Facial Rejuvenation

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Complete facial rejuvenation takes into account the correction of volume, tightening of the skin, and removal of the superficial signs of photoaging. Chemical peels, lasers, intense pulsed light (IPL) sources, light-emitting diode devices, photodynamic therapy, infrared light sources, radiofrequency (RF) systems, neurotoxins, and fillers have been developed to aid clinicians in providing patients with a middle ground between growing old gracefully and the surgical intervention of a face-lift. This article reviews the theories behind these medical devices and how each applies to patients undergoing facial rejuvenation.

The difference between a youthful-appearing face and an aged face encompasses many factors. The youthful epidermis is smooth and soft with a satin appearance that is pigmented homogeneously. The tissue of the face sits on or above regional margins defined by the bony rims and prominences of its underlying skeletal framework. The shape of the lower face is an inverted triangle extending across both zygomatic arches to the inferior margin of the central chin. This triangle is formed by the malar fat pads and the fusion of septa, which hold them in place.[1] As individuals age, the epidermis loses its youthful luster and stretches, and its even pigmentation may become permeated by solar lentigines. Changes in the dermis lead the skin to become thin and lose its elasticity. Underlying static muscle contraction leads to the formation of rhytides, folds, and furrows. The tissue of the face migrates below its margins, which leads the tissue to show signs of aging, such as heavy brows, jowls, and intensification of nasolabial folds. Further, volume is lost, malar fat pads shift, and the bony skeleton changes, which all contribute to the aged appearance of the face. In the lower face, these changes can be seen as an inversion of the youthful triangle that is based at the jowls, and has its tip at the root of the nose.[1]

Complete rejuvenation of the aging face requires correction of each of the problems described above. The epidermis is rejuvenated to a youthful appearance by treatments such as lasers, chemical peels, intense pulsed light (IPL), and cosmeceuticals. Deeper treatments such as radiofrequency (RF), infrared lasers, and fillers will help to rebuild the tissue foundation of youth. Neurotoxins will relax the muscles that cause dynamic and static lines of the face and will smooth its overall appearance. To successfully rejuvenate the aged face and maintain the youthful appearance of the skin, agents from the aforementioned groups have to be employed and patients must exercise proper daily photoprotection by using a broad-spectrum sunscreen.

The epidermis is under constant assault from damaging environmental factors. The main insults come from free radicals and exposure to UV radiation. These 2 factors are responsible for aging the face through

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various biochemical pathways as well as developing skin cancer. A study by Cao and Wan[2] reviewed how UV radiation damages the skin through either a direct photochemical reaction or the generation of free radicals, which in turn damage the cellular mechanisms of signaling pathways such as mitogen-activated protein kinase, protein kinase B, adenosine monophosphate kinase, and p53. Alterations in these signaling pathways directly change the apoptotic response of cells to UV radiation damage. The transcription of cellular hydration channels, called aquaporins, also is negatively effected by UV radiation. This leads to decreased moisture in the cells of the stratum corneum, which accentuates rhytides as well as gives an overall dry appearance to the photodamaged epidermis.[2]

The foundation of any skin-rejuvenating process should start with diligent use of a broad-spectrum sunscreen and a moisturizer. The application or ingestion of common antioxidants alone or in combination may further protect the epidermis. However, there are mixed results in the literature to support the ingestion of a combination of antioxidants.[3,4] These agents include α-lipoic acid, L-ascorbic acid (vitamin C), niacinamide (vitamin B_3), coffeeberry extract, green tea extract, *N*-acetylglucosamine, α-tocopherol, and ubiquinone (coenzyme Q_{10}), ferulic acid, and grape seed extract.[5]

Application of a topical vitamin A derivative such as tazarotene, tretinoin, or retinal (aldehyde form) results in an overall improvement in skin texture and appearance, and a reduction in fine lines and wrinkles.[6,7] Vitamin A derivatives decrease adhesion between corneocytes, thus increasing the overall rate at which the epidermis turns over and stimulates new collagen and elastin formation.[8] Patients will notice an improvement in skin smoothness early on, followed by an improvement in pigmentation and rhytides that becomes apparent after 3 months of use.[9]

CHEMICAL PEELS

Agents that can be used as chemical peels for facial rejuvenation include, α- and β-hydroxy acids, trichloroacetic acid (TCA), Jessner solution, retinoic acid, phenol, and dry ice/acetone slush.[10] These agents cause a reliable and reproducible level of destruction when applied to the skin. The 3 classes of chemical peels are superficial, medium, and deep. Repetitive superficial chemical peels, which peel the upper epidermis, will improve conditions such as melasma, postinflammatory hyperpigmentation, acne, lentigines, photoaging, and fine rhytides. These chemical peels should be used in conjunction with some of the aforementioned treatments to maximize their effect.[11] It also is important for patients to understand that superficial chemical peels will not achieve the same effects as deeper chemical peels.[12] Medium-depth chemical peels, which peel to the papillary dermis, will improve dermal pigmentation and rhytides and also are effective against growths such as actinic and seborrheic keratoses. Reepithelization will be completed approximately 7 days after phenol peels or combination peels with 35% TCA**,** and erythema will diminish over the next 2 to 4 weeks. To achieve a medium-depth chemical peel with TCA, a combination of a light-peeling agent such as Jessner solution or glycolic acid and 35% TCA is used. Peeling with TCA solutions higher than 40% is not recommended because of the increased incidence of scarring.[13,14] Deep chemical peels will penetrate into the midreticular dermis and are ideal for removal of deep wrinkles as well as benign and precancerous growths. The remodeling that occurs will be evident for 1 to 2 decades after this type of peel. The risks of cardiac or renal toxicity, scarring, and lines of demarcation always must be at the forefront of clinicians' minds when choosing this depth of chemical peeling.[14-17]

LASERS

Lasers came to the forefront of the clinicians armamentarium for facial rejuvenation after the groundbreaking work of Anderson and Parrish,[18] who hypothesized and proved the theory of selective photothermolysis. Laser skin resurfacing refers to eliminating photodamage such as dyschromias, poikiloderma, enlarged pores, and coarse-textured wrinkles as well as to improving acne or surgery scars. Pulsed CO_2 lasers (10,600 nm) are the gold standard of laser skin resurfacing. It not only improves skin texture but also tightens the skin. Although this is an effective procedure, it does have limitations and risks. Because this procedure ablates the entire epidermis, patients have a 2-week clinical downtime. Having a compromised skin barrier for this length of time has a risk for infection, which can cause scarring and pigment alteration. Pulsed CO_2 laser resurfacing is safest for treating patients with lighter skin types and is not safe for facial rejuvenation. Most patients who undergo this procedure are given general anesthesia. It also requires a skilled clinician to perform this procedure.

CO_2 and Er:YAG are the 2 most common ablative laser–based systems available. Both lasers target water and lead to tissue vaporization as well as generate a surrounding thermal damage zone. CO_2 laser systems will ablate to a depth of 20 to 60 µm and have a zone

of thermal damage up to approximately 150 µm.[19,20] A shallower vaporization depth of 2 to 4 µm with a thermal damage zone extending to 50 µm occurs when using the Er:YAG laser.[21]

Because of the risks and clinical downtime associated with ablative CO_2 laser treatments, nonablative laser treatments such as Nd:YAG were developed for skin resurfacing. However, the results were not as dramatic or reproducible.[22-28] Thus, a nonablative resurfacing laser technology with reproducible results was developed. This has driven the laser industry to develop novel laser technologies. One of the 2 main trends is the development of Er:YAG (2940 nm) laser systems, which can achieve the same long-term improvement seen with CO_2 laser systems while keeping the recuperation times close to those seen with an Er:YAG instrument.[29-31] The second trend is to decrease the overall risks and recuperation period that occurs with any ablative laser treatment. To address these challenges, the laser industry has developed systems such as pulsed CO_2/Er:YAG laser systems, dual Er:YAG laser systems, and fractional CO_2/Er:YAG laser systems.[32]

The ablation caused by these systems removes the epidermal signs of photoaging and clears the facial surface for repopulation with new healthier epidermal cells.[19,33] In the thermal damage zone, collagen bundles coagulate to one-third their length at the time of treatment. During the healing period, the photodamaged dermis is replaced by new orderly collagen bundles.[32-39] Treatment with an Er:YAG laser system results in only a fraction of the collagen coagulation compared with the CO_2 laser systems because of the decreased thermal damage zone depth.[40]

Fractional photothermolysis technology entered the market and further refined the field of nonablative lasers.[41-48] These lasers include the erbium-doped fiber amplifier (1550 nm) and the fractional Er:glass laser (1540 nm). The systems tout the benefits of having shorter recovery times than ablative lasers while giving the patient improved skin texture and homogeneous pigmentation by the end of a series of treatments. Between 4 and 6 treatments are needed to see the best improvement. Studies with these systems have shown that more superficial treatments with increased column density work best for pigment disorders while deeper, less dense treatment settings allow the best improvement in texture without greatly increasing the risk for adverse events.[41-48]

A nonablative fractional photothermolysis resurfacing device was developed by Reliant Pharmaceuticals, Inc, in 2004.[41-48] This laser creates millions of microscopic thermal damage zones in the treatment area. The undamaged epidermis between each of these thermal zones acts as a reservoir of epidermal cells and allows for rapid reepithelization. In fact, the thermally damaged epidermis acts as a barrier until the new epidermis forms underneath. These necrotic plugs are exfoliated as the new skin grows. The face will be red and swollen for 2 to 5 days but the epidermis will remain intact. Patients need a series of 4 treatments spaced 2 to 4 weeks apart. This is an excellent resurfacing device for all skin types and body areas. The clinician can choose the depth of laser penetration and percentage of skin coverage to fit each patient's rejuvenation needs. Fractional photothermolysis works well for acne scarring, melasma, photodamage, striae, and surgical scars. Patients need only topical anesthesia.[41-48]

Even though fractional photothermolysis works well, it does not tighten the skin or improve deep wrinkles as traditional CO_2 laser resurfacing does.[41-48] Thus, fractional CO_2 laser devices were developed to maintain the safety profile of the fractional system while producing results closer to the traditional devices. Fractional CO_2 laser devices differ depending on the manufacturer; for example, the Fraxel re:pair laser treatment system by Solta Medical, approved by the US Food and Drug Administration (FDA) in 2008, uses similar technology to the nonablative version except for the laser energy source. This laser vaporizes columns of tissue instead of thermally damaging them so the skin barrier is not intact after the treatment. As with the aforementioned laser, the surrounding unaffected skin acts as a reservoir of keratinocytes and replaces the ablated epidermis within 48 hours. Rather than 2.5 to 4 weeks of clinical downtime like traditional CO_2 lasers, this laser decreases the downtime to 1 week, which includes less than 2-day wound care. After 48 hours, the skin will be intact, and the face will be red, swollen, and dry for 5 days. Risks for infection and scarring are decreased greatly because of the decreased interruption of the epidermis. This laser is safer for treating patients with lighter skin types and even can be used to treat the chest and neck areas on conservative settings. The depth of penetration and percentage of coverage can be adjusted for individual patient needs. This laser can penetrate to a depth of 1.6 mm. There have been cases of infection and scarring especially on the neck when aggressive settings are used. However, to date, there have been no reports of permanent hypopigmentation. This device does not leave a line of demarcation on the jawline like traditional CO_2 lasers. Still, clinicians who perform this procedure must be skilled to avoid unnecessary complications. This treatment works well for the

treatment of skin laxity on the eyelids, deep rhytides, severe photodamage, surgical scars, poikiloderma, and rhinophyma.[41-48] Other available light-based rejuvenation technologies and procedures include IPL, lasers that target hemoglobin or melanin, light-emitting diode devices, photodynamic therapy systems, and infrared light sources.

Intense pulsed light platforms use a cooled contact crystal to deliver the light energy (500–1200 nm).[49-57] The internal technology surrounding the light source limits the available wavelengths to this range. Cutoff filtering crystals then are used to further select the wavelengths needed for treatment. The primary use of IPL is the removal of undesired pigmented lesions and vessels seen in photoaged skin. Further, there are mixed results reported in the literature regarding the textural improvements to the facial skin with this procedure.[49-57]

The pulsed-dye (585 or 595 nm) laser or the frequency-doubled potassium titanyl phosphate (532 nm) laser targets hemoglobin and can effectively remove erythema and telangiectasia. Some studies have shown that the pulsed dye laser treatments stimulate collagenization by a thus far unknown method.[32,58-60]

Pigmented lesions that result from photoaging can be treated using the Q-switched ruby (694 nm), Q-switched alexandrite (755 nm), pulsed-dye (510 nm), or potassium titanyl phosphate (532 nm) lasers, whose shorter wavelengths selectively target melanin and have shallow tissue penetration.[61-64] Light-emitting diodes are devices that can be designed to emit a limited spectrum of photoenergy within the electromagnetic range from UV to infrared radiation. It is hypothesized these devices illicit their biologic effects in vitro as well as in the cells and biologic systems of integument through the principle of photomodulation.[53,58,65-69] Studies performed using this technology have shown measurable yet limited improvement in a small percentage of study participants.[67-71] In one study, improvement was noted by only the participants and not by the blinded clinician reviewers.[72]

PHOTODYNAMIC THERAPY

Photodynamic therapy commonly is used to treat photodamaged skin as an adjuvant or substitute for liquid nitrogen to remove actinic keratoses. The most common photosensitizing agent in the United States is aminolevulinic acid. This agent is preferentially taken up by actinically damaged cells and converted into protoporphyrin IX. When this molecule is excited via its absorption of light energy, it generates singlet oxygen species. These reactive oxygen species are toxic to cells, have deleterious effects on the damaged cells, and result in a decreased actinic burden of the treated area.[73,74] Further studies have shown varying amounts of rejuvenation to the treated area in patients using an array of light-emitting diode–based or IPL-based devices to drive the photochemical reactions.[75-78]

Infrared light devices use photoenergy in the range of 800 to 1800 nm to heat the water in the dermis and cause collagen damage. The damage from these devices stimulates remodeling through collagen and elastin production, which leads to tightening of the skin in the treated area. Infrared light device units have some form of contact cooling technology to keep the epidermis in an acceptable thermal range while they heat the underlying dermis.[79-81] The studies have not been large or of the type that produce the highest grade of evidence; however, there are reports of limited improvement in the treated population.[81-83]

Another nonablative facial rejuvenation technology uses an RF field to drive electrons through tissue.[84-88] This technology is used to treat general facial laxity that results from photoaging and gravitational forces on the facial suspensory system. The resistance inherent in the tissue through which the electrons travel generates heat in the dermis, which is hypothesized to result in collagen shortening and collagenization. The first-generation RF devices used higher energy and were associated with significant patient discomfort and increased risk for adverse events. The next generation of devices uses new treatment protocols, better cooling technology, and lower energy, resulting in a more comfortable and safer treatment. The immediate clinical effects seen result from tissue edema and collagen shortening. The continued improvement seen in responding patients is hypothesized to result from the aforementioned collagenization.[84-88] The subtle tightening that is achieved from this technique is not equivalent to a surgical effect; however, it works synergistically with laser resurfacing. Laser resurfacing affects the epidermal and dermal collagen bundles, while the RF effect primarily occurs in the subcutaneous fat septa, tightening these deeper structures. However, more objective controlled studies need to be performed to realize its true benefit to rejuvenation.

NEUROTOXINS

Cosmetic dermatology is probably most associated with botulinum toxin. The injection of this neurotoxin locally blocks the acetylcholinergic neurons in the treatment field by binding these neurons and inhibiting the release of the transmitter.[89,90] Rejuvenation of the face using this agent can be accomplished in 2 different

ways. Chemical denervation of part or all of the corrugator, procerus, frontalis, nasalis, and orbicularis oculi muscles stop the contractions that lead to dynamic lines and formation of folds or furrows. Further, altering brow position or widening the vertical opening of the eyes may be achieved by using small amounts of the toxin. When used in the lower face and neck, botulinum toxin can enhance the lips, raise the lip commissures, smooth the mentalis crenulations, or soften the platysmal bands of the neck. Typical dilution of the toxin ranges from 1 to 4 cc of solvent per 100 U bottle of freeze-dried toxin. Injection depth, toxin quantity, placement, overall technique, and most importantly, desired clinical end effect or "freeze" vary greatly between clinicians.[90-97]

FILLERS

The final component needed for facial rejuvenation is a filler. As individuals age, volume is lost around the mouth, midface, and temples. As mentioned earlier, losses of fat volume, bone structure, and increased laxity of the suspensory system are responsible for the shape of the aged face.[1] It is important to replace this volume to recreate the fullness and roundness of the youthful face. Fillers can be used to add volume to the midface, temples, lateral face, perioral area, and jawline. The addition of fillers to these areas will lift the face to a more youthful position. Fillers are not just for nasolabial folds. In fact, after improving the volume status of the midface, cheeks, and temples, often the nasolabial folds have softened and do not need to be injected.

There are a variety of soft tissue fillers available on the market, each with different advantages and disadvantages. Fillers can be classified based on their duration, makeup, or intended function. Extensive cadaver work performed by Rohrich and Pessa[98] has shown that the fat of the face is compartmentalized. Each of these compartments is separated by fascial planes or fibrous septa. Further, there are superficial and deep compartments. In a second study that focused on the cheek, water was injected into the deep fat compartment of one of the cheeks.[99] The subsequent increase in volume both restored the forward projection and raised the cheek position, giving it a more youthful appearance. Using this knowledge in the placement of fillers will enhance the results that can be achieved with this procedure. This new understanding has allowed the use of fillers to evolve from correcting specific lines to lifting the face and recreating the volume seen in youthful cheeks and temples.

Four commonly used restorative, deep, permanent/semipermanent fillers are autologous fat, calcium hydroxylapatite (CaHA), polymethylmethacrylate (PMMA), and poly-L-lactic acid (PLLA), which are used to rebuild the foundation of the aged face. Autologous fat has the benefit of no type of acute or chronic immune response to its implantation. Because of the fragility of the fat cells, there often is unpredictable resorption of the fat from the implantation area, which causes asymmetry. Current recommendations for this type of augmentation try to minimize the loss of adipocytes by emphasizing gentle harvesting and preparation, smaller injection volumes, and implantation of the cell into well-vascularized tissues, such as muscle.[100-102]

The next filler CaHA microspheres suspended in a nonreactive gel.[102-105] The gel is absorbed slowly over 1 to 2 months, leaving behind the CaHA microspheres, which act as niduses of fibroblast aggregation and new collagen formation. The reported longevity of this filler is 2 to 5 years. To minimize the risk for any adverse nodule formation, deposition of this agent into the subdermal or intramuscular compartment is recommended.[102-105]

The next agent in this category is a permanent filler that consists of PMMA microspheres suspended in bovine collagen.[105-107] As this product's vehicle is made from reduced antigenic bovine collagen, a skin test is required prior to implantation. The current agent is the third-generation design and uses more strictly-controlled PMMA microsphere size and bovine collagen from a closed herd in the United States. As the collagen is resorbed and the PMMA microspheres remain, fibroblasts produce collagen to refill the spaces left by the resorbed collagen as well as a reaction to the PMMA microspheres. Clinically, overall maintenance of the correction is seen when the filler is added. Studies with long-term data have shown this filler to be resilient, safe, and reliable for patients who chose to undergo permanent correction.[105-107]

The last commonly used filler in this class is PLLA. The FDA approved this agent as a treatment for facial human immunodeficiency virus–associated lipoatrophy; however, after its success in that patient population, some clinicians now use PLLA as a semi-permanent deep filler.[102,105,108,109] This agent is reconstituted with a minimum of 5 mL of saline or sterile water and lidocaine. The mixture should be allowed to dissolve for at least 24 hours before it is implanted. These steps decrease the risk for granuloma formation. The PLLA particles initially act as a filler, but as they degrade over the next 6 months their presence stimulate fibroblasts to produce collagen. The exact mechanism with which the PLLA particles stimulate this is not yet elucidated. This filler is used primarily

in the periorbital and temple areas for volume restoration and is injected around the periosteum.[102,105,108,109]

Temporary fillers, such as HA fillers and collagen-based products, are used to correct rhytides, folds, and furrows. Their depth of implantation and subsequent recommended usage are determined by the cross-linking of the collagen or hyaluronic acid that composes the filler. Collagen-based products are derived from bovine, porcine, or human sources. The bovine-based products require skin testing, as previously mentioned. The longest lasting of these agents is the cross-linked porcine-based collagen product, which lasts for up to 1 year.[110] Currently, a finer-consistency porcine-based product that is ideal for treating fine lines and wrinkles or lip augmentation is available outside the United States.[111] Both the bovine- and human-based collagen fillers have formulations that are ideal for fine lines and wrinkles as well as for folds and furrows. Bovine- and human-based collagen fillers last between 3 and 6 months. Hyaluronic acid products can be used for the same facial corrections as the collagen products, depending on the amount of cross-linking present in the products, and have correction durations from 6 to 12 months.[102,104,105,112,113]

COMMENT

As we age, our faces change because of the constant and unrelenting external effects of free radicals, UV radiation, and gravity. These environmental factors are coupled with intrinsic facial-skeletal changes and resorption as well as fat compartment migration and volumetric loss. These insults progressively shift the zygoma-based triangular facial shape that we visually associate with youth, vitality, and attractiveness to the mandibular-based triangle associated with the aged face. Every patient will manifest these changes differently. A good rejuvenation program will incorporate multiple treatments to restore and rebuild what has been lost while balancing the amount of acceptable downtime the patient will tolerate. A proper and complete rejuvenation program will maintain and/or restore the youthful appearance of patients. It is the bridge between growing old gracefully and using corrective surgical techniques to restore lost youth.

ADDENDUM

The authors may discuss off-label uses of some of the medical devices mentioned in this article. The authors do not recommend or support the use of any medication or medical device for any treatment that exceeds the specified FDA–approved use.

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