DERMAL FILLERS FOR FACIAL SOFT TISSUE AUGMENTATION

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Nowadays, patients are demanding not only enhancement to their dental (micro) esthetics, but also their overall facial (macro) esthetics. Soft tissue augmentation via dermal filling agents may be used to correct facial defects such as wrinkles caused by age, gravity, and trauma; thin lips; asymmetrical facial appearances; buccal fold depressions; and others. This article will review the pathogenesis of facial wrinkles, history, techniques, materials, complications, and clinical controversies regarding dermal fillers for soft tissue augmentation.

Key Words: dermal fillers, collagen injections, soft tissue augmentation, macro esthetics

INTRODUCTION

Dental implants have revolutionized the field of dentistry. Due to their ability to preserve bone and provide proper emergence profiles, dental implants are usually the ideal treatment option in the esthetic zone, which focuses on microesthetics (anything inside the oral cavity). They provide patients with what they are more commonly seeking—a highly esthetic appearance. There are other aspects of facial esthetics—the so-called “macroesthetic” profile that focuses on the overall facial appearance of the patient. Many patients are hyper-aware of rhytides, or wrinkles, in the perioral region which may detract from an overall pleasing appearance. A rhytide may be divided into dynamic and static conditions. Dynamic wrinkles occur during the contraction of muscles, and are most prominent in the forehead and eyes region of the face. These wrinkles are best treated by a paralyzing drug, such as botulinum toxin.

Botulinum toxin (Botox, Allergan, Inc, Irvine, Calif) is a deadly poison produced by the Clostridium botulinum bacterium. Clinical applications include blepharospasm, strabismus, and hemispatial spasm. New clinical uses in the fields of cosmetic dermatology include its use for the management of hyperfunctional facial lines, most commonly in the regions of the glabella, periorbital crow’s feet, and forehead lines.

Static wrinkles are present, even when the face is relaxed. The most prominent static wrinkles are in the inferior third of the face, between the nose and the chin. This region is of primary importance to the dentist and will be addressed in this article.

Deep nasolabial folds, prominent “marionette” lines at the inferior corners of the mouth, or flat and thin lips suggest an elderly and less attractive appearance. Figure 1 describes the difference among lines, folds, and wrinkles. An emerging treatment option for such patients is soft tissue augmentation via dermal filling agents. These materials have the ability to decrease the appearance of wrinkles, enhance the fullness of lips, and yield a more youthful facial appearance. Coupled with intraoral esthetics in dentistry, soft tissue augmentation can provide the patient with a highly esthetic result. This article will discuss this history, materials, general techniques, and other important considerations for successful facial soft tissue augmentation.

LIP ESTHETICS

Full-looking lips have been popular since the late 1980s. Female actresses and models boast luscious, well-defined lips that portray exotic, erotic, and
sensual images. Just as the eyes and nose are hallmarks of the middle third of the face, the lips are the focal point of the lower third of the face. Full, well-defined lips symbolize youth, beauty, attractiveness, and sensuality. Conversely, lips that are thin or flat create an illusion of emotional coldness or insensitivity and seem to imply age and unattractiveness.

In general, youthful qualities set the standard for what constitutes beautiful lips. They are: (1) an elevated and well-demarcated shape to Cupid's bow; (2) fullness, projection, and bulk to the lips with a slight emphasis on the lower lip; and (3) a modest, rather than excessive, or short distance from the nose to the upper lip.

As a result, public demand for lip augmentation procedures has evolved. A number of operations have been developed for the purposes of (1) increasing or decreasing lip fullness, (2) changing the length of the upper lip, and (3) attempting to achieve esthetic definition of the vermilion border and filtrum. Most importantly, individual preferences and desires must be considered when considering lip augmentation procedures. For example, although the literature suggests a 20° to 30° prominence of the upper lip over the lower lip as an esthetic standard, some patients' expectations of their final result may deviate greatly from these standards.

The projection, support, and bulk of the maxillary lip are of considerable importance to the overall macroesthetics of the inferior third of the face. When an edentulous maxilla is restored, the dentist is very aware that the position of the labial flange of the denture affects the fullness of the lip, the depth of facial lines in the face, and even the length of the upper lip. The further forward the denture flange, the shorter the maxillary lip is at repose and vice versa. Dermal fillers may be placed on the maxillary bone between the mucogingival junction and the base of the nose to increase the support to the maxillary lip for dentate patients. A canine eminence may be developed with dermal fillers to help support the maxillary corners of the lip in partially edentulous patients missing the canines. Hence, these typical dental procedures for edentulous patients may be extended to dentate and partially edentulous patients to further support the lip, shorten the lip length during repose, and give the appearance of a fuller maxillary lip.

The injection of dermal fillers may also be inserted into the maxillary lip. An emphasis is usually made to increase Cupid's bow height and to increase the size of the lip in the mid third to one-half regions of the lip. These procedures are less familiar to the dentist and are also more challenging to obtain a consistent result.

**PATHOGENESIS OF FACIAL WRINKLES**

Facial wrinkles are the product of repeated and habitual contraction of the underlying muscles of facial expression. When the contraction of a facial muscle is accompanied by a lack of shortening of the skin, a wrinkle is produced. The amount of facial changes is related to the depth of the depression within the mucosa or submucosa of the tissue. The terminology for the degree of relative change to the skin includes folds, wrinkles, and lines (Figure 1). A fold develops when the depression extends through the dermis and approximates the subcutaneous tissues. A wrinkle proceeds through the epidermis and extends to the dermis of the skin. A line remains completely within the epidermis and does not approach the dermis of the skin. Factors that can affect the depth of the wrinkle include skin texture, the amount of subcutaneous fat, the water content of the skin, the distribution and ratio of collagen and elastic fibers, and the biochemical changes in the connective tissue, and interstitial spaces.

Age is a major cause of facial wrinkles. Tissue laxity occurs as a function of age, especially in the nasolabial fold areas. The effect of gravity can lead to deepening of facial wrinkles. Additionally, atrophy of the skin occurs: there is loss of dermal papillae, reduction in the number of Langerhans cells, and presence of melanocytes. The total amount of dermal connective tissue (which is composed of glycosaminoglycans and proteoglycans) decreases. There is a significant loss of collagen fiber to the point that the elastin to collagen ratio may change in favor of elastin.

Another cause of wrinkles is damage to the skin. Harmful doses of ultraviolet radiation have been recorded in normal sunlight, most fluorescent light, and in sun-tanning booths. Ultraviolet radiation, via...
generation of superoxide radicals, causes actinic skin damage which manifests as a decrease in mature type I collagen and an increase in immature type III collagen. Other causes of facial wrinkles include trauma, scarring, and disease processes that alter the quality of collagen in the dermis, which can present as excessive skin laxity or premature aging. Such conditions which enhance facial wrinkles include Ehlers-Danlos syndrome, progeria, and pseudoxanthoma elasticum.

Wrinkles in the perioral region can detract from the overall esthetics of the face and are in the privy of most dentists from an overall esthetic appearance. Areas of primary concern for many patients are the “marionette lines,” which form at the inferior corners of the mouth and the chin and the so-called “smile lines,” which are the nasolabial folds. A rating scale based on visual assessment of the length and apparent depth of the nasolabial fold was reported by Narins et al in 2003 (Table 1). The ideal wrinkle group to treat with dermal fillers is score 3, followed by score 4, then 2. A score of 5 on the severity scale is unlikely to have a satisfactory correction with only injectable dermal fillers.9

Decreasing the appearance of such lines by augmenting the soft tissue with dermal fillers can restore a youthful appearance. In addition, a multitude of lines may be found along the upper lip or at the corners of the mouth. Again, preoperative communication is of vital importance. Most patients simply desire a return to their youthful image and not complete dissolution of all lines. Every attempt should be made to fulfill the patient’s desires and not create a result that is esthetic only to the dentist.

**History**

Attempts to augment the soft tissue to enhance macro facial esthetics dates back to the 1800s when Neuber reported the use of small pieces of fat harvested from the upper arm to reconstruct depressed facial defects.10 The first instance of the use of an injectable filler can be attributed to Gersuny who used low melting point paraffin to correct cosmetic deformities.11 The use of this material, however, was discontinued around the 1930s because it was associated with high incidences of inflammatory reactions and foreign-body granuloma formation.12 Other injectable materials that have been used over the years include vegetable oil, mineral oil, lanolin, and beeswax. These materials, however, were discarded because they were associated with undesirable tissue reactions such as movement of the material, chronic edema, scarring, and granuloma formation.

Severe tissue reactions and unpredictable long-term results of such materials led to investigations using highly purified polymers such as silicone as dermal fillers. Introduced in 1962, medical grade liquid silicone was widely used to correct a variety of cosmetic defects. Currently, its use is banned in the United States due to its high abuse potential and adverse effects such as foreign body granuloma formation from adulterated compounds.

Over the next 4 decades, attention was turned toward alternative materials, both tissue-derived and synthetic. These materials have included injectable bovine collagen, autologous fat, hyaluronic acid derivatives, and allo genic and synthetic products. Randomized, long-term clinical trials are still needed to evaluate efficacy, longevity, and long-term effects of these products. Continuing research promises that advances, such as recombinant human collagen, are on the horizon.

**Ideal Filler**

The search for the ideal dermal filler is constantly occurring. Table 2 lists the properties of the ideal dermal filler. Currently, no substance for soft tissue augmentation satisfies all of the suggested criteria. Only autologous fat produces no risk of allergy. Popular bovine-derived collagen products tend to have some allergenic potential, which must be determined prior to use. The newer, longer lasting hyaluronic acid fillers, such as Restylane (Q-Med, Uppsala, Sweden) and Perlane (Q-Med) come close to being ideal; however, they have their disadvantages as well. Proper selection of a material depends on the inherent

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
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<tbody>
<tr>
<td>5</td>
<td>Extreme: Extremely deep and long folds, detrimental to facial appearance; 2- to 4-mm visible V-shaped fold when stretched; unlikely to have satisfactory correction with injectable implant alone.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Very long and deep folds; prominent facial feature; less than 2-mm visible fold when stretched; significant improvement is expected from injectable implant.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Moderately deep folds; clear facial feature visible at normal appearance but not when stretched; excellent correction is expected from injectable implant.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: Shallow but visible fold with a slight indentation; minor facial feature; implant is expected to produce slight improvement in appearance.</td>
</tr>
<tr>
<td>1</td>
<td>Absent: No visible fold; continuous skin line.</td>
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</tbody>
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advantages and limitations of the material, the specific clinical indication, and personal experience.

**TYPES OF DERMAL FILLERS**

Generally, the various dermal fillers used for soft tissue augmentation can be divided into 4 categories as indicated in Table 3.

**Xenografts**

*Bovine Collagen*

Xenografts are products that are derived from other species. More recently over the years, bovine-derived collagen products are the most commonly used dermal fillers in the United States and often are used as a basis to which all other products are compared. They are composed of sterile, purified, fibrillar, suspensions of type I collagen from domestic cattle. Pepsin degradation during processing removes the more antigenic end portions of the bovine collagen molecule (the telopeptides) without disturbing the natural helical structure. This is critical for the resulting agent to be more immunologically compatible with the human host. These products are generally 95% to 98% type I collagen, with the remainder being type III collagen. The products are suspended in phosphate-buffered physiologic saline solution containing 0.3% lidocaine to reduce the pain during injection. Once injected, the human body temperature causes the products to undergo consolidation into a solid gel as intermolecular cross-linking occurs in the suspension with the generation of a high proportion of larger fibrils.

Zyderm I (Inamed, Santa Barbara, Calif) was introduced in 1977 as the first injectable bovine collagen and received Food and Drug Administration (FDA) approval in 1981. Zyderm II (Inamed) and Zyplast (Inamed) were FDA approved soon after and differed in the amount of collagen contained in the suspension as well as in the amount of collagen cross-linking. Generally, results from these products last from 3 to 18 months; however, repeat treatments are usually required around 4 months. Zyplast is a somewhat more stable product because it contains collagen cross-linked with 0.0075% glutaraldehyde, which adds strength to the collagen fibers. This yields decreased proteolytic degradation rates once injected. For the deepest furrows, it may be necessary to immediately layer Zyderm I over Zyplast. The simultaneous use of 2 products can often provide increased longevity of correction and improved esthetic results.

Complete correction of the defect can be achieved at 1 visit if enough material is used. Seventy percent of patients require touch-up treatments at intervals of 3 to 12 months as the collagen is displaced from its site of implantation in the dermis into the subcutaneous space. Often, these materials are used as first-line fillers in an attempt to demonstrate to patients the results of therapy. Because they are not permanent, they are an excellent material for the dentist to develop an early learning curve; if an ideal result is not achieved, patients are not left with an unpleasing result long term. If they are pleased with the results, patients have the option to have corrective procedures done or opt for a more permanent filling material.

The application of these products in the perioral area is the largest single indication for which they are used. It should be noted, however, that while injection of this product into the skin surrounding the lips is an FDA approved procedure, injection into the mucosa of the lip is not. There is, however, considerable interest in using these materials for increasing the fullness of the lips, and clinical trials are currently underway.

*Artecoll* (Artes Medical, San Diego, Calif) is an injectable implant containing polymethylmethacrylate (PMMA) microspheres suspended in a 3.5% bovine...
collagen solution. Host collagen replaces the bovine collagen within 3 months after injection, while the 30 to 40 μm microspheres remain. PMMA is commonly used for dentures, Plexiglas, and bone cements in orthopedics. The relatively large size of the microspheres prevents phagocytosis or migration of the product. The microspheres become surrounded by a fine fibrous capsule within 2 to 4 months and remain in place as the capsule develops. Theoretically, a longer-lasting result is achieved because the microspheres are inert and nonbiodegradable. To reduce the pain of injection, 0.3% lidocaine is added to the product. Artecoll is available in Canada, Europe, and South America, but has not yet been approved by the FDA for use in the United States. A dentist should not attempt to inject the PMMA used for dentures or transitional prostheses into the soft tissue because these materials are different in their manufacturing process and are not developed to be used within the soft tissue.

Complications

There is a mild chance that patients will experience a delayed-type hypersensitivity reaction to bovine collagen implants with or without PMMA. It is suggested that as many as 3% to 5% of patients may experience such reactions. This is due to antibovine collagen antibodies which do not cross react with human collagen.14–16 Therefore, 2 skin tests performed 2 weeks apart, with the last test at least 4 weeks before treatment, is now required. A positive test is defined as erythema, induration, tenderness, or swelling that persists for more than 6 hours after implantation of a small amount of material into the dermis of the arm. Both tests must be negative in order to safely use the material. So far, there has been no proven association between bovine collagen and autoimmune disease.17

Porcine Collagen

Fibrel (Mentor, Goleta, Calif) is an injectable collagen-based material approved by the FDA for the correction of soft-tissue defects. The material consists of gelatin foam, ε-aminocaproic acid, and human plasma. The gelatin foam consists of denatured porcine type II and III collagen and serves as a scaffold for the trapping of clotting proteins. The ε-aminocaproic acid inhibits fibrinolysis and allows a solid clot to form. As the clot later matures, normal wound healing processes occur and new collagen is laid down. The patient’s plasma supplies supplemental fibrinogen. Contraindications for the use of this material are history of keloids, history of anaphylactic reactions, and allergic reactions to any of its constituents. A Fibrel skin test is required before treatment is initiated. Fibrel should be placed in the mid-to-deep dermis. Placement in the superficial dermis can result in prolonged surface irregularities. Therefore, this material is indicated for deeper wrinkles and folds.

Results have been generally promising with this product. A clinical trial evaluating 850 scars in 300 patients treated either once or twice with Fibrel was evaluated by physicians and patients and by photogrammetric analysis. In general, more than one half of the scars showed more than 65% improvement at the 1-year follow up appointment. When patients were followed up for 5 years, more than 50% of the scars maintained significant correction. The scars only lost an average of 35% of their original correction.18

Hyaluronic Acid

Hyaluronic acid is a constituent of the ground substance of normal dermis and has considerable water-binding capabilities which influence dermal volume and compressibility. It is a glycosaminoglycan composed of repeating dimeric units of D-glucuronic acid and N-acetyl-glucosamine, which provide a fluid matrix on which collagen and elastic fibers can develop. It is obtained from either avian or bacterial culture sources. Its derivatives that are used for soft tissue augmentation are cross-linked to decrease proteolytic degradation rates. Hyaluronic acid is highly suited for soft tissue augmentation because it is insoluble, resists degradation, does not migrate, and retains a high water content.

A major advantage of hyaluronic acid is due to the fact that its chemical structure is uniform throughout all living species, rendering a minimal chance of immunogenicity. Therefore, pretreatment allergic skin testing is not necessary. Also, unlike collagen products, these products are colorless; therefore, they can be injected superficially without concern of discolorations showing through the skin. The handling of these products is generally considered to be superior to bovine collagen because of easier flow rates. Additionally, they need not be refrigerated; however, if they are exposed to heat, monomers will form which can contribute to inflammation. They do not contain lidocaine, so slight pain may be associated with injection.

These products are not permanent and therefore generally require reinjection at 3 to 6 months.19 The more active the tissue movement, the less time the material will last. When placed in a very active area, as the lip, the material may last only a few months. On the other hand, the marionette lines of a lower lip region
may last longer than 6 months. Figure 2 shows how this material is being used to correct nasolabial folds.

A recent randomized, double-blind, multicenter clinical trial comparing a bacterial cultured hyaluronic acid derivative (Restylane) with bovine collagen (Zyplast) was conducted. One hundred thirty-eight patients with prominent nasolabial folds were treated and followed up for 6 months. Results showed that less injection volume was required to achieve optimal cosmetic results when hyaluronic acid was used. Both patients and investigators judged hyaluronic acid gel to be more effective in maintaining cosmetic correction. The frequency, intensity, and duration of local injection site reactions were similar for the 2 products. The investigators concluded that nonanimal stabilized hyaluronic acid provides a more durable esthetic improvement than bovine collagen.9

Another study of 158 patients receiving Restylane with a follow-up of 8 months revealed satisfactory results as evaluated by both physicians and patients. Photographic evaluation revealed even better results with an 80.4% chance of moderate or marked improvement. Histologically, at 1 year, the product was shown to be long-lasting and well-tolerated.20 A drawback of this study is that there were no positive or negative control groups. A recent multicenter, longitudinal clinical trial, however, included collagen filler (Zyplast) as a control group. Blinded examiners evaluated 68 patients randomized to receive either filler for the treatment of nasolabial folds. Evaluations were performed up to 1 year after treatment. Clinically significant better results were found in the group of patients that received hyaluronic acid as a filler. Optimal cosmetic results were achieved with a smaller volume of the test filler. Additionally, the test group demonstrated less local injection site inflammation.21

Since hyaluronic acid fillers are less expensive than the bovine collagen products, these products may be a better option for patients with financial difficulties. Due to the many advantages of this product, when experience grows within the United States, hyaluronic acid dermal fillers may replace bovine collagen as the most used product. Table 4 summarizes the composition, indications, duration, and FDA approval status of various xenograft dermal filler products.

**Autogenic products**

The advantages of autogenic products are obvious. Because they are derived from the patient’s own tissue, immunogenic reactions can be avoided as well as any chance of microbial disease transmission. Also, there is a theoretic unlimited supply. Disadvantages of such products are that a donor site is required and the harvested material must be processed before use. Options for autogenous dermal fillers include fat, dermal grafts, plasma, cultured fibroblasts, and collagen.

**Autologous Fat**

Since the late 1800s, the injection of fat tissue has been an option for reconstructive surgery. Autologous fat transplantation is indicated for correction of facial wrinkles, depressed or atrophic areas in the face (malar, cheek, and chin augmentation), and acne or traumatic scars. Such injections are more successful in the facial areas as compared to other areas due to the availability of a richer vascular supply that can support the fragile adipose implants. Approximately 15 to 20 mL of fat is suctioned from an area where it is not needed, usually the upper and outer area of the hips, the medial knee, inner and outer thighs, abdomen, or buttocks. Using the same needle to minimize handling...
of the graft, the practitioner can inject the fat into an area where it is needed. Excess fat tissue can be frozen for up to 6 months so that it can be available for touch-ups.

Advantages of autologous fat include that it poses no risk for allergies, there is unlimited supply of the material, and it is cheap for both the physician and the patient. The primary disadvantage of using autologous fat is that the material is quite viscous, necessitating the use of a large injection needle which can result in bruising, swelling, and tenderness at the injection sites. Varying success rates have been reported and they are generally lower than that of bovine collagen. Survival of grafts has been reported to be between 40% and 60% one year after transplantation. At 2-year follow-up, an average of 50% of the graft remained. The longest lasting results are seen when autologous fat is used for atrophic conditions such as scleroderma, postsurgical or traumatic atrophy, and depressed scars. When used for changes that occur due to aging, results are not as favorable. Uncommonly, side effects such as local tissue necrosis and blindness have been reported with glabellar injections.

Autologous Collagen

The use of autologous collagen involves the transplant of collagen from one part of the body to another. Autologen (Collagenesis, Beverly, Mass) is a process of autologous collagen preparation in which collagen is obtained from skin that is removed during abdominoplasty, breast reduction, excision, or face lift. The tissue is frozen and sent to a processing company where it is condensed into a powder and suspended in saline. The material is placed in a syringe and returned to the practitioner. No skin testing is required and results can last up to 18 months.

Harvested Fibroblasts

Another kind of autogenous filler is based on injection of the patient’s own cells to correct a dermal defect. Fibroblasts, harvested from a 3-mm punch biopsy of the postauricular skin are cultured, sent to a laboratory such as Isolagen Technologies (Houston, Tex), and processed into injectable fillers. The laboratory returns a syringe containing 1 to 1.5 mL of the patient’s cells and collagen for implantation within 48 hours after its receipt. The fibroblasts generate new collagen once injected. The product is currently marketed under the term name Isolagen, and it is still waiting for FDA approval. The company can make this amount available every 2 to 3 weeks as needed. Usually, to obtain the desired result, 2 to 5 treatments may be needed in a single site.

Although there is minimal risk of hypersensitivity, the practitioner should perform a skin test 2 weeks prior to treatment. Indications include correction of facial lines, wrinkles, and scars. Disadvantages of this
product include the necessity for a skin biopsy, high costs, long processing time (6 weeks), and the need to inject the material within 48 hours of receipt. Also, patients who expect immediate improvement may be dissatisfied because it takes time for the implanted fibroblasts to grow and ameliorate the treated area. Table 5 summarizes the composition, indications, duration, and FDA approval status of various autologous dermal fillers.

### Allogenic products

**Cadaveric Collagen**

In order to overcome disadvantages of autologous dermal fillers, such as the necessity for a donor site, attention has turned toward other sources. Allogenic dermal fillers used for soft tissue augmentation originate from other humans. It is obtained from cadaveric dermis or fascia, or engineered using human cell lines. One such material is AlloDerm (Lifecell, Birmingham, Ala), which is acellular human dermal allograft. It has been used in the treatment of burn victims and in oral and periodontal surgery. Guided tissue regeneration and root coverage has seen a dramatic increase in this product over more recent years. AlloDerm grafts are processed from human donor skin obtained from approved tissue banks. No allergy testing is required prior to use. Tissue recovery follows guidelines of the American Association of Tissue Banks. After being screened for HIV, hepatitis, and other disorders, the harvested skin is processed in such a way that all cellular components are removed. The remaining collagen matrix is washed and incubated in a cryoprotective solution which preserves the biochemical and structural integrity of the dermal matrix. The graft is then packaged and freeze dried and can remain refrigerated for more than 2 years. Rehydration of the graft is required before use. It is important to remember that the graft is supplemented with an antibiotic (gentamicin) and that allergy to this antibiotic is a contraindication for its use.

AlloDerm can be used for lip, glabellar, and nasolabial augmentation, elevation of depressed scars, and for camouflaging in rhinoplasty. It may also be used to further support the maxillary lip or form a canine eminence after the loss of a canine to a partially edentulous patient. This material may be rehydrated with 1 cc of lidocaine, saline, or platelet poor plasma. Thick AlloDerm grafts (>1 mm) are preferred for soft tissue augmentation of the lips and nasolabial folds. Figure 3 demonstrates how this material (AlloDerm, BioHorizon Inc, Birmingham, Ala) is used to augment ridge thickness around a dental implant. The thinner AlloDerm grafts (<1 mm) are indicated for camouflaging superficial textural skin irregularities. Unlike synthetic grafts, these grafts may be folded or rolled upon themselves to obtain extra thickness and to achieve a smooth contour at the edge of the defect. The material can also be sutured to the submucosal tissue using resorbable sutures which gives it another advantage over synthetic materials. Dermal allografts usually demonstrate slight resorption initially. Additionally, swelling usually persists for 1 week, which is longer than that for bovine collagen and autogenous grafts. Therefore, the size of the graft should be approximately 20% larger than the desired augmentation. A cryofractured, injectable form of AlloDerm called Cymetra is available for correction of finer defects. This material obviates the need for incisions and surgical dissection and allows for more precise placement of material.

The longevity of AlloDerm for soft tissue augmentation is still under investigation. It is yet to be determined how resorption rates compare to other more commonly used fillers. One case series of 25 patients who received AlloDerm grafts behind one ear and bovine collagen grafts behind the other ear was conducted recently. At 1 month, AlloDerm implants retained a higher percentage of the original implant volume than Zyplast at 1 and 3 months. Histologically, AlloDerm implants were extensively invaded by host fibroblasts without any foreign body reaction. Longer randomized controlled clinical trials are needed to verify such results.
FIGURE 3. (a) A deciduous canine is extracted. The patient had no permanent canine and therefore a lack of canine eminence. (b) After the AlloDerm is folded upon itself and shaped to the canine eminence, it is positioned under the labial mucosa of the canine site. (c) The canine eminence and implant in position. (d) After 6 months of healing, the canine eminence is present. (e) The final crown is inserted for the maxillary right canine implant.
Collagen Derived From Fibroblasts

Another type of allogenic dermal filler is tissue-engineered collagen derived from human fibroblastic cell cultures. CosmoDerm 2 (Inamed) has almost twice the collagen concentration as CosmoDerm 1 (Inamed). CosmoPlast (Inamed) is produced when CosmoDerm 1 is cross linked with glutaraldehyde to increase viscosity and longevity. These products have the same indications and techniques as injectable bovine collagen; however, no allergy testing is required. Additionally, results have yet to be confirmed with randomized controlled longitudinal trials. Table 6 summarizes the indications, duration, and FDA approval status of various allogenic dermal filler products.

Synthetics

There are advantages of synthetic products as dermal fillers. Unlike biologic products, results with synthetics are generally not transient and since they are biologically inert, there is little antigenicity. Additionally, they can be identically mass-produced at much lower costs. However, adverse events can be serious and long-lasting. Options for permanent synthetic dermal fillers include silicone (currently its use is off label due to reports of granulomatous responses), hydrogels and polymers which draw water into the area, polylactic acid, polyalkylamide, polyacrylamide, and polytetrafluoroethylene. The most commonly used products will be further discussed.

Calcium Hydroxylapatite

Calcium hydroxylapatite is a major constituent of bone and has been extensively used in reconstructive surgery and in dentistry. Its use in soft tissue augmentation is via an injectable material called Radiance (Bioform Inc, San Mateo, Calif). It is composed of calcium hydroxylapatite microspheres that are 24 to 45 μm in size suspended in an aqueous gel formulation. It does not require allergy testing or refrigeration. Due to its highly viscous nature, subdermal and intramuscular placement is recommended since intra-dermal placement will lead to nodule formation. Incidence of nodule formation in the lips has been reported to be as high as 20%. Side effects such as granuloma and nodule formation have been reported with superficial placement. This material is radiopaque and will show up in radiographs, which is important.

Table 6

<table>
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<tr>
<th>Class</th>
<th>Product</th>
<th>Indication</th>
<th>Duration</th>
<th>FDA Approval</th>
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<tr>
<td>Cadaveric collagen sheets</td>
<td>AlloDerm</td>
<td>Deep rhytides or scars, lip augmentation</td>
<td>3–12 months</td>
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<td>Cadaveric injectable collagen</td>
<td>Cymetra</td>
<td>Deep rhytides or scars, finer rhytides, lip augmentation</td>
<td>3–4 months</td>
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<td>Collagen derived from fibroblasts</td>
<td>CosmoDerm I &amp; II</td>
<td>Superficial defects, lip augmentation</td>
<td>3–4 months</td>
<td>Yes</td>
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<tr>
<td>Collagen derived from fibroblasts and cross linked with glutaraldehyde</td>
<td>CosmoPlast</td>
<td>Deeper defects, lip augmentation</td>
<td>3–4 months</td>
<td>Yes</td>
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FIGURE 4. (a) Dense hydroxylapatite is added to the labial aspect of the maxillary anterior bone and under the labial tissues, to help support the maxillary lip above the fixed implant restoration. (b) The fixed maxillary implant prosthesis after soft tissue healing. Note the labial soft tissue above the implant prosthesis is in a similar plane.
for the dentist to know. Since the effects of this material last much longer than other dermal fillers, adverse events can be unforgiving, and the clinician should be cautious with this product until results from long-term clinical trials are available. Currently, the use of calcium hydroxyapatite is not FDA approved for cosmetic purposes.

Calcium hydroxyapatite has also been widely used for bone augmentation and for edentulous sites for denture support (Figure 4). When placed directly with bone, under the intraoral flap in the maxillary arch, it may be used as a long-term support for the maxillary lip. It may also be used in maxillary anterior pontic regions for fixed prosthesis to reduce the pontic size of the teeth and to give more support to the lip.

**Expanded Polytetrafluoroethylene**

Expanded polytetrafluoroethylene (ePTFE) is a synthetic dermal filler that is FDA approved for soft tissue augmentation of deep defects such as nasolabial folds and also for lip augmentation. It is essentially a hollow

<table>
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<th>Table 7</th>
<th>Summary of expanded polytetrafluoroethylene implants</th>
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<tr>
<td>Low-porosity</td>
<td>Tube</td>
</tr>
<tr>
<td>High-porosity</td>
<td>UltraSoft UltraSoft RC</td>
</tr>
<tr>
<td>Dual-porosity</td>
<td>Tube</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 8</th>
<th>Advantages and disadvantages of various dermal fillers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product</strong></td>
<td><strong>Advantages</strong></td>
</tr>
<tr>
<td>Bovine collagen (xenograft)</td>
<td>- Contains lidocaine - Long track record for safety - Not permanent - No donor site</td>
</tr>
<tr>
<td></td>
<td>o May see white bumps through skin on superficial injections</td>
</tr>
<tr>
<td>Hyaluronic acid derivatives (xenograft)</td>
<td>- Colorless - No allergic potential - Safe - Cheaper than bovine collagen - Reliable - User-friendly - Predictable results - No refrigeration necessary</td>
</tr>
<tr>
<td>Autogenous</td>
<td>- Immunogenic reactions avoided - No need for allergic skin testing needed - No chance for microbial disease transmission - Unlimited supply</td>
</tr>
<tr>
<td>Allogenic</td>
<td>- No donor site required - Easy to shape and contour - No allergy testing - Easy handling and manipulability of AlloDerm</td>
</tr>
<tr>
<td>Synthetic</td>
<td>- Cheaper than other products - Less hypersensitivity reactions - No allergy testing - Longer lasting results or permanent results</td>
</tr>
</tbody>
</table>
tube that is palpable and easy to obtain. Fibroblasts migrate into the hollow part of the tube and anchor it in place. The extent of tissue in-growth is determined by the pore size of the product. More porous products promote fixation through encapsulation but limit in-growth, which provides stability in mobile areas. Higher porosity products offer more integration with the tissue, less migration, and a softer feel. ePTFE’s inert, strong, and flexible nature has allowed it to be used safely in millions of vascular surgery procedures.26 ePTFE can also be obtained as sheets, strips, or strings. No injectable forms of the material are currently available. The product can be threaded or tunneled into defects under local anesthesia. The cosmetic effect is immediate and permanent and there is no need for allergy testing. Possible complications include unnatural feel of the final result, migration of the material, granuloma formation, and postimplantation skin infection. Antibiotic administration is recommended after placement of the material to minimize postoperative infection. Table 7 summarizes the advantages and disadvantages of various ePTFE dermal filler products.

**Silicone**

The use of silicone injected into facial tissues was popularized in the 1960s and 1970s.27 Microdroplets of silicone are dispersed within the dermal tissues and subsequently encapsulated by fibrous tissue. The material is user-friendly, inexpensive, and results are permanent. In small quantities it seems to be biologically well-tolerated; however, over time it may induce a foreign body reaction. Chronic inflammation results in granuloma formation which is avascular and a potential site for infection.28–31 Additionally, removal can be problematic and lead to further complications. As a result, silicone is not FDA approved for cosmetic purposes and is illegal in many states.

Table 8 summarizes the advantages and disadvantages of the 4 main classes of dermal fillers.

### Complications of Dermal Fillers

Any clinician who wishes to use dermal fillers to enhance the esthetic appearance of their patients must be well informed about the possible complications.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Cause</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>Medications (ASA, NSAIDs, vitamin E, various herbal medications)</td>
<td>Discontinue medications 1 week prior to procedure with physician consult</td>
</tr>
<tr>
<td>Infection</td>
<td>Colonization by pathogenic bacteria; herpes simplex</td>
<td>Remove makeup; Preoperative alcohol or chlorhexidine scrub; Possible antiviral for patients with history of herpes</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Anxious personality, first time patient is having procedure</td>
<td>Offer full explanations; Answer all questions; Consider light sedation</td>
</tr>
<tr>
<td>Immunologic reaction</td>
<td>Allergy to component of filler</td>
<td>Obtain thorough medical history; Allergy testing per product recommendations</td>
</tr>
<tr>
<td>Pain</td>
<td>No anesthetic used, large-bore needle</td>
<td>Use smallest needle possible; Anesthesia (topical for superficial injections, nerve or field blocks for lips); Postoperative cold packs</td>
</tr>
<tr>
<td>Sensitivity reaction</td>
<td>Antibodies against material</td>
<td>Palliative treatment; 2.5–5 mg/mL intralesional triamcinolone</td>
</tr>
</tbody>
</table>

### Table 9

<table>
<thead>
<tr>
<th>Soft tissue augmentation and the management of possible complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complication</td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>Bleeding</td>
</tr>
<tr>
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<tr>
<td>Pain</td>
</tr>
<tr>
<td>Sensitivity reaction</td>
</tr>
</tbody>
</table>

**TABLE 10**

<table>
<thead>
<tr>
<th>Problem</th>
<th>Description</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solar elastosis</td>
<td>Furrows between areas of elastosis often dislodge fillers</td>
<td>Removal of elastotic material with ablative resurfacing</td>
</tr>
<tr>
<td>Superficial contour defects</td>
<td>Fine defects may be too shallow for dermal fillers</td>
<td>Ablative resurfacing</td>
</tr>
<tr>
<td>Significant laxity</td>
<td>Excessive fillers in these areas may result in lumpiness</td>
<td>Surgical correction (rhytidectomy, liposuction) or nonablative tightening</td>
</tr>
<tr>
<td>Deep dynamic folds</td>
<td>Fillers may dislodge easily in dynamic areas</td>
<td>Dermal fillers or Botox therapy</td>
</tr>
</tbody>
</table>
tions of treatment and the management of these complications (Table 9).

Not all wrinkles are amenable to dermal filler treatment. It is important to evaluate the cause of the soft-tissue defect and in many cases decide on another treatment of choice. Often, referral to a physician is needed to provide proper treatment. Table 10 summarizes various problems and appropriate treatments as described by Murray.32

**CONCLUSION**

The dentist has been well trained in the facial macroesthetics of the inferior third of the face. The ideal and compromised esthetic condition for edentulous patients has primarily been under the privacy of dentists. Recently, the esthetic conditions of the partially edentulous and dentate patient have been emphasized. Dental esthetics must include macroesthetics of the inferior third of the face. Since many of these techniques include resorbable dermal fillers, the dentist is even more encouraged to provide these procedures. Table 11 summarizes the currently available treatment options for folds, wrinkles, and lines. The dentist is one of the few medical professionals routinely visited by patients every 3 to 6 months, during health or disease of the circumoral system. Hence, the dental profession is ideally positioned to treat patients with prescribed biannual treatment of facial wrinkles, at the same time their teeth and intraoral conditions are evaluated.

For optimal results, the clinician must be aware of the indications for all available products and know how to manage complications. Many products are not currently FDA approved, and until long-term randomized clinical trials are completed, they should be used with caution. Nevertheless, the techniques and products presented in this review offer exciting options for patients who desire a younger and healthier appearance.

**NOTE**

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**REFERENCES**


