Injectable Skin Fillers

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Recent advances in soft tissue augmentation have expanded our options in the search for an ideal filling agent, and several new fillers have recently been approved by the US Food and Drug Administration (FDA). Fillers can be used aesthetically to reduce the effects of aging and to de-emphasize previous scars. With aging, there is shifting and loss of connective and subcutaneous tissue, most notably in the face, neck, and hands. Subcutaneous augmentation in appropriate areas with injectable fillers replaces this lost tissue, producing a rejuvenating effect. Fillers can work synergistically with surgical procedures (eg, facelifts) to improve results. Patients who do not want to undergo a surgical procedure can often obtain excellent results noninvasively using fillers combined with other modalities (eg, laser resurfacing, peels, botulinum toxin).

Facial fillers are most useful in the lower third of the face. The gravitational effects of aging mean that tissue shifts inferiorly, resulting in accentuated nasolabial and melolabial folds. Moreover, botulinum toxin is unmatched in its ability to rejuvenate the upper third of the face. Scars from acne, surgery, or trauma that result predominantly from loss or contraction of tissue can also be improved greatly with fillers. Each type of filler has different strengths and weaknesses (Table 1). Physicians who are familiar with many fillers thus are best equipped to maximize the benefits of this class of agents and to serve their patients.

The ideal filler would be easy to use and give reproducible and long-lasting results. It would be able to pass through a small needle, be painless on injection, and fill both superficial lines and deep folds or furrows. It would be nonallergenic and hence would not require a skin test (ie, it could be injected on the day of initial consultation). It would be noncarcinogenic, nonteratogenic, and nonmigratory, and it would store and ship at room temperature and have a long shelf life. It would be free of transmissible diseases and have minimal postoperative morbidity, such as swelling, redness, or bruising.

To achieve the desired result using fillers for soft tissue augmentation, the practitioner must make several determinations, based on the specific situation:

Choice of filler. Different filling substances have different characteristics (strengths and weaknesses) and must be chosen accordingly, based on the task at hand. For example, a nonorganic, thick, high-viscosity filler that requires a large needle for injection and is permanent once injected may do well for a large, atrophic scar but would be a poor choice for improving fine, superficial rhytids of the upper cutaneous lip.

Proper placement and location. Optimal performance of a filler requires appropriate anatomic placement, consistent with its intended use. (For instance, a filler substance designed for subcutaneous augmentation should not be placed superficially in the papillary dermis...
and vice versa.) This placement can be affected by injection technique (eg, linear threading versus serial puncture, fanning, cross-hatching) and other factors (eg, needle gauge, needle angle and direction, needle tip depth).

Amount of implant deposited. This question sounds like a matter of common sense, but all too often the potential benefit is not realized and the patient is not satisfied simply because too little product was used. Nasolabial folds and other large furrows can be deceptive as to how much filling they require. This comment does not necessarily imply that complete correction must be achieved at the initial session. On the contrary, gradually achieving the final result over several sessions has several advantages. These include more exact correction in some areas (eg, lips) by elimination of the product, which is partially resorbed, and the acute swelling associated with local anesthesia or tissue edema, and guarding against overcorrection (a very personal and subjectively defined factor with large interpatient variation) by requiring the patient to agree that “more is needed.”

Timing (of repeat injections). Different fillers have different tissue residence times, ranging from a few months to many years. Patients benefit from re-evaluation and “touch-up” injections before the implant is completely absorbed to maintain clinical effect. On a related note, beware of placing a permanent filler in a patient who has never had fillers before. The authors like to use a nonpermanent filler first, then after several months to replace it with a longer-lasting, closer to permanent filler if the patient decides he or she likes the effect. (You will only make this mistake once.)

Nonpermanent fillers

Zyderm/Zyplast

Zyderm I and II and Zyplast (Inamed, Santa Barbara, California) have been used successfully as fillers for many years [1–5]. Zyderm I first appeared in 1976 and was FDA approved in 1981. The off-white, opaque products are derived from bovine collagen from an isolated United States–raised herd. Both come prepackaged in 1- to 2-mL syringes for single use. Zyderm is excellent for superficial etched-in lines, and Zyplast fills in deeper folds and lines. For both, a double skin test with Zyderm I is the norm, with treatment following the first skin test at 6 weeks and the second occurring at 2, 3, or 4 weeks. Generally, the product lasts for 4 or 5 months in the nasolabial folds and 2 or 3 months in the lips, with the duration of action dependent on the amount injected.

Zyderm I is injected through a 30- to 32-gauge needle into the superficial papillary dermis to raise a bleb as it flows along the superficial lines, whereas Zyplast is injected through a 30-gauge needle into the middermis or deep dermis to lift deeper folds. These fillers should spread smoothly into the tissue and be massaged lightly after injection. It is necessary to overcorrect with Zyderm, because it is diluted with saline, which is reabsorbed over 24 hours. If placed too superficially, it can impart a flat, yellow look to the skin.

Zyplast may be placed along the vermilion border of the lips or the filtrum or injected into the musculature of the lips themselves, a procedure that has been called the “Paris Lip.” For the glabella, Zyderm works best and lasts longest when used in conjunction with botulinum toxin injections. One case of blindness was reported after injection into the...
glabella caused vascular occlusion. For this reason, Zyderm (which is injected more superficially) rather than Zyplast (which is injected deeper and closer to the blood vessels) is recommended for this area. For nasolabial and melolabial “puppet” lines, Zyderm is often layered over Zyplast to obtain the best correction.

Zyderm and Zyplast have a long track record of safety, come prepackaged with 30-gauge needles, and are easy to use. In addition, they have the capacity to treat etched-in lines as well as folds and are formulated with 0.4% lidocaine to minimize injection pain.

Their disadvantages are the need for refrigeration (they do not freeze), the possibility of allergic reactions (they require skin testing), the short duration of improvement, and the need for ample use of product in older patients, making treatment expensive. Sensitivity reactions (erythema, swelling, induration, or urticaria) occur in 1% to 3% of patients and can last for 1 to 9 months. Treatment includes topical, intralesional, and oral corticosteroids and nonsteroidal anti-inflammatory medication.

### Table 1
Comparison of filler characteristics

<table>
<thead>
<tr>
<th>Filler</th>
<th>Material (Source)</th>
<th>Duration in tissue</th>
<th>Primary use</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artecoll</td>
<td>Collagen (bovine), PMMA (synthetic)</td>
<td>Permanent</td>
<td>Folds, lips</td>
<td>Long-lasting</td>
<td>Permanence a problem?</td>
</tr>
<tr>
<td>Cosmoderm</td>
<td>Collagen (human)</td>
<td>3–5 mo</td>
<td>Wrinkles, fine lines</td>
<td>Not painful</td>
<td>Skin tests required</td>
</tr>
<tr>
<td>Cosmoplast</td>
<td>Collagen (human)</td>
<td>3–5 mo</td>
<td>Deep folds/wrinkles, lips</td>
<td>Not painful</td>
<td>Skin tests required</td>
</tr>
<tr>
<td>Cymetra</td>
<td>Micronized dermis (human cadaver)</td>
<td>5–7 mo</td>
<td>Lips, scars, folds</td>
<td>No allergy/skin test</td>
<td>Short-lasting</td>
</tr>
<tr>
<td>Dermalive/</td>
<td>Hyaluronic acid (bacteria), HEMA,</td>
<td>3–6 mo</td>
<td>Lips, deep defects</td>
<td>No allergy/skin test</td>
<td>Results not reproducible?</td>
</tr>
<tr>
<td>Dermadeep</td>
<td>EMA (synthetic)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fascian</td>
<td>Fascia lata (human cadaver)</td>
<td>3–6 mo</td>
<td>Lips, deep defects</td>
<td>No allergy/skin test</td>
<td>Results not reproducible?</td>
</tr>
<tr>
<td>Fat</td>
<td>Fat (autologous)</td>
<td>Months–years</td>
<td>Deep defects</td>
<td>No allergy/skin test</td>
<td>Separate procedure required to harvest fat</td>
</tr>
<tr>
<td>Gore-Tex</td>
<td>ePTFE (synthetic)</td>
<td>Permanent</td>
<td>Deep furrows, lips</td>
<td>Long-lasting, low tissue reactivity</td>
<td>Difficult to remove</td>
</tr>
<tr>
<td>Hylaform</td>
<td>Hyaluronic acid (rooster comb)</td>
<td>6–9 mo</td>
<td>Lips, nasolabial folds, wrinkles</td>
<td>No allergy/skin test</td>
<td>Slightly more pain/erythema</td>
</tr>
<tr>
<td>Radiance</td>
<td>Calcium hydroxyapatite (bacteria)</td>
<td>2–5 y</td>
<td>Deep folds, lips</td>
<td>No allergy/skin test</td>
<td>Painful on injection</td>
</tr>
<tr>
<td>Restylane</td>
<td>Hyaluronic acid (bacteria)</td>
<td>6–12 mo</td>
<td>Lips, nasolabial folds</td>
<td>No skin test required</td>
<td>Painful on injection</td>
</tr>
<tr>
<td>Sculptra</td>
<td>Poly-L-lactic acid (synthetic)</td>
<td>1–2 y</td>
<td>Lipohypertrophy, scars, medium wrinkles</td>
<td>No allergy/skin test; store at room temperature</td>
<td>Reconstitution required; multiple treatment sessions; painful on injection</td>
</tr>
<tr>
<td>Silicone</td>
<td>Silicone oil (synthetic)</td>
<td>Permanent</td>
<td>Wrinkles, scars</td>
<td>No skin test, inexpensive</td>
<td>Several sessions often required</td>
</tr>
<tr>
<td>Zyderm</td>
<td>Collagen (bovine)</td>
<td>3–5 mo</td>
<td>Wrinkles, fine lines</td>
<td>Not painful</td>
<td>Skin tests required</td>
</tr>
<tr>
<td>Zyplast</td>
<td>Collagen (bovine)</td>
<td>3–5 mo</td>
<td>Deep folds/wrinkles, lips</td>
<td>Not painful</td>
<td>Skin tests required; avoid glabella</td>
</tr>
</tbody>
</table>

Abbreviations: EMA, ethylmethacrylate; ePTFE, expanded polytetrafluoroethylene; HEMA, hydroxyethylmethacrylate; PMMA, polymethylmethacrylate (Plexiglas).

CosmoDerm/CosmoPlast

CosmoDerm I and II and CosmoPlast (Inamed, Santa Barbara, California) contain purified collagen derived from cell cultures of human fibrocytes. These are the only FDA-approved, commercially available dermal fillers that contain human collagen. The cell line has been tested for viruses, tumorigenicity, retroviruses, and so forth and was obtained from the...
foreskin of a newborn. Because these products contain the basic human collagen molecule stripped of antigenic determinants, no skin testing is necessary. Hence they may be used during the consultation visit. The material is whitish and opaque and flows through a 30-gauge needle easily. The products are prepackaged in 1-mL syringes and are meant for single use only.

Injection is similar to that of Zyderm and Zyplast. CosmoDerm is injected into the superficial papillary dermis, and CosmoPlast is injected into the mid- to deep reticular dermis. It is necessary to overcorrect with CosmoDerm, as with Zyderm, because it is diluted with saline, which is reabsorbed over 24 hours. Care should be taken in thin-skinned areas around the eyes and mouth. CosmoDerm is often layered over CosmoPlast for the best results. The products should not be injected into patients with allergy to lidocaine. Other precautions are similar to those for Zyderm and Zyplast.

The advantage of these fillers over the previously described collagen products, Zyderm and Zyplast, is that the formulation may be used at the initial consultation visit, because no skin testing is necessary. The disadvantages are the same as those of Zyderm and Zyplast: the need for refrigeration (they do not freeze), the cost, the duration, and the need for an ample amount of product in the patient with deeper lines. Flulike symptoms have been reported in 2% to 4% of patients.

**Fat**

Fat is an autologous filling substance that is usually available in large quantities, enabling the dermatologic surgeon to fill in large defects, perform mini–face lifts, and rejuvenate the hands. It can be frozen for later use and often lasts for years in the hollows of the cheeks and after repairing surgical defects. The technique the authors use (description to follow) is based on that of Dr. Sidney Coleman [6]. For completeness, many physicians use the micro-infiltration technique described by Dr. Roger Amar, in which fat is injected directly into the muscles for better blood supply [7].

Only a small amount of equipment is necessary: a sterile tray with several 10-mL syringes, a female–female luer-lock adapter, a test-tube rack in which the syringes can be placed upright, various needles (including 30-gauge, 0.5-in and 18-gauge, 16-gauge, and 22-gauge spinal needles), a Coleman extraction/injection cannula, red syringe caps, and gauze pads. Tumescent lidocaine solution, spinal needles, and syringes or a pressure pump with intravenous tubing are also needed for anesthesia.

The recipient and donor sites are prepared with povidone iodine, and a small amount of tumescent anesthetic is injected with a 30-gauge, 0.5-in needle using a 3-mL syringe in the “incision” area of the donor site. Tumescent anesthesia is injected radially through this incision site using 10-mL syringes and a spinal needle or using the IV pump (very low setting) and intravenous tubing with an 18-gauge or 20-gauge spinal needle.

The incision sites of the recipient areas are then similarly injected, and a small amount of tumescent anesthetic is delivered radially into the reinjection area using a 30-gauge, 1-in needle or, if the area is large, a 22-gauge spinal needle. In this area, very little anesthesia is needed, and it should be delivered under barely any pressure with a syringe, so that there is no distortion of the tissue. This slight anesthesia of the recipient area makes reinjections much more comfortable for the patient. Tiny needles are necessary to minimize the risk of bleeding, especially in this area, because fat is so vascular. When augmenting the nasolabial fold, commissures of the mouth, lips, puppet lines, and cheeks, one reinjection site can be used on each side, just lateral to the lips. If the chin or area anterior to the jowls is being enhanced, two incision sites are used, and the fat is injected at multiple levels from both incision sites.

Fat is harvested using syringes rather than a liposuction aspirator, because high pressure can injure the fat cells. The skin at the donor site is pierced with a 16-gauge needle; no mark is left by this incision and no suture is necessary. Through this opening, a Coleman extractor attached to a 10-mL syringe can be inserted and used to harvest the fat. Negative pressure is obtained in the syringe by pulling the plunger out and holding it there while the syringe is moved back and forth in the subcutaneous tissue. Fat and fluid fill the syringe, which is then placed in the container plunger up, so that the fluid can settle to the bottom and fat can rise to the top. This procedure may be repeated with as many syringes and donor sites as are necessary. The negative pressure on the plunger should be small; pull back 0.5 to 1 mL, and the fat will come out easily.

The infranatant fluid collects at the bottom of the syringe and is easily expelled with the plunger. A cap is put on the tip of the syringe, and the plunger is removed before centrifuging for 1 or 2 minutes. After centrifuging, any oily supranatant fluid is poured off (the final amount may be wicked off with sterile gauze), the plunger is replaced, and the
resultant clean yellow fat is ready for transplantation. Fat to be implanted immediately is transferred into 1-mL luer lock syringes through a female–female adaptor. Any remaining fat is frozen in the 10-mL syringes after they are capped. Each syringe is carefully labeled with the patient’s name, social security number, and date before being placed in the freezer at −20°C.

Fresh fat is reinjected through an incision with an 18-gauge NoKor needle (Robbins Instruments, Inc., Chatham, NJ) using a 1-mL luer lock syringe attached to a Coleman injection cannula. Two or fewer injection sites should be used per area to avoid extrusion of the fat through multiple openings. The cannula is inserted to the farthest point, and a tiny aliquot of fat is injected as the syringe is pulled out. This procedure is performed at multiple levels of the skin and subcutaneous tissue. After injection, the fat should be massaged in so that it fills the area smoothly. When injecting, placing a hand around the perimeter of the treatment area can help keep the transplanted fat within the desired site. Some surgeons overcorrect to compensate for fat that is re-absorbed over the first few postoperative days, but the authors prefer not to overcorrect, because more may always be added later. When injecting the hands, a single injection site on the back of each wrist should suffice. Five mL of fat are injected and massaged to allow an easy spread over the entire hand.

Fat that was previously harvested and frozen is injected into recipient sites using the same technique. It is a good idea to confirm with the patient the day before the procedure that he or she is still coming in; the amount of fat needed for reinjection is then removed from the freezer for thawing a few hours before the appointment. The frozen syringes are placed upright in a container, and the tray is arranged as for fresh fat. The top 0.5 to 1 mL is not used, because it is usually just triglycerides and other fatty acids. The fat is then pushed through a female–female adapter into 1-mL luer-lock syringes for injection. Some physicians use a sharp 18-gauge needle to reinject fat monthly with no local anesthetic. The authors find that less frequent injections suffice when a blunt-tipped instrument is used for injection. They do use local anesthetic, because undermining or subcision with the blunt-tipped instrument appears to improve cosmetic results.

The advantage of autologous fat is that it enables the physician to harvest, use, and then freeze a large quantity of material. This factor makes it versatile: it may be used to fill large and small areas over much of the body (eg, face, hands). Because it is the patient’s own fat, there is no problem with allergenicity. The disadvantages are the need for a surgical procedure to harvest the fat, the need for frequent touch-ups in areas of heavy movement (nasolabial folds and marionette lines), and the need for a local anesthetic before reinjection.

**Hyaluronic acid gels (hylans)**

Hyaluronic acid (hyaluronan, sodium hyaluronate; HA) is a naturally occurring linear polysaccharide. Unlike collagen, it exhibits no species or tissue specificity; its chemical structure is uniform throughout nature, and it thus has no potential for immunogenicity in its pure form. In the skin, it forms the elastoviscous fluid matrix in which collagen fibers, elastic fibers, and other intercellular structures are embedded.

HA gels (hylans) are swollen with water (95% of weight) and have the unique attribute of dynamic viscosity, which decreases with increasing shearing force. Under pressure of injection (high shear rate), the gel can pass through a small-gauge needle. On removal of the shearing force, viscosity increases, forming a thick gel at the site of tissue implantation, which is unlikely to migrate. Unlike other temporary soft tissue fillers, such as collagen, HA fillers disappear from tissue following isovolemic degradation. As individual molecules of HA are degraded, those remaining are able to bind more water, so that the overall volume of the gel remains unchanged. In other words, the concentration of the gel decreases during reabsorption, but volume remains steady until the last molecules of HA are degraded. Clinically, this translates to an implant that maintains more than 95% of its initial space-filling volume until the last of the material is completely resorbed.

**Hylaform**

The first hylan preparation widely used for soft tissue augmentation was hylan B gel (Hylaform Gel, Biomatrix, Ridgefield, New Jersey), which was developed in the mid-1980s. It uses HA derived from the dermis of rooster combs, which is then purified and chemically cross-linked with divinyl sulfone. It is distributed in Canada by Collagen Aesthetics (Palo Alto, California) and in Europe by Collagen International. It has been used in the treatment of soft tissue defects and facial augmentation throughout most of the world (Canada, Europe, Australia, South America, Asia) for many years and recently became available in the United States (April 2004). In clinical studies, treatment reactions have included mild
erythema, itching, swelling, and pain, which usually resolve in less than 1 week.

Restylane

Restylane (Q-Med AB, Uppsala, Sweden) is a stabilized, partially cross-linked HA gel. The HA is produced from cultures of *Streptococcus equi* by fermentation in the presence of sugar, which is alcohol-precipitated, filtered, and dried. The HA chains are then chemically stabilized through permanent cross-linking with epoxides. The material is heat-sterilized in its final container and has a shelf life of 1.5 years from the date of manufacture. Because its production does not require an animal source, it has been termed a non-animal, stabilized hyaluronic acid.

In a Swedish study of the clinical safety and efficacy of Restylane [8], physician evaluation revealed that treatment sites maintained an average of 82% and 69% of correction at 12 and 26 weeks, respectively, whereas subjects self-reported 75% and 61% improvement at these same time points. An Italian study of Restylane’s clinical efficacy and tolerability also showed favorable results [9], with 78% of patients maintaining moderate to marked improvement after 8 months, and nasolabial folds and lips faring the best. An American study comparing Restylane with Zyplast in the treatment of nasolabial folds reported Restylane to be superior to Zyplast in 56.9% of patients, Zyplast to be superior in 9.5%, and both fillers to be equal in 33.6% after 6 months [10].

Injection-related reactions include redness, swelling, darkening of the treatment site, and slight pain, most of which resolve spontaneously within several days. In the early efficacy studies of Olenius [8] and Duranti et al [9], investigators reported such adverse events at an incidence of 13%. Subsequent retrospective reviews of Q-Med Esthetics’ adverse events database reported much lower incidences, with only 1 out of every 650 (0.15%) of an estimated 144,000 patients treated in 1999 reporting temporary redness, swelling, localized granulomatous reactions, bacterial infection, or acneiform lesions [11]. No patients were reported to have systemic symptoms or anaphylaxis, although two cases of injection-site necrosis were recorded, both of the glabellar area. Clinically speaking, compared with collagen, hylan preparations are slightly more painful on injection (more viscous, with no lidocaine in current preparations) and can result in more erythema at the injection site, persisting for several days to a week.

Although early studies did not demonstrate hypersensitivity or other allergic reactions to hylans, delayed implant-site reactions have now been reported in several case series at incidences from 0.4% to 3.7% [12–14]. In these rare cases, delayed inflammatory reactions of redness, pruritus, painful swelling, or “nettle-like” rash occurred. None appeared sooner than 6 to 8 weeks after injection; some were reported to last up to 4.5 months without oral treatment. In one instance, patients developed anti-Restylane and anti-Hylaform antibodies [14].

### Treatment with hylan fillers

At the time of this writing, Restylane and Hylaform are the only FDA-approved hylans available in the United States, and these are only indicated for the treatment of moderate to severe facial wrinkles and folds, such as the nasolabial folds. All other uses are currently considered off-label. They have not been studied in patients who are pregnant, breastfeeding, under 18 years of age, or on immunosuppressive therapy.

The Restylane family of products is a good example of different hylan formulations designed for use at different dermal depths: Restylane, Restylane Fine Lines, and Restylane Perlane (Table 2). The concentration of HA is identical in all three preparations at 20 mg/mL. What differs is the size of the HA particles, expressed in number of gel particles per milliliter, and the target depth for implantation. Restylane Fine Lines has the smallest particles and

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Restylane</th>
<th>Restylane Fine Lines</th>
<th>Restylane Perlane</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composition</td>
<td>20 mg/mL stabilized HA</td>
<td>20 mg/mL stabilized HA</td>
<td>20 mg/mL stabilized HA</td>
</tr>
<tr>
<td>No. of gel particles/mL</td>
<td>100,000</td>
<td>200,000</td>
<td>10,000</td>
</tr>
<tr>
<td>Indications</td>
<td>Wrinkles, lips</td>
<td>Thin superficial lines</td>
<td>Deep folds (eg, nasolabial), lip augmentation, facial contouring</td>
</tr>
<tr>
<td>Target depth</td>
<td>Middermis</td>
<td>Upper dermis</td>
<td>Deep dermis/Upper subcutis</td>
</tr>
<tr>
<td>Degree of correction</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Syringe volume</td>
<td>0.7 mL, 0.4 mL</td>
<td>0.4 mL</td>
<td>0.7 mL</td>
</tr>
<tr>
<td>Needle size</td>
<td>30-gauge</td>
<td>31-gauge</td>
<td>27-gauge</td>
</tr>
</tbody>
</table>
hence is the least viscous. It is injected through a 31-gauge needle and is designed for use in the most superficial dermis to correct fine lines and superficial, easily distensible defects. Restylane, with larger particles that are injected through a 30-gauge needle, is placed in the middermis to correct moderate nasolabial folds and provide lip augmentation. Perlane has the largest particle size, making it the most viscous of the three preparations, and requires a 27-gauge needle for injection. It is designed for implantation into the deep dermis and superficial subcutaneous tissue to treat deep folds and provide facial contouring (eg, cheek and chin augmentation). The three different products can be used in concert, layering one over another for optimal clinical results. Currently, only Restylane is FDA-approved for use in the United States (marketed through Medicis Aesthetics, Scottsdale, Arizona since December 2003) and is officially indicated only for the treatment of moderate to severe facial wrinkles and folds, such as the nasolabial folds.

None of the hylan preparations include lidocaine (unlike collagen products such as Zyderm and Zyplast), and they may require separate anesthesia before treatment. Topical anesthetics (eg, LMX) can be useful but must be thickly applied for 15 minutes before injection, and the degree of pain reduction provided may not warrant the preparation time. Alternatively, small amounts of local anesthetic or a nerve block may be used. Some patients can tolerate treatment of nasolabial folds, oral commissures, or the glabellar area without any anesthesia (Figs. 1–3). For injections of the lips, however, peripheral nerve or field blocks are usually needed.

The linear threading technique is probably the most commonly used. Holding the syringe parallel to the length of the wrinkle or fold to be treated, pierce the skin and advance the needle to its fullest extent. Then, while slowly withdrawing the needle, apply even pressure on the plunger to dispense material into the dermis. (For very fine, superficial wrinkles, picture the extrusion of material from the needle tip pushing the needle backward.) Relieve pressure just before withdrawing the needle from the skin to avoid leakage and wastage of gel. Short, superficial lines and wrinkles can be ablated with a single injection; several successive “threads” below, above, or beside previous injections may be required to fill larger folds, lines, or wrinkles. Deeper defects may require layering with thicker preparations (ie, Restylane Perlane).

Some practitioners enter the skin with a needle angle of 30° or 45°. Others prefer it closer to parallel with the skin; this is a matter of personal preference. Most authors recommend keeping the needle bevel-up, but this is not essential; studies have shown that the direction of the bevel does not influence the direction of flow of the material, which follows the course of least resistance [15]. The authors like to start with the bevel up to see the tip of the needle and control more precisely where it pierces the skin.
The practitioner should keep the tip of the needle at constant depth during implantation, depositing all filler material within the same plane to get even results. The depth of needle placement (and hence of filler implantation) should be high dermis for superficial lines, middermis for more substantial wrinkles, and deep dermis/subcutaneous border for heavy folds. A rule of thumb to gauge needle depth is that, for middermis placement, the needle’s contour should be visible but not its color. The practitioner should guide treatment while injecting by visual response when placing thinner material high in the dermis (Restylane Fine Lines) and by tactile response when placing thicker material more deeply (Perlane). Resistance should be felt when placing thicker substances into deep dermis; a sudden drop in such resistance may indicate injection into the subcutaneous plane. The fanning and cross-hatching techniques are merely variations on the linear threading technique, most often used when placing a larger amount of filler more deeply.

The most difficult part of the technique for beginners is developing a feel for needle depth. It is better to err on the side of injecting too deeply, which will simply not give as much benefit. In contrast, injecting too superficially can overcorrect defects and leave surface irregularities. Although the clear hylan gels are not as unsightly as collagen (visible as white material) when placed too superficially, they can tend to make the epidermis transparent, leading to red or gray spots.

After injection, some practitioners manually gently massage the area to smooth out any nodular or uneven areas and ensure that the implanted material conforms to the contour of surrounding tissues. Using an ice pack or other cold compress can help to minimize swelling (especially on lips); some patients also feel it alleviates postinjection discomfort. Unlike collagen implants, which lose some volume after injection because of the accompanying lidocaine, hyalans should only correct to 100% of the desired volume. If the area is overcorrected, massage firmly between fingers or against underlying bone to obtain optimal results. Approximately 20% of overcorrection can be massaged out; more will lead to a persistent unwanted cosmetic result. Patients can return to normal activities almost immediately after treatment (eg, can apply make-up, if desired). The duration of correction depends on the character of the defect being treated, tissue stress at the implant site (frequency of muscular activity), implant depth, and injection technique. Most authors suggest limiting treatment to 1.5 to 2.0 mL per treatment session and planning a “touch-up” 2 to 4 weeks later.

**Radiance**

Radiance FN (Bioform, Franksville, Wisconsin) is composed of microscopic calcium hydroxyapatite particles suspended in a gel. It has been FDA-approved and used for years in dental reconstruction and bone, bladder, neck, and vocal cord implants. Technically, it comprises calcium hydroxyapatite microspheres suspended in an aqueous polysaccharide gel, similar to Coaptite. The polysaccharide, carboxymethylcellulose, stays in place long enough for the body’s own tissue to move in and hold it in place. Radiance FN supposedly acts as a scaffolding for bone or collagen to grow in soft tissue, thereby creating volume. Use in the skin is FDA–off label.

No skin testing is necessary, because Radiance FN contains no animal products. Therefore, treatment may be given on the day of consultation. Radiance FN is reported to last from 2 to 5 years. One milliliter treats more areas than 1 mL of collagen, and it is said to look and feel natural.

Dental blocks and local anesthesia are necessary, because the injections are more painful than collagen. Swelling can occur for 2 days postinjection, and sometimes calcium deposits (easily excised) rise to the surface of the skin. Granulomas sometimes occur. Radiance FN is not to be used for superficial lines but is reported to be good for deeper folds, wrinkles, and lip enhancement. If it is injected too superficially, extrusion, infection, firmness, and lumps may occur. Complications include lumpiness, extrusion, granulomas, infection, and firmness.

**Cymetra**

Cymetra (LifeCell, Branchberg, New Jersey) is micronized acellular human cadaveric dermis. It is supplied in a prepackaged 5-cm³ syringe of dried powder. The powder is reconstituted to 1 mL with saline or lidocaine and is for single use only. The human tissue has been tested, sterilized, and treated so that it is accepted without rejection. It is a soft implant without allergies that is reported to last slightly longer than collagen. It should be refrigerated when received to lengthen its shelf life.

To treat nasolabial folds, 1.5 to 2 units are usually required on each side. After subcising the injection site with an 18-gauge, 1.5-in needle, the practitioner should inject the material with a threading technique. If no subcission is desired, the material may be threaded with multiple injections using 23- to 25-gauge needles or with serial injections using 25- to 27-gauge needles.
Techniques for injecting the lip vary depending on location. For the vermilion border, use a 22- or 23-gauge, 1.5-in needle and inject with the bevel up, tenting the skin while withdrawing the needle. First inject from the Cupid’s bow on one side to the opposite commissure. Then repeat for the other side (the middle third of the lip is overlapped, for double treatment), using a total of 0.5 to 1.5 units per lip. To treat the vermilion itself, use the same technique, injecting from a third of the way across the lip to the other side to deposit roughly twice the amount of Cymetra in the middle third of the lip. Use about 1.2 units per lip. To treat perioral rhytids, a 26-gauge, 0.375-in needle should be used in a similar manner to deposit material immediately subdermally. A small amount should be injected parallel to and just above the white roll in the same manner.

For the triangular depression of the marionette complex, combine the threading and serial-puncture techniques. The threading technique works best with a 25-gauge, 1.5-in needle using subdermal subcision from below the fold. Inject while withdrawing the needle, keeping the bevel up and the tissue tented. Use 0.5 to 1 unit of Cymetra on each side, then follow this procedure with serial-puncture implantation into the immediate subdermal plane.

The malar area should be treated with a 22-gauge, 1.5-in needle. In the subdermal plane, thread the implant three times horizontally and three times vertically for an even criss-cross pattern. The area can then be rolled, even with a common cotton-tipped applicator, or massaged bimanually. For all areas, gentle massage is performed after injection, and the patient is warned to avoid facial expressions as long as possible (6 hours or more). More than one treatment may be necessary for optimal improvement.

The advantages of Cymetra include the possibility of treating at the initial consultation visit, because no skin test is necessary. It can be stored at room temperature and lasts up to 6 months. However, it must be stored refrigerated and be rehydrated before injection. The manufacturer recommends Cymetra not be used in patients who have a collagen autoimmune disease. It also advises its physicians not to use Cymetra around the eyes and in the glabella. More than one treatment may be necessary for optimal improvement.

**Fascian**

Fascian is preserved fascia lata in particulate form made from screened human cadavers and was introduced in 1999. It is quite dense and takes the body many months or years to absorb. Fascian comes in prepackaged 3-cm\(^3\) luer-lock syringes of dried material. The tissue is tested for various diseases, irradiated, particulated, and vacuum sealed. Fascian particles come in various sizes: less than 0.25 mm, less than 0.5 mm, and less than 2.0 mm; all three need to be rehydrated in 3 to 5 mL of saline or lidocaine solution before injection. After rehydrating the material and anesthetizing the area with a local anesthetic or anesthetic block, the practitioner sub-cises the area to be injected with a 20-gauge needle and injects the material subdermally with a 16- to 29-gauge needle, depending on the particle size. Fascian should not be injected into the dermis, because inflammation with erythema and swelling and lumpiness can occur. After injection, collagen is said to form around the graft and act as a scaffolding.

The advantages of Fascian are that it may last slightly longer than collagen, it can be stored at room temperature, and no skin testing is required. However, it must be rehydrated before injection, and a local anesthetic or anesthetic block must be used. Trace amounts of polymyxin sulfate, bacitracin, or gentamycin may be present, so it should not be used in patients who are allergic to any of these substances. Fascian should not be used for superficial lines, because intradermal injection can lead to lumpiness or inflammation.

**Sculptra**

Sculptra (Dermik Aesthetics, Berwyn, PA) is an injectable form of poly-L-lactic acid (a compound that has been used in absorbable suture material for more than 40 years). It is a nontoxic, synthetic, immunologically inactive, biodegradable lactic acid polymer. It has been approved in Europe (where it is marketed as “New-Fill”) for the treatment of scars and wrinkles and was recently approved by the FDA for the treatment of facial lipoatrophy associated with HIV disease. It is sold in a kit of two vials, each containing 367.5 mg of powdered product. Three to five mL of sterile water with or without lidocaine are added to each vial to reconstitute it for injection. The vials must then stand for 2 hours to ensure complete hydration of the product. The product requires a 26-gauge or larger needle for injection and must be used within 72 hours of reconstitution.

Sculptra should be injected into the deep dermis or subcutaneous space after the area is adequately anesthetized with local anesthetic. The recommended maximum dosage is one vial per side per treatment.
session. It is injected into the deep dermis and subcutaneous space of the cheeks and nasolabial folds using a threading (also called “tunneling”) technique. In the temporal and zygomatic areas, depot-type injections are used instead to place the product just above the temporal fascia or zygomatic periosteum, respectively. Only a small amount of product is deposited with each injection, and many injections applied in a “criss-cross” pattern may be needed to address large areas. The fluid is absorbed in 1 week, and the poly-L-lactic acid particles are said to stimulate collagen growth. Multiple sessions, spaced at least 2 weeks apart, are needed for significant improvement. Initial studies of Sculptra demonstrated an increase in skin thickness as early as 6 weeks after injection, which persisted for up to 96 weeks [16].

The advantages of Sculptra are that it does not need to be refrigerated, and no skin test is necessary. However, it must be reconstituted 2 hours before use, a local anesthetic is usually required, and multiple sessions are needed. Granulomas have been reported.

Permanent fillers

Unlike the previously discussed fillers, these synthetic substances remain permanently at the implantation site. Unfortunately, longer tissue residence does not always translate to a better result or a more satisfied patient. On the contrary, permanent fillers can be a poor choice: first-time filler patients who find that they do not like the effect of fillers are “stuck” with them when they are permanent! Hence it is almost always preferable to use nonpermanent agents first, then advance to permanent fillers if the patient decides he or she likes the effects. In addition, because facial contour changes naturally with time (aging), any type of permanent implant that will not naturally change with the rest of the face may become more prominent than desired.

Artefill/Artecoll

Artecoll (Artes Medical, San Diego, California) is a permanent filler consisting of polymethylmethacrylate microspheres (PMMA; Plexiglas beads) in collagen (microscopic homogenous polymethylmethacrylate beads in 3.5% collagen suspension, mixed with 0.3% lidocaine) [17,18]. PMMA, commonly called Plexiglas or Lucite, has been used in artificial eye lenses, dentures, and bone cement. The PMMA is polymerized into 30- to 40-μm spheres that are then suspended in the collagen. The collagen is degraded after injection, leaving the PMMA spheres to remain permanently. The company reports that these spheres cannot migrate, because they are encapsulated by the patient’s own tissue in 2 to 4 months [19–21].

Artecoll is injected deeply, using a threading or tunneling technique at the junction between the dermis and subcutaneous tissue, through a 27-gauge, 0.5 in needle. If it is injected intradermally, the skin will blanch; injection should stop immediately, because small nodules may form and prolonged erythema may occur. The product is then massaged and molded with the fingers. Two treatment sessions should be used so as not to overcorrect during implantation. Patients should be advised to minimize facial expressions for 3 days after treatment to reduce the likelihood of muscular contraction’s pushing the substance more deeply into the subcutaneous tissue.

Because Artecoll contains collagen, the product must be refrigerated, and skin testing must be performed before injection. It is contraindicated in people with thin skin, because it can be palpable or visible after implantation. Patients may experience swelling, redness, and pain over the first few days. Granulomas, some occurring more than 10 years after injection, have been reported. Long-lasting redness can occur when the injection is too superficial, and itching may occur and persist for weeks to months.

Dermalive and Dermadeep

Dermalive (Dermatech, Seven Hills, NSW, Australia) is a semipermanent nonanimal filler composed of HA and acrylic hydrogel fragments. Here the HA is merely the delivery system (accounting for 60% of the volume); the acrylic hydrogel filler is a copolymer of hydroxyethylmethacrylate and ethylmethacrylate, a nonbiodegradable material belonging to the acrylate family that has demonstrated a good level of tolerance for many years in eye surgery. (It is the same acrylic hydrogel that is used in intraocular lens implants in cataract surgery.) The smooth-walled 45- to 65-micron hydrogel particles are intentionally irregular (nonspherical), which is thought to help integrate them into newly formed collagen fibers and prevent concentric fibrosis. It is supplied in 0.8-mL syringes and delivered through a 27.5-gauge needle. The product was first marketed in France in 1998 and has become popular throughout Europe. The manufacturer suggests several treatment sessions, each separated by a minimum of 3 months. Reports exist of granulomatous reactions from the acrylic
particles, manifesting as palpable nodules appearing about 6 months after injection. As with other HA products, no preoperative skin tests are required. Dermadeep is similar to Dermalive, except that the acrylic particle sizes are larger, from 80 to 110 μm. It is provided in 1.2-mL syringes and delivered through a 26.5-gauge needle. One study describing the use of Dermalive and Dermadeep in 455 patients (859 syringes) over 3 years reports that patients were satisfied in 88% of cases, with 20% developing transient redness or edema at the injection site [22,23].

**Gore-Tex**

Gore-Tex (W.L. Gore and Associates, Flagstaff, Arizona) is a permanent filling substance made of expanded polytetrafluoroethylene (ePTFE) created by the extrusion of Teflon. Nodules of ePTFE are connected by a multidirectional fibril structure to make a polymer. This soft and pliable polymer comes in sheets, patches, and tubes of various sizes. It has been used in the body since 1971, including abdominal wall and hernia repairs, and has been used for skin augmentation since 1991. It is inert and nonallergenic, with low tissue reactivity and minimal capsule formation. Its 20- to 30-μm pores allow tissue to grow into and anchor the material, although this anchoring also makes it more difficult to remove. Softform is a tubular form of Gore-Tex that comes prepackaged in a trocar to be used in the nasolabial folds and the vermilion border of the lips. After implantation, fibroblastic tissue grows into these tubes within 6 months and anchors them in place.

After anesthetizing the implantation site, the practitioner uses a hollow trocar to tunnel subcutaneously through the deepest part of the fold. The implant is then pulled through by dragging back with the trocar, needle, or suture and trimming excess ePTFE. The 3- to 5-mm incision sites are then sutured. Collagen can be layered over this material if more correction is needed.

An advantage of Gore-Tex is that it is stored at room temperature. The disadvantages are that implantation is a surgical procedure with incisions and suturing, the material may be palpable (irritating to some patients) or require repositioning, and removal is difficult.

**Silicone**

The silicone oil used today is Silikon 1000 (Alcon Laboratories, Fort Worth, Texas), which has a density of 1000 centistokes. The original Dow Corning silicone was 350 centistokes. Its use is off-label for wrinkles and scars. It is a purified product, because it has been FDA-approved for retinal detachment and has been used for the lipoatrophy seen in patients with AIDS. Problems seen in the past were usually due to excessive volume injected or adulteration of the fluid with substances such as mineral oil. Silikon 1000 is a sterile, clear, colorless gel that is relatively inert. There are no preservatives or other ingredients. It is distributed in 10-mL vials with 8.5 mL of sterile silicone oil that can be stored at room temperature. Silikon 1000 may be used off label, but because it is a device and not a drug, the physician may not advertise its use in the office, the phone book, on a Web site, or in other media.

A microdroplet serial injection technique is used to inject silicone oil. Multiple treatments are necessary at intervals of 4 to 6 weeks or more, and results may not be apparent until after two to three treatments. A 1-mL luer-lock syringe is used and attached to a 27-gauge needle or the RJ Flo 30-gauge, large-bore needle (RI Development Corp., Peabody, MA) that patients find more comfortable.

Silicone oil is an ideal filling substance in many ways. It is permanent, needs no skin testing (because there are no antibodies to liquid silicone), is stored at room temperature, does not support bacterial growth, can be used to treat many areas, is not painful when an anesthetic cream is used before injection and a modified dental block is used for the lips, and does not cause postinjection morbidity. It is inexpensive and has a long shelf life. Granulomas and other side effects are extremely rare when the proper volume of unadulterated, purified silicone is used.

**References**


