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The Role of Stimulatory Fillers in Aesthetic Facial Rejuvenation

Proceedings From a Clinical Roundtable

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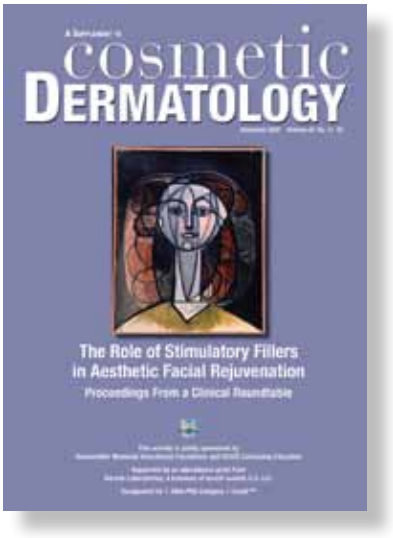

On the cover:
Pablo Picasso (1881–1973)
Face of Woman with Curly Hair, 1946
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EDUCATIONAL METHOD

Welcome to this continuing medical education program, titled *The Role of Stimulatory Fillers in Aesthetic Facial Rejuvenation*. This activity is certified for continuing education credits by the Dannemiller Memorial Educational Foundation, which offers credits for physicians. Participants should, in order, read the objectives, then read the supplement. This activity should take approximately 1 hour to complete. To obtain credit, you must complete and return the posttest answer sheet and application, found on pages 19 and 20. Please follow instructions provided on the application. Continuing medical education (CME) credit is available through the November 30, 2008, expiration date. No credit will be awarded after this date.

The evaluation form provides each participant with the opportunity to comment on the quality of the instructional process, the perception of enhanced professional effectiveness, the perception of commercial bias, and his or her views on future educational needs.

This CME activity was developed for dermatologists, plastic surgeons, specialists in the management of the human immunodeficiency virus (HIV), and other physicians managing dermal atrophy.

LEARNING OBJECTIVES

At the end of this CME activity, participants should be able to:

1. Assess the changes that characterize the aging face
2. Develop a plan to rejuvenate the face that balances the principles of aesthetics with the capabilities and limitations of currently available dermal fillers
3. Establish guidelines for reconciling the patient's expectations with realistic outcomes
4. Describe the optimal techniques for reconstituting and administering dermal fillers
5. Administer dermal fillers, singly or in combination, to achieve optimum results without "overcorrecting" the signs of aging

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The Role of Stimulatory Fillers in Aesthetic Facial Rejuvenation

Gregory Alan Buford, MD; Cheryl M. Burgess, MD; Victor G. Lacombe, MD; Richard N. Sherman, MD; Danny Vleggaar, MD; Susan H. Weinkle, MD; Wm. Philip Werschler, MD

As the population of the United States continues to age and cosmetic procedures become more accepted, adults of all ages and socioeconomic levels will seek to counteract the effects of facial aging. Today, there are many nonsurgical cosmetic treatment options that can aid in rejuvenation, and more are being developed every year. To use these treatments effectively, physicians must understand the cellular and molecular events that result in an aged appearance and be able to match the procedures and products available to certain types of wrinkles, folds, and furrows.

Dermal fillers are used widely for rejuvenation. Once the proper rejuvenation treatment has been chosen, optimal aesthetic cosmetic results can be achieved only with optimal administration techniques. Unfortunately, many residency programs have failed to emphasize the importance of these techniques.

This supplement, based on a roundtable discussion among plastic surgeons, aesthetic dermatologists, and dermatologic surgeons, provides an overview of real-world approaches to aesthetic rejuvenation of the aging face.

The use of aesthetic procedures is growing exponentially. According to the American Society for Aesthetic Plastic Surgery, physicians performed nearly 11.5 million surgical and nonsurgical cosmetic procedures in the United States in 2006.[1] Surgical procedure rates alone have increased by 98% since 1997. Nonsurgical cosmetic procedure rates, including injections of botulinum toxin and laser skin resurfacing, have increased by 747% over the same period. In 2006, nonsurgical procedures accounted for 83% of the total, or about 9.5 million procedures (Table 1).[1]

This shift from a reliance on plastic surgery to an exploration of the less costly and less invasive options afforded by cosmetic dermatology is noticeable and promises to continue. The epidemiologic and sociologic changes currently fueling this shift in demand are also expected to become more pronounced.[2] As reported by the American Society for Aesthetic Plastic Surgery, many of the cosmetic procedures in the United States were performed on persons who were old enough to opt for physician-assisted rejuvenation of their aging bodies and faces: 47% were performed on those aged 35 to 50 years, 25% on those aged 51 to 64 years, and 5% on those aged 65 years or older.[1] The more surprising statistics speak to the trend toward proactive cosmetic rejuvenation or enhancement in younger segments of the population (22% of procedures were performed on those aged 19–34 years) and an increase in procedures performed on racial and ethnic minorities, who now make up 22% of all patients undergoing cosmetic procedures.[1] The availability of a variety of dermal fillers that yield natural-looking results may be the single most important factor in broadening the capabilities of cosmetic dermatology and attracting this growing population of patients.

The use of stimulatory dermal fillers has already altered the way practitioners assess and treat candidates for cosmetic procedures. The durability and versatility of these products make them ideal for subsurface sculpting, contouring, and volumizing. Because these fillers are so durable, their potential to effect truly balanced aesthetic rejuvenation is great. Achieving optimal correction with stimulatory fillers demands proper reconstitution of the product before injection, a high level of proficiency in injection technique, and the skills to assess what the targeted area will look like after the collagen stimulator has had a chance to maximize its tissue-building properties. Until these

TABLE 1

The Top 5 Nonsurgical Cosmetic Procedures in 2006[1]

Procedure	Number Performed
Botulinum toxin injections	3.18 million
Hyaluronic acid fillers	1.59 million
Laser hair removal	1.47 million
Microdermabrasion	993,000
Laser skin resurfacing	576,000

proficiencies are consistently reflected in the standard of care, the threat of long-lasting suboptimal correction poses a risk that many potential patients may not want to take. The versatility of stimulatory fillers—which can be used alone, in combination with replacement fillers, or as adjuncts to plastic surgery—is prompting plastic and dermatologic surgeons to forge professional alliances to bridge the gap between their respective areas of practice. This collaboration has the power to yield a greater array of options to patients as well as erect a strong theoretical foundation on which to build educational and training curricula for the next generation of skilled practitioners.

This supplement is based on a roundtable meeting held in February 2007 at which a panel of plastic surgeons, aesthetic dermatologists, and dermatologic surgeons convened to consider the use of dermal fillers in aesthetic rejuvenation. More specifically, the panel members shared their experiences with reconstitution and injection techniques for poly-L-lactic acid (PLLA), a semipermanent agent that stimulates neocollagenesis and produces long-lasting results. Their discussions took place within the real-world context of assessing the face of a typical candidate for facial rejuvenation. This supplement summarizes that discussion and includes a posttreatment assessment of the results of the patient's rejuvenation procedures.

CURRENT CONTROVERSY: CLASSIFICATION OF DERMAL FILLERS

Fat is the oldest of the dermal fillers. Its transfer from areas of relative abundance in the body to areas in need of augmentation was first reported in 1893.[3,4] By the 1970s, physicians were using viscous fluids, such as silicone, to plump the face. In 1981, the US Food and Drug Administration (FDA) advanced the capabilities of cosmetic dermatology by approving collagen derived from animal sources for use in the correction of wrinkles associated with the skin's loss of natural collagen.[5] Hyaluronic acid (HA), which restores facial volume by attracting and binding water, gained FDA approval in 2004.[6] Up through the introduction of HA, the classification of dermal fillers was based on the duration of their effects, which were either temporary, semipermanent, or permanent (Table 2).[1]

The 2004 approval of PLLA for facial lipoatrophy related to human immunodeficiency virus infection[7] led to the realization that dermal fillers could be designed to work in tandem with the body's own physiologic processes to stimulate the growth of endogenous tissue. Until then, dermal fillers had been viewed as inert substances that effected immediate change in the face by replacing lost volume or adding desired volume simply by occupying space. The idea that a dermal filler could increase volume gradually through dynamic biologic processes, such as initiating soft tissue growth, increasing the existing tissue growth rate, or reducing soft tissue breakdown, led to a change in the way dermal fillers were categorized (Table 3).

This classification scheme is not without controversy, as evidenced by the recent implication

TABLE 2

Dermal Fillers: Categorized by Duration of Effect*

Temporary	Semipermanent	Permanent
Fat	PLLA	Combinations of collagen and PMMA
Collagen	CaHA	Silicone
HA	Polyalkylimide hydrogel	

*HA indicates hyaluronic acid; PLLA, poly-L-lactic acid; CaHA, calcium hydroxylapatite; PMMA, polymethylmethacrylate.

TABLE 3

Dermal Fillers: Replacement Versus Collagen Stimulators*

Replacement Fillers	Collagen Stimulators
Fat	CaHA
Collagen	Combinations of collagen and PMMA
HA	PLLA
Polyalkylimide hydrogel	Silicone

*HA indicates hyaluronic acid; CaHA, calcium hydroxylapatite; PMMA, polymethylmethacrylate; PLLA, poly-L-lactic acid.

of HA in fibroplasia and collagen production. A recent clinical study concluded that HA did stimulate collagen synthesis, probably by inducing mechanical stretching of the dermis and, in turn, stretching and activating dermal fibroblasts.[8] However, in vitro tests suggested that HA is not directly stimulatory, as it did not bind the filler. For our purposes, it is less important how individual agents are classified than that a variety of dermal fillers with different properties, mechanisms of action, sites of optimum efficacy, and durations are available to help practitioners achieve aesthetic facial rejuvenation. We have, in essence, determined to rely on a fairly traditional categorization of fillers as temporary, semipermanent, or permanent and accorded HA the status of a stimulatory filler while reserving judgment on whether it actually stimulates neocollagenesis.

ASSESSING THE FACE

Before planning the course of rejuvenation, the physician must assess the face for signs of aging while taking a variety of factors into consideration. Although the patient's primary concern may be to improve the appearance by reducing the signs of aging, the physician may need to enumerate the signs of aging, discuss how they are assessed, and determine whether or to what degree those signs can be modified by available treatment options. Peripheral concerns must be brought center stage and addressed before treatment can begin. These concerns run the gamut from the need to treat frank or incipient skin cancers to discussing how the current treatment might affect aging in the future. Honestly assessing what the patient can afford in terms of cost and recovery time is also important. The most successful assessments conclude with the patient and physician agreeing on a plan for facial rejuvenation that is realistic and comprehensive in its attention to preserving facial balance. It is important to note that the duration of results varies depending on the products used, the procedures performed, and the patient's health and lifestyle choices.[9] Getting the patient to understand that facial rejuvenation is ultimately a work in progress is crucial to the establishment of realistic expectations.

FACIAL AGING

Many factors contribute to an aged facial appearance. Superficial changes include alterations in pigmentation, texture, and hair growth[10]; dulling of the skin due to slow turnover of skin cells; and the presence of keratoses, lentigines, redness, and telangiectasias.

Extensive subsurface changes that result in volume loss, including bone resorption, muscle atrophy, and fat redistribution, are also of paramount concern.[10] With aging, fat redistribution changes facial contours, as the smooth primary arcs and convexities of the young face reshape into hills and valleys.[11] The loss of fat converts primary arcs to straighter lines, and excess skin begins to sag.[12] Fat atrophy affects the periorbital, forehead, buccal, temporal, and perioral areas. Loss of fat under the lower eyelids causes a sunken appearance of the eyes, and loss of cheek fat causes a gaunt appearance.[13] Hypertrophy causes fat to accumulate in the submental area, jowl, lateral nasolabial fold, labiomental crease, and malar area.[12] The lower half of the face becomes heavy, with sagging and drooping in the jowl area and under the chin. Because fat plays such an important role in facial appearance, the restoration of youthful fat distribution is a primary goal in facial rejuvenation.[12]

Ideally, the physician should have access to photographs of the patient in his or her youth. Being able to see the specific changes wrought on a face by age, photodamage, and, possibly, a previous plastic surgery gives the physician an aesthetic ideal to which to aspire. The aesthetic is specific to the patient and allows for a realistic appraisal of what is possible.

CASE HISTORY: ASSESSMENT

The patient is a 63-year-old woman with Fitzpatrick skin type II. She will tan with careful sun exposure but has not tried to tan since her 20s and wears sunscreen every day at the recommendation of her doctor. She has had a procedure to freeze an emerging actinic keratosis on her nose, but no other cosmetic procedures. She considers her wrinkling minor but is concerned about heavy eyelids, hollows under the eyes, and some jowling.

Figure 1. Pretreatment evidence of aging in a 63-year-old woman from 3 perspectives: right lateral (A), frontal (B), and left lateral (C) views.

Photographs were taken before treatment at various angles against a neutral background with consistent lighting to avoid shadows so that results can be reviewed and compared over time (Figure 1). Each series of photographs taken throughout the rejuvenation process should, ideally, have 5 views: frontal, left and right lateral, and left and right oblique. Photographs can also be useful when explaining procedures to patients.

Superficial Changes

The panel agreed that the patient showed evidence of photodamage, particularly on the neck, which required that she be examined and treated for precancerous and cancerous lesions before undergoing any aesthetic procedures. It was also recommended that she wear sunblock every day to protect against further photodamage. The panel then weighed the specifics of how facial rejuvenation would be achieved. Each panelist was mindful of the effect that a proposed correction would have on the patient's appearance and took care to suggest compensatory corrections to maintain the overall balance of her face.

When queried by the moderator about the nature and extent of superficial changes and how best to address them, the panelists initially focused their comments on the minimization or eradication of signs of photodamage and rhytides.

Photodamage

Dr. Burgess: I would use a trichloroacetic acid peel or erbium laser to deeply exfoliate the skin surface and address the discoloration and the precancerous lesions.

Dr. Sherman: I agree; a chemical or laser peel would help minimize the signs of photoaging. However, if she does not want the downtime associated with a 25% or 35% trichloroacetic acid or laser peel, a series of lighter peels using α-hydroxy acid, β-hydroxy acid, or both may provide an alternative for treating sun-damaged skin. In addition to peeling, I would supplement treatment of focal brown spots (lentigines) and telangiectasias with a laser such as the Vari-Lite™ dual-wavelength (532 nm and 940 nm) laser system.

Dr. Buford: For a less invasive option, intense pulsed light therapy could be used to remove the brown spots and telangiectasias and rejuvenate the skin.

Rhytides

Dr. Burgess: She has a few rhytides in a horizontal plane on the forehead and vertical lines in the glabellar area and across the nose bridge. Her hyperkinetic musculature definitely could be relaxed with botulinum toxin. Because of the laxity of her upper eyelids, botulinum toxin injections in the forehead lines will probably cause brow ptosis, thereby increasing the hooding of her upper eyelids. Outside of using botulinum toxin type A to produce a brow-lift, I would refer her to a plastic surgeon to consider blepharoplasty. There are also rhytides around the mouth, which could be treated with botulinum toxin and any temporary filler.

Dr. Sherman: I am also concerned about the heavy appearance of the upper eyelids and would recommend consultation with a plastic surgeon for blepharoplasty. In the region of the superior temples, there is a crepelike appearance to the skin and the superior-lateral brows seem to fall downward. PLLA may be used to volumize the temples and will create a vector to help lift the lateral brows. If she opted for a face-lift, I would recommend volumization with PLLA 4 to 6 months postsurgery. Tear troughs are another prominent feature and may be minimized using small volumes (0.25–0.05 mL) of

Table 4

Hyaluronic Acid*

FDA approval	First HA product approved by the FDA in 2004[6]
Components	Some products contain avian HA, some manufactured by fermenting streptococcal bacteria[5]
Mechanism of action	Restores volume immediately. Also acts as a sponge to attract and bind water, maintaining fullness in injected areas for varying lengths of time, depending on specific product
Duration of effect	Claims of ≥4–6 mo[14]
Uses/advantages	Best used to augment lips; fill lower eyelids, tear troughs, and wrinkles; correct fine lines. Effective in all areas of the face and at multiple dermal tissue depths. Structurally identical in all species; therefore, pretreatment skin testing not necessary[5]
Disadvantages	Relatively short duration of results. Produces soft volume enhancement; therefore, less suitable and less cost-effective than other products for facial contouring.[15] Tissue injection required, and tissue in thin areas may become discolored. Adverse events associated with the use of these products include noninflammatory nodules and inflammatory granulomas
Current controversy	Cross-linked HA injected into forearms of 11 healthy volunteers stimulated collagen synthesis and partially restored components of the dermal matrix that had been lost to photodamage.[8] Investigators hypothesized that stimulatory effects were due to activation of dermal fibrolasts and that cross-linked HA may have some utility in treating atrophic conditions. Other clinicians warn that the collagen-stimulation properties of HA have not been proven conclusively

*FDA indicates US Food and Drug Administration; HA, hyaluronic acid.

PLLA to create a series of vectors that would help not only elevate the depressions but also lower the eyelids. She has very prominent tear troughs, and using small volumes of PLLA to create a series of vectors would help elevate the lower eyelid area.

Dr. Buford: I'm concerned that if you adequately took away the forehead transverse lines, you might block brow compensation, which might make her feel claustrophobic, so I would use botulinum toxin medially in the forehead. Botulinum toxin at the orbicularis oculi might raise her eyelids a little. In reality, though, I think she is a surgical patient. If she does not want surgery, she must be willing to accept a less-than-optimal result with injectables. I see the whole midface coming down against the mandibular ligament and against the nasolabial fold, and I think it would be difficult to bring that up with PLLA alone. If surgery were unacceptable, I would proceed conservatively with botulinum toxin. I would use botulinum toxin in the crow's-feet area and medial brow but, for the previous reasons, would most likely avoid the lateral forehead.

Dr. Weinkle: I think what definitely needs to be addressed is the glabella, because that's what communicates stress and anger. I would use a little filler in conjunction with botulinum toxin to enhance this area. I would concentrate on relaxing the orbicularis oculi, which would lift the brow and soften the upper face. It's also important to address the perioral region. I would also use some botulinum toxin in the depressor anguli oris (DAO) to turn up the mouth, as well as a filler to support the buttress of the lip to improve the overall facial appearance.

Dr. Lacombe: Clearly, the forehead is a dynamic area, so I would present the patient with 2 options: have botulinum toxin injected every 3 to 4 months or interrupt the muscle fibers surgically. When performing a blepharoplasty, I make my incision in the crease. However, because her hooded upper eyelid

TABLE 5

Poly-L-lactic Acid*

FDA approval	First brought to market in France in 1999 and promoted principally as an aesthetic treatment. Approved by the FDA in 2004 to treat HIV-related facial lipoatrophy.[7] Dramatic results have led to widespread off-label use for cosmetic rejuvenation in the United States
Components	Hydrogel suspension containing microparticles of PLLA, an α-hydroxy acid, in sterile water[16]
Mechanism of action	Immediate volumizing effect of hydrogel and water, which lasts ≤1 wk. Once carrier suspension and water are absorbed, collagenesis is stimulated and progressive volumizing begins[11]
Duration of effect	Suspension gradually degrades over time, requiring reinjection for maintenance of effect
Uses/advantages	Best used for sculpting, contouring, and volumizing. Rapid administration, requires little downtime; final results appear gradually over ≥3–5 treatments. Optimal depth of implantation is at dermal-subcutaneous junction, but can also be implanted within superficial subcutaneous fat or just above periosteum.[7] Directly addresses problem of dermal atrophy; improve skin's look and texture by producing natural collagen. Useful on hands, chest, and other areas, in addition to the face. Requires patient compliance with self-massage for several days after treatment to help minimize formation of nodules and repeat injections over 3–5 mo, usually at monthly intervals Because PLLA is a synthetic, no animal sensitivity is involved and no pretreatment testing is required[16]
Disadvantages	Not recommended for volumizing lips, treating specific superficial wrinkles, or superficial or site-specific enhancement. More costly than other dermal fillers. Adverse effects include noninflammatory micropapules, papules, nodules, and inflammatory granulomas

*FDA indicates US Food and Drug Administration; HIV, human immunodeficiency virus; PLLA, poly-L-lactic acid.

extends in a fold past the corners of the eyes, I would have to extend the incision further. Typically, this doesn't heal as nicely in this thicker skin. My solution would be to perform an endoscopic brow-lift. This would elevate the eyelid, eliminating the fold; then I could limit the incision to the crease. When the eyelid incision heals, it is hidden in this natural crease. She already has a relatively arched brow, so I would not try to lift it too much more centrally. I would use muscle transaction and excision to produce a lateral elevation, a little separation in the center, and a release around the temple. The result would be a softening of the upper half of the face. In the lower half, I get pretty good results with botulinum toxin around the DAO. I find that I get crisper results with HA or CaHA than with PLLA in the corners of the mouth and along the marionette lines (Tables 4 and 5).[5-8,11,14-16] I put the filler into the lip border and all around the corner, and the lips turn up immediately.

Subsurface Changes

Because the correction of the subsurface changes associated with aging very often requires extensive sculpting, contouring, and volumizing of targeted areas, the fillers used must provide strong structural tissue support that yields a long-lasting, natural-looking result. Stimulatory fillers offer the best options for achieving these types of aesthetic goals because they are injected deep into the dermis and subdermis (Figure 2). In addition, each filler has its own sites of

Product Name	Depth of Injection	FDA Indication
Poly-L-lactic acid	Deep dermis–subdermis	Restoration or correction of HIV-associated lipoatrophy
Calcium hydroxylapatite	Deep dermis	Oral and maxillofacial defects; vocal fold insufficiency, radiographic tissue marking
Collagen and hyaluronic acids	Upper dermis–mid dermis; mid dermis–deep dermis	Correction of soft tissue contours (eg, those created by wrinkles and acne scars); correction of moderate to severe facial wrinkles and folds (eg, nasolabial folds)
Silicone	Deep dermis	Prolonged retinal tamponade in cases of complicated retinal detachments

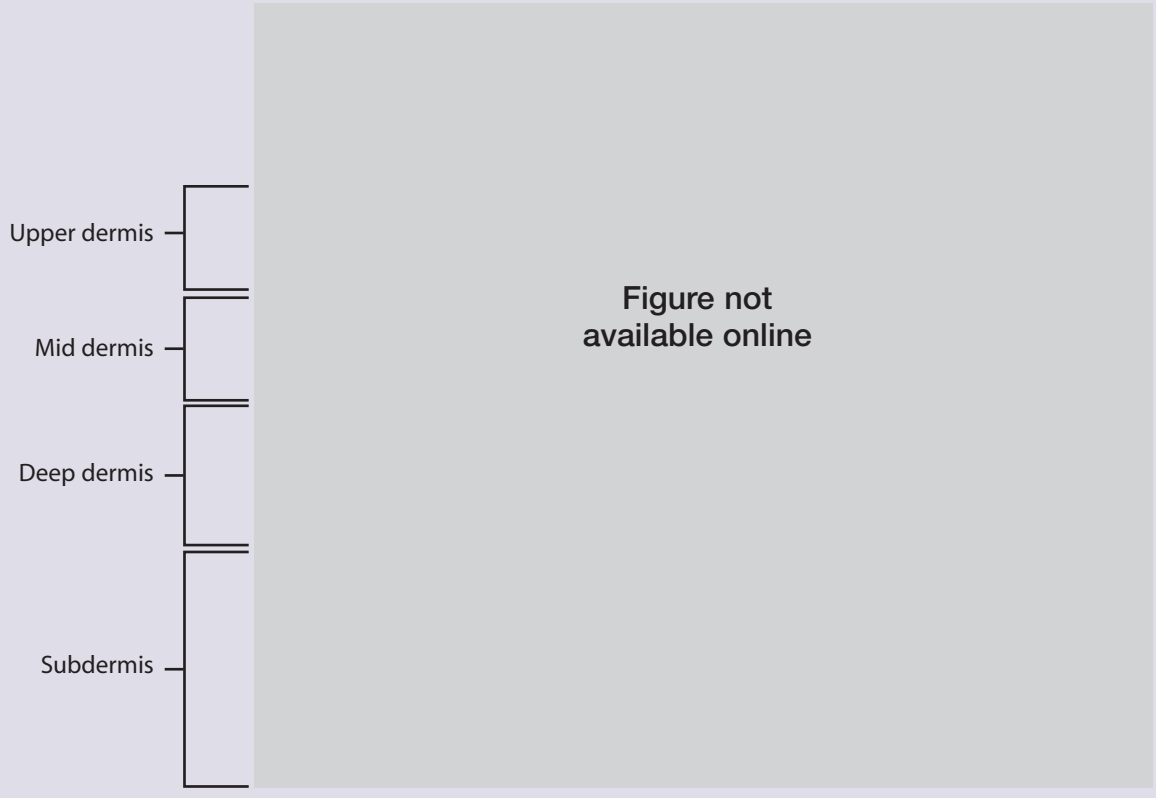

Figure 2. Depth of injection of various fillers. FDA indicates US Food and Drug Administration; HIV, human immunodeficiency virus. Adapted with permission from *Cosmetic Dermatology.* 2006;19(suppl 2). ©2006, Quadrant HealthCom Inc. Illustration by Christy Krames.

optimal efficacy. (These will be examined in more detail in the Treatments section.) The ability to inject these products to create a layered effect further enhances their versatility and the chances of achieving a more natural look. This versatility also makes stimulatory fillers ideal adjuncts to plastic surgery and useful elements in combination treatment with botulinum toxin and HA.

Because the long-term effects of stimulatory fillers occur gradually, optimum aesthetic correction is a matter of successive approximations to the ideal look. The mantra "treat, wait, and assess" should be used to guide stimulatory filler injections in any patient.[7] The usual recommendation is to schedule a reassessment for a possible second treatment 4 to 6 weeks after the first.

Loss and Redistribution of Facial Fat

Dr. Burgess: This patient has a lot of facial fat loss around the mouth, which pushes the skin against the nasolabial folds, cupping the perioral region. I would recommend using a stimulatory filler such as PLLA in the malar and preauricular regions to pull away from the perioral region. In the midface area, she has prominent nasolabial folds, which could be diminished by supporting and restructuring beneath with any of the fillers. I would use a stimulatory filler for the bilateral prejowl sulcus. Although a surgical jowl-lift might be indicated, the filler would make a significant difference without plastic surgery.

Dr. Sherman: If she didn't want to have a lower face-lift, I would volumize and support her cheeks (the mid-third of the face) with PLLA, beginning at the nasojugal fold (tear trough) and progressing from the medial, mid-, and lateral cheek at the zygomatic arch and finally upward into the temple area. Using a series of vectors to bolster and buttress soft tissue, blending concavity and convexity, 3-dimensional volume with contour is reestablished. My goal would be to move the cheeks in a posterolateral direction, minimizing the heaviness of the central face associated with fat loss and redistribution.

After volumization of the mid-third of the face, I would assess the nasolabial folds. Often, the nasolabial fold appears less prominent after correction of the mid-third of the face. She has a mild troughlike area just above the vermilion border of the upper lip. To volumize this area, small aliquots of 0.025 to 0.05 mL of PLLA may be injected, requiring only 1 or 2 treatment sessions 4 to 6 weeks apart. Her prejowl sulcus is a prominent concavity and may be minimized with PLLA, which may also be used to strengthen the chin and lessen marionette lines.

Dr. Buford: The malar prominence basically gives out medially, so I would inject PLLA to get a vector laterally and superiorly to produce a lifting effect. For the soft tissue loss around the maxilla, I would inject PLLA into the perioral crescent, establishing a vector to support that area laterally. Filling or strengthening of the modiolus may strengthen or lift the oral commissure. I think anything else would warrant surgical correction.

Dr. Weinkle: I would address the prejowl sulcus with a depot injection of CaHA. Then I would use a little HA to address the fine lines. The effect would be a softening of the face. I agree that she should consider surgery with some volumizing as the ultimate package. For the present, though, the fillers and botulinum toxin would make a big difference in her appearance, with no downtime.

Dr. Lacombe: She has some skin redundancy in the lower eyelid area. There is a concavity, and I can feel skin, muscle, and bone but no fat. I would use a stimulatory filler like PLLA in this area. She has obviously lost volume in the cheek; the area is flattened all the way down. This could be corrected with a vertical face-lift to reposition the fat upward and backward. There is some ptosis of subcutaneous fat in the buccal and malar areas. With surgery, I would either reposition or remove some fat, correcting the jowliness. There is some concavity around the prejowl sulcus and marionette lines. I would use PLLA there after I saw the results of the surgical procedure because surgery will restore some of this volume. The area will be relatively less concave or will be further back. I would use some lifting underneath the subcutaneous musculoaponeurotic system to bring that whole subcutaneous musculoaponeurotic system and skin layer back together and keep the natural volume and thickness. There is some platysmal separating in the neck and some volume that is probably hereditary. Obviously, surgical reconstruction of these areas would produce a dramatic change. However, many patients who cannot afford the downtime or are not psychologically prepared for surgery are pleased with the results of volumetric fillings.

Dr. Vleggaar: I agree that surgery might be the best option to enhance certain areas of the face and would explain to the patient the limitations of what we can do without surgery. Her lips are full and don't need correction, but the lip fullness combined with the fat absorption from the maxilla to the mandible gives her an appearance of forward projection or pouting. I would correct this by volumizing the area of the alar sulcus. I would use PLLA if a gradual procedure were acceptable or HA if she wanted an immediate result. If she were definitely against surgery, I would compromise by using volumizers from the chin to the ear, but my best recommendation would be a blepharoplasty followed by contouring with injectables.

Administration

The panel concentrated on the use of PLLA because proper reconstitution of the injectable before treatment and skillful massage of the injected area after treatment are crucial to the attainment of optimal aesthetic correction.

Dr. Werschler: I always fill the vial of PLLA to capacity with 3 to 5 mL of 1% lidocaine with epinephrine at

the time of injection, unless the patient is sensitive to epinephrine. This is done after the initial reconstitution of the filler with 4 to 5 mL of sterile water for injection, a minimum of 2 hours before injection and, preferably, 12 to 24 hours before use. The total volume of solution to be injected is, therefore, 7 to 10 mL.

In most applications, I prefer to use the 1½-in 25-gauge needle. I am a "threading/fanning/cross-hatching" injector. I must admit, however, that any of the various methods of injection techniques, in skilled hands, will yield the same final results. I prefer the 1-mL silicone-lubed syringe with a Luer-Lok™ hub.

It is important to think of global areas when using PLLA, as it is a global volumizer, or panfacial sculpting agent, which acts as a collagen stimulator. It is not a wrinkle filler. Therefore, its highest and best use lies in increasing dermal structure and support and reducing volume deficits.

I always use a washable crayon-type marker to "sketch" a treatment on the patient's face. This is done to confirm with the patient the overall treatment program and to demonstrate unique individuality in treatment design.

Dr. Weinkle: PLLA is the only filler that needs reconstitution. For most of my standard facial injections, I reconstitute it with 5 mL of bacteriostatic sterile water and then just before injection add 2 mL of 1% lidocaine with epinephrine, for a total of 7 mL. This is a slightly increased volume and seems to go into suspension more evenly, preventing needle clogging. For suspension that is prepared a minimum of 2 hours ahead of time, warming it slightly aids in reconstitution. I use a 1-in 25-gauge needle with a 1-mL Luer-Lok syringe. I feel that I can watch small aliquots more easily with the 1-mL syringe than with the 3-mL syringe. My assistant draws up the next syringe as I am finishing the first, so there is no time for the suspension to precipitate. With this technique, I have very minimal needle clogging. Before injecting, I use only a topical anesthetic.

Dr. Lacombe: I also use a 7-mL solution of PLLA, with 5 mL of sterile water and 2 mL of 1% lidocaine. I don't think that epinephrine really prevents bruising, as bruising happens when you first put the needle in and by the time the epinephrine takes effect—a minute or 2 later—the bruising has already happened. I will use 1% lidocaine with epinephrine for tiny blocks, maybe 2 mL; in this case, I can see where the epinephrine went and that becomes the injection point. I use mental and orbital nerve blocks in all patients. It takes only about 20 seconds to do and is effective quickly. Using a topical anesthetic takes too long, and it can't be used too close to the eyes.

I do all my injections from 4 basic spots to avoid multiple injection sticks and to produce less bruising. Once I inject the first bolus, the lidocaine begins working, so there is no pain in that area. Warming the suspension is important. We warm the solution by placing it in a pocket or holding it in our hands to bring it closer to body temperature. My assistant agitates the hydrogel when she has the lidocaine ready for injection and then draws it into six 1-mL Luer-Lok syringes with 1½-in 25-gauge needles. If we are going to do 2 vials, she prepares the next 6 syringes as I am finishing the first 6. I don't have problems with clogging. The saline is added at least a day or 2 before, and the lidocaine is added 20 minutes before injection to allow time for agitation.

Dr. Vleggaar: I was using a PLLA dilution with 4 mL of water and 1 mL of 2% lidocaine but found that 1 mL was not enough to provide comfortable anesthesia. Now I use 4 mL of water and 2 mL of 2% lidocaine, which I inject with a 5/8-in 26-gauge needle. The nurse prepares the suspension but doesn't agitate it and just stores it in the refrigerator. I add epinephrine if I am treating the preauricular region years after a face-lift, when there is obvious atrophy and the tissues are attached firmly. For these patients, I use 6 mL of water and 4 mL of 1% lidocaine with epinephrine in a 10-mL 25-gauge syringe with a 1½-in needle. In this case, I am really using the highly diluted solution to dissect the tissue and deposit small amounts of product. The epinephrine limits the extent of bruising.

I use a special technique for injecting PLLA into the DAO area. If injecting HA in this area, you can focus on a small surface of the lateral corner. However, because PLLA is a particulated product, it is injected more deeply, and when you hit that tendon part of the DAO, it doesn't diffuse very well. If you keep repeating the injection here, the particles bulk at the DAO and the muscle becomes inflamed or fibrotic, developing a nodule. To avoid this situation, I inject the PLLA just medial to the tendon of the DAO, heading the needle toward the vermilion border on a level with the muscle. I tilt the needle until it just touches the mucosa and use the bevel to rupture the muscle a bit, injecting at the same time. You can feel and hear a snap when the muscle ruptures. One side of the sandwich of dermis and muscle will fall outward, and the mucosa and a bit of muscle will fall backward. Then you can add bulk between these layers, keeping the 2 sides apart with product. The effect is visible immediately.

Dr. Burgess: For PLLA, I use a 5.5-mL dilution, with 5.5 mL of water. Occasionally, I add 1% lidocaine with epinephrine; this allows for some vasoconstriction and minimizes bruises and cutaneous bleeding with

injection. If time allows, I have the patient sit with a topical anesthetic on the face for about an hour, and I usually perform infraorbital blocks or mental nerve blocks (or both) that contain 1% lidocaine with epinephrine. I also use 0.5 mL of lidocaine in a ring block if I am injecting the temple area. I have found that heat actually helps with the covalent bonding of the PLLA particles. Before administration, the reconstituted vial is submerged in hot water (≈98–100°F) for about 30 minutes. The hot water improves the consistency of the hydrogel. A baby-bottle warmer could be used as well to maintain a constant heated temperature.

For administering PLLA, I like to use a 3-mL syringe with a 1½-in 25-gauge needle, and I find in teaching other physicians that the 1½-in needle provides room for error. The needle length allows a longer track with a steady stream for retrograde injecting. I probably am using 1 in of my 1½-in needle because I am injecting into the skin and not completely retracting the needle. I keep reangling the needle at 15° to create a fanning pattern and to lattice the product. I withdraw the needle completely only when I am ready to inject the next site. When the patient's skin is totally anesthetized, I can inject PLLA in 15 minutes. I can visualize the elevation of the skin as the product is being injected; therefore, I don't generally watch the syringe gauge. For depot injections in the temple areas, I use a ⅝-in 26-gauge needle. After injecting PLLA, I do a lot of massage. I instruct my patients to report any nodules or thickening of the skin and to massage them at home if they appear.

Dr. Sherman: I prefer the use of topical anesthetic ointment in conjunction with ice packs. The use of 1% lidocaine in the reconstituted hydrogel provides a tumescent anesthetic effect quickly. I do not use regional blocks of local anesthetic injections. To reconstitute, I add approximately 5.5 mL of sterile bacteriostatic water the night before use. Immediately before use, I slowly add 1 mL of 1% lidocaine with epinephrine to avoid precipitation of PLLA particles. I have found that this provides 6 mL of injectable PLLA hydrogel. The extra 0.5 mL of sterile water is absorbed by the PLLA. Once reconstituted, I withdraw from the vial using an 18-gauge needle, which provides easy flow into syringes. I use 3-mL Terumo® syringes and 1-in 25-gauge needles, which provide a uniform pressure gradient for injection. I find that the 1-mL silicone-coated syringes move product quickly and, for novice injectors, may be associated with a bolus injection, leading to papule or nodule formation. I use the retrograde injection technique, increasing the pressure of injection as the needle is withdrawn. When I thread the needle through the skin, I am looking for a roll of skin over the needle shank to illustrate proper depth, optimally at the dermal subcutaneous junction. I am not concerned with the exact volume of each injection but rather gauge the amount of each injection by the skin response. I use the retrograde injection technique throughout the entire face, including the tear trough, cutaneous lip, and temples. I no longer use the depot technique. I use small volumes (0.025–1.0 mL) of product, which vary based on the area of injection. I place injections close together (2–3 mm apart) and use both a cross-hatching and a fanning pattern. I massage as I move from one cosmetic unit to the next, so when the case is complete, so is the massage. A full-face cosmetic case is scheduled for 30 minutes and human immunodeficiency virus infection cases for 45 minutes. Patients are instructed to ice on and off for approximately 2 hours and massage at home twice daily for 5 minutes for 1 week. Follow-up injection sessions are scheduled at 4- to 6-week intervals.

Dr. Buford: For numbing, I use a topical anesthetic for about 10 minutes. I have done training sessions where I have not used any numbing, and the patients said that the discomfort was about 2 on a scale of 1 to 10 (where 1 indicates least uncomfortable and 10 indicates most uncomfortable). I used a nerve block only once, for a patient with almost no pain tolerance. I reconstitute PLLA with 5 mL of sterile water and 2 mL of 1% lidocaine with epinephrine. My assistant prepares the suspension the night before treatment or in the morning, then just before injection, agitates the hydrogel and draws up all the injections. I use 1-mL syringes so I can move very fast and there is much less clogging; this also helps to achieve an even distribution. It takes me approximately 10 minutes to do the entire face.

Usually, I have about 6 full syringes and 1 half-full syringe. I use 3 per side. With a 3-mL syringe, clogging becomes more of an issue. I use a 1½-in 25-gauge needle, so there are fewer needle sticks. I use an eyeliner to mark the injection sites before treatment. When injecting, I use a combination of fanning and cross-hatching. I inject deeply and with very low volumes along the periosteum to correct tear troughs. I don't do much injecting in temple areas because my patients don't have much temple wasting. I might inject along the brow, but too much volume can obliterate the nice sweep of the cheek bone. I inject one side of the face, then show the patient what I have done, for comparison.

PROPOSED TREATMENTS: STIMULATORY FILLERS AND PLASTIC SURGERY

In considering all available options for aesthetic rejuvenation, the patient had to weigh the risks and

Serial Puncture

Needle punctures are placed in the skin at closely spaced intervals and into each is placed a small quantity of filler. This technique relies on a fixed needle position and is particularly useful to novice injectors. *Strengths*: Allows for controlled delivery of product and minimizes the risk of overfilling. *Drawbacks*: Time-consuming and greater risk of bruising.

Figure not available online

Serial Threading

This technique combines the best of serial puncture and linear threading and is used as a transitional technique between serial puncture and linear threading/fanning. Several contiguous small tracks are created and injected with filler. *Strengths*: Allows for controlled delivery of product while maintaining all the benefits associated with threading and fanning, such as speed, comfort, and decreased bruising.

Figure not available online

Linear Threading

A long needle (1–1.5 in) is used to deposit a long, continuous thread of product into the skin. *Strengths*: In small areas, only one injection point is needed. *Drawbacks*: Difficult to control for even delivery of product. The advanced nature of this technique requires that the injector first demonstrate proficiency with serial puncture and serial threading.

Figure not available online

Figure 3. An overview of injection techniques. Adapted with permission from *Cosmetic Dermatology*. 2006;19(suppl 2). ©2006, Quadrant HealthCom Inc. Illustrations by Christy Krames.

benefits of surgical intervention with or without stimulatory fillers. These useful adjuncts to plastic surgery may be used before or at the time of a face-lift to help stimulate collagen production during the healing phase. Stimulatory fillers also may be useful for patients who are considering repeat face-lifts 5 to 10 years after the initial surgery. Usually, significant skin laxity does not develop after a face-lift, but appearance is compromised as the patient continues to age. Although the skin becomes somewhat less elastic, the underlying skeletal framework changes, and there is increasing lipoatrophy. In many cases, the lost volume can be replaced with a stimulatory filler.

Other than relating the administration of stimulatory fillers to the time of surgery, there are no differences in the administration techniques used by plastic surgeons and dermatologists. The usual regimen is to perform 1 or 2 stimulatory filler treatments before surgery, then fine-tune with 1 or more treatments after the surgical swelling has dissipated, usually 3 to 6 months after surgery. Differences in results can, however, be traced back to the sophistication of the clinician's injection technique (Figure 3). Being proficient in a variety of techniques ranging from the novice-friendly serial puncture technique to the advanced techniques of cross-hatching and fanning gives the clinician varying degrees of control over placement of product, the speed with which the injection is performed, and the amount of bruising and discomfort experienced by the patient.

Collaboration between dermatologists and plastic surgeons is becoming increasingly common. Some patients who would probably benefit most from plastic surgery may be satisfied with a

Figure not available online

Cross-Hatching

A variation on threading, this technique calls for the repeated threading of single threads of filler at 90° angles. Injectors must attain proficiency in linear threading before attempting cross-hatching. *Strengths:* This technique provides greater tissue stability and increased bulk and volume. *Drawbacks*: Suboptimal cosmetic results can arise from uneven product delivery.

Figure not available online

Fanning

This injection technique uses a repetitive "in-and-out" movement to deliver the filler without removing the needle from the skin. *Strengths*: With this technique, pain is minimized and deposition of filler is achieved more quickly than with threading or cross-hatching. *Drawbacks*: Overinjection of product at the base of the fan can produce a bulky effect.

less-than-perfect result that can be achieved with stimulatory fillers. It is also true that the initial use of fillers might affect the type of surgery needed later, especially if injections have involved permanent fillers. In addition, there are many volume issues that cannot be treated with surgery. Optimal results are achieved when dermatologists and plastic surgeons work together to coordinate the various types of procedures available.

A unique feature of stimulatory fillers that is both an advantage and a disadvantage is that the final results are not immediate. For various reasons, some people are not interested in immediate results. They want to look rejuvenated, but they want to do so gradually and unobtrusively. Patients who are not fully aware that it may take weeks or months to see the final effects of stimulatory fillers may be disappointed with the immediate results of treatment. Carefully explaining the gradual nature of the rejuvenation will help manage the patients' expectations and influence their degree of satisfaction with results. Alternatively, layering injectables with different onsets of action is a good way to provide both immediate and progressive, longer-term results.

THE IMPORTANCE OF THE AESTHETIC EYE

One of the most important factors in the success of facial rejuvenation is the physician's ability to analyze the patient's face aesthetically—to appreciate what is missing, what needs to be embellished, how changes to one part of the face will affect other parts of the face, and which final effects are desired. For example, a patient's face may appear full, but assessing the patient with an aesthetic eye reveals a face that is centrally full but with lateral atrophy. Adding volume to the atrophic area changes the proportions, and the whole face appears smaller. Throughout any injection procedure, the physician must stop and reanalyze the face so that volume is added strategically and the face

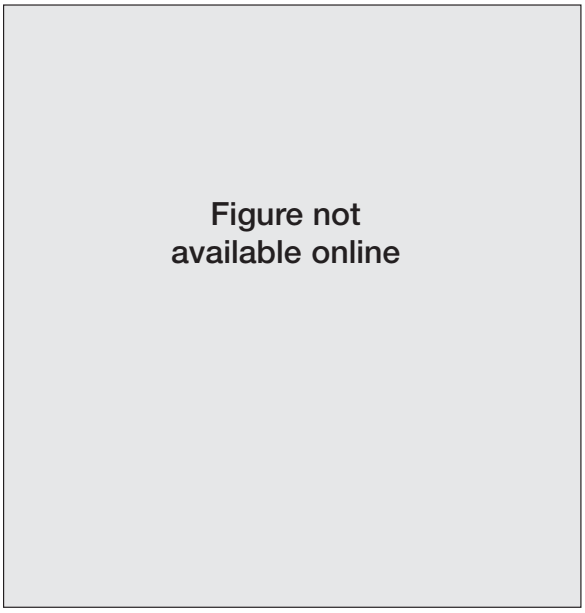

Figure 4. Areas of the face treated with botulinum toxin, hyaluronic acid, and poly-L-lactic acid.

is not distorted. It is extremely important to tailor the treatment to the patient's underlying facial anatomy and bone structure so that the corrections are unique to that patient. Patient expectations are important also. The patient must be educated about what constitutes a youthful face and how the physician plans to achieve that look.

An injection procedure is not always a direct replacement of volume. When using stimulatory fillers, clinicians should inject the product to create vectors that move the soft tissue in a medial to lateral, superior, or anterior direction. The goal is to volumize concave areas and blend them into convex areas, establishing a smooth transition, maintaining facial contour, and eliminating fine lines and wrinkles. For example, establishing a vector by volumizing the cheeks tends to draw the tissue away from the mouth so that nasolabial folds are corrected. Significant superolateral enhancement may minimize the need to inject the nasolabial folds.

The practice of aesthetic dermatology must evolve the way plastic surgery has evolved: from concentrating on reconstruction to improving appearance. Those responsible for dermatology training programs must be encouraged to educate residents about how to assess faces aesthetically and how and why certain techniques used in combination can produce better results than can any one technique used alone. Board certification and postresidency training, in fellowships and continuing medical education courses, should become standard for any physician who practices cosmetic rejuvenation.

TREATMENTS

After considering all options for facial rejuvenation, the patient decided that she was not ready for plastic surgery (Figure 1). She was, however, interested in treatments with botulinum toxin and dermal fillers, which she had over the course of 3 sessions.

Session 1: March 16, 2007

Pretreatment—Pretreatment of the face took place 1 hour before fillers were injected and consisted of the following: facial cleansing with povidone-iodine solution and alcohol, application of topical anesthetics (lidocaine and prilocaine) to cheeks allowed to remain on the face for 45 minutes, injection of 2-mL infraorbital nerve blocks (1% lidocaine with epinephrine), injection of 2-mL mental nerve blocks (1% lidocaine with epinephrine), and local anesthetization of small areas with 1% lidocaine with epinephrine.

Injection of Dermal Fillers—Three products were strategically administered to provide a subtler, more natural-looking appearance: botulinum toxin, HA, and PLLA (Figure 4). Forty-four units of botulinum toxin were used in the upper midforehead and under the arch of the eyebrows to elevate brows, glabella, and marionette lines (DAO). In the lips, 0.5 mL of HA was used; a total of 0.5 mL was also used in nasolabial folds and chin crease. PLLA was injected into each side, in doses of 7.5 mL each to correct prejowl sulci, nasolabial folds, preauricular areas, marionette lines, and tear troughs, to volumize the lower face. A total of three 5.5-mL vials were used.

Posttreatment—The face was cleansed with peroxide, and moisturizing sunscreen was applied.

Session 2: May 11, 2007

Eight weeks after initial treatment, the patient reported for a follow-up visit. At that time, it was determined that there had been less than 50% improvement in her facial appearance (Figure 5). Another round of injections was administered. Pretreatment varied just slightly from the first visit, with minor adjustments in the amount of 1% lidocaine with epinephrine used to block specific nerves: 2-mL infraorbital nerve blocks, 1-mL intradermal ring blocks, and 1-mL mental nerve blocks.

The primary purpose of this touch-up session was to soften the lines etched into the forehead and enhance the lift of the eyebrows. To this end, 1 mL of HA was injected into the glabella and under the eyebrows; 20 U of botulinum toxin was used for additional relaxation of the glabella.

Posttreatment consisted of cleansing with peroxide and the application of moisturizing sunscreen.

Figure 5. A 63-year-old woman 8 weeks after initial treatment with 44 U of botulinum toxin in the upper midforehead, under the arch of the eyebrows, glabella, and marionette lines; 0.5 mL of hyaluronic acid in the lips and 0.5 mL in the nasolabial folds and chin crease; and 15 mL of poly-L-lactic acid in the prejowl sulci, nasolabial folds, preauricular areas, marionette lines, and tear troughs.

Session 3: June 22, 2007

Six weeks later, the patient returned for another follow-up treatment. Her appearance showed a marked improvement over that of her initial visit and an incremental improvement since her second visit. She and her doctor were satisfied with the results and decided not to administer additional fillers. They did, however, discuss the potential need for future treatment with dermal fillers. "I'm very happy with the results," she said (Figure 6). "The wrinkles in the forehead and around the mouth are gone, the tear troughs have disappeared, and my cheeks are full. I look younger and more rested, and my skin has a youthful glow. My friends say they are seeing a gradual change and they think I look good. Having a younger appearance is refreshing, and now I feel like I have more energy and a more positive outlook on life."

THE ROLE OF STIMULATORY FILLERS IN NONFACIAL REJUVENATION

Although experience in this use is limited, the panel members discussed how they use stimulatory fillers to rejuvenate hands.

Dr. Buford: More patients are asking to have their hands rejuvenated. I like to use a more dilute PLLA suspension for this, using 10 to 12 mL of sterile water.

Dr. Vleggaar: Originally, I used a 6- to 8-mL suspension but then realized that I don't need to sculpt or contour the hand, just plump it with a diffusion. The more water I add, the more it diffuses. With a 6- to 8-mL dilution, you also risk creating nodules. Now I use about three quarters of a vial of PLLA, which is about 9 mL, with 12 mL of sterile water. I split this between 2 hands.

Dr. Burgess: I usually dilute to a 10-mL suspension and use 5 mL per hand (approximately 1 mL into the subcutaneous plane of the interosseous space).

CONCLUSION

The success of facial rejuvenation is influenced by many factors. One of the most important is an agreement between physician and patient about which effects can be expected. Optimum results can be achieved only when the physician understands

Figure 6. At 14 weeks posttreatment, evidence of facial rejuvenation in a 63-year-old woman from right lateral (A), frontal (B), and left lateral (C) views. At her first session, the patient was treated with 44 U of botulinum toxin in the upper midforehead, under the arch of the eyebrows, glabella, and marionette lines; 0.5 mL of hyaluronic acid in the lips and 0.5 mL in the nasolabial folds and chin crease; and 15 mL of poly-L-lactic acid in the prejowl sulci, nasolabial folds, preauricular areas, marionette lines, and tear troughs. At her second session, the patient received a touch-up, including 1 mL of hyaluronic acid injected into the glabella and under the eyebrows and 20 U of botulinum toxin type A to relax the glabella.

the physiologic causes of facial aging and is able to tailor various rejuvenation techniques based on an aesthetic appraisal of the patient's face both before and during treatment. The ultimate goal of aesthetic facial rejuvenation is to achieve the greatest improvement with the least amount of treatment.

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The Role of Stimulatory Fillers in Aesthetic Facial Rejuvenation

Expiration Date: November 30, 2008

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For each question listed below, select the one best answer.

1. The oldest known dermal filler is:
   a. poly-L-lactic acid (PLLA)
   b. fat
   c. collagen
   d. hyaluronic acid (HA)

2. PLLA effects immediate change in the face by replacing lost volume or adding desired volume.
   a. true
   b. false

3. Hypertrophy causes fat to accumulate in which of the following areas?
   a. periorbital area
   b. forehead
   c. lower eyelids
   d. submental area

4. Treatment options for sun-damaged skin include which of the following?
   a. trichloroacetic acid
   b. erbium laser peel
   c. intense pulsed light
   d. all of the above

5. Which of the following statements about HA is incorrect?
   a. HA treatment produces permanent results.
   b. HA acts as a sponge to attract and bind water.
   c. Regardless of its provenance, HA restores volume immediately upon administration.
   d. Because HA produces soft volume enhancement, it is less suitable and less cost-effective than other products for facial contouring.

6. PLLA is recommended for all the following areas EXCEPT:
   a. face
   b. hands
   c. lips
   d. chest

7. Which of the following dermal fillers must be reconstituted before use?
   a. PLLA
   b. HA
   c. collagen
   d. none of the above

8. When using stimulatory fillers as an adjunct to plastic surgery, the usual regimen is to give 1 or 2 injections before surgery, then fine tune with 1 or more treatments after the surgical swelling has dissipated, usually _____ after surgery.
   a. 10 to 15 days
   b. 4 to 6 weeks
   c. 3 to 6 months
   d. 8 to 12 months

9. Injection with which of the following products is a good option for elevating the brows in a patient who does not want to undergo surgery?
   a. botulinum toxin
   b. HA
   c. collagen
   d. none of the above

10. A unique feature of stimulatory fillers that is both an advantage and a disadvantage is that _____.
    a. they are injected superficially into the dermis and subdermis
    b. they do not demand a high proficiency in injection technique
    c. the final results are permanent
    d. the final results are not immediate

The Role of Stimulatory Fillers in Aesthetic Facial Rejuvenation

Released: November 2007

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❑ Yes, via e-mail (address above) ❑ No, please do not contact me.

	Strongly Agree	Agree	Disagree	Strongly Disagree
1. The program objectives were fully met.	❍	❍	❍	❍
2. The quality of the educational process (method of presentation and information provided) was satisfactory and appropriate.	❍	❍	❍	❍
3. The educational activity has enhanced my professional effectiveness in treating patients.	❍	❍	❍	❍
4. The educational activity will result in a change in my practice behavior.	❍	❍	❍	❍
5. The information presented was *without* promotional or commercial bias.	❍	❍	❍	❍

(When answering this question, please refer to the following guidelines set forth by the ACCME regarding commercial bias and fair balance: *Discussion of commercial products must be free of bias for or against any one product and must present objective information about each product discussed; only generic names of therapeutic options should be used. However, if trades names are used, those of several companies must be discussed in the activity.)*

6. What new information did you learn from this activity?

_____

_____

7. Please provide us with suggestions for improving this activity.

_____

_____

8. Recommendations for topics of future presentations.

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If CME credit and a certificate are desired, please mail/fax this completed form or a copy of it. Keep a copy of this form for your records until you receive your certificate.

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