Dermal Fillers

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The dermal filler market is rapidly growing worldwide. According to the American Academy of Aesthetic Plastic Surgeons, 1,448,716 people received hyaluronic acid (HA) injections by plastic surgeons in 2007 (Table 23-1). The actual number is likely much higher when factoring in procedures performed by dermatologists and other aesthetically oriented physicians and physician extenders. Although collagen products (Zyplast and Zyderm) were the first dermal fillers to become widely available, collagen fillers have largely been replaced by HA fillers.

The ultimate goal of dermal fillers is to smooth out wrinkles and folds, even out scars, volumize furrows and sunken valleys, contour unevenness and laxity, and sculpt skin into a 360-degree, rejuvenated look. Over the last quarter century, several kinds of products suitable for soft tissue augmentation have become available, with intense industry research yielding more and more filler options with increasing regularity. Different regulatory mechanisms usually leave the US a few months or years behind other developed countries in making the latest products available to patients.

### HISTORY

In 1893, by transplanting fat from the arms into facial defects, Neuber became the first physician to practice soft tissue augmentation. In the middle of the 20th century, soft tissue augmentation could best be characterized by the use of silicone. Although popular in the 1940s and 1950s, silicone use was associated with the development of foreign body granulomas, which ultimately prompted the banning of silicone in 1992 until a new form of the substance (intended for ophthalmologic use) was approved by the United States Food and Drug Administration (FDA) in the late 1990s. In the meantime, though, the field of soft tissue augmentation had come into its own, in the 1970s, with the introduction by Stanford University researchers of animal-derived collagen implants. By the 1980s, the use of collagen injections for wrinkles had entered the mainstream. While Americans were enjoying the benefits of bovine collagen fillers (i.e., Zyderm and Zyplast), other countries began to experiment with dermal HA fillers such as Hylaform and later Restylane in the mid to late 1990s. The beginning of the 21st century ushered in the introduction of newer nonbovine collagen fillers, Cosmopolitan and Cosmoblast, and HA fillers, such as Captique and Juvederm, as well as other synthetic fillers, Sculptra, Radiesse, and Artefill into the United States market. With different forms of soft tissue augmentation agents currently available in the United States and others in the pipeline, selecting the appropriate filler is challenging for physicians and patients alike. In order to achieve optimal cosmetically-pleasing results, it is incumbent upon dermatologists to obtain thorough comprehension of the characteristics of available fillers, their indications, contraindications, benefits and drawbacks, and ways to resolve potential complications. In this chapter, we will review the basics behind the art and science of the broad array of dermal fillers on the market in the United States. This will be preceded by a brief discussion of regulatory issues and the patient evaluation and consultation.

### PATIENT EVALUATION AND CONSULTATION

When embarking on soft tissue augmentation, proper preparations are essential. An initial consultation should include distant and close evaluation of the patient's facial structure and discussion of the cosmetic treatment options. The patient's history is taken to assess contraindications including allergy to filler components, herpes facialis, pregnancy/lactation, keloid predisposition, and autoimmune diseases. In addition, use of medications that inhibit clotting such as aspirin and ibuprofen should be examined. The ideal cosmetic outcome is achieved through a combination of various cosmetic procedures in order to attain an even tone, smooth texture, and adequate facial volume and shape. The discussion of the sequence and description of each proposed procedure, alternatives, risks and benefits, financial cost, and recovery period prepares the patient for realistic expectations and informed decision-making. After the treatment procedures are selected and informed consent is signed and witnessed, the patient should undergo pretreatment photography for the purpose of documentation; posttreatment photography is scheduled immediately after and on the follow-up visits. For novice patients, it is better to start the soft tissue intervention with the temporary and predictable fillers (e.g., collagen and HA), and then gradually advance with more lasting fillers (e.g., Sculptra and Radiesse) based on their comfort level and desire. The best approach to minimizing the side effects of soft tissue augmentation.

### TABLE 23-1

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Number Performed in 2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat injections</td>
<td>44,547</td>
</tr>
<tr>
<td>Calcium hydroxylapatite</td>
<td>119,397</td>
</tr>
<tr>
<td>(Radiesse/Radiance)</td>
<td></td>
</tr>
<tr>
<td>Collagen</td>
<td>63,769</td>
</tr>
<tr>
<td>Hyaluronic acid</td>
<td>1,448,716</td>
</tr>
<tr>
<td>Sculptra (not yet FDA approved)</td>
<td>34,972</td>
</tr>
<tr>
<td>Polyethyl methacrylate</td>
<td>12,075</td>
</tr>
<tr>
<td>(Artecoll, Artefill)</td>
<td></td>
</tr>
</tbody>
</table>

Data obtained from www.surgery.org.
Dermal fillers can be classified based on various criteria: depth of implantation (superficial upper and middermis, deep dermis, and subcutaneous levels); longevity of correction (temporary, semipermanent, and permanent); allergenicity (whether preprocedure allergic testing is required); composition of the agent (xenografts, allografts, or autologous, semi/fully synthetic); and stimulatory behavior (capacity to drive physiologic processes of endogenous tissue proliferation) versus replacement fillers (space-replacing effect). Safety and efficacy studies of the available fillers are required by the FDA; however, studies looking at the durability of the filler are not required and, therefore, subject to disagreement and frequent citing of anecdotal evidence. The lasting effect of the filler is dependent on the composition, amount used, depth injected, and carrier of the agent. Our discussion of fillers will proceed by dividing them according to composition: collagen fillers will be discussed first, followed by HA fillers, and then other agents.

### TEMPORARY FILLERS

Injectable fillers such as collagen and HA are biodegradable and last from 4 to 9 months. These fillers commonly serve an important role as the initial step for new patients interested in soft tissue augmentation. Because of their transient effect, the potential patient dissatisfaction and side effects are also short-lived. Therefore, temporary fillers should always be the first line of therapy, saving the longer-lasting fillers for future patient visits.

#### Collagen

The major structural component of the dermis, collagen, is the most abundant protein in the human organism as well as the skin, in particular, and confers strength and support to the skin. Collagen is also one of the strongest natural proteins, imparting durability and resilience to the skin, and comprising 70% of dry skin mass (see Chapter 2). What is known as “collagen” is actually a meshwork of scaffolding-like structures composed of a complex family of over 18 types, 11 of which are found in the dermis. Type I collagen (80%–85%) and type III collagen (10%–15%) are the primary collagen constituents in the dermal matrix of adult human skin. Dermal fibroblasts produce a precursor form of collagen, α procollagens, which in turn produce both collagen types I and III, each of which is composed of three collagen chains.

Skin fragility and wrinkles result from the loss of collagen, which occurs with aging as well as solar exposure and other insults. UV light, free radicals, and other factors cause the body to produce collagenase, an enzyme that breaks down collagen. The injection of various forms of collagen into the skin helps it regain a youthful appearance, but such results are temporary. The range of collagen products has increased in recent years as manufacturers have worked to extend the duration of product effects.

#### BOVINE COLLAGEN

**Overview** With a record of safety and efficacy spanning over two decades, bovine collagen was the traditional dermal filler agent used to ameliorate undesirable signs of cutaneous facial aging. In 1977, Zyderm I was introduced as the first injectable bovine collagen implant; it was approved by the FDA in 1981 for fine lines and shallow acne scars. Zyderm II and Zyplast were introduced and approved, respectively, in 1983 for moderate lines and deeper acne scars and 1985 for deep dermal folds and lines. Although these products were the standard for years to which newer implants were compared, because of better safety profiles, human-derived collagen and HA products have become more widely used. Zyderm I is 96% type I collagen and 4% type III collagen derived from the bovine skin of US enclosed cattle herds. Zyderm I and II differ only by collagen concentration. Zyderm I contains 35 mg/cc, while Zyderm II contains 65 mg/cc. The difference in concentration is significant insofar as it renders Zyderm II thicker and stiffer than Zyderm I. Like Zyderm I, Zyplast contains 35 mg/cc of collagen, but this collagen is cross-linked with glutaraldehyde, which makes it last longer via resistance to degradation (Table 23-2). Consequently, Zyplast is more viscous and less immunogenic than Zyderm.

Zyderm and Zyplast are white substances prepackaged in 0.5-, 1-, and 2-mL syringes and injected with a 30-gauge 0.5-inch needle. The product should be stored in the refrigerator ideally at 4°C. While Zyderm I is properly injected into superficial dermis at 20- to 30-degree angles with the expectation of temporary skin blanching, Zyderm II can be injected slightly deeper at 35- to 45-degree angles with less anticipated blanching and minimal overcorrection.

#### TYPES OF FILLERS

Dermal fillers can be classified based on various criteria: depth of implantation (superficial upper and middermis, deep dermis, and subcutaneous levels); longevity of correction (temporary, semipermanent, and permanent); allergenicity (whether preprocedure allergic testing is required); composition of the agent (xenografts, allografts, or autologous, semi/fully synthetic); and stimulatory behavior (capacity to drive physiologic processes of endogenous tissue proliferation) versus replacement fillers (space-replacing effect). Safety and efficacy studies of the available fillers are required by the FDA; however, studies looking at the durability of the filler are not required and, therefore, subject to disagreement and frequent citing of anecdotal evidence. The lasting effect of the filler is dependent on the composition, amount used, depth injected, and carrier of the agent. Our discussion of fillers will proceed by dividing them according to composition: collagen fillers will be discussed first, followed by HA fillers, and then other agents.

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**TABLE 23-2**

<table>
<thead>
<tr>
<th>Collagen from Cow Hide</th>
<th>Collagen from Bioengineered</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zyderm I</td>
<td>CosmoDerm I</td>
<td>35 mg collagen/cc</td>
</tr>
<tr>
<td>Zyderm II</td>
<td>CosmoDerm II</td>
<td>65 mg collagen/cc</td>
</tr>
<tr>
<td>Zyplast</td>
<td>CosmoPlast</td>
<td>35 mg collagen/cc cross-linked with glutaraldehyde</td>
</tr>
</tbody>
</table>
Since Zyderm is diluted with phosphate-buffered sterile saline, which is rapidly reabsorbed in skin, to achieve the optimal effect, overcorrecting implantation is necessary. Zyplast is implanted into even deeper dermis at 45- to 90-degree angles with minimal delayed blanching and without overcorrection.

**Benefits** Bovine-derived collagen dermal filling agents effectively reduce wrinkles and scars. Zyplast is appropriate for shaping the vermilion border of the lips and treating moderate and deep wrinkles, such as nasolabial folds and atrophic scars. Zyderm I is well suited for treating superficial rhytides (e.g., horizontal forehead wrinkles, crow’s feet, fine perioral wrinkles, and scars) or for use over Zyplast in deeper wrinkles. The higher concentration of collagen in Zyderm II renders this product more appropriate for acne scar revision (see Chapter 26), but Zyplast lasts longer because it is cross-linked. Collagenase ultimately succeeds in degrading these products, returning the skin to its appearance prior to injection. Zyplast is the most commonly used bovine collagen product and lasts approximately 4 months, just slightly longer than Zyderm I and II. Bovine collagen can be safely reinjected 3 to 4 times per year if needed. Zyderm and Zyplast are the least expensive dermal fillers on the market and typically engender less bruising than products that contain HA. All the bovine collagen products contain 0.3% lidocaine to reduce the pain associated with the procedure.

**Drawbacks** Two skin tests, 6 and 2 weeks before the scheduled treatment, are required before the use of bovine collagen agents to reduce the risk of inducing hypersensitive or allergic reactions. Such responses can occur as early as 6 hours after the test, but are more likely to emerge 48 hours or 4 weeks after the test. A positive skin test disqualifies a patient for treatment with bovine collagen.

Approximately 3% of the general population is thought to be sensitive to bovine collagen. Although a patient is unlikely to react to bovine collagen implants after two negative skin tests, the risk is never completely eliminated. The risk of hypersensitive reaction is 1.3% to 6.2% after one negative test and 0.5% after two negative tests (Fig. 23-1). Patients should be advised that should such a reaction occur, it can be expected to spontaneously resolve within 4 to 24 months. Allergic reactions also arise, albeit rarely, following multiple treatments. Topical, intralesional, or a brief course of systemic corticosteroids can be effective to treat these reactions. Oral cyclosporine and topical tacrolimus have also reportedly been used for the successful treatment of recalcitrant hypersensitive reactions to bovine collagen. Patients with lidocaine hypersensitivity are contraindicated for obtaining these injections because the fillers contain lidocaine.

Nonhypersensitive reactions to bovine collagen fillers can also infrequently occur (e.g., abscesses, bacterial infections, beading, cyst and granuloma formation, ecchymoses, and local necrosis). Several previously discussed preventative steps can be taken to reduce the likelihood of such outcomes. Because of its viscosity, Zyplast should not be injected into the glabellar region, as there have been reports of local necrosis and retinal artery occlusion leading to visual loss. However, Zyderm I or II can be injected into the glabellar area very slowly and with extreme caution. Vascular occlusion or compression manifests as prominent...
immediate blanching and pain. Warm compresses, topical nitroglycerin, and meticulous wound care are necessary treatments. Prior to 1990, beads and cysts were reported at the injection site in 0.04% of patients treated with Zyderm or Zyplast, most likely caused by injections that were too superficial. Injections should be made only into the dermis to avoid such reactions. Abscesses should be treated with incision and drainage and a combination of antibiotics and corticosteroids to reduce secondary scarring. More than a decade ago, there was some speculation that autoimmune diseases, namely, polymyositis and dermatomyositis, might be induced by the injection of bovine collagen, but studies have demonstrated that antibodies to bovine collagen do not cross-react with human collagen. Therefore, the FDA has agreed that it is unlikely that bovine collagen causes connective tissue disease in humans. Further, a study by Hanke et al. showed that the incident rate of polymyositis/dermatomyositis in patients receiving bovine collagen was not higher than the control-matched population. However, the authors recommend avoiding the use of bovine collagen-containing fillers in patients with a history of autoimmune disease. Another major downside to using bovine collagen is the minimal durability of about 3 to 4 months.

**Bioengineered Human Collagen**

*Overview* Over the last 10 years, several companies, motivated by the drawbacks of bovine-derived collagen, have developed human-derived soft tissue fillers. Unlike earlier cadaver-derived collagen (i.e., Cymetra) and, more recently, autologous collagen (i.e., Isolagen), bioengineered human collagen is pregenerated to ensure ease of accessibility. The manufacturing process begins with the harvesting of dermal fibroblasts from bioengineered human skin and placement into a three-dimensional mesh. The fibroblasts are then cultured in a bioreactor that simulates the conditions of the human body. Then, the fibroblasts synthesize collagen and extracellular matrix proteins. The derived collagen is purified to enhance safety. Human-bioengineered collagen implants include CosmoDerm I, CosmoDerm II, and CosmoPlast (Allergan Corporation, Irvine, CA), which contain human collagen types I and III, and were approved by the FDA in March 2003. CosmoDerm I is composed of 35 mg/cc human-bioengineered collagen distributed in a phosphate-based saline solution and 0.3% lidocaine. CosmoDerm II contains twice the collagen concentration of CosmoDerm I. CosmoPlast contains the same ingredients as CosmoDerm I, but is cross-linked by glutaraldehyde, yielding a product more resistant to degradation, thus lasting longer, and more appropriate for use in treating deeper furrows. While CosmoDerm is indicated for superficial wrinkles and shallow scars, CosmoPlast, which exhibits a stiff consistency (even more so than products containing HA), is well suited to treating the vermilion border of the lips (Fig. 23-4), as well as raising the corners of the mouth. In addition, it is a good choice to correct deformities of the bridge of the nose or to raise the nasal tip (Fig. 23-5). CosmoPlast is typically used in combination, usually with an HA agent, to treat medium and deep wrinkles, with the collagen product injected first to create a volume-filling base and the HA filler injected more superficially into the same location.

Similar to bovine collagens, CosmoDerm and CosmoPlast are white substances prepackaged in 1-mL syringes and injected via 30-gauge 0.5-inch needles. Although some anecdotal reports indicate better rheology of human collagen fillers, their technique of injection, cosmetic outcome, and durability are
CosmoPlast or Restylane is This patient has a dropped nasal tip. Options to raise the tip include a dermal filler or a botulinum toxin. This acellular and purified filler 21

Tunneling and threading CosmoPlast can create the HA, Given the absence of allergy B. Approved by the FDA in Based on the composition of addition, to treat medium and deep wrinkles, HA fillers can be superimposed in the skin and other tissues (specifically, connective, epithelial, and neural tissues) as space-occupiers of the

Benefits Given the absence of allergy risk associated with these agents, no skin testing is required. This allows for patients to be treated in their initial visit to the physician. The cosmetic effects of CosmoDerm and CosmoPlast are immediate, lasting about 3 months for the former and about 4 months for the latter, and are typically associated with less bruising than the effects of procedures using agents containing HA. Also similar to the bovine-derived fillers, CosmoDerm and CosmoPlast contain lidocaine to mitigate the pain of injection and lower the risk of edema and ecchymoses by inhibiting the activation of eosinophils. CosmoPlast can create the beautiful “Snow White line” and “Cupid’s bow” shape of the lip borders as well as upturn the tip of the nose to create a poised appearance. Although HA fillers are favored because they last longer and are softer, CosmoDerm I can be used to plump the body of the lip. CosmoDerm I can be layered over CosmoPlast for the purpose of ideal contouring of deep lines, such as nasolabial folds and marionette lines. In addition, to treat medium and deep wrinkles, HA fillers can be superimposed on top of CosmoPlast or injected in the same plane as CosmoPlast. Although fillers should be used rarely and with great caution in the glabellar rhytides because of the potential risk of tissue necrosis, CosmoDerm I can be used with great care in this region. At the time of publication of this text, there were no HA fillers geared for superficial placement, although Prevelle, Juvederm, and Restylane may have superficial fillers soon. Therefore, CosmoDerm I, although it lasts only about 3 months, is the filler of choice for peri-orbital wrinkles and smoker’s lines above the top lip. CosmoDerm II is most often used for acne scars.

Drawbacks Bioengineered human-derived collagen is expensive to produce, rendering these agents somewhat costly. Further, the cosmetic effects from these products do not last, on average, any longer than the bovine-derived products. The duration is thought to be around 4 months. However, these products are associated with less bruising, erythema, and pain than other filling agents and, consequently, remain desirable options for those who cannot afford to have downtime. Excluding the reduction in immunogenic potential, human collagen fillers have similar side effect profiles to bovine collagen fillers. Likewise, patients with lidocaine allergies should avoid these agents.

CADAVERIC COLLAGEN Overview Approved by the FDA in 2000 for soft tissue augmentation, Cymetra® (LifeCell Corp., Palo Alto, CA) is a micronized collagen derived from processed human cadaver skin. A similar product, Fascia (Fascia Biosystems, Beverly Hills, CA), is obtained from cadaver fascia, and has a heavier consistency. Cymetra is packaged as a 330-mg white powder in a 5-cc syringe, stored at room temperature and reconstituted with 1 ml of 1% lidocaine to create a thick paste. Tunneling and threading injection methods are accomplished through a 26-gauge syringe into a subcutaneous plane, avoiding overcorrection.

Benefits This acellular and purified filler negates a potential sensitivity reaction and pretesting is, therefore, unnecessary. The cadaver collagen has somewhat longer durability versus other collagen products, lasting from 3 to 9 months, although durability is controversial. Cymetra is indicated for use in deep rhytides (i.e., nasolabial folds), depressed scars, and volumizing of the lips. Reconstitution with lidocaine yields reduction in intraprocedural pain.

Drawbacks Based on the composition of the product, Cymetra is contraindicated in patients with gentamicin allergies. The product is very viscous, which makes it difficult to operate, generating more local tissue discomfort and trauma as well as leading to longer recovery time for patients. Fascia is an even thicker and stiffer product, which translates to more side effects and difficulty in administration. The implantation of cadaver products into superficial and mobile wrinkles can induce migration and, therefore, is discouraged. The major issues with employing these agents are the cumbersome preparations and deficit of adequate clinical trials demonstrating their long-term efficacy and safety.

Hyaluronic Acid In the last few years, HA filler substances have become the new gold standard, far outpacing in usage the other soft tissue augmentation agents. HA, or hyaluronic, is a nonsulfated glycosaminoglycan (GAG) that occurs naturally in the skin and other tissues (specifically, connective, epithelial, and neural tissues) as space-occupiers of the
extracellular matrix. HA is also ubiquitous across animal species, which makes it nonimmunogenic. This polysaccharide has the capacity to bind water up to 1000 times its mass. The biologic behavior of HA is predictable; it creates lubrication and volume with an aqueous and pliable framework that suspends and adheres to collagen, elastin, and cells. With age, the concentration of HA in skin decreases, translating to more lax, sallow, and dull skin. The viscoelastic qualities of HA serve to plump up the skin, yielding a more youthful appearance. Naturally-occurring, unmodified, or uncross-linked HA has a half-life of about 24 hours. For this reason, HA is cross-linked when formulated into a dermal filler product. Higher concentrations and moderate cross-linking of the HA in a product impart greater longevity. There exists a certain threshold where beyond that value additional cross-linking can cause biocompatibility issues. In effect, cross-linking has to be in the right balance to maintain duration and biocompatibility of the HA filler. HA is readily metabolized by the liver into by-products, water, and carbon dioxide. In the skin, HA is broken down by hyaluronidase, mechanical degradation caused by facial movement, and by free radicals. Supplementation with oral antioxidants theoretically will increase the duration of HA fillers, but this has not been proven (see Chapter 34).

There are two main categories of HA fillers: animal derived (e.g., Hylaform) and bacteria derived (e.g., Restylane, Captique, Juvederm, etc). Medicis, the company that sells Restylane, trademarked the name “nonanimal derived synthetic hyaluronic acid (NASHA)” to show that their products, Restylane and Perlane, are not animal based. Because of the expense of animal-derived products, the vast majority of HA products are bacterial derived. At the time this chapter was written, no HA products on the market contained lidocaine and, therefore, were more painful than fillers that contain lidocaine. However, lidocaine-containing injectables, such as Prevelle Silk, have recently entered the market. Because of their nonallergenic nature and manufacturing, HA fillers do not require prior testing and can be stored at room temperature. Their advantages over collagen products are longer duration (6–12 months), better pliability, and less immunogenic and allergic side effects. On the whole, side effects of various HA fillers are similar, mild, and rare; these include bruising (Fig. 23-6), temporary swelling, lumps, acneiform eruptions, and, rarely, acute hypersensitivity. In addition, arterial occlusion, thought to be due to swelling of the HA implant, causing vascular compromise, can rarely occur. (Fig. 23-7). A major advantage of HA fillers is that if skin nodules do arise, these reactions can be easily dissolved with intralesional hyaluronidase (Fig. 23-8). The disadvantages of the currently available HA fillers are increased pain on injection and post-procedure edema, erythema, and ecchymoses as compared to CosmoPlast injections.

CONSIDERATIONS IN CHOOSING AN HA FILLER HA fillers do not require skin testing and the risk of allergy with all products that are FDA approved is minimal. Cost, availability, duration of correction, and size of the required needle for injection all play a role in product selection and manufacturers all strive to create an affordable, long-lasting product that can be injected with a 30-gauge or smaller needle. However, there are other, less obvious, scientific considerations to be taken into account when choosing a filler (Table 23-3). The stiffness or G’ (G prime) of a product is one of the most important considerations. G’ is a measurement of gel hardness. It is obtained when a gel is placed on a plate. A second plate is placed over the

**FIGURE 23-6** This is a common site at which bruises occur after a dermal filler is injected.

**FIGURE 23-7** This patient developed redness, blisters, and lumps after receiving an HA injection. The most likely cause was vascular compromise due to swelling of the implant. All cultures were negative, other treated sites were normal and the lesions resolved without scarring.
CHAPTER 23
DERMAL FILLERS

**TABLE 23-3**
Factors to Consider When Choosing a Hyaluronic Acid Filler

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration of HA</td>
<td>Cost</td>
</tr>
<tr>
<td>Cross-linking</td>
<td>Degree of cross-linking</td>
</tr>
<tr>
<td></td>
<td>Quantity of HA cross-linked versus uncross-linked</td>
</tr>
<tr>
<td></td>
<td>Type of cross-linking technology used</td>
</tr>
<tr>
<td></td>
<td>Duration of correction</td>
</tr>
<tr>
<td></td>
<td>G’ (elastic modulus)</td>
</tr>
<tr>
<td></td>
<td>Hydration level of product in the syringe</td>
</tr>
<tr>
<td></td>
<td>Presence of lidocaine</td>
</tr>
<tr>
<td></td>
<td>Required needle size for injection</td>
</tr>
<tr>
<td></td>
<td>Sizing technology</td>
</tr>
<tr>
<td></td>
<td>Syringe</td>
</tr>
<tr>
<td></td>
<td>Design of syringe</td>
</tr>
<tr>
<td></td>
<td>Size</td>
</tr>
</tbody>
</table>

Gel and a lateral force is applied. The measurement of resistance to deformation is known as the elastic modulus or the G’ (Fig. 23-9). Together with the cohesivity of the product, G’ values could be used to determine the appropriate placement of an HA dermal filler. For example, more robust products (higher G’ values and higher cohesivities) such as Juvéderm Ultra Plus and Perlane, in the primary author’s opinion, should be used in deeper lines, such as nasolabial folds and marionette lines, as well as to lift the lateral brow, to correct the nasal bridge, to give the ear lobe youthful volume, to evert the nipples, and to raise the nasal tip. More fluid products such as Juvéderm Ultra and Restylane are better suited to be used over large areas such as the cheekbones and cheeks. Low G’ products such as Hylaform and Juvéderm Ultra are necessary in areas that require a softer agent, such as the body of the lip or the tear trough. As new products reach the market, knowing the G’ will help practitioners match fillers with indications.

The concentration of HA in a product is important to consider as well (Table 23-4). Many authorities believe that the higher the concentration of HA, the stiffer the product and the longer its duration. This is true in general when comparing products within a brand, for example, when comparing Juvéderm 18 to Juvéderm 24. However, this does not hold true across brands because not all of the HA in the dermal fillers is cross-linked. Many HA fillers contain uncross-linked HA and lightly cross-linked chains and fragments. The uncross-linked HA, fragments of HA, and lightly cross-linked HA are included in the overall concentration measurement but only remain in the skin for a limited time and should minimally contribute to the longevity of the filler. The uncross-linked HA does help decrease extrusion force and make injection easier, which is the main reason it is included. Therefore, the fact that Restylane contains 20 mg of HA/cc and Juvéderm contains 24 mg of HA/cc does not give a physician enough information to decide which filler will have longer duration. It is actually the amount of modified HA that plays the primary role in duration.

The type of modification (cross-linking) and the cross-linking agent used is also important. Cross-linking can be best visualized by imagining a ladder (Fig. 23-10). Each side of the ladder is an HA chain. The rungs of the ladder are the cross-links. When the “rungs” of the ladder attach to both sides of the ladder, the agent is considered completely modified. However, the cross-linking agent used may incompletely cross-link the chains of HA, leaving the sides of the rungs unattached and resulting in incomplete modification. Such a product might not be as durable as a completely modified product. In addition, there are two types of rungs in the HA ladder. One is called an ether linkage and the other is called an ester linkage. Ether linkages are formed by 1,4-butanediol diglycidyl ether (BDDE, the cross-linking agent in Restylane and Juvéderm) and divinyl sulfone (DVS, the agent used in Prevelle Silk, Captique, and Hylaform). The cross-linking agent used in Prevelle Dura, 1,2,7,8 diepoxyoctane (DEO), forms both ether and ester linkages (known as “double cross-linking”). It is

![FIGURE 23-8](image) Visible lumps of Hylaform in the upper lip.

![FIGURE 23-9](image) Measurement of G’. A force is applied laterally on the top plate. The more the gel resists the movement, the harder the gel, the higher the G’.

![FIGURE 23-10](image) Cross-links that occur during the cross-linking process may be complete or incomplete.
unknown at this time what advantages, if any, ether linkages impart to a dermal filler.

The hydration status of the filler once it is packaged in the syringe also affects filler performance. HA is well known to bind up to 1000 times its weight in water. The amount of water bound to the HA prior to its packaging in the syringe determines how much more water the filler can absorb once it is injected into the skin. In other words, fillers that are completely hydrated in the syringe will bind less water on injection and the volume will expand less upon injection as compared to fillers that are not completely hydrated in the syringe. Fillers that are not completely hydrated in the syringe will bind less water on injection and the volume will expand less upon injection as compared to fillers that are not completely hydrated in the syringe. Therefore, it consists of randomly sized and broken into sized pieces while the small pieces such as Restyline Fine Line can be more superficially. The Juvéderm family of products is not sized. In other words, Juvéderm is not pushed through a screen. The Juvéderm family of products is not sized. In other words, Juvéderm is not pushed through a screen. This produces various sizes of the gel and therefore, it is prudent to slightly underestimate with these substances. In addition, patients can be told that they will "look even better" 24 hours after the injection. Restyline and Juvéderm are not completely hydrated in the syringe while Captique and Hylaform are close to being fully hydrated (Table 23-5).

Another process that may affect the performance of the filler is referred to as "sizing technology." This term is used by Allergan to differentiate Juvéderm from the other HA fillers. When an HA filler is cross-linked, the chains of modified sugars form a gel. In the process of manufacturing Restyline, Restyline Fine Line, Restyline Lip, Restyline Touch, Perlane, and Restyline Sub-Q, this gel is extruded through a screen. This produces various sizes of the gel that are considered "sized." The large pieces become Perlane or Restyline Sub-Q, while the small pieces are marketed as Restyline Fine Line or Restyline Lip. The medium-sized pieces are Restyline. The larger pieces yield products that are best used in the mid to lower dermis while the small pieces such as Restyline Fine Line can be used more superficially. The Juvéderm family of products is not sized. In other words, Juvéderm is not pushed through a screen and broken into sized pieces and, therefore, it consists of randomly sized and shaped pieces. It is unknown at this time what role sizing technology plays, if any, in the performance of a filler.

There are many factors that must be understood in order to make the most suitable choice of HA filler. There are no peer-reviewed publications that review the above mentioned properties so it is difficult at this point to know how important these various characteristics are in choosing a filler. More data need to be collected to properly ascertain if, for example, sizing technology makes a difference or if ester bonds last longer than ether bonds. These distinctions will become clearer and more important as more HA fillers are introduced onto the market and more data are collected. A discussion of the individual HA brands follows.

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### TABLE 23-5

**Hyaluronic Acid Filler Hydration in the Syringe**

<table>
<thead>
<tr>
<th>Product</th>
<th>Cross-Linking Agent</th>
<th>Concentration (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captique</td>
<td>DVS</td>
<td>4.5–6.5</td>
</tr>
<tr>
<td>Hylaform</td>
<td>DVS</td>
<td>4.5–6.5</td>
</tr>
<tr>
<td>Juvéderm Ultra and Ultra Plus</td>
<td>DEO</td>
<td>24</td>
</tr>
<tr>
<td>Prevelle Dura</td>
<td>DEO</td>
<td>20</td>
</tr>
<tr>
<td>Prevelle Silk</td>
<td>DVS</td>
<td>4.5–6.5</td>
</tr>
<tr>
<td>Restyline and Perlane</td>
<td>BODE</td>
<td>20</td>
</tr>
</tbody>
</table>

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**HYLAFORM (NO LONGER ON THE MARKET)**

**Overview** Although Hylaform is no longer on the market, it will be discussed because it was the first product on the market that used the DVS cross-linking system. The knowledge gleaned from this revolutionary agent has led to many spin-off products using similar technology such as Captique and Prevelle. Hylaform is an animal-based HA product derived from rooster comb. It is produced by cross-linking the hydroxyl groups of HA with DVS to yield a gel-like substance that is sized by extruding the gel through a sieve in the production process discussed above. The smallest pieces of the gel are packaged as Hylaform Fine Line, which is indicated for superficial wrinkles, but has never been approved for the US market. Hylaform, composed of medium-sized (average size 400 μm) particles, is indicated for injection into the middermis for medium facial wrinkles and fine lines. Hylaform Plus is composed of larger particles (average size 700 μm) and is used for deeper furrows. In 2004, the FDA approved two products in this family, Hylaform and Hylaform Plus (Allergan, Irvine, CA), the latter of which remains on the US market. The moderate density of cross-linking renders the Hylaform fillers biocompatible, soft, and pliable. The G’ of this filler is low compared to other HA products on the market; therefore, this is the softest HA filler currently on the market. This softness makes it an ideal filler for use in the lips. The Hylaform products contain 5.5 mg/mL of cross-linked HA.

**Benefits** Hylaform has a low G’, which means that it is not very stiff and has a very natural feel in the skin. It is soft and malleable making it ideal for use in the body of the lip, smoker’s lines, and the periorbital tear-trough as well as in large areas such as the cheekbones and jowls. Hylaform is very easy to inject with a low extrusion force through a 30-gauge needle. The side effects of Hylaform are rare, mild, and temporary.

**Drawbacks** Side effects, which are rare and relatively mild, typically include bruising, erythema, induration, and pruritus. The contraindications for Hylaform products are similar to those for most fillers (e.g., autoimmune and inflammatory disorders, allergic background, history of anaphylactic reactions, immunosuppressant therapy, and pregnancy or breastfeeding). In addition, patients allergic to products of avian origin (e.g., eggs) cannot use these agents. Hylaform is close to being fully saturated with water in the syringe; therefore, there is no volume expansion of the filler after injection. Additionally, the injection of Hylaform, as with other fillers that do not contain an anesthetic, could be painful. However, the softness of Hylaform renders it less painful than other HA fillers to inject. The use of topical anesthetics reduces the pain on injection. The cosmetic effects of Hylaform and Hylaform Plus are believed to last only about 3 to 4
months, most likely because of their cross-linking properties and lower concentration of HA than the newer HA fillers (e.g., Restylane and Juvederm).

**CAPTIQUE (NO LONGER ON THE MARKET)**

**Overview** Captique (Allergan, Irving, CA) differs from Hylaform only insofar as the former is derived from bacterial fermentation rather than rooster combs; otherwise, it is also composed of 5.5 mg/mL of HA. In 2004, it was approved by the FDA for moderate to severe wrinkles. The bacterial origin of Captique renders it slightly stiffer than Hylaform, but not as firm as Restylane. Captique is packaged as a clear gel in a 0.75-mL syringe and injected dermally with a 30-gauge needle via the serial puncture method. Like Hylaform, Captique is no longer available.

**Benefits** This product is suitable for treating similar periorbital and perioral wrinkles as Hylaform as well as enhancing lip fullness and shallow scars. No testing or refrigeration is required and the agent can be injected in the initial physician’s visit. As an HA filler, it has a low side effect profile because of its immunogenic inertness and low likelihood of allergic reactions. The equilibrium hydration of Captique is comparable to Hylaform, meaning that it is fully hydrated with water in the syringe. In the primary author’s experience, patients complained of less stinging after injection with Captique as compared with Juvederm.

**Drawbacks** The longevity of Captique is questionable but believed to be about 4 to 6 months. Few duration studies were performed, however. It has a high extrusion force when injected through a 30-gauge needle, which renders injection more difficult than that for Hylaform or Restylane. Captique does not contain lidocaine, thus it is similar to other HA fillers in the capacity to cause moderate pain, bruising, edema, and redness on injection. Captique has been taken off the market because its parent company, Allergan, is focusing on promoting Juvederm.

**RESTYLANE**

**Overview** Restylane (Medicis, Scottsdale, AZ) was the first nonanimal HA product approved in the US. It is a NASHA gel formulated through fermentation, with sugar present, in bacterial cultures of eumyc streptococci. Restylane has a higher concentration of HA compared to Hylaform and Captique and the highest G’ of the fillers currently on the market, denoting that it is a slightly stiffer product. It is the most popular of the HA fillers in the US because of its safety profile, brand recognition, and ease of injection. Restylane is composed of approximately 100,000 particles/mL (approximately 250 μm on average) and contains 20 mg/mL of HA. Restylane is indicated for middermal wrinkle reduction and was the first HA filler approved in the US in 2003. Perlane, another product in the Restylane family, was more recently approved by the FDA for significantly deeper folds and furrows. Restylane is made of medium-sized particles of HA gel, while Perlane is composed of larger HA gel particles (approximately 1000 μm), but with the same HA concentration. The Restylane family of products also includes Restylane Fine Line, Restylane Touch, Restylane Lip, and Restylane Sub-Q, which are not currently approved for use in the US. These products have the same formulation as Restylane and differ only in their particle size. Restylane and Perlane are packaged as transparent gels, with a shelf life of 18 months, and stored at room temperature. Restylane is enclosed in 0.4- and 1-mL syringes while Perlane is packaged in a 0.7-mL syringe; both are injected via a 27-gauge needle. Restylane is implanted using linear threading antegrade or retrograde techniques. It is important to avoid injecting at withdrawal of the needle, which can result in superficial injection, creating blue-colored nodules. A fanning threading technique can also be employed with Restylane at the nasolabial fold or lip commissures.

**Benefits** The stiffness of Restylane renders it well suited for moderate to deep wrinkles and it is this quality among other factors that is thought to impart greater longevity in human tissue as compared to Hylaform and Captique. The cosmetic effects of Restylane are thought to last over 6 months; Perlane delivers a durability of 6 to 9 months. Product stiffness makes Restylane and Perlane more suitable for moderate and deep wrinkles than for use in the body of the lips or the tear trough. Restylane is ideal to fill nasolabial and marionette lines, chin and jowl depressions, nasal deformities, and for nasal tip-lift as well as acne scars and other defects.

**Drawbacks** Bruising is associated with injection. Captique has been taken off the market. Captique does not contain an anesthetic, the injection of Restylane can be painful. The use of topical anesthetics and/or dental nerve blocks is recommended to reduce the pain on injection. Restylane tends to sting less after injection when compared to Juvederm. It is unknown why this occurs as they are both the same pH of approximately 7.0.

**JUVEDERM™**

**Overview** Juvederm (Allergan, Irvine, CA), is manufactured by a bacterial fermentation process similar to that used for other stabilized bacterial-based HA fillers and was approved by the FDA in late 2006. There are many products in the Juvederm line (Juvederm 18, Juvederm 24, Juvederm 24 HV, Juvederm 30, and Juvederm 30 HV), but only Juvederm 24 HV (also known as Juvederm Ultra) and Juvederm 30 HV (also known as Juvederm Ultra Plus) are currently approved by the FDA and sold in the US. All the products in the line vary by the amount of HA concentration, the amount of cross-linking, and the regularity of the cross-linking. Both Juvederm Ultra and Ultra Plus consist of 24 mg/cc of HA, but Juvederm Ultra Plus has a higher degree of cross-linking than Juvederm Ultra, which makes Ultra Plus more suitable for the deepest facial grooves and furrows. Unlike Restylane, which consists of stiff and a fairly narrow range of particle sizes, Juvederm is a smooth consistency gel composed of a broad range of particles of various sizes and shapes (referred to as “Hyalacross technology”).

Juvederm products are packaged as a clear gel in 0.8-mL syringes. They are stored at room temperature. Juvederm Ultra is injected into the middermis via a 30-gauge needle while Juvederm Ultra Plus is implanted deeper via a 27-gauge needle. The needles must be tightly attached to the Luer-lock syringe to prevent detachment during
injections. Various techniques of injection can be used with Juvederm, including serial puncture and tunneling.

**Benefits** Juvederm Ultra and Ultra Plus are in the medium range of stiffness; therefore, they can be used in any wrinkles, moderate or deep, and to correct scars. Juvederm Ultra is easily placed in the vermilion border or the body of the lips. The high concentration of HA in Juvederm Ultra and Ultra Plus and the high degree of cross-linking results in longer-lasting aesthetic effects as compared to products such as Hylaform. As other HA products, these agents have an overall low, mild, and transient adverse-event profile. Juvederm is not an overall superior product to products such as Hylaform. As compared to products such as Hylaform. The gel contains 5.5 mg/mL of cross-linked HA with an average particle size of 500 μm. Prevelle is safe for treating shallow to moderate wrinkles, lips, and scars. The longevity of the product is unknown but reported to be about 4 months. Prevelle Silk contains 0.3% lidocaine. It was approved in the United States in 2008. This product is suitable for use in the lips since it generates less pain during injections. Side effects, which are rare and relatively mild, include redness, swelling, and pruritus.

**Benefits** This product is softer than other products on the market since Hylaform and Captique were discontinued. It can be used in any moderate to deep facial wrinkles, the body of the lip, and periorbital areas. Prevelle Silk is the first lidocaine-containing HA in the United States.

**Drawbacks** Prevelle Dura is slightly more viscous and, therefore, requires more pressure on injection.

**Hyaluronidase**

Hyaluronidase is a soluble enzyme that hydrolyzes HA, other GAGs, and other connective tissue components in the skin and vitreous humor of the eye. It has been approved by the FDA, as Vitrase and Amphadase, for enhancement of injectable drug absorption and resorption of radiopaque agents. However, effective off-label uses include wound care and postsurgical flap care among other uses.

Several reports have indicated the usefulness of hyaluronidase to dissolve HA filler overcorrection for symmetric contouring, as well as to manage impending tissue necrosis because of HA skin injections. Specifically, Hirsch et al. published two cases of imminent tissue necrosis caused by intra-arterial injection of HA and surrounding tissue compression of vital vessel, which resolved with employment of hyaluronidase. After using other appropriate techniques to manage impending tissue necrosis including systemic aspirin, Nitro BID under occlusion, and hot compresses with massage without significant response, the authors injected 30 units of hyaluronidase into deep dermal tissue and subcutis using a serial puncture method along the distribution of affected arteries, which led to the resolution of symptoms within a day. Although early reports have recommended the utility of hyaluronidase only within 16 minutes of the critical event, Hirsch et al. reported successful responses after several days. Furthermore, the effectiveness of hyaluronidase for bluish (Tyndall) manifestations and asymmetric lumpiness from HA overcorrection has also been reported at various concentrations.

Because of the described benefits of hyaluronidase for the treatment of complications of the popular HA fillers, it has been recommended as a necessary agent to keep in an aesthetic physician’s office. Hyaluronidase is a clear liquid that is stored in the refrigerator and reconstituted with 1 mL of normal saline to generate 150 units. Very rare adverse acute and delayed-type hypersensitivity reactions to hyaluronidase have been reported, so it may be prudent to perform a skin test prior to the use of this agent. Injection of hyaluronidase into patients with an allergy to hymenoptera stings and thimerosal is contraindicated.
Semipermanent Fillers

Fat, Radiesse, and Sculptra are considered semipermanent; because they are partly biodegradable, they are less likely to cause sensitivity or inflammation and are therefore considered biocompatible. Furthermore, the technique of fat implantation has undergone remarkable polishing over many years, especially with the advent of harvesting subcutis through liposuction techniques. The procedure is a multistep process, whereby the fat cells are obtained from the buttock, thigh, and abdominal regions, then segregated, stored (refrigerated up to 18 months), and injected back into the patient’s subcutis on the face, hands, and any other areas requiring volume enhancement. As anticipated, this process is more invasive, time-consuming, both for the clinician to prepare and perform as well as the patient to recover from, as well as more costly. In effect, the optimal efficacy with minimal adverse effects is mainly achieved in the hands of a qualified dermasurgeon. Approximately 0.1 cc aliquots of fat are inserted into subcutis through a 17- to 18-gauge needle via a tunneling technique, without overcorrection. Postprocedure massage is recommended for proper shaping of contours.

Benefits

Because of its autologous character, lipotransfer is unlikely to cause sensitivity and reactivity of the tissue, minimizing potential long-term side effects and obviating prior testing. Nasolabial folds, sunken cheeks, tear troughs, marionette lines, scars, and lips are the most appropriate areas of correction with fat. Furthermore, fat transfer provides a reported duration of about 12 months although the concrete duration is controversial. Because the injectable material used is the patient’s own tissue, its use decreases the amount of money spent on the actual filler. The procedure also has an attractive double-gain, where two cosmetic areas can be simultaneously addressed, liposuction and lipodystrophy. Stem cells have been isolated from fat cells. It is believed that the stem cells found in fat lead to increased skin rejuvenation (see Chapter 6). When performed by a skilled physician, the results of lipotransfer are remarkable.

Drawbacks

Fat injections require prophylactic local or regional anesthesia. Because of the fact that the procedure is more surgically invasive, more complex preparations and settings are required with longer and more frequent office visits. Although the harvesting portion can cause a longer recovery time and an increased risk of side effects (e.g., infection, scarring), the actual injection has a similar adverse event profile to the other fillers (e.g., edema, redness, bruising, and discomfort lasting a few days). Another variable to consider when selecting candidates for this procedure is to ensure that the patient has a sufficient graft supply. In some patients, the fat injections last several years and in other patients the injections last merely months. Many tricks are employed to try and increase longevity, but at this time there are no guarantees.

RADIESSE

Overview

Radiesse (BioForm Medical, San Mateo, CA) was approved by the FDA in 2006 for the correction of moderate to severe folds and wrinkles along with HIV-associated lipodystrophy. It is composed of 90% calcium hydroxyapatite (CaHA) microspheres (25-45 μm) suspended in an aqueous gel carrier (1.3% sodium carboxymethyl cellulose, 6.4% glycerin, and 36.6% sterile water). As the gel carrier of this filler dissipates within several months, the microspheres stimulate cutaneous cells to generate focal foreign body reaction and neocollagenesis. This leads to envelopment of the microspheres by fibrin, collagen, and fibroblasts, and slows the degradation by macrophages and metabolism into calcium and phosphate ions. Because of a similar mineral constitution as human bones, and no foreign antigenic properties, CaHA is particularly biocompatible. It is critical for patients to be aware that Radiesse is a radioopaque material that can be visualized and misinterpreted on facial radiographs, but importantly, it does not radiographically mask surrounding tissues.

Drawbacks

The main drawback of Radiesse is that it is not reversible like HAs. Radiesse also does not contain an anesthetic and because of its high viscosity, requires administration through a high-bore needle. However, Radiesse can be combined with lidocaine in the syringe to decrease pain on injection. Hence, the use of topical or regional anesthesia is recommended. Minimal side effects such as ecchymoses, edema, and erythema appear soon after Radiesse injection and are transitory. Rare nodules have also been associated with Radiesse and can be managed with intralesional steroids or excision. Similar to Sculptra, an implantation of Radiesse in the superficial and mobile wrinkles (e.g., lips and periorbital area) and the body of the lips is discouraged because of the palpable and visible white papules that can develop (also known as “popcorn lips”). Radiesse should not be performed in the nose of a patient anticipating rhinoplasty. Several facial plastic surgeons have given anecdotal reports in lectures suggesting that this complicates rhinoplasty surgery. An HA or collagen filler would be a more appropriate...
choice in preoperative rhinoplasty.

**SCULPTRA**

**Overview.** Sculptra is a synthetic, biodegradable, biocompatible, immunologically inert peptide polymer (also known as NewFill).44–46 Sculptra (Dermik Laboratories, Sanofi-Aventis, Bridgewater, NJ) is composed of poly-L-lactic acid (PLLA) microspheres, sodium carboxymethylcellulose, and nonpyrogenic mannitol and is manufactured from powdered, absorbable suture material (e.g., Vycryl). This agent is not a true dermal filler because it does not fill the dermis the way collagen and HA do but, rather, it promotes the production of new and organized collagen in the dermis. Many physicians refer to it as a “dermal stimulator.” Sculptra is thought to foster neocollagenesis by stimulating fibroblasts and gradually restoring facial volume.47–48 However, Sculptra is eventually cleared from the skin via phagocytic digestion. In the US, Sculptra was approved by the FDA in 2004 for the treatment of HIV-associated facial lipoatrophy, but it has been used off-label for cosmesis, and Dermik is currently applying for approval for its use in facial rejuvenation. NewFill has been used in Europe and Asia for many years. When it was first introduced, NewFill was diluted with a lower amount of saline and many granules and nodules were reported. This led to new recommendations to dilute one bottle with 5 to 10 cc of sterile water and massage after application. With the new recommendations, adverse events have been minimal.

Freeze-dried Sculptra powder is stored at room temperature and reconstituted approximately 2 to 4 hours prior to injection. The package label states that the product should be used within 72 hours. In our practice, we prefer using Sculptra that has been reconstituted for at least 2 days because the solution is easy to work with and results in less needle clogging. Sculptra is reconstituted and kept in the refrigerator for 2 days to 2 weeks. Although the package label recommends that the formulation be reconstituted with 5 cc of sterile water, many physicians reconstitute with 4 mL of sterile water and 1 mL of 2% lidocaine with epinephrine. The lidocaine decreases pain while the epinephrine reduces bruising. Strong agitation of the filled syringes is recommended directly before injection to homogenize the white suspension. (Sculpta tends to settle in the bottom of the syringe.) By means of tunneling and threading techniques, a 25- or 26-gauge needle is used to implant Sculptra into overlapping deep dermal and subcutaneous layers of the skin.

The mechanism of action and proper technique of injecting Sculptra require practitioners to restore volume to a selected treatment plane rather than a specific wrinkle.49 Indeed, injecting Sculptra is more similar to fat injection procedures than collagen or HA injections, because it serves to sculpt the prominent hollows and deep grooves associated with loss of deep soft tissue. In addition, specialized training to use Sculptra is required prior to injections. Small and exact aliquots of Sculptra are injected in the correct tissue plane without overcorrection. In general, 2 to 3 cc of the product are used for patients in their thirties, 4 cc for patients in their forties, and 5 cc or more for older patients. The cost is approximately $250 per syringe.

Once Sculptra is injected, there is a transient period lasting about 1 hour during which the patient can see a slight effect because of the volume of fluid injected. Once this resolves, results are not seen until about 4 weeks after treatment when results may begin to appear. Injections are performed on a monthly basis until desired results have been obtained. The number of injection sessions required varies greatly from person to person and it is difficult to predict the total number of sessions needed. Injections are performed 3 to 6 weeks apart. Ancedotal reports state that premenopausal women and postmenopausal women on hormone replacement therapy (HRT) require fewer sessions than postmenopausal women not on HRT. Postmenopausal women not on HRT may require up to eight sessions. Men tend to correct more quickly than women for unknown reasons. After the procedure, the patient’s skin is strenuously massaged with topical arnica (for its anticoagulant properties) for about 30 minutes to an hour. Patients should be told to massage the treated area for 5 minutes every night for five nights.

Sculptra treatments can be combined with other fillers for instant gratification. In this case, Sculptra is injected first, the massage with arnica is performed, and then the HA or collagen filler is applied in the treatment area. Sculptra is often used in the cheeks and cheekbone area, while an HA filler is used in the nasolabial folds, marionette lines, and the lips. Alternatively, a course of three to four Sculptra treatments is used and then an HA filler is used after Sculptra at the last visit. Sculptra should always be used first, then massaged, before the HA is injected so that the lidocaine and epinephrine in the Sculptra will reduce the pain and bruising of the HA injection, and the massaging will not affect the placement of the HA filler.

**Benefits** Sculptra does not require prior skin testing. It is ideal for treating volume loss in the cheeks, nasolabial folds, and the malar area. Once the desired result is achieved, results last about 18 to 24 months.50,51,52 The correction is very natural looking. Having been used successfully in various medical devices for more than 30 years, PLLA has an established safety record.53 Moreover, new product guidelines and injection techniques (e.g., using a more dilute product, avoiding overcorrection, not injecting too superficially, and postinjection massage) have reduced the incidence of side effects (i.e., formation of granulomas and nodules) as compared to when the product was originally packaged as NewFill.54

**Drawbacks** Sculptra injection results are not immediate and multiple courses are required to achieve the optimal cosmetic effect, with the number of treatments depending on volume of the defect being treated.45 Preinjection reconstitution can contribute to scheduling limitations because it must be made at least 2 hours in advance. Injecting suspension can be slightly difficult because of recurrent clogging of the needles, which leads to frequent needle changes. Adverse events are rare, but PLLA can cause postinjection site pain, bruising, and swelling, as compared to other products, partly because of the larger needle used. Adding lidocaine to the diluent mitigates injection pain. Ecchymoses can be reduced by mixing epinephrine into the PLLA suspension and taking bromelain supplements (500 mg twice daily) after injection (see Chapter 21). Hyperkinetic areas (e.g., crow’s feet and the corner of the mouth) and regions with thin skin (e.g., around the eyes, smoker’s lines above the lips) should not be treated with Sculptra because of irregular papules that can emerge. Most lumps that do arise are from superficial administration of Sculptra and are not visible, although they are palpable by the patient. Reassuring patients that these lumps are transient in nature is important. Nodule and hematoma formation are the other rare adverse effects that
have been reported, but are less likely if the new injection technique is altered. The injection technique is very different than that of HA fillers and the learning curve is higher. In addition, there is lack of reversibility as with HA fillers. Specialized training is required by the manufacturer of Artecoll before they will sell the product to a physician.

Permanent Fillers
Although the current momentum in the cosmetic market is toward the less invasive procedures, some are safer, permanent fillers are very popular outside the US because of the lower cost. Many of these products are used by unskilled practitioners and lead to disfiguring results. If practitioners are to use a permanent filler, they should be skilled in the technique and certain of the patient’s expectations. In the primary author’s opinion, it is best to use a temporary filler first, to make sure that a patient is pleased, before proceeding to a permanent or semi-permanent option. Newer fillers (e.g., Artefill) as well as older fillers (e.g., silicone) are being used for this purpose. These non-biodegradable fillers stay encased by the skin for an indeterminate and lasting period of time. However, these fillers are not to be used for and by the inexperienced. They are associated with rare, significant side effects such as granulomas, migration, and asymmetry and are best implanted into a patient experienced with prior soft tissue augmentations and by a proficient physician. Remember, as with anything enduring, if one is not pleased with the results, one has to live with long-term consequences.

Artefill
Overview
In October 2006, the FDA approved the novel permanent filler Artefill (Artes Medical, Inc., San Diego, CA) for the correction of nasolabial folds. Artefill is constituted with 20% homogenous polymethylmethacrylate (PMMA) suspended in equilibrium with 0.3% lidocaine. As opposed to the original European product, Artecoll, which contained different size microspheres of PMMA, Artefill is essentially homogenous polymethylmethacrylate (PMMA) suspended in equilibrium with 0.3% lidocaine. As opposed to the original European product, Artecoll, which contained different size microspheres of PMMA, Artefill is constituted with 20% homogenous polymethylmethacrylate (PMMA) suspended in equilibrium with 0.3% lidocaine. As opposed to the original European product, Artecoll, which contained different size microspheres of PMMA, Artefill is constituted with 20%

Benefits
Artefill offers the dual action of immediate wrinkle correction from collagen (lasting about 1–3 months) and permanent deep-fold ablation from PMMA (lasting for more than 5 years). The long-term efficacy is believed to be because of the stimulatory influence of PMMA on the surrounding skin, causing fibroblast and collagen proliferation around the material starting at 1 month. Although approved only for nasolabial folds, PMMA has also been successfully used in other deeper defects (e.g., the cheek and malar regions). Lidocaine content eliminates the necessity for alternative anesthesia and alleviates intrajejunum discomfort. As compared to the standard of bovine collagen, PMMA filler has been found to be superior in efficacy with a comparable safety profile. Widely used in implantable medical devices for more than 50 years, PMMA has a long safety record.

Drawbacks
Artefill contains bovine collagen; therefore, skin testing prior to injection is strongly advised to reduce the incidence of hypersensitivity. This means that patients cannot be treated on the initial office visit. Furthermore, because of Artefill’s higher viscosity, more administration pressure is required by the clinician, and the product is more difficult to inject than collagen and HA fillers. Although the majority of side effects caused by Artefill are mild and transient (e.g., swelling, redness, hypersensitivity, and temporary lumpsiness, which is amenable to massage), rare moderate-to-severe effects have been reported (e.g., granuloma and inflamed node formation, manageable with intraleosomal steroids or excision). Because of the reported lumpiness with this product, it is currently discouraged for lip augmentation or any superficial wrinkle correction. Having to inject through a larger bore needle may induce more posttreatment edema and ecchymoses, which require slightly longer downtime. The disadvantage of implanting permanent fillers such as Artefill is the inability to foretell the long-term appearance of the patient, since the skin changes with age, the natural look may be altered. Time will tell the exact risk-to-benefit ratio of this filler.

Silicone
Overview
Silicone is composed of dimethylsiloxane chains linked by oxygen with varied viscosity based on the length of the polymer. Used in patients since the 1940s, the liquid form of this product is one of the oldest soft tissue augmentation materials. The use of this injectable filler is fraught with controversy because the initial unpurified product was associated with long-term disfiguring side effects, including migration and granuloma formation. It was illegal to perform silicone injections in the US in some states until recently. However, because of the purification of liquid silicone and homing of the injection technique, this soft tissue filler has returned and is very popular in Brazil. At the turn of the 21st century, the FDA approved two forms of medical-grade silicone oils: ADATO (or Sil-ol 5000, Bausch & Lomb Surgical, Inc., San Dimas, CA) with 5000 centistoke (cs) viscosity and Silikon 1000 (Alcon Laboratories, Inc., Fort Worth, TX) with 1000 cs viscosity. These are both indicated for the ophthalmologic uses of retinal tamponade and detachment. Although neither of these products have been approved by the FDA as skin injectables, they are used off-label. Furthermore, there are ongoing studies in the US assessing the safety and efficacy of SilSkin (a 1000 cs, highly purified polydimethylsiloxane, OFAS-Therapeutic Silicone Technologies, Inc., New York, NY) for the correction of nasolabial folds and HIV-associated lipoatrophy. Pilot studies in patients with HIV-lipoatrophy have revealed satisfactory results with minimal side effects.

Similar to PMMA and PLLA, silicone oil biostimulates the surrounding skin to slowly generate a focal fibro-granulomatous reaction that leads to a permanent volumizing. Zappi et al. analyzed the microscopic biologic behavior of liquid silicone and concluded that it was an effective, durable (up to 23 years), and immunologically compatible filler.
Silikon 1000 is the preferred injectable filler over ADATO because of its lower viscosity and therefore easier injectability. It is stored at room temperature and packaged as clear oil. The proficiency in the injection technique is the crucial variable in achieving successful soft tissue augmentation with silicone. The favored technique is a serial puncture of microdroplets and subdermal implantation of 0.01 to 0.02 mL silicone aliquots at 2- to 4-mm intervals using a glass syringe with a 30-mL needle. The key is not to overcorrect. Instead, patients should anticipate steady changes with multiple treatment sessions, 1 to 2 months apart, in order to achieve the most natural and safe outcome in several months.

Benefits
Since it is immunologically inert, no prior skin testing is required. Practitioners with experience in using Silikon have reported its value in correcting wrinkles and scars, augmenting lips, and panfacial contouring of deeper folds and valleys. Its low cost and longevity are obvious benefits.

Drawbacks
As with any temporary filler, potential long-term consequences should be broached when discussing this treatment option with patients. Most side effects associated with medical-grade silicone injectables are minimal and include anticipated temporary pain, edema, bruising, and redness. The pain is likely because of the absence of anesthetic as part of the product formulation, so appropriate preprocedure anesthesia should be provided. However, it is important to keep in mind that rare reports of appropriately-injected, purified silicone causing significant nodules, granulomas, cellulitis, and ulceration also exist. The skill of the physician is crucial as this is a permanent filler. The primary author has seen myriad unhappy patients who have lumps and asymmetry after treatment by other physicians (Figs. 23-11 and 23-12). In addition, many patients who are treated by nonphysicians are treated with impure silicone. This results in disfiguring edema and long-term complications. In our clinic, we have tried to treat complications of silicone injections by nonphysicians with injectable steroids, tacrolimus, cyclosporine, and Aldara with minimal and short-term improvement. Surgical excision has remained the only effective long-term treatment.

POLYTETRAFLUOROETHYLENE
Overview
Approved by the FDA in the 1990s for the purpose of soft tissue augmentation, several forms of expanded polytetrafluoroethylene (PTFE) are currently on the market: Gore-Tex strings or strands (Gore Advanced Technologies Worldwide, Newark, DE); Soft-Form and UltraSoft tubes (Tissue Technologies, Inc., San Francisco, CA); and newer dual-porous, soft, varied-shape Advanta (Atrium Medical Corporation, Hudson, NH). PTFE is a synthetic material used in medical devices since the 1970s with a good safety record. These are spongy products that provide significant volume enhancement and stimulate local tissue fibrosis and integration, which relays permanence and stability. PTFE is
biocompatible with rare instances of inflammatory reactions.

The extended PTFE subdermal implants require a more invasive procedure via surgical implantation, which translates to higher procedural risks and the necessity for a more specialized setting and training. Because of these complex features and generally lower physician satisfaction, the use of these devices by cosmetic dermatologists is not popular.67

**Benefits** PTFE fillers have been shown to impart an enduring correction of the nasolabial folds, marionette lines, malar and mandibular deficits, and enhancement of the lips.56 Additionally, these products do not require prior testing because of immunologic inertness. Although the implants are considered permanent, if patients are dissatisfied with their image alterations, the products can be removed in bulk within 3 months.

**Drawbacks** The side effects of bleeding, bruising, redness, postoperative pain, scarring, palpability, and secondary infection occur more frequently with PTFE fillers as compared to HA fillers.68 These products have high displacement and extrusion rates and an unnaturally stiff appearance.58 In addition, they can shrink with time leading to an asymmetric correction.

**Fillers on the Horizon**

As noninvasive cosmetic interventions have become more prominent, the manufacturing market has responded by developing newer products. In fact, there are so many products to consider, it has become ever more challenging for regulatory organizations, physicians, and patients to discern their differences. While some clinicians opt to jump on the bandwagon and use novel filling agents by interpreting newer as better, others await satisfactory clinical evidence before integrating these fillers into their practices. It is crucial to appreciate the fact that the products once proclaimed innovative have either stood the test of time, with manufacturers reaping the rewards, or they have been superseded. This section provides an overview of the up and coming soft tissue augmentation devices.

**EVOLENCE**

**Overview** Evolence (Collar LifeScience Ltd., Herzliya, Israel) is cross-linked porcine-derived collagen (30 mg/mL concentration). Because of the greater biologic similarity between pig and human skin versus bovine and human skin, this filler has potentially lower immunogenicity than bovine collagen fillers, with no preprocedure sensitivity testing required.65 It is currently only approved in Europe and Israel as two products, Evolence and Evolence Breeze (finer version), for soft tissue augmentation.

Evolence is injected through a 25- to 27-gauge 1.25- to 1.5-inch needle into mid-depth dermal space using tunneling and cross-hatching techniques, while Evolence Breeze is injected in 0.1-mL aliquots via a 31-gauge needle using a serial puncture technique into the superficial dermis; overcorrection is to be avoided.66 Postimplantation massage is advised to enhance molding.

**Benefits** Without prior allergy testing needed, these products can be injected on the first visit. Special cross-linking technology, Glymartix, yields a more stable collagen product that creates immediate effects potentially lasting for up to 1 year. Evolence products may be used in combination with other agents such as HA fillers. This collagen filler is stored at room temperature. A recent study comparing the safety and efficacy of Evolence and Restylane showed that Evolence performed similarly to Restylane.67

**Drawbacks** Evolence does not contain lidocaine as other collagen fillers do. It is more difficult to inject than Restylane and Juvederm. Needle jamming has been noted on occasion, which makes injections a bit awkward.60 Religious beliefs have to be considered prior to implantation because this product contains porcine collagen, which may be rejected on religious grounds by Jewish and Muslim patients. This product had not yet been approved by the FDA at the time of publication, but approval is expected shortly. Although postprocedure side effects of porcine collagen fillers are comparable to HA fillers (e.g., transient edema, erythema, pain, ecchymoses), the development of infrequent lumps and nodules that last several months has also been noted.60 These papules can be treated with massage and intralesional corticosteroids. Because of these side effects, injecting Evolence into thin skin areas should be avoided.60 This filler is new and does not have the years of experience associated with other collagen and HA fillers. Its use should be approached with caution.

**ISOLAGEN**

**Overview** Although presently approved in the UK, Isolagen (Isolagen Inc., Exton, PA) is undergoing clinical studies in the US to obtain FDA approval. Utilizing the patient’s skin, fibroblasts, which provide ameliorative effects by increasing the production of desired cytokines and growth factors, stimulating collagen and elastin production. Correction is believed, but not proven, to last about 6 to 12 months. As other collagen fillers, it is injected at superficial and moderate dermal depth to treat rhytides and nasolabial folds as well as the lips.

**Benefits** The crucial benefits of Isolagen are biocompatibility and safety. This product contains the donor’s own fibroblasts, which may provide ameliorative effects by increasing the production of desired cytokines and growth factors, stimulating collagen and elastin production. Correction is believed, but not proven, to last about 6 to 12 months. As other collagen fillers, it is injected at superficial and moderate dermal depth to treat rhytides and nasolabial folds as well as the lips.

**Drawbacks** This product is particularly expensive because of the specific engineering technique of cultured autologous fibroblasts and collagen. There is a waiting period of 2 months and the product derived from the biopsy is relatively sparse. However, this product can be used in conjunction with other fillers to make up the volume difference. Special product shipping, handling and storage, as well as a narrow time-frame of implantation (within 24 h of Isolagen delivery) are limitations. The side effects of the product have not been clarified, but are likely similar to other fillers on the market.

**LA RESSE**

**Overview** Laresse is a novel dermal filler composed of two polymers in solution, carboxymethyl cellulose (CMC) and polyethylene oxide (PEO), both of which are hydrophilic. The product is a viscoelastic gel that is injected into the dermis as a space-filling substance. Although the clinical data are limited, it has been available in the UK since mid-2006 and has become a competitor to
cross-linked HA products. Since Laresse is not cross-linked, it is smoother to inject than HA fillers and imparts a soft contour to the dermis.

**Benefits** Skin testing is not required with this product. The components have been used in numerous injectable therapeutics and medical devices and are known to be immunologically inert. Laresse is easily injected and is reported to produce less pain on injection than other fillers. The product is particularly smooth and natural feeling in the skin and it has been used in nasolabial folds and other superficial wrinkles. Because of its ability to stabilize and compact in higher concentrations without a need for cross-linking, it is hypothesized that Laresse will have longer durability than HA fillers. However, no studies have been published in the US to support these claims.

**Drawbacks** Although studies have shown that Laresse lasts 6 months in some patients, limited clinical studies have been performed so its duration will become evident as it becomes available in the marketplace. The extent of its potential applications in facial augmentation is unclear as the product has been used clinically only since 2007 and its use in the hands of practitioners is still being evaluated. Laresse does not contain lidocaine and, therefore, preprocedure anesthesia is usually topical or a nerve block, similar to HA fillers. Side effects are analogous to the HA fillers and consist mainly of transient swelling, bruising, and redness. Other adverse events are yet to be revealed as Laresse is being investigated by the FDA.

**AQUAMID**

**Overview** A novel permanent filler, Aquamid (Ferrosan A/S-Consuldn International SA, Cophenhagen, Denmark) has been approved and used in Europe, South America, and the Middle East for the past few years. Aquamid is composed of 97.5% pyrogenic water linked to 2.5% cross-linked polyacrylamide polymer. When it is introduced into skin tissue, acrylamide stimulates fibrotic and localized foreign-body reactions. The gel is packaged in a 1-mL syringe and stored at room temperature. It is injected through a 27-gauge needle using a threading technique without overcorrection.

**Benefits** The material is inert, obviating prior sensitivity testing. Aquamid is biocompatible and nonabsorbable, which yields an inert and durable device that can last indefinitely. Aquamid has shown efficacy in lip augmentation, correction of nasolabial folds, depressed mouth commissures, as well as glabellar and perioral rhytides. However, no studies have been published in the US to support these claims.

**Drawbacks** Lacking lidocaine content, Aquamid requires local or regional anesthesia prior to the procedure. Although postimplantation side effects are similar to those of HA fillers (e.g., temporary erythema, edema, redness), rare long-term and more severe adverse effects are more prominent with Aquamid. The primary author has seen several patients treated in South America with prolonged swelling and edema (Fig. 23-13). The exact duration of Aquamid in the skin is still unclear,

### TABLE 23-6

<table>
<thead>
<tr>
<th><strong>The A, B, C, D Approach to Choosing the Appropriate Filler</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>A—Assess the patient</strong></td>
</tr>
<tr>
<td>a. Which areas show aging or asymmetry?</td>
</tr>
<tr>
<td>b. Which areas can be easily corrected?</td>
</tr>
<tr>
<td>c. Imagine how the patient will look if various areas are corrected.</td>
</tr>
<tr>
<td>d. Determine the best areas of injection and proceed to next step.</td>
</tr>
<tr>
<td><strong>B—Budget</strong></td>
</tr>
<tr>
<td>a. Determine the patient's financial budget.</td>
</tr>
<tr>
<td>b. Determine the patient's time budget.</td>
</tr>
<tr>
<td>c. Refine plan in your mind about which areas are most important to treat.</td>
</tr>
<tr>
<td><strong>C—Considerations</strong></td>
</tr>
<tr>
<td>a. Learn more about the patient.</td>
</tr>
<tr>
<td>b. What bothers the patient most?</td>
</tr>
<tr>
<td>c. Ask about prior experience with fillers.</td>
</tr>
<tr>
<td>d. Are there any religious restrictions?</td>
</tr>
<tr>
<td>e. Can the patient return for future treatments?</td>
</tr>
<tr>
<td>f. Does the patient have an event coming up?</td>
</tr>
<tr>
<td>g. Is the patient on anticoagulants?</td>
</tr>
<tr>
<td>h. Are there any concerns about outcome?</td>
</tr>
<tr>
<td>i. Are there any product promotions going on?</td>
</tr>
<tr>
<td><strong>D—Device</strong></td>
</tr>
<tr>
<td>a. Assess pros and cons of available fillers.</td>
</tr>
<tr>
<td>b. Match attributes of fillers to what was learned in steps A, B, and C.</td>
</tr>
<tr>
<td>c. Choose the appropriate device.</td>
</tr>
<tr>
<td>d. Discuss the plan with the patient.</td>
</tr>
</tbody>
</table>
with most recent studies demonstrating about 2-year durability. Rare hematomas, lumps, granulomas, and indurations do occur with the use of Aquamid. Use of this filler should be discouraged until more safety data are gathered.

**HOW TO SELECT A FILLER**

There are many filler options available, so deciding on which filler to use is difficult. The A, B, C, D approach can help (Table 23-6). “A” stands for assess the patient. Determine which areas can be treated with the greatest potential for improvement. Look at the entire face and decide where to get the “best bang for the buck.” For example, if the patient has prominent nasolabial folds, there are two main options: treating the nasolabial folds, or treating the cheek or cheekbone area to add volume that will improve the fold by pulling the skin back. A patient with large round cheeks would do better to have the nasolabial fold treated (Fig. 23-14), while a patient with thin cheeks and facial volume loss would have a better result if the cheeks were treated (Figs. 23-15 and 23-16). As a practitioner, it is important to form your own impression first before the patient tells you their thoughts. In some cases you may notice factors that the patient does not even realize are contributing to an aged appearance (Figs. 23-17 and 23-18). These observational skills are developed with experience. Table 23-7 provides an overview of which fillers are best suited for each facial area. Once you have an idea of what areas would make the most significant impact if treated, then move to the “B” section, which is budget. It is crucial to determine how much money the patient is willing to spend. It is often the case that the budget is lower than what is necessary, so the physician must determine what areas to treat to achieve the best cosmetic effect possible within the patient’s budget. In addition, the practitioner must consider the patient’s time budget or schedule. For example, if a patient is visiting from another country and planning to leave the following day, a course of Sculptra injections is not an option. Once the time and financial budget have been determined, the practitioner should talk to the patient about other considerations. The most important question is what bothers them about their face. It is often different than what the physician sees.

**FIGURE 23-14** A. Those with a normal to large buccal fat pad are best treated with injections directly into the nasolabial folds and marionette lines. B. Immediately after treatment of nasolabial folds and marionette lines.

**FIGURE 23-15** This patient has thin cheeks from buccal fat pad wasting; therefore, she is a good candidate for a filler such as Sculptra, Juvederm Ultra, or Restylane to the cheek area below the cheekbones.

**FIGURE 23-16** This patient appears to have buccal fat pad wasting, but actually is missing a tooth on this side, leading to the defect. A dental consult is more appropriate for this patient rather than a dermal filler.

**FIGURE 23-17** (A and B) Soft tissue loss around the mental area is often one of the first signs of facial aging. It is hard to capture on film and patients do not really notice it until it is pointed out to them.
Patient happiness is contingent on improving what they see as the problems on their face, not what bothers the physician. The following or similar questions may be appropriate to frame such a discussion, then, in the attempt to identify the most suitable filler for a patient: What have you tried before? Were you satisfied with the results? Why or why not? What concerns do you have? Are you a frequent bruiser? Are you worried that your lips will look too big? Do you hate it when your lipstick bleeds up into the lines on the top lip? Do you have any religious restrictions? Do you have any events coming up? What amount of downtime can you tolerate? These are all critical issues in determining the most appropriate filler. Once all this information has been gathered, the physician must choose a filling device that meets all the criteria. It is a relatively easy choice after the preceding questions have been answered. In addition, the physician should have many filler choices on hand to give the patient the best result.

**Injection Technique**

Injection technique varies from filler to filler. Most physicians use either an anterograde, retrograde, or serial puncture technique. Most collagen and HA fillers are injected at a 45-degree angle (Fig. 23-19). It is important to be individually trained on the injection techniques of each filler. Fillers can be used in combination with botulinum toxins and other cosmetic procedures (Fig. 23-20). Although this chapter focused on facial use, fillers can also be injected in other areas of the body such as the hands (Fig. 23-21). Many injection techniques can be used. However, it is difficult to teach various techniques without video and live demonstrations. In the future, instructional videos will be available at www.derm.net and training courses will be offered at the University of Miami. In addition, the American Academy of Dermatology and the American Society of Dermatologic Surgeons offer training courses for dermatologists.

**SUMMARY**

Filling agents for soft issue augmentation procedures are now widely available, based on the long-standing successful track records of the earliest products. Most agents in the soft tissue augmentation armamentarium can be safely used alone or in combination. The

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**TABLE 23-7**

<table>
<thead>
<tr>
<th>Filler by Region (Listed from the Top of the Face Down)</th>
<th>Nasolabial folds</th>
<th>Vermilion border of the lip</th>
<th>Tear trough (soft fillers preferred)</th>
<th>Body of the lip</th>
<th>Marionette lines</th>
<th>Cheek bones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forehead lines</td>
<td>CosmoDerm I</td>
<td>CosmoPlast</td>
<td>Hylaform</td>
<td>CosmoDerm I</td>
<td>Prevelle Silk</td>
<td>Juvéderm Ultra</td>
</tr>
<tr>
<td>Restylane Fine Lines, Juvéderm, or Prevelle Silk</td>
<td></td>
<td>Evokevence</td>
<td>Juvéderm Ultra</td>
<td></td>
<td>Prevelle Silk</td>
<td>Juvéderm Ultra Plus</td>
</tr>
<tr>
<td>Zyderm I</td>
<td></td>
<td>Juvéderm Ultra Plus</td>
<td>Prevelle Dura</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
</tr>
<tr>
<td>Raising lateral brows (almost any will work)</td>
<td>CosmoPlast</td>
<td>Prevelle Silk</td>
<td>Radiesse</td>
<td>Prevelle Silk</td>
<td></td>
<td>Prevelle Dura</td>
</tr>
<tr>
<td>CosmoDerm I</td>
<td>Evokevence</td>
<td>Prevelle Dura</td>
<td>Restylane</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
</tr>
<tr>
<td>Juvéderm Ultra</td>
<td>Juvéderm Ultra Plus</td>
<td></td>
<td>Restylane</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
</tr>
<tr>
<td>Juvéderm Ultra Plus</td>
<td>Perlane</td>
<td>Prevelle Silk</td>
<td>Restylane</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
</tr>
<tr>
<td>Prevelle Silk</td>
<td>Prevelle Silk</td>
<td>Radiesse</td>
<td>Sculptra</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
</tr>
<tr>
<td>Prevelle Dura</td>
<td>Radiesse</td>
<td>Sculptra</td>
<td>Zyplast</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
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<tr>
<td>Prevelle Silk</td>
<td>Restylane</td>
<td>Sculptra</td>
<td>Zyplast</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
</tr>
<tr>
<td>Zyplast</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sculptra</td>
</tr>
<tr>
<td>Glabella (use with caution)</td>
<td>CosmoDerm I</td>
<td>Prevelle Silk</td>
<td>Juvéderm Ultra</td>
<td>Sculptra</td>
<td>Prevelle Silk</td>
<td>Prevelle Silk</td>
</tr>
<tr>
<td>Zyderm I</td>
<td></td>
<td>Prevelle Dura</td>
<td>Radiesse</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
</tr>
<tr>
<td>Tear trough (soft fillers preferred)</td>
<td>Hylaform</td>
<td>Prevelle Dura</td>
<td>Restylane</td>
<td></td>
<td></td>
<td>Pre-jowl sulcus</td>
</tr>
<tr>
<td>Hylaform</td>
<td></td>
<td>Prevelle Silk</td>
<td>Restylane</td>
<td></td>
<td></td>
<td>CosmoPlast</td>
</tr>
<tr>
<td>Juvéderm 18</td>
<td>Prevelle Silk</td>
<td>Restylane</td>
<td>Prevelle Silk</td>
<td></td>
<td></td>
<td>Evokevence</td>
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<tr>
<td>Prevelle Silk</td>
<td></td>
<td>Restylane</td>
<td>Prevelle Dura</td>
<td></td>
<td></td>
<td>Juvéderm Ultra</td>
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<tr>
<td>Restylane Touch</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
<td></td>
<td></td>
<td>Juvéderm Ultra Plus</td>
</tr>
<tr>
<td>Crow’s feet</td>
<td>CosmoDerm I</td>
<td></td>
<td>Prevelle Dura</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
</tr>
<tr>
<td>Juvéderm 18</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
<td></td>
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<td>Prevelle Dura</td>
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<tr>
<td>Prevelle Silk</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
</tr>
<tr>
<td>Restylane Touch</td>
<td></td>
<td></td>
<td>Prevelle Dura</td>
<td></td>
<td></td>
<td>Pre-jowl sulcus</td>
</tr>
<tr>
<td>Zyderm I</td>
<td></td>
<td></td>
<td>Pre-valle Dura</td>
<td></td>
<td></td>
<td>CosmoPlast</td>
</tr>
<tr>
<td>Cheek bones</td>
<td>Juvéderm Ultra</td>
<td></td>
<td>Juvéderm Ultra</td>
<td>Sculptra</td>
<td>Prevelle Silk</td>
<td>Prevelle Silk</td>
</tr>
<tr>
<td>Juvéderm Ultra Plus</td>
<td>Perlane</td>
<td></td>
<td>Juvéderm Ultra Plus</td>
<td></td>
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<td>Prevelle Dura</td>
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<tr>
<td>Prevelle Dura</td>
<td>Preuvee Silk</td>
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<tr>
<td>Prevelle Silk</td>
<td>Radiesse</td>
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<td>Radiesse</td>
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<tr>
<td>Radiesse</td>
<td>Restylane</td>
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<td>Restylane</td>
<td></td>
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<td>Pre-jowl sulcus</td>
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<tr>
<td>Restylane</td>
<td>Sculptra</td>
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<td>Zyplast</td>
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<td></td>
<td>CosmoPlast</td>
</tr>
<tr>
<td>Sculptra</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Evokevence</td>
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</tbody>
</table>
most frequently used agents are those that contain HA. Given the widespread popularity of soft tissue augmentation and the ever-present need to develop safer fillers that last longer than the current products, new fillers frequently enter the market. Soon to be made available in the US is an HA filler that contains lidocaine as well as more durable and safer synthetic agents. In short, the demand for soft tissue augmentation procedures has steadily increased since their inception and research is ongoing to develop products that address the shortcomings of the earlier products while incorporating and expanding on their advantages. Moreover, the “coupling” of fillers with other cosmetic interventions (e.g., Botox injections) enhances their longevity and efficacy, and creates an overall realistically aesthetic appearance. To keep abreast with the rapidly changing cosmetic dermatology arena, it behooves the aesthetic practitioner to be aware of the current availability, application, and future potential of dermal fillers.

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