younger" rate of epidermal renewal. It also induces a significant deposit of fibrillin-rich microfibrils in the papillary dermis of photo-aged volunteers[18] and reverses steroid-induced atrophy.[19] Twice daily application for 3 months resulted in significant improvement of crow's feet wrinkles, skin texture, and reduction in facial skin pores. Other restoring approaches are illustrated by the results of studies on a new C-xylopyranoside derivative and fragmented hyaluronic acid that respectively show improved morphogenesis of the whole dermal epidermal junction and clues to the remodeling of the dermal architecture network.

4. "Boosting" or Stimulating Cell Metabolism

The daily use of mild exfoliating agents such as alpha hydroxy-acids (AHA's) has been widely recommended to help remove the outermost layers of SC and improve epidermal renewal. In this respect, a close member of this family (β-hydroxyacids), n-capryloyl salicylic acid (LHA), has been demonstrated to have unique properties. Being lipophilic, with slow penetration into the SC layers, LHA acts on loose interfaces, closely mimicking the normal physiological process of desquamation through a controlled thinning of SC leading to epidermal cell renewal similar to that of younger skin. It thus reduces age-related changes including hyper pigmentation, fine lines, and wrinkles.[20]

An interesting boosting approach is by modulating the glucosaminoglycan (GAG) and proteoglycan (PEG) content of the skin. GAG and PEG are major players in inter-cellular communications, cell migration, and tissue modeling. Significant changes in GAG's and PEG's have been identified in aged skin. Hyaluronic acid (HA) is a unique non-sulfated GAG the role of which appears essential in re-epithelialization process, control of proliferation, and migration of keratinocytes from the epidermal basal layer. The high molecular weight (MW) of HA (around 10^6 Da) makes it a surface protective film that cannot penetrate when applied as a lotion onto skin but maintains hydration by trapping water. A fragmented HA, with low MW fragments, that can penetrate and contribute to remodel the architecture of the collagen network has been tested successfully in reconstructed skin models.[21]

Skin aging entails dramatic changes in the extracellular matrix (ECM), particularly in the superficial dermis and dermal epidermal junction (DEJ), the outline of which loses papillary structure and anchor fibers, thus flattening with age. These alterations gather pace with exposure to extrinsic factors. A C-xylopyranoside derivative (C-xyloside) was shown to stimulate the expression and deposit of GAG and key ECM proteins in the superficial dermis, thereby improving the morphogenesis of the whole functional DEJ.[22-25]

The clinical efficacy of C-xyloside combined with blueberry extract was shown on diabetic subjects older than 50 yrs where

fine lines were found significantly decreased.[26] In a multicenter blinded study, C-xyloside was also found significantly effective in alleviating skin aging signs in menopausal women.[27, 28]

CONCLUSION

Advances in methods for quantitative and reproducible evaluation of aging signs by clinicians, trained individuals, and panelists have resulted from outstanding progress in imaging techniques with high resolution level and software for observing, recording, and collecting data up to the ultrastructural level. Skin aging status and appearance can thus be objectively assessed to provide optimal answers to huge demand for skin anti-aging options for all skin types. New strategies using prevention, protection and boosting skin metabolism have been devised to test new evidence-based ingredients for skin antiaging benefits. Sun and associated oxidative stress are clearly causative factors in premature altering of the facial appearance and exposed areas. These obviously make sun avoidance and protection by broad spectrum sunscreens with strong absorption in the UVA range a primary daily care, especially when coupled with antioxidants. Mild exfoliative products that smooth coarse or rough skin can prompt a faster epidermal turnover. A large range of carefully composed combinations of evidence-based ingredients can now be used for preventing or reversing troublesome concerns about the deterioration of the facial look and its related aged skin appearance.

DISCLOSURES

Dr. Verschoore and Dr. Nielsen are full-time employees of L'Oréal Research & Innovation.

REFERENCES

1. Lavker RM. Cutaneous aging: Chronological versus photo-aging. In Gilchrest BA (ed): Photodamage. Cambridge: Blackwell Science, 1995:123-135.
2. Ou-Yang H, Kollias N. Dermal contribution to UVA-induced oxidative stress in skin. *Photodermatol Photoimmunol Photomed.* 2009;25(2):65-70.
3. Bazin R. Skin Aging Atlas, Vols I (Caucasian type), II (Asian type), III (African American type). MED'COM 2007, Paris, France.
4. Urbanska M, Nowak G, Florek E. Cigarette smoking and its influence on skin aging. *Przegl Lek.* 2012;69(10):1111-4.
5. Krutman J, Liu W, Li L, et al. Pollution and skin: from epidemiological and mechanical studies to clinical implications. *J Dermatol Sci.*2014;76: 163-168.
6. Lefebvre MA, Pham DM, Boussouira B, et al. Evaluation of the impact of urban pollution on the quality of skin: a multicentre study in Mexico. *Int J Cosmet Sci.* 2015;37(3):329-338.
7. Lefebvre MA, Pham DM, Boussouira B et al. Consequences of urban pollution upon skin status. A controlled study in Shanghai area. *Int J Cosmet Sci.* 2016;38(3):217-23.
8. Krutman J, Bouloc A, Sore G, et al. The skin aging exposome. *J Dermatol Sci.* 2017;85:152-61.
9. Non invasive methods and imaging techniques for investigating the skin in vivo. Lévêque JL, Li L, Verschoore M. Basic Science for Modern CosmeticDermatologyp. 85-96 Verschoore M., Liu Wei editors people's Medical Publishing House, Beijing.
10. Lévêque JL1, Querleux B SkinChip, a new tool for investigating the skin surface in vivo. *Skin Res Technol.* 2003;9(4):343-7.
11. de Rigal J, Escoffier C, Querleux B, Faivre B, Agache P, Lévêque JL. Assessment of aging of the human skin by in vivo ultrasonic imaging. *J Invest Dermatol.* 1989;93(5):621-5.
12. Tancrède-Bohin E, Baldeweck T, Decencière E, Brizion S, Victorin S, Parent N, Faugere J, Souverain L, Bagot M, Pena AM. Non-invasive short-term assessment of retinoids effects on human skin in vivo using multiphoton microscopy. *J Eur Acad Dermatol Venereol.* 2015;29(4):673-81
13. Halder R, Rodney I., Munhutu M., et al. Evaluation and effectiveness of a photoprotective composition sunscreen) on subjects of skin of color. XXII International Pigment Cell Conference, Singapore 2014. doi: 10.1111/pcmr.12292, Abstract P185.
14. Nusgens BV, Humbert P, Rougier, A, et al. Topically applied vitamin C enhances the mRNA level of collagens I and III, their processing enzymes and tissue inhibitor matrix metalloproteinase 1 in the human dermis. *J Invest Dermatol.* 2001;116:853-859.
15. Murray JC, Burch JA, Streilen RD, et al. A topical antioxidant solution containing vitamins C and E stabilized by ferulic acid provides protection for human skin against damage caused by ultraviolet radiation. *J Am Acad Dermatol.* 2008;59:418-25.
16. Kofi R1, Kwak HS, Schumacher WE, et al. Improvement of naturally aged skin with vitamin A (retinol). *Arch Dermatol.* 2007;143(5):606-12.
17. La Roche-Posay Scientific Dossier data on file
18. Tran C, Michelet JF, et al. In vitro and in vivo studies with tetra-hydro-jasmonic acid (LR2412) reveal its potential to correct signs of skin ageing. *J Eur Acad Dermatol Venereol.*2014;28(4):415-423.
19. Alexiades M., Clinical assessment of a novel dehydrojasmonate cosmeceutical, LR2412-CX, for the treatment of skin aging. *J.Drugs Dermatol.* 2016;15(2):209-15.
20. Saint-léger D, Lévêque JL, Verschoore M. The use of hydroxy acids on the skin: characteristics of C8-lipohydroxy acid. *J Cosmet Dermatol.* 2007;6:59-65.
21. Girardeau-Hubert S, Teluob S, Pageon H, et al. The reconstructed skin model as a new tool for investigating in vitro dermal fillers: increased fibroblast activity by hyaluronic acid. *Eur J Dermatol.* 2015;25(4):312-22.
22. Sok J, Pineau N, et al. Improvement of the dermal epidermal junction in human reconstructed skin by a new c-xylopyranoside derivative. *Eur J Dermatol.* 2008;18(3):297-302.
23. Cavezza A, Boulle C, et al. Synthesis of Pro-Xylane : a new biologically active C-glycoside in aqueous media. *Bioorg Med Chem Lett.* 2009;19 (3):845-9
24. Pineau N, Carrino DA et al. Biological evaluation of a new C-xylopyranoside derivative (C-Xyloside) and its role in glycosaminoglycan biosynthesis. *Eur J Dermatol.* 2011;21(3):359-70.
25. Vassal-Stermann E, Duranton A et al. A new C-Xyloside induces modifications of GAG expression structure and functional properties. *PLoS One.* 2012;10:e47933.
26. Draelos ZD, Yatskayer M et al. An evaluation of the effect of a topical product containing C-Xyloside and blueberry extract on the appearance of type II diabetic skin. *J Cosmet Dermatol.* 2009;8(2):147-51
27. Bouloc A, Roo E et al. A compensating skin care complex containing Pro-Xylane in menopausal women: results from a multicenter, evaluator-blinded, randomized study. *Acta Derm Venereol.* 2017;97:541-52.
28. Deloche C, Minondo AM, Bernard BA, Bernerd F, Salas F, Garnier J, Tancrede E. Effect of c-Xyloside on morphogenesis of the dermal epidermal junction in aged female skin. An unltrastuctural pilot study. *Eur J Dermatol.* 2011;21(2):191-6.

AUTHOR CORRESPONDENCE

Michèle Verschoore MD

E-mail:.....mverschoore@rd.loreal.com

Alternatives to Standard Injectables and Devices for Rejuvenation

Sabine Zenker MD
Dr. Zenker Dermatology Clinic, Munich, Germany

ABSTRACT

Introduction: Looking at alternatives to standard injectables and devices for rejuvenation, typical indications for facial rejuvenation are poor skin quality, pigmentary changes, and the loss of shape. Looking for effective treatments for those indications in the aesthetic field, one can notice a kind of "retro"-trend: easy-to-perform, non- or minimally-invasive, low-investment-requiring procedures are regaining a lot of popularity. And, over time, those treatments are becoming well defined and far more specific.

Objective: To discuss an indication-specific full-face concept for facial rejuvenation using alternatives to standard injectables and devices for rejuvenation.

Materials and Methods: The strategy of this indication-specific full-face concept is based on a three-pillar-principle: regeneration, regulation, and reshaping. In parallel to this concept, major indications such as poor skin quality, pigmentary changes, and loss of shape and definition are discussed. To address those indications, therapeutic principles such as topicals (cosmeceuticals, magistral formulations), mesotherapy, needling, chemical peelings, injection lipolysis, and thread lifting will be demonstrated.

Conclusion: As an alternative to standard injectables and devices, an indication-specific approach for a concept of full-face rejuvenation is based on the three-pillar-principle of regeneration, regulation, and reshaping by easy-to-perform, non- or minimally-invasive procedures for rejuvenation.

J Drugs Dermatol. 2017;16(6 Suppl):s98-103.

INTRODUCTION

Facial aging is a complex process affecting different areas and structures of the face in various ways. This article focuses on the most common problems our patients complain about and present in the doctor's consultation, and outlines a science-based, indication-specific, therapeutic concept focusing on alternatives to standard injectables and devices for rejuvenation in aesthetic dermatology.

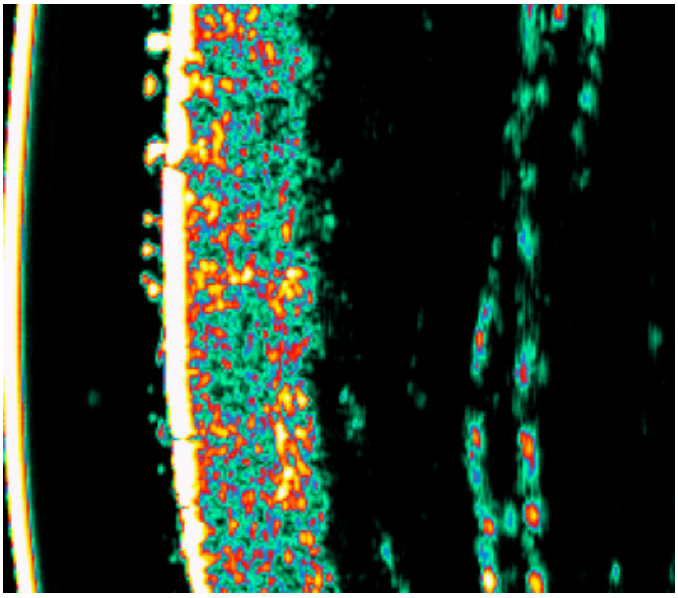
Skin Aging and Beyond

Skin aging is a continuous ongoing process typically dividable into two mechanisms, extrinsic and intrinsic aging. Photoaging is the major trigger for skin changes from extrinsic factors. The predominant pathomechanism is the formation of free radicals causing oxidative damage and induction of an inflammatory milieu taking place in the epidermis and dermis but mainly in the dermis. The results are a decrease in collagen type I and degeneration of extracellular fibers.[1] Clinically speaking, the skin atrophies in all layers, gets thinner and less elastic, and presents wrinkles and folds (solar elastosis) as well as irregular pigmentation, broken vessels, and possibly skin cancer and its precursors.

Intrinsic skin aging is a process based on chronobiologic, genetically determined aging, and can be influenced by hormones as the skin is a typical target organ for those molecules: estrogens are responsible for elasticity, water retention, and circulation; androgens increase sebum production; gestagens inhibit the enzymatic depletion of connective tissue. The drop in hormones in menopause result in typical skin changes: the thickness of the epidermis decreases through the reduced proliferation activity of keratinocytes and restricted capacity for differentiation. Throughout the dermis, a depletion of up to 30% of the collagen fibers occurs in the first five years of menopause. Further to this, skin matrix proteins get reduced. Additionally, the skin's function wanes in terms of sebum and sweat production, and overall, the skin gets thin (like cigarette paper), rough, wrinkly, more sensitive, and easily vulnerable. Benign lesions such as seborrheic keratosis can occur. So, looking at the overall structural and functional changes of the epidermis and dermis throughout the aging process, one can see again alterations in dermal collagen, elastin, and glycosaminoglycans,[1] a loss in the content of hyaluronic acid with an overall thinning and loss of elasticity, impaired response to ultraviolet light, etc.[2]

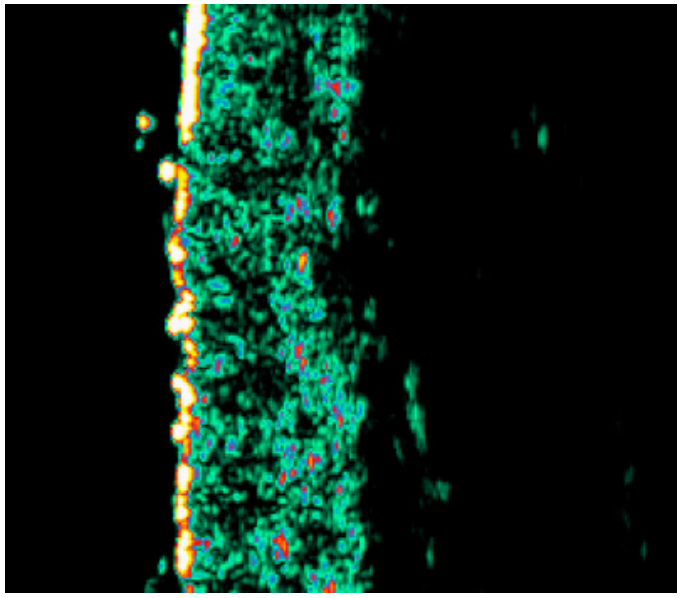
Even though facial aging starts at the surface by showing signs of aging on the skin, the aging process goes far beyond and finally involves all facial structures such as the muscles, retaining ligaments, fat pads, and bone structures. But, over time, the facial fat pads get redistributed, atrophying and separating. Further to this, a remarkable bony resorption takes place and doesn't give the needed structural support. All this results in deflation and sagging of the midface in a three-dimensional

FIGURE 1. 20MHz Ultrasound 20-year-old skin.



©Cortex/Sabine Zenker MD

FIGURE 2. 20MHz Ultrasound 50-year-old skin.



©Cortex/Sabine Zenker MD

way. Facial shape loses its definition in volume and shape due to alterations in all different anatomical layers.[3]

So aesthetically speaking, facial aging shows overall changes from the surface to three-dimensional changes in shape. Young looking and healthy skin is ideally glowing, firm, smooth, even, and flawless. In addition, the architecture and position of the fat pads is predominantly important for a youthful and appealing shape of the face.

Indication

Any therapeutic approach to target changes "from surface to shape" must be done in an indication-specific way[4]: Typical indications for facial rejuvenation in aesthetic dermatology are dull skin and hyperpigmentation as these represent the typical changes of the surface and lost definition of a face and the most frequent clinical findings of changes in facial shape.

Strategy

The key to facial rejuvenation is to tailor any treatment to the needs of the patient. So, looking at the surface, the goal is to regenerate dull skin and regulate hyperpigmentation. Targeting the shape, the goal is to reshape lost definition.

Therapy

There are various therapeutic options for facial rejuvenation. This article focuses on alternatives to standard injectables and devices for rejuvenation such as topicals, mesotherapy, needling, chemical peeling, injection lipolysis, and absorbable lifting sutures.

Surface

Topicals

Cosmeceuticals are cosmetics with biologically active ingredients such as antioxidants, peptides, and plant extracts, obviously not regulated as medication[5] to typically hydrate and protect the skin with additional features such as anti-pigmentation, anti-oxidation, anti-inflammation, increased cell-turnover rate, etc. Topical antioxidants such as vitamin C/E/A derivatives, polyphenols, etc can reduce harmful effects by neutralizing free radicals, known and widely accepted as one major reason leading to skin aging as they can directly damage various cellular structural membranes, lipids, proteins, and DNA. Basically, one can agree on the fact that high sun-protection indices against UVB and UVA rays offer optimal prevention against skin aging. The technical difficulty is to find a suitable daily skincare cream with ideal anti-aging properties in combination with a preferably high SPF. So, especially hydration, as well as protection, are important strategic ways to improve the skin's quality.

Magistral formulations are epicutaneous topical medications provided in different textures such as cream, ointments, etc, with drug content. Mishandling topical medication can lead to certain complications.[6] Typical topical prescription drugs used frequently in aesthetics to treat dull skin are eg, retinoic acid and hormones, etc. To treat hyperpigmentation, hydroquinone is still the gold standard. Resorcinol is also frequently used. Being able to prescribe individual formulations by combining different topical drugs depends on the doctor's expertise.

FIGURE 3. Before treatment with Chemical Combination Peel (Dr. Zenker DFP©).

©Sabine Zenker MD

FIGURE 4. One month after treatment with Chemical Combination Peel (Dr. Zenker DFP©).

©Sabine Zenker MD

Mesotherapy

Mesotherapy works by multiple, micro-dosed, superficial injections using specific injection techniques such as epidermal-, nappage-, micro-papular, or point-by-point technique to inject bioactive substances into the skin to treat cosmetic conditions.[7] The therapeutic aim of mesotherapy for skin rejuvenation is to increase the activity of fibroblasts by inducing an optimal physiologic environment to enhance the cell activity and therefore the synthesis of collagen, elastin, and hyaluronic acid. The desired clinical result is a firm, bright, and moisturized skin. Typically, a liquid mixture of compounds such as hyaluronic acid, pharmaceutical and homeopathic medications, plant extracts, vitamins, and other ingredients such as platelet rich plasma are used to improve the overall quality of the skin.[8] Hyaluronic acid especially has proven to increase the skin's elasticity, hydration, and firmness.[9]

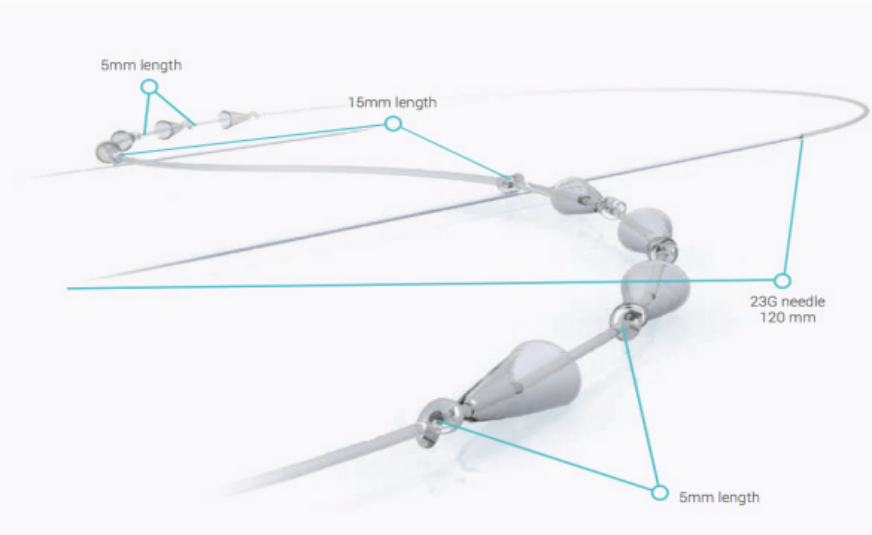
Needling

Needling is a medical procedure that involves repeatedly puncturing of the skin with tiny, sterile needles by a micro-needling device equipped with needles with a maximum length of 150 µm. The therapeutic principle is to increase the formation of new tissue by activating the wound healing cascade.[10] The resulting micro-channels leave the epidermis intact. Consecutive inflammation leads to gene expression of numerous growth factors, collagen I, and glycosaminoglycan. For example, TFG-β3 is regulated beyond the initial phase to provide scar-free healing and a normal collagen structure.[11] Due to the low risk of developing post-inflammatory hyperpigmentation, micro-needling can be used for all patients regardless of their skin type and color as well as throughout the year. The immediate painting-on of appropriate actives such as non-prescription agents and prescription agents (eg, glycolic acid, retinoic acid, hyaluronic acid, trichloroacetic acid, vitamin C/A, grow factors, etc.) acts for additional skin rejuvenation effects and regulates hyperpigmentation (eg, hydroquinone, retinoic acid, resorcinol, kojic acid, pyruvic acid, etc) and therefore is an elegant way to treat the discussed indications.[12]

Chemical Peeling

Chemexfoliation by chemical peels does effect controlled exfoliation, destruction, and/or inflammation of skin in a superficial, medium depth, or deep level, depending on the chemicals used for any individual indication. The combination of peeling agents for a customized treatment has been presented in the dermatologic cosmetic literature with scientific clinical trials and histology a long time ago.[13] It is the responsibility of the dermatologic surgeon to be in control of the chemicals and products used and to understand all the products and peeling formulations. A typical bleach-peel concept used for regulating hyperpigmentation is one of a controlled skin barrier disruption and exfoliation in combination with a controlled melanin breakdown. Therefore, the strategy is to intervene before the melanin synthesis takes place by alteration of the melanosome structure and function, during the melanin synthesis by tyrosinase- and peroxidase-inhibition and by ROS-scavenging and after the melanin synthesis by melanin dispersion and inhibition of melanosome transfer.[14] The author uses individual combinations of non-prescription as well as prescription agents to formulate any peel individually and in a tailored and customized way. The typical agents used are hydrochinon HQ (1,4 Dihydroxybenzol), tretinoin (Trans-retinoic-acid), resorcinol, salicylic acid, alpha-hydroxy acid (AHA), and vitamin C (ascorbic acid). The agents are applied in two layers to the affected skin area and stay there for an individually determined exposure time. The post-operative treatment protocol consists of an

FIGURE 5. Silhouette InstaLift™.



individual post-peel-care program (desquamation, hydration, as well as a daily applied post-peel cream to sustainably enhance the lightening process), as well as an effective sunscreen.

Injection Lipolysis

Injection lipolysis is a therapeutic tool to reduce localized fat pads by targeted destruction of the structure of the adipocyte. For this purpose, polyenyl-phosphatidylcholin (PPC, a membrane phospholipid that contains unsatorized fatty acids), and deoxycholic acid (DCA, a gallic acid which acts as solvent) are injected into the fat pad directly.[15] Thanks to the action of the two chemicals, the membrane of the adipocytes ruptures and the free fat is emulgated by the detergenting action of PPC/DOC. The fat is finally degraded to tiny fat particles of nano-size and broken down to triglycerides and finally monoglycerides, transported to the liver as lipoproteins, and – thanks to beta-oxydation – eliminated via the citric acid cycle; a small amount is excreted via the renal system. To reduce localized fat pads and consecutively re-shape the jawline as well as the underchin area, polyenyl-phosphatidylcholin and deoxycholic acid are injected with a sharp needle through a single- or multishot-injector by administering a maximum of approximately 0.5 cc per point, 1.5 cm gapped.

Shape

Thread Lifting

Absorbable lifting sutures counteract the forces of gravity by lifting and re-suspending sagging skin and facial soft tissue in a quick and expeditious fashion. The procedure of absorbable lifting sutures doesn't leave scars, is performed on an outpatient basis with local anesthesia, and combinable with any other aesthetic procedure "from surface to shape" such as the above named technologies as well as with botulinum toxin and fillers. The history of lifting facial tissue with threads dates back to the sixties of the last century: "Suspension-" and "rejuvenation- threads" derive from a technique invented by Dr. Guillemin in 1965, the curl lift: Surgical threads are placed under the skin making up a loop in such a way as to "suspend" the tissues. But the threads used slipped and the result didn't last. Dr. Sulamanidze then developed notched threads (2-0 polypropylene (non-absorbable suture and cut barbs), which hooked into the tissues, correcting sagging with a longer lasting effect. In 2005, Contour Threads™ (2-0 polypropylene with unidirectional barbs placed in a helical configuration) were approved by the FDA (Food and Drug Administration). As other threads of this kind, they had to be anchored in place proximally. Silhouette InstaLift™, bidirectional Poly-L-lactic acid (PLLA) sutures with tiny transparent cones (small umbrella-like attachments) are known for years in many parts of the world and have now launched in the US.

Typical indications for absorbable lifting sutures in an aging face are mid-face skin ptosis, loss of malar volume, jaw line ptosis, and eyebrow ptosis. Patient selection is key here: The ideal patient shows a good skin quality (not too thin neither too thick), a moderate sagging of the midface with jowling, visible marionette lines, and nasolabial folds. The lifting test should be positive: Evaluating the effect by lifting the tissue with a fingertip should affect a hoisting of the targeted tissues. The procedure itself is performed with local anesthesia (typically, lidocaine 1% mixed with adrenaline in a ratio 1:200.000 is injected to each entry point, approximately 0.5 cc per point). The entry points are done with an 18 G sharp needle. The sutures are then placed to the subcutaneous layer. The strategy of how the sutures are placed is decided individually and depending on each clinical case accordingly. A typical placement

FIGURE 6. Before treatment with Silhouette Soft Silhouette InstaLift™.

©Sabine Zenker MD

FIGURE 7. After treatment with Silhouette Soft Silhouette InstaLift™.

©Sabine Zenker MD

pattern is eg, the in-line-technique, a straight technique to lift the midface and the angle-pattern to redefine the jawline. Suspension sutures show good medium-term outcome 12 to even 24 months after surgery.[16] The formation of fibrous tissue was examined in patients before planned post-bariatric abdominal surgery[17]: A progressive increase of tissue formation was observed around the sutures; after one year, the cones in polylactic and glycolic acids had been replaced by scar tissue. So, this easy-to-perform procedure repositions volume and lifts the overlying skin in the midface and immediately gives a firmer and more regular contour of the jawline as well as in the long term in a micro-invasive way and the downtime is minimal.

CONCLUSION

There are various therapeutic modalities and alternatives to standard injectables and devices for facial rejuvenation. The concept for facial rejuvenation described here is an indication-specific one: Typical indications frequently found in our patients are the ones resulting from changes of the surface up to changes due to the three-dimensional aging process resulting in changes of the facial shape. The approach for a concept of full-face rejuvenation is based on the principles of regeneration, regulation, and reshaping. A customized concept uses therapeutic tools separately or in combination such as topicals, mesotherapy, needling, and chemical peeling to target the most common surface changes and injection lipolysis as well as absorbable lifting sutures to re-shape facial contours.

DISCLOSURES

Dr. Zenker is on the Speakers Bureau and Advisory Board for Sinclair Pharma and has no conflicts of interest to declare.

REFERENCES

1. Fisher, G et al. Looking older: Fibroblast Collapse and Therapeutic Implications. *Arch Dermatol.* 2008;144(5):666–672.
2. Fenske NA et al. Structural and functional changes of normal aging skin. *J Am Acad Dermatol.* 1986;15(4 Pt 1):571-85.
3. Coleman SR et al. The anatomy of the aging face: volume loss and changes in 3-dimensional topography. *Aesthet Surg J.* 2006;26(suppl 1):S4-S9.
4. Zenker, S. Combination Therapies: From Surface to Shape. *Anti Age Magazine* 18, 2015; 110-111.
5. Kligman A. Cosmeceuticals: do we need a new category? In: Elsner P, Maiback H, editors. Cosmeceuticals. New York: Marcel Dekker; 2000. p. 1.
6. Zaghi, D et al. Survey of Safety and efficacy information in drug inserts for topical prescription medications. *Am J Clin Dermatol.* 2007. 8(1):43–46.
7. Baspeyras M et al. Clinical and biometrological efficacy of a hyaluronic acid-based mesotherapy product: a randomised controlled study. *Arch Dermatol Res.* 2013 Oct;305(8):673-82.
8. Herreros FO. Mesotherapy: a bibliographical review. *An Bras Dermatol.* 2011;86(1):96-101.
9. Reuther T et al. Effects of a three-session skin rejuvenation treatment using stabilized hyaluronic acid-based gel of non-animal origin on skin elasticity: a pilot study. *Arch Dermatol Res.* 2010;302:37–45.
10. Fernandes D Minimally invasive percutaneous collagen induction. *J Oral Maxillofac Surg Clin North Am.* 2005;17:51-63.
11. Aust MC et al. Percutaneous collagen induction. Scarless skin rejuvenation: fact or fiction? *Clin Exp Dermatol.* 2010;35:437–439.
12. Badran MM et al. Skin penetration by a microneedle device in vitro: Dependency on needle size and applied formulaton. *Europ J Pharm Sci.* 2009 36:511-23.
13. Monheit GD. Chemical peels. *Skin Therapy Lett.* 2004;9(2):6-11.
14. Briganti S et al. Chemical and Instrumental Approaches to Treat Hyperpigmentation. *Pigment Cell Res.* 2003;16:101-110.

15. Reeds DN et al. Metabolic and structural effects of phosphatidylcholine and deoxycholate injections on subcutaneous fat: a randomized, controlled trial. *Aesthet Surg J*. 2013 Mar;33(3):400-8.
16. Maschio F et al. Suspension sutures in facial reconstruction: surgical techniques and medium-term outcomes. *J Craniofac Surg*. 2013;24(1):e31-3.
17. Consiglio F et al. Suture With Resorbable Cones: Histology and Physico-Mechanical Features. *Aesthet Surg J*. 2016;36(3):NP122-7.

AUTHOR CORRESPONDENCE

Sabine Zenker MD
E-mail:..... kontakt@dr-zenker-services.de

The Future of Non-Invasive Rejuvenation Technology: Devices

Michael H. Gold MD
Gold Skin Care Center, Tennessee Clinical Research Center, Nashville, TN
Vanderbilt University School of Nursing, Nashville, TN
Meharry Medical College, School of Medicine; Huashan Hospital, Fudan University, Shanghai, China;
The First Hospital of China Medical University, Shenyang, China
Guangdong Provincial People's Hospital, Guangzhou, China
First People's Hospital of Foshan, Guangzhou, China
The First Affiliated Hospital of Zhejiang University, Hangzhou, Zhejiang, China
The People's Hospital of Hunan Province, Changsha, Hunan Province, China

ABSTRACT

Non-invasive rejuvenation of the skin is performed regularly in many cosmetic offices. Using evidence-based medicine, we will review the various technologies being used for non-invasive rejuvenation. This includes the use of intense pulsed light (IPL), which has been thoroughly studied and shown to be quite useful for this type of rejuvenation in removing the red and brown pigments, as well as affecting collagen. Fractional lasers, both non-ablative and ablative in nature, also can show dramatic improvements in the skin and associated clinical studies are reviewed here. Also described are radiofrequency (RF) fractional pin devices and RF microneedles used for non-invasive rejuvenation. Picosecond lasers are showing very positive results in the non-invasive rejuvenation market. Finally, absorbable sutures are being used to lift the skin and add volume in the skin over a duration of time. They are quickly becoming more popular.

J Drugs Dermatol. 2017;16(6 Suppl):s104-107.

INTRODUCTION

Non-invasive rejuvenation with technology devices, or energy based devices (EBDs), has become standard in many offices. We need to examine the evidence-based medicine behind this increasing technology, to make sure that we are dealing with fact over fiction, with reproducibility over one great case, and making the technology legitimate while demanding to learn the safety of these devices along with their efficacies. We need to be assured that our patients are taken care of, and that utilizing this technology will improve their well-being. This article will review some of the exciting new technological advances with EBDs.

We have been using intense pulsed light (IPL) sources for many years. Originally designed to treat vascular lesions, we soon learned that they are effective for other indications as well, including hair removal and pigmentary concerns. Soon we learned that collagen and elastin changes occurred with their use and this led to the term photorejuvenation being coined, which has become common term among laser surgeons. In 2000, Biter[1] reported on the use of IPL over a period of time to affect textural changes in the skin along with improving the reds and browns and even pores in the skin. In 2015, Ping et al[2] published their findings in a retrospective analysis of the long-term effects of using an IPL over time in a group of Chinese patients. Their group in Foshan, China has treated over 5300 patients with the IPL and studied the first 2354 patients who received treatment to examine the clinical facial features that occurred over time. Each patient was required to have received at least three IPL treatments to be included in the analysis and most of the patients who were studied had yearly IPL treatments as well. Clinical photographs were taken yearly during the 12 years of follow-up in this group of patients, and an independent panel studied the effects seen.

The results showed that there was an effective rate between 88.24% and 96.45% in the study participants for improving signs of photodamage and for the rejuvenation of the skin. It is the single largest clinical evaluation in IPL history and as shown in Figure 1, has had and will have profound effects on our patients.

Fractional skin resurfacing has also gained popularity all over the world. Whether we are using ablative fractional lasers or non-ablative fractional lasers, we have seen great effects from these devices in our patients. With the ablative fractional CO2 lasers, one thing we have learned from our colleagues is that long-term results with them are achievable. The work by Clementoni showed one- and two-year results following fractional CO2 lasers.[3] In 2014, evaluations by Tan et al[4] took this work further and looked at 56 patients and followed them for one month post laser resurfacing and then 30 patients at five years. Photodamage scores in those 30 patients were significantly changed

FIGURE 1. Before and after 14 IPL treatments.

Photos Courtesy of Dr. Ping Chen, Foshan, China.

(P<0.01) at one month, one year, and five years as compared to baselines. An example is shown in Figure 2.

Fractional laser skin resurfacing for hypertrophic scars also has become a popular treatment in recent years, thanks to the work of Waibel and Beer, who first reported on treating these lesions successfully.[5] Tan et al[6] have also reported on the use of fractional CO2 lasers in the treatment of scars and have shown that with fractional CO2 lasers, treating these lesions can be accomplished. A case is shown in Figure 3.

Fractional EBDs are not limited to lasers and recent work with radiofrequency (RF) energy has shown that these too can be used successfully to treat wrinkles and rhytids, as well as acne and traumatic scars. Work by Hruza et al[7] and Gold and Biron[8] showed that pin-based delivery of bipolar RF energy into the skin would have an effect on wrinkle and scars. RF energy is color-blind and therefore useful in all skin types with minimal risks of pigmentary concerns following treatment. What made these devices popular and makes them continue to be popular today is that they all work by having minimal epidermal destruction and allowing delivery of RF energy at varying depths into the dermis. Collagen destruction and collagen remodeling will follow and lead to positive results. Several devices for pin-type RF energy delivery are now available and we have reported on scanning technologies and newer delivery methods being successful in this regard.[9, 10] Fractional EBDs with microneedles and RF are also becoming very popular. Some of the devices in this category have insulated microneedles and some in this category have non-insulated microneedles to deliver their RF energy into the skin. From all published studies, it appears that both forms of microneedling, insulated and non-insulated, work well in treating wrinkles and lax skin, and both have shown positive effects in skin lifting as well.[11,12] One must decide which modality works best for them – RF destruction at the tip of the needle or RF destruction along the course of the entire needle. Both penetrate the dermal-epidermal junction before delivering their RF energy, which is why post-inflammatory pigment changes are not very common with these modalities. Examples of RF fractional therapies are shown in Figures 4 and 5.

Pigmentary concerns are some of the most common and problematic changes that we face daily in our clinical practices. EBDs have treated these conditions over the years with modest effects. In recent years, picosecond lasers have been introduced into the cosmetic armamentarium. These newer lasers not only treat tattoos faster and better than the traditional Q-switched

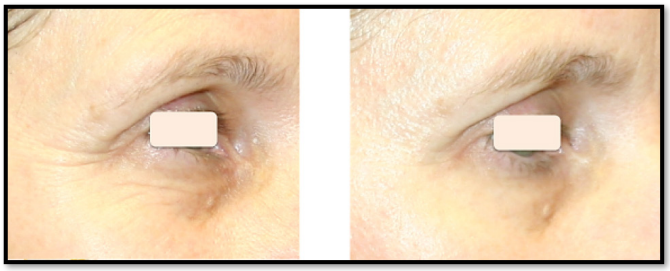
FIGURE 2. Fractional CO2 laser treatment. One treatment 5 years after CO2 laser.

Photos Courtesy of Dr. Ping Chen, Foshan, China.

FIGURE 3. A case of scar treatment with fractional CO2 lasers – baseline and 6 months.

Photos Courtesy of Dr. Ping Chen, Foshan, China.

FIGURE 4. Intensif Microneedling. Before and 1 month post 3 Tx.



Photos Courtesy of Michael H. Gold MD.

FIGURE 5. Intensif microneedling before and post 2 Tx.

Photos Courtesy of Michael H. Gold MD.

lasers. Recent studies have shown that the picosecond lasers are useful in treating various pigmentary concerns. Some of the newer fractionated picoseconds are not just producing results with pigment, but are addressing wrinkles and texture as well. Picosecond lasers are becoming more and more useful, not only for tattoo removal, but also for pigment and rejuvenation effects seen in our patients.[13, 14]

RF energy also is popular to use for skin tightening. Many of the laser companies have entered this market and claim superiority over others in how well their device tightens the skin. Bulk RF heating through either monopolar, unipolar, or bipolar RF has shown, in multiple clinical studies, to have a positive effect for skin tightening. The effects work over a time period, and multiple treatments will normally be required to achieve the desired effects. Maintenance treatments will also need to be given, although this part of the equation has never been fully elicited from an evidence-based method. Many devices exist in this category as noted and we always recommend that one study the published reports on these individual devices and that choose one based on science rather than on hype from the manufacturer. These devices differentiate themselves by varying the RF electrode configuration and by how many electrodes are actually employed with each system.[15-17]

We will move away from non-invasive rejuvenation and EBDs and describe one of the more exciting trends that has entered the US market recently – the use of absorbable sutures for skin lifting. The use of permanent threads is not new to the US market and over the past decade we have seen several of these products come and go. Some have left the market because they were fraught with adverse events that were not acceptable to any of us. This led to the adoption by many of an absorbable suture, known as the Silhouette InstaLift, which has become the go-to product for skin lifting in our era. The material used in the US is poly-glycolic acid, although outside the US, polylactic acid is used. For all practical purposes, the products act identically. The sutures are composed of bidirectional cones and knots, as shown in Figure 6. When applied through proper vector placement within the skin, immediate and dramatic lifting is accomplished, which actually improves over time as the suture materials absorb and form

FIGURE 6. Absorbable sutures, known as the Silhouette InstaLift; the sutures are composed of bidirectional cones and knots.

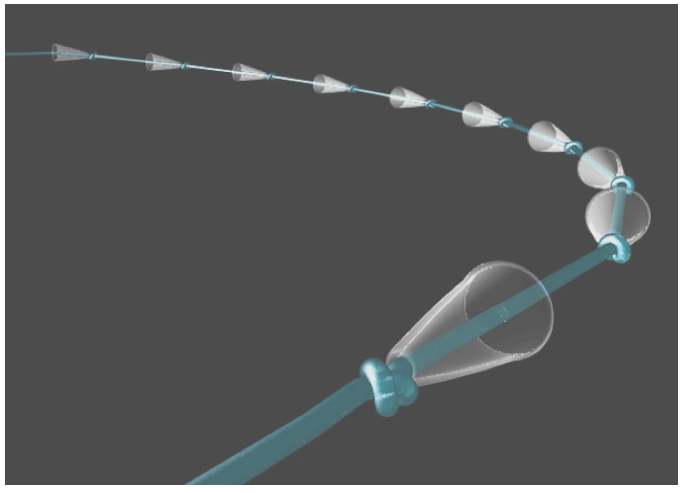


FIGURE 7. Examples of clinical work with this material and its effects.

Photos Courtesy of Michael H. Gold MD.

new collagen. Clinical work with this material has shown its effects and an example is shown in Figure 7.[18,19]

EBDs have been very useful for rejuvenating the skin over the years. Newer technologies following evidence-based medicine have made these devices a reality for all of us in the laser and EBD field. As noted earlier and throughout this article, we can live in a world of hype or a world of reality. We need to choose to live in a world where well-done clinical studies pave the way for real science to explain how these devices work, to show the results that these devices can deliver, and to be truthful and honest in how we share these works with the world.

DISCLOSURES

Dr. Gold is a consultant for the following: Lumenis, Syneron-Candela, Venus Concept, EndyMed, and Sinclair.

REFERENCES

1. Biter PH. Noninvasive rejuvenation of photodamaged skin using serial, full-face intense pulsed light treatments. *Dermatol Surg.* 2000;26:835-843.
2. Ping C, Xueliang D, Yongxuan L, Bilai L, Shaoming L, Gold MH. A retrospective study of the clinical efficacy of the intense pulsed light source for photodamage and skin rejuvenation. *J Cosm Laser Ther.* 2016;18(4):217-24.
3. Clementoni MT, Galimberti M, Tourlaki A, Catenacci M, Lavagno R, Bencini PL. Random fractional ultrapulsed CO2 resurfacing of photodamaged skin: Long-term evaluation. *Lasers Surg Med.* 2013;28(2):643-650.
4. Tan J, Lei Y, Ouyang HW, Gold MH. The use of the fractional CO2 laser resurfacing in the treatment of photoaging in Asians: Five year long-term results. *Lasers Surg Med.* 2014;46:750-756.
5. Waibel J, Beer K. Fractional laser resurfacing of thermal burns. *J Drugs Dermatol.* 2008; 7(1): 59-61.
6. Ying L, Li SF, Yu YL, Tan J, Gold MH. Clinical efficacy of utilizing fractional CO2 laser for the treatment of hypertrophic scars in Asians. Submitted for publication.
7. Hruza G, Taub AF, Collier SL, Mulholland SR. Skin rejuvenation and wrinkle reduction using a fractional radiofrequency system. *J Drugs Dermatol.* 2009;8:259-265.
8. Gold MH, Biron JA. Treatment of acne scars by fractional bipolar radiofrequency energy. *J Cosm Laser Ther.* 2012; 14: 172-178.
9. Hongcharu W, Gold MH. Expanding the clinical application of fractional radiofrequency treatment: Findings on rhytids, hyperpigmentation, rosacea, and acne redness. *J Drugs Dermatol.* 2015;14(11):611-617.
10. Ray M, Gold MH. A retrospective study of patient satisfaction following a trial of nano-fractional RF treatment. *J Drugs Dermatol.* 2015;14(11):618-621.
11. Cohen JL, Weiner SF, Pozner KN, Ibrahimi OA, Vasily DB, Ross EV, Gabriel Z. Multi-center pilot study to evaluate the safety profile of high energy fractionated radiofrequency with insulated microneedles to multiple levels of the dermis. *J Drugs Dermatol.* 2016;15(11): 1308-1312.
12. Gold M, Taylor M, Rothaus K, Tanaka Y. Non-insulated smooth motion, microneedles RF fractional treatment for wrinkle reduction and lifting of the lower face: International Study. *Lasers Surg Med.* 2016;48:727-733.
13. Letters and Communications, Picosecond 532 nm Neodymium-Doped Yttrium Aluminium Garnet Laser for the Treatment of Solar Lentigines in Darker Skin Types: Safety and Efficacy. *Dermatol Surg.* 2016;0:1-3
14. Kono T, Shek S, Chen H, Groff W, Imagawa K, and Miyasada M, Comparison Study of a 532nm Picosecond Laser vs A 532nm Nanosecond Laser in the Treatment of Pigmented Lesions in Asians. *Cosmetic Laser Dermatol.* San Diego, CA.
15. Gold MH. Update on Tissue Tightening. *J Clin Aesthet Derm.* 2010;3(5):36-41.
16. Harth Y, Vider I, Elman M, Shemer A, Gottfried V, Kamin A. Long term anti-wrinkle reduction using a novel multisource of RF phase controlled radiofrequency treatment system. *Lasers Surg Med.* 2010;42(S22):94-95.
17. Elman M, Vider I, Harth Y, Gottfried V, Shemer A. Non-invasive therapy of wrinkles, lax skin using a novel multisource phase controlled radiofrequency system. *J Cosm Laser Ther.* 2010;12:81-86.
18. Isse N. Silhouette sutures for the treatment of facial aging: Facial aging, rejuvenation, remodeling, and facial tissue support. *Clin Plastic Surg.* 2008;35:481-486.
19. Gamboa GM, Vascomez LO. Suture suspension techniques for midface and neck rejuvenation. *Ann Plast Surg.* 2009;62:478-481.

AUTHOR CORRESPONDENCE

Michael H. Gold MD
E-mail:..... drgold@goldskincare.com

JOURNAL OF DRUGS IN DERMATOLOGY
JDD
DRUGS • DEVICES • METHODS

JO0617