Facial Rejuvenation: A Regional Assessment

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Facial volume loss as a result of aging can be partially attributed to bone resorption and cartilage remodeling, although certain areas of the face undergo fat redistribution. The underlying anatomic structure of the face allows the signs of aging to be regionally assigned to the upper, mid, or lower face. Aging in the upper face, ascending from the zygoma and including the orbits, is characterized by horizontal hyperkinetic rhytides on the forehead, glabellar wrinkles, and lateral canthal rhytides, with occasional lipoatrophy in the temple and periorbital regions. The use of botulinum toxin type A and hyaluronic acid products is common in upper-face rejuvenation. Nasolabial folds and volume loss in the preauricular, malar, and buccal regions are common targets for facial rejuvenation in the mid face, descending from the zygoma to the oral commissure. Liquid silicone, autologous fat, calcium hydroxylapatite, and poly-L-lactic acid are injectable products that can be used to correct the appearance of lipoatrophy and volume loss in the mid face. The perioral region and the area inferior to the oral commissure are described as the lower face. Resurfacing techniques, collagen hyaluronic acid fillers, as well as poly-L-lactic acid and polymethylmethacrylate beads are useful in these areas. Lips should be treated only with collagen and hyaluronic acid supplemented by resurfacing procedures. Complete facial treatment requires multiple approaches; each must be sensitive to the needs of the patient and to the area requiring treatment. This review will discuss the regional categorization of the aging face and rejuvenation options currently available.

The skin, like all other organs, undergoes genetically programmed chronologic aging. However, unlike other organs, the skin is directly exposed to the external environment with the added extrinsic factors of aging. UV irradiation from the sun causes sunburn, immune suppression, skin cancers, and photoaging.[1,2] Histologic changes associated with photoaging include the disorganization of collagen fibrils and the accumulation of abnormal elastin-containing material. Also, areas of photoaged skin do not produce as much collagen types I and III as younger skin, and the ratio of type II to type I collagen declines in photoaged skin.[2]

As collagen fibrils are responsible for the strength and resilience of the skin, the loss and reorganization of these molecules may be responsible for the sagging appearance of aged skin.[3] Photoaged skin is characterized by wrinkles, uneven pigmentation, brown spots, and a leathery appearance.[4] Although chronologically aged skin that has been protected from the sun is smooth, it is thinner, less elastic, and more prone to perturbations of barrier function than younger skin.[2]

In the face, changes that occur as a result of aging also include volume loss. This is attributed to bone resorption and cartilage remodeling, as well as to fat redistribution in certain areas of the face.[5,6] Facial lipoatrophy is most visible as a reduction in the buccal fat pads, such that the

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cheeks appear to sink into the face. More pronounced nasolabial folds and malar, preauricular, periocular, and temple concavities are also linked with this degenerative change. Facial lipoatrophy usually only becomes apparent, and is usually mild, after approximately 30 years of age.[5] However, in patients infected with human immunodeficiency virus (HIV), antiretroviral therapy can cause severe accelerated lipoatrophy, irrespective of age, which can be stigmatizing and psychologically disturbing.[7]

Volume loss, skin laxity, wrinkles, and folds have characteristic patterns related to underlying anatomic structure and can thus be regionally described. By simplifying discussion of facial defects into patterns in the upper, mid, or lower face, the level of discourse between patient and physician can be improved; this might also help establish where products are likely to be most effective.

REGIONAL CHARACTERIZATION OF THE AGING FACE

Upper Face

Ascending from the zygoma and including the orbits, the upper face is associated with distinct aging characteristics, such as horizontal hyperkinetic rhytides on the forehead, glabellar wrinkles, and lateral canthal rhytides. Lipoatrophy can occur in the temple and periorbital regions. Whereas temporal lipoatrophy is most commonly associated with HIV and the antiretroviral therapy used to treat the disease, orbital hollowing in concert with lateral eyebrow ptosis becomes more prevalent with age and disease. This is partly a result of changes in the structures that promote mobility of the eyebrow, such as the galea fat pad, the preseptal fat pad, and the subgalea fat pad glide plane space.[8]

Mid Face

The mid face can be described as descending from the zygoma to the oral commissure. Within this region, nasolabial folds and volume loss in the preauricular, malar, and buccal regions are common targets for facial rejuvenation. Descent of the buccal fat pad accentuates not only the tear troughs but also the nasolabial folds and marionette lines.

Lower Face

The lower face includes the perioral region and the area inferior to the oral commissure. As the lip line thins, the vermilion border tends to diminish with aging, a process characterized by the increasing visibility of fine perioral lines, more distinct marionette lines, and downturned oral commissures. Skin laxity, fine lines, and wrinkles are commonly found in the lower cheeks and chin. Volume loss in the cheeks and lower face produces redundant chin skin with jowls.

With age, superficial wrinkles are likely to occur in any facial region; therefore, wrinkle fillers, such as collagen and hyaluronic products, can be used on any part of the face. Laser and chemical peels can also be used on all areas of the face to treat fine lines. Resurfacing techniques and wrinkle fillers do not have the capacity to restore areas that have suffered volume loss as a result of lipoatrophy, commonly seen in the mid and lower face. Conversely, volume enhancers are not the most appropriate tools for correcting hyperkinetic lines, such as those found in the forehead, although they may be useful in softening lines of areas that have suffered volume loss. Thus, botulinum toxin products are more appropriate in the upper face, and volume enhancers, such as collagen and hyaluronic acid products, are needed in the mid and lower face.

TREATING THE UPPER FACE

Botulinum Toxin Type A

The basis of treating lines caused by muscle movement is chemodenervation of the underlying muscle. Botulinum toxin type A is generally used for the amelioration of superficial dynamic wrinkles in the forehead and the glabellar and periorbital regions (Figure).

Patients can expect noticeable results quickly. Effects in the glabellar region can be observed 6 to 36 hours postinjection and can last for up to 3 or 4 months.[9] Consistent efficacy has also been observed in the lateral canthal area. One study showed that injection of botulinum toxin type A into this region resulted in a significant improvement of crow's-feet over 4 months. Interestingly, results lasted longer after the second botulinum toxin type A injection than the first, suggesting that longer-lasting changes are effected beneath the dermis by administration of botulinum toxin type A.[10] Because of its efficacy and favorable safety profile, botulinum toxin type A is the most widely used cosmetic intervention in the United States.[11] However, the short-term effects of botulinum toxin type A may mean frequent repeat injections, resulting in increased costs and time at the clinic for the patient. For the eradication of lines caused by processes other than muscle movement, botulinum toxin type A alone is not usually the most effective intervention.

Hyaluronic Acid–Based Products

Hyaluronic acid is a polysaccharide naturally found in the human dermis. It functions to stabilize the extracellular matrix, bond water, and assist in hydrating the skin. The use of hyaluronic acid–based products in facial rejuvenation is founded on the principle that the injected substance replaces natural hyaluronic acid lost with age. Bonding the hyaluronic acid polymers gives the filler stability and longevity that the natural hyaluronic acid

does not have. There are a number of different hyaluronic acid–based products, differentiated on the basis of particle size, bonding, and product stiffness. Despite their widespread use, only 4 hyaluronic acid products are currently used in the United States: Captique™, Hylaform®, Juvéderm®, and Restylane®.

As unmodified hyaluronic acid naturally degrades within days, the manufacturing of injectable products involves the introduction of chemical cross-links between polysaccharide chains, resulting in hydrophilic, insoluble polymers that are more resistant to enzymatic degradation.[12] The extent of this cross-linking dictates density, which relates to where the product can be used and the durability of results. Fine lines require injection with a correspondingly fine needle, so relatively fluid products are needed to prevent blockages.

Hylaform Fineline® (derived from rooster combs) is often used to correct fine lines, such as those occurring around the eyes in young patients, with results generally lasting 2 to 3 months.[13] Medium-density products are generally used to correct deeper lines and wrinkles, as might be found in slightly older patients. For example, Restylane (derived from bacterial fermentation) has been shown to produce effective results in some patients for 6 months and, in some cases, for close to 1 year[14,15]; however, most physicians recommend retouch injections every 6 months. A representative of the densest class of agent, Juvéderm 30, is particularly effective at correcting deeper lines, the results of which can last for 12 to 15 months in some patients.[9]

TREATING THE MID FACE

Injectable products that correct the appearance of lipoatrophy and volume loss in the mid face include liquid silicone, autologous fat, calcium hydroxylapatite, and poly-L-lactic acid (Figure).

Silicone

Medical-grade silicone (Silikon® 1000 and AdatoSil® 5000) is approved by the US Food and Drug Administration (FDA) for ophthalmologic use pertaining to complicated retinal detachment. These approvals have reignited interest in silicone as a means of achieving facial rejuvenation. By injecting medical-grade liquid silicone into areas of depression using the microdroplet technique, the product itself provides volume augmentation by stimulating a limited foreign-body reaction, which creates additional volume as collagen surrounds the injected droplets.[16]

A recent trial of 77 patients with severe facial HIV-associated lipoatrophy was designed to investigate the volume of silicone, number of treatment sessions, and time required to return their appearance to their prelipoatrophic state.[17] The severity of patient lipoatrophy was initially rated using the 5-point James and Carruthers scale (ranging from 0 [no lipoatrophy] to 4 [very severe lipoatrophy]).[18] Patients were then treated using the microdroplet technique previously described until an independent investigator deemed that total correction had been achieved.[16] Sessions were spaced approximately 1 month apart. On average, patients with lipoatrophy stage 1, 2, or 3 required 17.1, 35.7, and 59.7 weeks to achieve total correction, respectively.[17] In this study, no adverse events were reported. However, complications, including chronic cellulitis, nodules, foreign-body reactions, and migration of material, have been noted many years after injection, despite sterile material and sound injection technique.[19] Questions arise as to whether this represents impurities in the products used or a true silicone complication. Until a controlled long-term study can assure patients and physicians of the safety of liquid silicone, many physicians prefer to avoid its use for cosmetic purposes.[20]

Fat Transfer

Structural autologous lipoaugmentation has been used to recontour the mid face, particularly the malar region, as well as other facial areas. There is no standard and accepted method of autologous fat transfer, but many physicians base their technique on that pioneered by Drs. Sydney Coleman and Roger Amar. Fat is removed from the donor site, such as the outer thighs or buttocks, with a 3-mm open-tipped cannula attached to a 10-mL syringe. The collected syringes are then spun in a sterile centrifuge for 20 seconds to separate the fat cells from the triglycerides and tumescent fluid, and the collected fat is transferred to smaller 1-mL syringes. Fat is then introduced in minuscule strands at the treatment site with a blunt 18-gauge cannula.[21] To recontour the face, small aliquots of fat are injected deeply into fat and muscle using a microdroplet technique, achieving excellent results in some patients. Disadvantages include injury to the donor site, occasionally prolonged bruising, edema, and the unpredictability of results. Controversy remains over optimal technique and the durability of results. A systematic review of the literature revealed that autologous fat can be absorbed in as little as 4 weeks, although correction has been shown to persist for up to 8 years.[22]

Calcium Hydroxylapatite

Calcium hydroxylapatite is a biocompatible product consisting of 30% calcium hydroxylapatite microspheres suspended in a carboxymethylcellulose gel. It is thought that calcium hydroxylapatite directly provides volume after injection and that the size of the calcium hydroxylapatite microspheres (25–45 µm) facilitates gradual

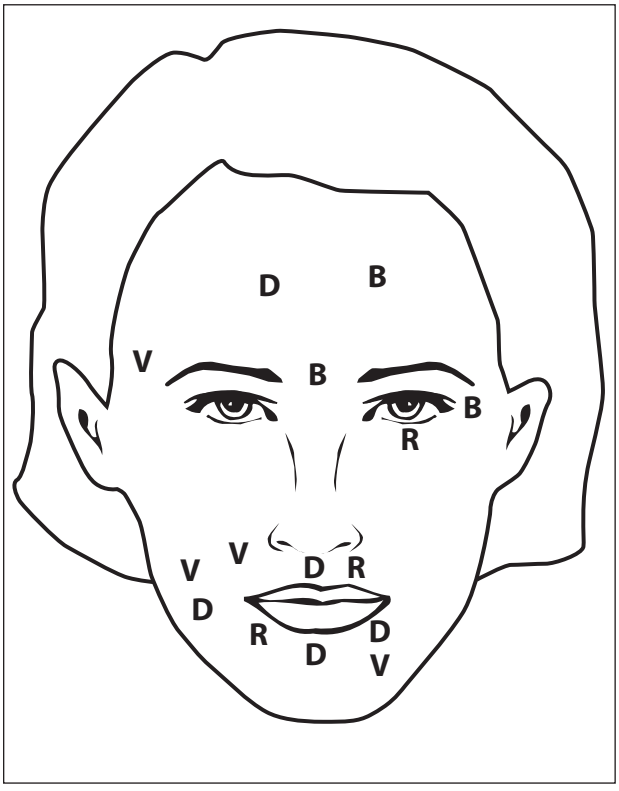
tissue ingrowth. Calcium hydroxylapatite is currently indicated in Europe for the subdermal augmentation and restoration of the facial area and is approved by the FDA for vocal cord injection and as a radiopaque tissue marker. Its usage for soft-tissue augmentation is off label.[23]

Calcium hydroxylapatite is not currently approved for cosmetic purposes in the United States; however, a recent cosmetic trial involving a total of 101 treatments on 64 patients seeking augmentation of a wide variety of facial defects has been published.[24] Patient satisfaction with the results was found to be high, with minimal downtime or side effects noted. The most common complication was palpable or visible nodules reported in 20% of patients who underwent lip augmentation.[24] Correction in all patients was immediate and persisted during the follow-up period of 6 months. However, the actual longevity of results from calcium hydroxylapatite in the face is unknown.[24]

Poly-L-lactic Acid

Poly-L-lactic acid is currently indicated in Europe as a suitable product for increasing the volume of depressed areas, such as wrinkles, folds, scars, and hollow eyes, and for skin aging. It is also indicated for large-volume corrections of the signs of lipoatrophy. In addition, poly-L-lactic acid is the only product currently approved by the FDA for correction of the signs of facial fat loss (lipoatrophy) in people infected with HIV. Poly-L-lactic acid is a biocompatible, biodegradable, and immunologically inert powder of poly-L-lactic acid microspheres (40–63 µm). It is composed of 40.8% poly-L-lactic acid, 24.5% sodium carboxymethylcellulose, and 34.7% nonpyrogenic mannitol, which is reconstituted with 5 to 6 mL sterilized water at least 4 hours prior to injection. Injectable poly-L-lactic acid was FDA approved on the basis of favorable efficacy and safety results from a number of clinical trials conducted in populations of patients with severe HIV-associated lipoatrophy.[25-27]

Results from treatment with poly-L-lactic acid have been shown to last up to 96 weeks in HIV-infected patients.[25] Studies and case reports of its use in cosmetic patients with facial lipoatrophy confirm its efficacy and durability,[15,28,29] with one report suggesting that results last for up to 40 months post–treatment initiation.[30] Injectable poly-L-lactic acid is also associated with a favorable safety profile. No serious adverse events have been linked to the product, and poly-L-lactic acid polymers have a strong heritage of safety by virtue of their long history of successful use in medical devices such as sutures.[31,32] The most common adverse event linked to injectable poly-L-lactic acid is the appearance of nonvisible subcutaneous papules at the treatment site.[33]



Simplified regional assessment of products used to provide facial rejuvenation. B indicates botulinum toxin type A; D, dermal filler; R, resurfacing; V, volume enhancer.

TREATING THE LOWER FACE

Fine lines are often targets of facial rejuvenation in the lower face, as are the deeper rhytides caused by photoaging and skin laxity seen in older patients. Resurfacing techniques and wrinkle fillers such as collagen products are commonly used to treat superficial lower-face defects (Figure).

Resurfacing Techniques

By injuring the epidermis and dermis, superficial lesions can be removed and the texture of the skin improved. How deep an agent penetrates, the extent of destruction, and subsequent inflammation vary according to product and technique; deeper peels are reserved for more severe photoaging, darker skin, or both.[34] Mild photoaging can be reversed with free-radical avoidance and topical skin care regimens, such as over-the-counter α-hydroxy acid products containing 3% to 10% glycolic acid (or other naturally occurring organic acids).

The typical α-hydroxy acid peel, recommended for mild photoaging, involves the use of glycolic acid at concentrations of at least 50%. Unlike other peeling agents, penetration of glycolic acid is time dependent; thus, the agent is applied for a specific amount of time and then neutralized.[35] For moderate and more advanced cases

of photoaging, the Jessner-trichloroacetic acid combination peel (Monheit peel) can be used, although the phenol peel remains the treatment of choice to reverse heavy lines and severe photoaging.[35] Laser resurfacing is especially useful for addressing skin laxity by shrinking collagen, resulting in collagen remodeling and skin contraction.[35] Complications associated with resurfacing include reactivation of herpes simplex virus (particularly when the perioral area is treated), prolonged hyperpigmentations, edema, and hypopigmentation.

Collagen Fillers

For fine lines, as well as deeper wrinkles and folds, collagen fillers (Zyderm® I, Zyderm II, and Zyplast®) are frequently used.[36] The Zyderms consist of a suspension of purified, sterile bovine dermal collagen in a physiologic saline solution containing lidocaine. Zyplast is similarly composed, but denser because of the cross-links between the collagen peptides, resulting in a longer-lasting product. Fine lines are generally treated with Zyderm I or II, with results lasting for up to 3 months, whereas Zyplast is used for deeper lines, with results lasting for 2 to 4 months.[9,37]

A major disadvantage of bovine collagen is that patients are required to undergo double skin testing prior to treatment. Bovine collagen is immunogenic in approximately 3% of skin-tested patients and in an additional 1.2% of patients with negative skin-test results.[38] Autogenic and allogeneic preparations of collagen have been designed to eliminate allergic reactions and to overcome the theoretical possibility of virus or prion transmission. CosmoDerm® and CosmoPlast®, derived from cultured human dermis, can be directly injected without the need for skin testing or preparation.

There are no published clinical trials comparing the effects of bovine versus nonbovine collagen products in the upper face, although it has been reported that the quality of improvements seen with autogenic and isogenic preparations of collagen is no better than that seen with conventional bovine collagen.[9]

DISCUSSION

Complete facial treatment requires multiple approaches that are sensitive to the needs of the patient and to the area requiring treatment. During the patient consultation, at least 3 levels of evaluation should be performed in addition to a global aesthetic appraisal. The first evaluation should investigate any signs of disease, such as actinic keratosis or skin cancer. Second, the extent of surface imperfections, such as wrinkling, should be assessed, and finally, an examination should be performed to determine the degree of volume loss, including that caused by lipoatrophy. These evaluations can be performed regionally, whereby the face is visually divided into the upper, middle, and lower thirds, relating to differences in underlying facial anatomy.

These variations in facial anatomy relate to the type of defect likely to occur and dictate the choice of appropriate corrective treatment. For example, where powerful muscle exists to aid facial expression, such as in the glabellar region, hyperkinetic lines are likely to form. As discussed, volume loss, hyperkinetic lines, and those caused by photoaging require different treatment approaches.

Patient desires are also pivotal to treatment choice. Such desires include the length of time required for results to appear. Although some patients want immediate and dramatic results, as can be achieved with collagen fillers, others prefer correction to be gradual, as is accomplished with poly-L-lactic acid. Similarly, whereas some patients want permanent results, others are more comfortable with regular visits. Although long-lasting or permanent treatments offer advantages in reducing inconvenient and costly retouch treatments, the inflexibility inherent with permanent products can be problematic. Nonbiodegradable treatments, such as silicone and polymethylmethacrylate, or very long-lasting products (as might be the case with calcium hydroxylapatite) can look unnatural as the patient ages or if facial volume is gained over time.

Therefore, long-lasting, biodegradable products such as poly-L-lactic acid or calcium hydroxylapatite (if results are less durable than have been reported for other indications) offer patients a favorable compromise. During the patient consultation, in addition to a full discussion of product safety, patients should be made aware of the extent to which treatment can ameliorate appearance and of the length of time results can be expected to last.

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