SCULPTRA INJECTIONS

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Facial volume restoration of the aging face with poly-l-lactic acid

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ABSTRACT: The purpose of this article is to discuss current techniques used with poly-l-lactic acid to safely and effectively address changes observed in the aging face. Several important points deserve mention. First, this unique agent is not a filler but a stimulator of the host’s own collagen, which then acts to volumize tissue in a gradual, progressive, and predictable manner. The technical differences between the use of biostimulatory agents and replacement fillers are simple and straightforward, but are critically important to the safe and successful use of these products and will be reviewed in detail. Second, in addition to gains in technical insights that have improved our understanding of how to use the product to best advantage, where to use the product to best advantage in facial filling has also improved with ever-evolving insights into the changes observed in the aging face. Finally, it is important to recognize that a patient’s final outcome, and the amount of product and work it will take to get there, is a reflection of the quality of tissues with which they start. This is, of course, an issue of patient selection and not product selection.

KEYWORDS: poly-l-lactic acid, Sculptra, volume restoration

Introduction

The purpose of this article is to discuss current techniques used with poly-l-lactic acid (PLLA) to safely and effectively address changes observed in the aging face. As with any esthetic procedure or product, recommendation guidelines are in a state of perpetual evolution and refinement. With this in mind, several important points deserve mention. First, this unique agent is not a filler but a stimulator of the host’s own collagen, which then acts to volumize tissue in a gradual, progressive, and predictable manner. This mechanism of action has important implications in the way the product is used in order to optimize outcomes and avoid adverse events. How to use the product to best advantage as a tissue augmentation device has evolved considerably since its introduction to the marketplace over one decade ago as a “facial filling” agent for human immunodeficiency virus (HIV)-associated facial lipodystrophy (1). As experience has been gained with this product, and parameters adjusted accordingly, we have seen a dramatic decrease in the number of device-related adverse events reported in these early HIV studies (2). The technical differences between the use of biostimulatory agents and replacement fillers are simple and straightforward, but are critically important to the safe and successful use of these products and will be reviewed in detail.

Second, in addition to gains in technical insights that have improved our understanding of how to use the product to best advantage, where to use the product to best advantage in facial filling has also improved with ever-evolving insights into the changes observed in the aging face. Current literature suggests that these changes are occurring in all tissue structures of the face and that a change in one area may greatly influence changes in neighboring tissues, leading to a cascade of secondary
Although a new patient may present pointing to a wrinkle, line, or fold they have noticed seemingly overnight, it is now becoming increasingly recognized by the medical community that these are really just the first obvious visible signs of a slow progressive change taking place in all structures of the face. As no two faces age identically, there is no one algorithm of what every face needs. PLLA is not used directly in these wrinkles, lines, and folds, but rather in multiple areas (and tissue structures) of the face in an attempt to address the volume loss that leads to their appearance. In our experience, this approach has proved capable of delivering the sort of subtle and natural-looking results desired by many patients (“I don’t want to look done, I just don’t want to look tired”) and is, in our opinion, the greatest strength of this product. Seemingly small changes in shape, proportions, balance, and symmetry can sometimes have a surprisingly large effect on our perception of the face. This shift in perspective, i.e., looking at the face as an interlocking 3D puzzle rather than focusing on individual lines and folds, such as nasolabial folds or marionette lines, as isolated entities, is the largest part of the learning curve with this product. Third, it is important to recognize that a patient’s final outcome, and the amount of product and work it will take to get there, is a reflection of the quality of tissues with which they start. Wasted faces (associated with HIV or endurance exercise) are harder to fill, and it is harder to sustain the fill (3,4). Older faces with advanced craniofacial remodeling, fat loss, and very poor skin quality can be treated successfully; however, they will need a lot of products to achieve a desirable result. Fillers of any kind may not be the most cost-effective choice in a cosmetic patient who would best benefit from fat augmentation and a face lift. Conversely, fuller and younger faces “bring in their own volume” and are therefore easily reshaped with a conservative amount of filler of any kind. This is, of course, an issue of patient selection and not product selection.

Finally, it should be noted that as PLLA is a bio-stimulatory agent and employs the host reaction for its effect, the effects are not immediate. A patient who wants a “quick fix” for an upcoming event such as a reunion or wedding may be more satisfied with an agent that provides immediate results. PLLA is, however, the only filler currently on the market that is approved by the Federal Food and Drug Administration to last up to 25 months (the cutoff time in the study used to gain Food and Drug Administration approval). The manufacturer
of the product, in order to highlight the benefit achievable from this long duration of action, funded three separate surveys of American women \( (n = 800–1000/\text{survey}) \) considering cosmetic injectable treatments through three separate organizations – the American Academy of Dermatologic Surgery, the American Academy of Facial Plastic and Reconstructive Surgery, and the American Academy of Plastic Surgery. The results revealed that the majority of cosmetic patients would choose duration over immediacy when considering an injectable filler treatment.

We all recognize that optimal, predictable, and reproducible patient outcomes are best facilitated by carefully predicting (patient selection), planning (facial analysis and mapping), and performing (proper preparation and injection of product) treatments in an informed manner. It is our hope that the information provided here, based on extensive personal experience with this product, will help to facilitate this goal.

**Product composition and mechanism of action**

PLLA is a synthetic polymer derived from the alpha-hydroxy-acid family that is both biocompatible and biodegradable. The currently commercially available injectable PLLA products are Sculptra and Sculptra Aesthetic (Dermik Laboratories, a business of Sanofi-Aventis, Bridgewater, NJ, USA).

These products are identical and are supplied as a lyophilized powder in a sterile glass vial containing nonpyrogenic mannitol, sodium carboxymethylcellulose, and microparticles of PLLA measuring 40–63 microns in diameter. This particle size ensures that the particles are large enough to avoid phagocytosis by dermal macrophages or passage through capillary walls, but small enough to be easily injected by needles as fine as 26 gauge (5).

This agent is not a filler but a stimulator of the host’s own collagen, which then acts to volumize tissues in a gradual, progressive manner. Biostimulatory agents work through employment of the host response, and their biocompatibility is contingent upon the ability of the material to perform with an appropriate host response in a specific application (6). The mechanism of action of all of the currently commercially available collagen-stimulating devices (including PLLA) in the specific application of tissue augmentation begins with a subclinical inflammatory tissue response following implantation, followed by encapsulation and fibroplasia. This fibroplasia produces the desired cosmetic result. There are some simple but critical technical differences in the manner in which bioactivators/collagen stimulators are used, as opposed to replacement fillers.

**PLLA: technical considerations**

Careful scrutiny of literature reveals that most problems are technical (2,7–9). Unlike hyaluronic acid fillers, which may be used in any amount desired to achieve full correction at a single session, the recommended strategy with collagen-stimulating fillers is gradual, progressive correction over multiple treatment sessions. Simple yet critical technical considerations of which the practitioner should be aware all relate to avoiding overcorrection (leading to lumps, bumps, and clumps) and include the following.

**Product reconstitution**

- **Recommended dilution:** \( \geq 5 \text{ cc with sterile water} \) for injection. A final dilution of 8–9 cc is most commonly used and may be achieved by the addition of 1–2% lidocaine with or without epinephrine added at the time of hydration or immediately prior to injection.
- **Add fluid gently and leave to hydrate. DO NOT shake the vial until adequately hydrated to avoid deposition of dry clumps of material on the wall of the vial.**
- **Hydration time:** \( \geq 2 \text{ hours (preferably overnight).} \)
- **Lidocaine 1–2% with or without epinephrine may be added at the time of hydration or immediately prior to injection.**

**Product amount**

The amount of product used at any single-treatment session should be determined solely and completely by the amount of surface area to be treated at that session. The appropriate volume of product to be used at each session is therefore easily predetermined.
The therapeutic end point for each session is to blanket the surface area to be treated at that session. The final volumetric correction is addressed by the number of treatment sessions.

Additional comments

The novice injector should be aware that it is initially difficult to resist the temptation to treat to full visual correction at any one session (although this may be possible with patients needing minimal treatment) and recall that “blanketing” the surface area to be treated at that session is the end point.

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Product placement

- Can be done with a 1-cc or 3-cc syringe, and a 25-gauge (long or short) or 26-gauge (short) needle
- Depth of placement varies with location (see below)
- Cheeks, nasolabial folds, lower face
  - Inject in the deep subcutaneous plane under the muscle in the medial cheek and the chin, and in the superficial subcutaneous fat (above the parotid gland and masseter muscle) in the lateral face
  - Use the cross-hatch or fanning technique using 0.1–0.3 cc/cm
  - May be placed as depot injections supraperiosteally along the zygoma, maxilla, and mandible using 0.2–0.3 cc/cm followed by firm massage
- Temple
  - Place deeply under the temporalis fascia. (Manufacturer instructions are to place 0.05 cc/depot; however, it is common practice among experienced users to place 0.3–0.5 cc/depot in this area, followed by firm massage)

Additional comments:

- The viscosity of PLLA is very low compared with hyaluronic acid gel; caution should be exercised to avoid inadvertent overcorrection. It may be prudent to inject slowly in a cross-hatch pattern while becoming familiar with the product.
- Fanning has the advantage of fewer needle sticks, but the novice injector should be vigilant to avoid multiple deposits at the apex of the fan.

Product placement precautions

- Avoid placement in or through areas of hyperdynamic muscle movement. Never inject through the inferior portion of the orbicularis oculi mm. or into the modiolus or proximal depressor anguli oris (DAO) mm. (muscle movement in these areas will clump the product, leading to localized overcorrection).
- Wait a minimum of 4 weeks between treatments.

Aftercare

- Massage after every two to three injections and again at the end of the treatment
- Instruct patients to massage over the 5 days following each treatment session using the “rule of 5s” (5 minutes, 5 times daily, 5 days).

Prevention of adverse events

As noted above, careful scrutiny of the available literature indicates that the majority of adverse events stem from suboptimal product reconstitution or placement 2,7–9, and can therefore be avoided by adherence to the above guidelines.

Subclinical granulomatous inflammation is a normal, expected, and desired tissue response to injected collagen stimulators and follows a predictable course in a normal host. Histopathology of a lump, bump, or clump of product will show an overabundance of product with a few foreign body giant cells, often surrounded by skeletal muscle as seen in FIG. 2A. Injection of steroids or antimitotics such as 5-fluorouracil will have little clinical effect on these lesions as the majority of the lesions is product and not host reaction to product.

Clinically relevant granulomatous reactions have been reported with all currently available commercial devices including collagen, hyaluronic acid, PLLA, silicone, calcium hydroxyapatite (CaHA), polymethylmethacrylate, and polyacrylamide gel. True inflammatory granulomas are unpredictable and rare (the reported rate of clinically detectable granuloma formation varies between 0.01% and 0.1%) (10).

Histopathology of a lesion such as this will show an overabundance of reaction to product with too numerous to count foreign body giant cells as seen in FIG. 2B. Injection of steroids or 5-fluorouracil will clear the lesion; however, fortunately, most resolve spontaneously over time (10).
“Lumping, bumping, and clumping” leading to papules and nodules is an iatrogenic issue caused by (predictable and preventable) suboptimal product reconstitution or placement. True Inflammatory granulomas are a rare and unpredictable event seen with all commercially available products.

Understanding and analyzing the aging face – volume loss and structural changes in multiple tissue layers

As stated earlier, current literature suggests that changes are occurring in all tissue structures of the face with aging and that a change in one area may greatly influence changes in neighboring tissues, leading to a cascade of secondary events. The central role of volume loss and deflation, rather than ptosis, in the aging face has been eloquently illustrated by Lambros in a longitudinal photographic analysis of >100 patients spanning an average period of 25 years (11). Recognizing where that volume has been lost (or sometimes lacking in the first place) in each individual will greatly enhance our ability to address it with site-specific corrections in order to achieve optimal and natural-looking results. Because of the importance of this concept to the optimal use of this product, it will be briefly addressed here with an emphasis on the changes seen in the bone and fat.

Bone

Craniofacial bony remodeling is increasingly being recognized as an important contributor to the facial aging process, and multiple studies have demonstrated significant craniofacial skeletal changes with age. Sharabi et al. recently reviewed and assembled this information in a concise and cogent fashion (12). The results of their review of work from Barlett et al. (13), Pessa et al. (14–19), Levine et al. (20), Farkas et al. (21), Mendelson et al. (22), and Shaw and Kahn (23–25) indicate that significant and consistent changes occur as the craniofacial skeleton ages. The most consistent findings were a change in contour of the orbit (with superior medial and inferolateral remodeling) and a decrease in the glabellar, pyriform, and maxillary angles.

A recently published retrospective review of computed tomography scans of 100 consecutive patients imaged at Duke University Medical Center including 50 men and 50 women from two age groups, younger (aged 18–30 years) and older (55–65 years), found similar changes (26). Although longitudinal studies would be ideal, the findings described in the aforementioned studies were all found to be statistically significant. These findings are all in agreement with observations published by Pessa et al. over a decade ago noting that an infant’s small craniofacial skeleton as well as age-related bony remodeling caused a decrease in the space available for the soft tissue in the midface, resulting in a “folding in” of the soft tissue in a configuration that resembles an accordion, referred as the “concertina effect,” whereas a youthful face seemed to represent a point in time when a particular set of skeletal proportions are ideal for their soft tissue envelope (27). They are also in agreement with the early work of Enlow (28) and the description of a “clockwise rotation” of the maxilla and mandible with aging as hypothesized by Pessa (17) and Lambros (also over a decade ago). These concepts are well illustrated in FIG. 3 and were, in fact, the impetus for most of the aforementioned studies.

The value of this work lies in its implications for treatment – that is, that the underlying bony structure may be augmented by solid implants, as has been done historically (see FIG. 4), or by

FIG. 2. Nodule versus granuloma. (A) Low-power histopathology of a nodule with an overabundance of product trapped in skeletal muscle. (B) Low-power histopathology of a true granuloma showing an overabundance of host reaction to a small amount of product. Photographs courtesy of Rebecca Fitzgerald, MD.
injectable shaping agents, resulting in the restoration of soft tissue support and therefore a reversal, to some degree, of the concertina effect. FIG. 5 is a computed tomography image of a patient from both the older and younger age groups of the study by Shaw and Kahn (23) illustrating the orbital, glabellar, maxillary, and pyriform aperture changes. Note that the areas of loss with aging correlate to the areas of augmentation with implants pictured in FIG. 4. Craniofacial skeletal support is an important determinant of facial shape. The young and aged face with extreme lipoatrophy shown in FIG. 6 illustrate both the shape of the underlying craniofacial skeleton in youth and aging, as well as the different clinical appearance noted when the overlying outer skin envelope is able, or less able, to accommodate the underlying volume loss.
During the last decade, substantial progress has been made toward understanding underlying mechanisms of human skin aging. A major feature of aged skin is fragmentation of the dermal collagen matrix. collagen fragmentation is responsible for loss of structural integrity and impairment of fibroblast function in aged human skin (29). Fragmentation results from actions of specific enzymes (matrix metalloproteinases) observed in both intrinsic and extrinsic aging. Fibroblasts that produce and organize the collagen matrix cannot attach to fragmented collagen and they subsequently collapse. In aged skin, collapsed fibroblasts produce low levels of collagen and high levels of collagen degrading enzymes. Once a critical amount of collagen has been lost, this imbalance advances the aging process in a self perpetuating, never ending deleterious cycle. The production of new collagen demonstrated by electron microscopy after the injection of hyaluronic acid is felt likely to be due to a mechanical stretch effect, serving to rebalance collagen production and degradation, and thereby slowing its loss (30). This same mechanism may account for the improvement in skin tone and quality seen after collagen-stimulating agents and even fat augmentation as well.

A significant point to note here is that a face with a very elastotic outer skin envelope is very difficult to volumize – with fat or fillers – and may take a substantial amount of product – any product – to achieve a desirable result. This should be expected in this patient population and discussed with a patient such as this prior to any filler treatment.

**Muscle**

The question of whether muscles age histologically or simply change physiologically in response to the aging process of underlying structures is not yet clear. The muscles of facial animation may adjust to shifts in underlying volume by adjusting their resting tone (31,32). It is interesting to note that patients with Bell’s palsy do not develop the same lines and folds as a face with normal innervation. It is also interesting to speculate whether or not this plays a role in the clinical development of peau d’orange of the chin or a downward pull on the oral commissures by the DAO muscles in an aging face losing fat and craniofacial support.

Le Louarn and colleagues (32) have proposed that in youth, deep fat beneath the muscles are responsible for a curvilinear shape and that these structures contribute to the anterior projection that is characteristic of a youthful face. They also hypothesize that loss of volume beneath the muscles occurring with age causes these structures to shorten and straighten, thus contributing to the changes in shape, morphology, and topography of the aging face. This may have important clinical implications pertaining to the depth at which we choose to place our facial fillers.

**Fat**

The youthful face has an ample amount of volume that is evenly distributed, which displays a smooth transition from one area to another and confers a well-rounded 3D topography delineated by a series of arcs and convexities (33). There is no clear distinction between areas such as the temple, lid, and cheek – just one unbroken reflection of light from a convex surface (34). In 2007, Raskin and LaTrenta used cadaver dissections to quantify the differential volume of fat in the human face and neck, as well as to determine the amount of subcutaneous fat both above and below the superficial musculoaponeurotic system. FIG. 7 offers an interesting illustration of the contribution of both superficial and deep fat to the contours and topography of the face. The face and neck were arbitrarily divided into subunits in these specimens (35).
Clinically, this topography is magnified enormously by the effect of light reflection or shadow. This is illustrated in FIG. 8 by high contrast black and white photography in a very lipoatrophic patient immediately after treatment in multiple fat compartments on only one side of the face. The face has an oval shape on the filled side that looks more like a “peanut” on the empty side.

More recently, a series of groundbreaking studies from Rohrich and Pessa et al. have demonstrated that facial fat exists as multiple well-delineated, independent compartments that have specific anatomic relationships to one another and that many of the retaining ligaments that support facial soft tissue originate within the septal barriers between these compartments (36,37). These fascial extensions form a framework that provides a “retaining system” for the human face. Implicit in this concept is the suggestion that the face ages three dimensionally, with separate compartments changing relative to one another by both position and volume.

These compartments exist in both superficial and deep fat, some of which are illustrated here (FIGS 9 and 10). There is good clinical evidence that individual fat compartments age independently, which may have a cascade effect on adjacent areas and have enormous relevance in techniques used for facial filling (38). Because the deep fat is compartamentalized in a fashion similar to the overlying subcutaneous fat, volume loss of specific deep fat compartments leads to predictable changes in the topography of the face. These researchers hypothesize that loss and/or ptosis of deep fat compartments leads to changes in shape and contour of the face. Folds, in contrast,
occur at transition points between thick and thinner superficial fat compartments such as that seen at the nasolabial fold, the labiomental fold, the submental crease, and the preauricular fold (39). This has led to the concept of “pseudoptosis” – that loss of volume in one area may lead to the development of folds in a neighboring area. This is well illustrated by the improvement seen in the nasolabial fold and “v-shaped deformity” under the eye with refilling of the deep medial cheek fat pad accomplished with saline from a single-injection point in the cadaver pictured in FIG. 10 (40). Again, these anatomical observations, combined with Lambros’ theory of age-related deflation, enable the clinician to approach facial rejuvenation in a site-specific manner (rather than

FIG. 7. Facial fat and facial topography. The face and neck are arbitrarily divided into 8 subunits (as numbered above). (A) First, a cadaver shown after the skin alone was dissected off, leaving all subcutaneous fat intact. (B) Second, the cadaver after removal of the superficial fat, the superficial musculoaponeurotic system (SMAS), and the facial mimetic muscles, revealing the deep subcutaneous fat, and (C) finally, the cadaver after removal of all the deep subcutaneous fat, showing enormous loss of contour. (This fat was weighed showing that 57% of the fat mass was found above the SMAS, and 43% was found below the SMAS.) Reproduced with permission from Raskin and LaTrenta (35).

FIG. 8. Clinically, facial topography is enormously magnified by the effect of light reflection or shadow as shown here in a very lipoatrophic face immediately after treatment in multiple fat compartments only on the left side. The face has an oval shape on the filled side that looks more like a “peanut” on the empty side. Photographs courtesy of Rebecca Fitzgerald, MD.
Rohrich and Pessa have performed multiple cadaver studies supporting the concept that subcutaneous fat is compartmentalized, specifically by fascial extensions that travel from superficial fascia to dermis. These fascial extensions form a framework that provides a “retaining system” for the human face. Implicit in this concept is the suggestion that the face ages three dimensionally, with separate compartments changing relative to one another by both position and volume. The nasolabial fat compartment is the most medial of the major cheek compartments. Blue dye has stained this region. The orbicularis retaining ligament is the superior boundary (ORL), and the suborbicularis fat is a lateral and deep boundary (SOOF). Medial cheek fat has been reflected off the nasolabial compartment. The zygomaticus major is tethered at its inferior border (ZM). The ORL is also the superior border of the medial cheek compartment. The middle cheek fat compartment lies between medial and lateral temporal-cheek fat. The superior border is defined by the superior cheek septum (SCS). Reproduced with permission from Rohrich and Pessa (36).
treating the nasolabial or marionette fold in all patients). It also suggests that some regions of the face may “auto” improve with what might be called “indirect treatment” – that is, treatment of one area can beneficially affect one or more adjacent areas.

Understanding and analyzing the aging face/where to place the replacement

In order to solve any problem, one must first define the problem, come up with a solution, and then successfully execute the solution. This section is about defining the problem. As mentioned above, a youthful face represents a point in time when a particular set of skeletal proportions is ideal for their overlying soft tissue envelope – a place we grow into from infancy and away from with age. We may all start, however, with more or less of one structural tissue or another. Additionally, although the sequence of events seen with facial aging are somewhat predictable, the pace of these events is very individualized (even within one tissue in one individual). Facial analysis, then, is a process of observation and palpation/provocation that allows us to determine the nature and extent of the structural tissue changes aging the face in front of us at that particular point in time. It is not a “recipe”; it is a “read.” What you choose to address depends on the extent of changes noted in each structural layer and the parity of these changes between layers. If there is a great deal of disparity, try to blend them all back to a more similar place – i.e., a young patient with severe HIV lipoatrophy, for instance, is a “one tissue issue” just needing volumization of empty fat pads. Most of us, however, tend to lose a little volume in all structural tissue layers. Obviously, all thirds of the face should be addressed so you do not end up with a cosmetic patient who has young lips and cheeks on an otherwise aging face. Patients new to fillers often bring up fear of this kind of “unnatural” result. It is useful to first evaluate the face in terms of the integrity of each structural tissue – skin, fat, muscle, bone. Then, look at what those changes are doing to the face in terms of morphologic changes – the shape, proportions, and topography of the face. This concept of the contribution of each structural layer to the appearance of the face is easy to appreciate when looking at a face with profound congenital asymmetry (FIG. 11). The less volumized side appears to have less brow support (bone and fat), less lateral projection of the cheekbone (bone), less maxillary support for the nose (bone), as well as a shorter chin length (bone and fat). A lid, lid cheek junction, and nasolabial fold are visible only on the less volumized side (perhaps in part because of less deep fat in the mid-cheek as seen on the cadaver specimen in FIG. 10), whereas no such demarcation is visible on the more volumized side.
Look again now at FIG. 1. All structural tissue layers are affected by aging, and there is a change in the topography, shape, and proportions of the face. In this sequence of women, note the deepening of the tear trough, nasolabial fold, and marionette fold as the face loses deep medial cheek fat, similar to the changes seen in FIG. 10. Note that the marionette fold appears more prominent as volume is lost both superior and inferior to the modiolus and the DAO muscle. Locating the precise area of fat loss is often easier to palpate or provoke than to visualize. Also, note the progressive change in the perioral ratio and the position of the nose, as well as the superiomedial and inferiolateral remodeling of the orbit, the flattening of the brow bone and lateral cheekbone, as well as the progressive change in the position of the nose and the perioral ratio (starting in the 30 year old as a 1/3 to 2/3 “golden ratio” and ending in the 60 year old as a 1 : 1 ratio). The 40-, 50-, and 60-year-old patients have all lost varying degrees of fat in the nasolabial compartment as well as the temple and lateral cheek compartment. The 50 and 60 year old also show atrophy of the medial and middle fat compart-ments, although the 50 year old has a large masseter that is compensating for some of this soft tissue loss, leaving her with a jawline that looks longer and straighter than that of the 40- and 60-year old patient. Look at the resting tone of the mentalis and DAOs in the 60 year old at rest (as well as in the 40 year old with mandibular insufficiency).

As the face loses volume with age, the skin also loses elasticity and is no longer able to accommodate the underlying volume loss, causing it to sag and fold.

Now, look at how these structural changes are affecting the morphology of the face. Look at light and shadow, and how it plays off of areas of depression and prominence (convexities and concavities) contributing to (sometimes subtle) changes in facial shape and topography. Palpate and provoke areas of shadow to reveal areas of atrophy.

Look at the shape of the orbits, the bony support under the brow and the nose, and the proportions in the lower third of the face.

Do not focus on just “lines and folds,” but consider all the structural changes in the face and the interdependency between them. Look at the whole face as a 3D interlocking puzzle where losing or correcting one thing may have a negative or positive impact on another. Utilize the emerging concepts of the anatomy of aging in the recent literature, which illustrate the role of bony support and how it changes over time, as well as the anatomy of facial fat compartmentalization to inform site-specific corrections in order to obtain natural-looking results with the least amount of product.

Patient cases

The following patients were analyzed, mapped, and treated with the above information in mind.

In the first case, the injection technique as well as the rationale for placement of product will be discussed. The additional cases were chosen in order to illustrate a couple of patients with a clear-cut “one tissue issue” (one needing only skeletal augmentation, another needing only fat augmentation), as well as some needing various amounts of both. It is our hope that these cases reflect the above description of “looking at the face as a whole” as well as simplify this concept as you begin to see the same pattern emerge on each face – just more or less of it depending on that specific patient. We have also attempted to mark the patients in a manner that illustrates how to best predict the amount of product necessary for a given session.
The legend for markings states the amount of product used in these treatments (FIG. 12). (We have attempted to draw it to scale, i.e., one large X in the temple is 0.3–0.5 cc; for cross-hatch/fanning, three small x’s = 1 cm.) As stated earlier, the amount of product used at any one session is determined solely by the amount of product it will take to “blanket” the surface area you want to treat at that session. The total number of sessions is determined by the total degree (not distribution) of atrophy. This will be illustrated in the following examples.

Patient 1

A 36-year-old woman is pictured in FIG. 13. Her face shows good craniofacial support around her brows and cheekbones, but with minor, early remodeling in the perioral area with a shadowing and depression in the area of the canine fossa/pyriform aperture as well as some shadowing on the chin. It is possible to palpate a slight depression over her mandible in this area. Her skin is very able to accommodate all underlying volume loss. She is very athletic, and her biggest issue is loss of facial fat. She has lost fat in the same pattern on both sides of her face, but both the distribution (surface area) as well as the degree of fat loss on the right are greater than that on the left (meaning she will need more products as well as more sessions on the less volumized side). On close observation of the less volumized side, you can appreciate the loss in the temporal and lateral cheek fat, as well as the nasolabial, medial, and middle superficial fat pads. This is somewhat compensated by her large masseter, which is providing some soft tissue convexity in this area. The area of fat atrophy in her lower face (superior and inferior jowl fat) on this less volumized side leaves a visible demarcation anterior to this muscle, as well as posterior to the orbicularis, that is not seen as a demarcation on the more volumized side.

Rohrich and Pessa feel that the term “malar fat” is likely a combination of nasolabial fat, superior medical fat, and the inferior infraorbital compartments. These lie above the superficial fascia and are therefore superficial compartments. Midfacial adipose tissue includes both malar fat and the deep medial cheek fat, as well as the medical and lateral suborbicularis oculi fat (41). Squeezing this midfacial fat gives an idea of the volume of both. On close observation, it is not hard to appreciate that there is less deep medial cheek fat (and consequently, less anterior projection of the mid-cheek) on the less volumized side. This area will be treated both superior and inferior to, as well as under, the pinched fat. Squeezing the modiolus/DAO reveals an area of atrophy both superior and inferior to this muscle, representing loss of fat in the lateral nasolabial fat compartment as well as loss of volume (both bone and fat) in the chin. Deep fat may contribute to the increased anterior projection of the chin on the more volumized side. Replacing volume lost from both bony remodeling and fat may serve to lengthen the chin.

FIG. 14 illustrates the areas to be injected. The areas that already show prominence and convexity will be avoided – the cheekbone, the masseter, the modiolus/DAO, and the “squeezable” fat in the mid-cheek. The marked areas around the canine fossa/pyriform aperture as well as the mandible will be treated with supraperiosteal injection. An outline of the skeleton was added to the figure for clarity in reference to these injections. The skeletal outline at the edge of the area of convexity where the masseter overlies the mandibular angle in this figure incidentally highlights the lateral cheek fat atrophy. The largest area of loss in this patient is in her temporal and lateral cheek fat. There is some loss in all other superficial and deep cheek compartments, as well as some atrophy of the (superior and inferior) jowl fat. The goal here is not to “fill” this area and make her face look fat or “chipmunked,” but to replace enough of the lost volume to blur the demarcation seen around the muscles on the less volumized side that is not noted on the more volumized side. (This can be accomplished because the total degree of volume is determined by the total number of sessions and not the amount used at one session, allowing for gradual progressive fill of this area and minimizing the risk of “overfill.”) Finally, the deep fat pad that has been
described under the superior and mid-aspect of the mentalis will be filled.

A 9-cc dilution was used for all injections. In the temple, ~7 depot injections of 0.4 cc/cm were carried out, placing the product deeply under the temporalis fascia followed by firm massage (using ~3 cc total) (FIG. 15). In the lateral cheek compartment, fanning injections were placed in the

FIG. 13. 36-year-old female with good craniofacial support, good skin tone, and global mild to moderate fat loss (R > L) most pronounced in her temples and lateral cheeks. Her large masseters are compensating for some of the fat loss in this area. Pinching her “malar” fat reveals the fat atrophy in her midface. Pinching the modiolus is followed by a slow “bounce back” of soft tissue both superior and inferior to the muscle, also indicative of some fat atrophy in this area. Photograph courtesy of Rebecca Fitzgerald, MD.

FIG. 14. Areas of volume loss to be treated in this patient include: (i) suprperiosteal injections along the canine fossa/pyriform aperture as well as the mandible; and (ii) global fat loss in the temple, lateral, and mid-cheek, as well as the lower face. Photograph courtesy of Rebecca Fitzgerald, MD.
subcutaneous tissue posterior to the masseter (FIG. 16). This temporal and lateral cheek fat compartment is the largest area of atrophy on this patient’s face.

FIG. 17 illustrates the technique used to replace deep fat in the medial and lateral cheek, as well as along the zygoma and anterior maxillary wall. These injections are approached with a 25-gauge 1 1/2-inch needle from a site distal to the insertion of the orbicularis oculi muscle. The soft tissue is lifted with the nondominant hand, and these injections are then done deep to this area. These can be done in the pattern of an X, with one diagonal and one horizontal injection with the center of the X at the most atrophic area of the mid-cheek. The superior portion of the diagonal injection is in the area of the deep medial cheek fat, and the inferior portion of this injection is along the medial border of the zygoma. The horizontal injection runs along the anterior surface of the maxilla out to the lateral border of the zygoma. This simple pattern allows for restoration of both anterior and lateral projection of the cheek (which can be likened to the shape of the Nike logo on a left-facing profile). In
this face, one diagonal and one horizontal injection were sufficient to blanket the surface area to be treated at that session. A face requiring more volume (a larger face, or one with more atrophy) may require more than one diagonal and/or horizontal injection. In this case, these injections should be carried out at least 1 cm apart.

In FIG. 18, the areas of loss in the lateral nasolabial, as well as superior and inferior jowl compartments are addressed. The areas of atrophy that most benefit from treatment here are found by provoking weaknesses in the area. The “crevice” created by this provocation is then filled as illustrated. The product is placed in the subcutaneous tissue, deep to the zygomaticus muscle. Product may be placed adjacent to, but not in, the modiolus and the lip depressors.

In some individuals (secondary to genetics, aging, or trauma), a depression referred to as the “canine fossa” can be palpated superior to the canine tooth as pictured in FIG. 19. This area, as well as the rim of the pyriform aperture (recall that the pyriform aperture was found to enlarge by 15–20% in the study by Shaw and Kahn (23)), may be approached directly. A 25- or 26-gauge short needle allows for the ability to reflux prior to each injection – an important consideration as vascular compromise around the angular artery has been reported in this area with use of bulking fillers (42,43). Clinically, injections in this area appear to “push” the soft tissue forward and away from the skeletal platform, resulting in the restoration of a more youthful position of the nose (look again at the position of the nose on the adolescent and the older face in FIG. 3). This may be accompanied by an increase of mucosal show in the upper lip and an accentuation of the philtrum and Cupid’s bow, making the lip appear more everted.
Finally, FIG. 20 shows a supraperiosteal injection done with a short 26-gauge needle along the mandible. A technique similar to that outlined above in the mid-cheek was used by first pulling the soft tissue away from the bone with the non-dominant hand, and then approaching the area from below. Injection of product into the proximal DAO or orbicularis muscle, as well as the mandibular septum will clump the product and should be avoided. The area of fat deep to the mentalis muscle can be approached from lateral to the muscle (which is difficult to lift) on each side. The small surface area to be covered here requires a very conservative amount of product (~0.3–0.5 cc per injection) and serves to efface the labiomental fold.

Eversion of the lower lip may be noted in a patient who still has a fair amount of soft tissue volume in the lips. Incidentally, these last two figures (FIGS 19 and 20) demonstrate a transient effect often seen with nerve blocks, as lidocaine was added to the suspension used here. This is not uncommon and clears rapidly.

FIG. 21 shows the patient before, immediately after, and 1 month after injection. The volume seen immediately after injection is felt to be mechanical distention from the water used to rehydrate the product, and resolves in a few days. In our experience, the patient, at this time, often appears as they would after ~3 total treatments. This can be used to help predict what will be necessary to achieve full correction, i.e., fat faced immediately after will need two or less sessions (as seen here), perfect immediately after will likely need three sessions total, and still atrophic immediately after will need three or greater sessions total. In this patient, another full treatment will be done on the right side of her face. The left side will be treated only in the area of the lateral and middle cheek fat compartment.

**Patient 2**

The 50-year-old female with familial lipoatrophy pictured in FIG. 22 has almost no craniofacial skeletal remodeling – note the prominent supraorbital rim, the position of her nose, and the youthful 1/3 to 2/3 ratio in her perioral area. She does, however, show lipoatrophy, which is both global in distribution and severe in degree of atrophy. Her skin has adjusted pretty well to this profound underlying volume loss, with only a small amount of laxity noted in her neck. This patient then has a clear-cut “one tissue issue,” requiring volumization of the fat compartments. It can be predicted that this patient will require a lot of product/session secondary to the large surface to be addressed, as well as a number of sessions secondary to the degree of atrophy to be addressed. As in the above case, the areas that already show prominance and convexity will be avoided – the cheekbone, the masseter, the modiolus/DAO, and the “squeezable” fat in the mid-cheek. All fat compartments were revolumized. A volume of >5 cc was placed in each temple with about 8 cc used in the cheeks and

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**FIG. 19.** The size of the canine fossa is determined by palpation above the canine tooth. This area is approached directly with a 26-gauge 1/2-inch needle. A reflux maneuver was carried out prior to each injection to ensure that the needle tip had not been placed in a vessel. Photograph courtesy of Rebecca Fitzgerald, MD.
lower face/side. Note again the amount of fat behind the hairline in the cadaver dissection used to demonstrate the borders of the temporal and lateral cheek fat pad in FIG. 9. Replacement of volume in this area serves to re-ovalize a “peanut”-shaped head as seen in FIG. 8. A total number of nine vials were used in this patient. The final picture was several months after the final treatment. More than this may be required in a large male face with severe HIV-related lipoatrophy. This is a face often felt to be “the perfect candidate” for PLLA. These are, in fact, difficult faces to fill with any product. Be aware that this is an issue of patient selection and not product selection.

**Patient 3**

The 40-year-old female pictured in FIG. 23 has great skin tone and a good amount of soft tissue in her face, but on close observation, she has a lack of underlying craniofacial support. This is likely a genetic issue now exacerbated by aging. Look at the subtle but pleasing result possible from addition of volume in a supraperiosteal location along the superior orbital rim, the canine fossa, anterior
FIG. 21. The patient is pictured here before, immediately after, and 1 month after injection. The volume seen immediately after injection is felt to be likely because of mechanical distention and resolves in a few days. In our experience, the patient, at this time, often appears as they would after ~3 total treatments. This can be used to help predict what will be necessary to achieve full correction, i.e., fat faced immediately after will need two or less sessions (as seen here), perfect immediately after will likely need three sessions total, and still atrophic immediately after will need three or greater sessions total. In this patient, another full treatment will be done on the right side of her face. The left side will be treated only in the area of the lateral and middle cheek fat compartment. Photograph courtesy of Rebecca Fitzgerald, MD.
maxilla and zygoma, as well as the mandible. Note that this required a very conservative amount of product – only one vial total, as only a small amount of surface area needed to be treated, and only a small degree of atrophy was present. The final picture was taken 1 month after the treatment.

**Patient 4**

In contrast to patient 2, the 52-year-old woman pictured in FIG. 24 has lost only a small amount of volume and only in very focal areas. It can be predicted that she will not need much product/session or many sessions to correct. A total of two
vials were used in this patient. Supraperiosteal injections along the superior orbital rim, lateral cheek, and mandible were done to address flattening seen clinically in those areas. Additionally, this patient is a good clinical example of the concept of “pseudoptosis” mentioned earlier. This was addressed with replacement of deep volume in the midface and lateral face. The treatments were

FIG. 24. In contrast to patient 2, the 52-year-old woman pictured here has lost only a small amount of volume (in fat and bone) and only in very focal areas. She has good skin tone. It can be predicted that she will not need much product/session or many sessions to correct. Photograph reprinted with permission from Fitzgerald R, Vleggaar D. Poly-l-lactic acid. In: Jones DH, ed. Injectable fillers: principles and practice. London: Wiley Blackwell, 2010: 54–74.

FIG. 25. A total of two vials were used in this patient carried out with one vial/session and two sessions placed in the areas pictured. She did not require treatment in her temples, which accounts for the small amount of product needed for this result. Photograph reprinted with permission from Fitzgerald R, Vleggaar D. Poly-l-lactic acid. In: Jones DH, ed. Injectable fillers: principles and practice. London: Wiley Blackwell, 2010: 54–74.
FIG. 26. This 30-year-old “baby-faced” woman presented with poor craniofacial support, resulting in a “concertina effect” as described earlier. Product was placed supraperiosteally along her superior lateral orbital rim, zygoma, canine fossa, and mandible in roughly the same areas that would be treated with a solid implant. Deep injections along the lateral zygoma and the temple were carried into the hairline. Deep soft tissue injections were done in the mid-cheek and chin, and a small amount of product was placed supraperiosteally 1 cm below the infraorbital rim. It can be predicted that she will need a fair amount of product in order to fill the large surface area of volume loss in her temples. Photograph reprinted with permission from Fitzgerald R, Vleggaar D. Poly-l-lactic acid. In: Jones DH, ed. Injectable fillers: principles and practice. London: Wiley Blackwell, 2010: 54–74.

FIG. 27. This patient was injected with two vials of poly-l-lactic acid/session over two sessions spaced 2 months apart. Almost an entire vial was split between her temples in each treatment. No other treatments were carried out in this patient (no botulinum toxin). Note the brow elevation as well as the change in her facial shape and perioral ratio with these treatments. Photograph reprinted with permission from Fitzgerald R, Vleggaar D. Poly-l-lactic acid. In: Jones DH, ed. Injectable fillers: principles and practice. London: Wiley Blackwell, 2010: 54–74.
carried out several months apart in order to avoid inadvertently “overvolumizing” her face. The results are shown in FIG. 25.

Patient 5
The 30-year-old “baby-faced” woman in FIG. 26 presented with poor craniofacial support, resulting in a concertina effect as described earlier. She was injected with two vials of PLLA/session over two sessions spaced 2 months apart. Almost an entire vial was split between her temples in each treatment. Additionally, the product was placed supraperoisteally along her superior lateral orbital rim, zygoma, canine fossa, and mandible in roughly the same areas that would be treated with a solid implant. Deep injections along the lateral zygoma and the temple were carried into the hairline. Deep soft tissue injections were done in the mid-cheek and chin, and a small amount of product was placed supraperiosteally 1 cm below the infraorbital rim. No other treatments were carried out in this patient (no botulinum toxin). Note the brow elevation as well as the change in her facial shape and perioral ratio with these treatments in FIG. 27.

Patient 6
The 47-year-old woman in FIG. 28 presented with clinical evidence of early mild bony remodeling noted in her canine fossa and mandible (a common finding in this age group). She also has a wide distribution, but small degree, of fat atrophy in her midface and lower face. She had only a small amount of loss in her temples (not pictured here). It can be predicted that she will need only a conservative amount of product. Photograph courtesy of Rebecca Fitzgerald, MD.

FIG. 28. This 47-year-old woman presented with clinical evidence of early mild bony remodeling noted in her canine fossa and mandible (a common finding in this age group). She also has a wide distribution, but small degree, of fat atrophy in her midface and lower face. She had only a small amount of loss in her temples (not pictured here). It can be predicted that she will need only a conservative amount of product. Photograph courtesy of Rebecca Fitzgerald, MD.

FIG. 29. The result above is after treatment with one vial/session, two sessions. Note the change in facial shape. Note also how the small change in topography of her face is magnified by light and shadow. Lastly, this patient is a good example of how the perioral ratio can be manipulated with injections. The deep injection along the bone and in the deep submental fat efface the labiomental fold, and the mentalis muscle seems to have relaxed, making the chin appear longer. This patient was also treated with one syringe of hyaluronic acid in her lower lip. Photograph courtesy of Rebecca Fitzgerald, MD.
injections. The deep injection along the bone and in the deep submental fat efface the labiomental fold, and the mentalis muscle seems to have relaxed, making the chin appear longer. This patient was also treated with one syringe of hyaluronic acid in her lower lip.

FIG. 30 summarizes the above concepts. Both of these patients were treated in a fashion similar to the above patients with supraperiosteal injection along the zygoma, anterior maxillary wall, canine fossa, and mandible. Fat atrophy was treated in the temporal and lateral cheek fat compartments as well as in fat compartments of the midface and lower face. Both of these patients were also treated with one syringe of hyaluronic acid in their lower lip.

The 42-year-old woman required much less products/session and fewer sessions than the 60-year-old patient with elastotic skin. Note the anterior and lateral projection of the cheeks achieved with the technique shown in FIG. 17. Also note the subtle change in the position of the nose and the lengthening of the chin with supraperiosteal injections around the canine fossa and mandible. Note that the increased surface area over which the outer skin envelope drapes leads to an improvement of laxity along the jawline without directly treating this area. Photograph courtesy of Rebecca Fitzgerald, MD.

**Conclusion**

The above summarizes our technique with PLLA in order to address the changes observed in the aging face. It is interesting to reflect that historically, we learned to use this product on the most difficult patients first, and with suboptimal techniques (almost like using a 10-cc dilution of botulinum toxin on the lower face before using a 2.5-cc dilution in the glabella), leaving a bit of a residual “fear factor” in some physicians.

As experience has been gained with this product and technical issues have evolved, it has been found to be a safe and effective product with predictable and reproducible results (2,7–9). Subtle, natural, and pleasing results of long duration can be obtained with a reasonable amount of product utilizing the emerging concepts of the pathophysiology of facial aging in order to optimize site-specific corrections. Evaluate each patient individually by looking for evidence (and location) of skeletal remodeling versus fat atrophy versus both processes. Determine prior to the start of treatment if fillers are a cost-effective choice for the patient. Remember that very empty and very elastotic faces are very difficult to fill (regardless of product choice). A patient with severe global lipoatrophy and a thin body with no fat donor sites may have limited choices for rejuvenation and may therefore choose fillers regardless of cost. This may be accom-
plished with less products in a patient with good skin elasticity. A patient with an outer skin envelope that is no longer able to accommodate any underlying volume loss should be made aware that replacement of volume may not give the results desired without also addressing the excess skin. A cosmetic patient with skeletal atrophy and/or fat loss, and an outer skin envelope with good tone is a great candidate for fillers, including PLLA. A cosmetic patient with skeletal atrophy and/or fat loss, and an elastotic outer skin envelope may be best served with surgical modalities such as solid implants or fat augmentation, as well as a surgical face lift. Remarkably, nice results may be obtained in these patients with fillers, including PLLA, but it requires a lot of product. Very pleasing results can be obtained with more conservative amounts of product in younger or fuller faced patients. Our experience with PLLA has been one of very high physician and patient satisfaction. Review of the current literature also reports a high patient satisfaction (44). Optimizing outcomes and minimizing adverse events with this product are not difficult but do require awareness of and attention to its specific and evolved injection methodology, and are enhanced by a careful facial analysis prior to treatment. It is our hope that this information will raise that awareness.

References

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