Chapter 6

Soft Tissue Augmentation

6

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Core Messages

- Facial aging is a growing concern among individuals in their 30s, 40s, and 50s and is driving increased demand for new products and techniques.
- Soft tissue augmentation is the fastest-growing segment among plastic and dermatologic cosmetic procedures and is one of the few cosmetic procedures that can be used in all skin types (Fitzpatrick I–VI).
- Soft tissue fillers and microimplants can be permanent, semipermanent, or temporary.
- Natural soft tissue filler materials are derived from sources that include bovine, porcine, human (autologous and cadaver), and recombinant bacteria.
- Synthetic soft tissue filler materials include silicone oil, expanded polytetrafluoroethylene (ePTFE), synthetic calcium hydroxylapatite, poly-L-lactic acid (PLA), and polymethylmethacrylate (PMMA).

Contents

6.1 Introduction

Many options are available to the individual wishing to ameliorate such facial signs of aging as rhytids (fine lines, creases, and wrinkles). In response to ongoing demand, research is focusing on new and better ways to do so. In consultation with the dermatologist or cosmetic surgeon, the patient can explore these options in detail and arrive at an individualized plan. In some instances, combining procedures may be an excellent choice.

Over time, senescence of the skin, elastosis, decreased collagen, and lipoatrophy lead to the loss of the face's youthful turgor and tightness, resulting in the appearance of radiating vertical lines around the lips and mouth, deepening and furrowing of the nasolabial folds, and the development of a longer and flatter upper lip leading to a thinner lip vermilion border. These changes begin to appear in a person's late 20s or early 30s, and they may become a growing concern for individuals in their 30s, 40s, and 50s [1]. People are living longer and want to achieve their best appearance for their entire life, and

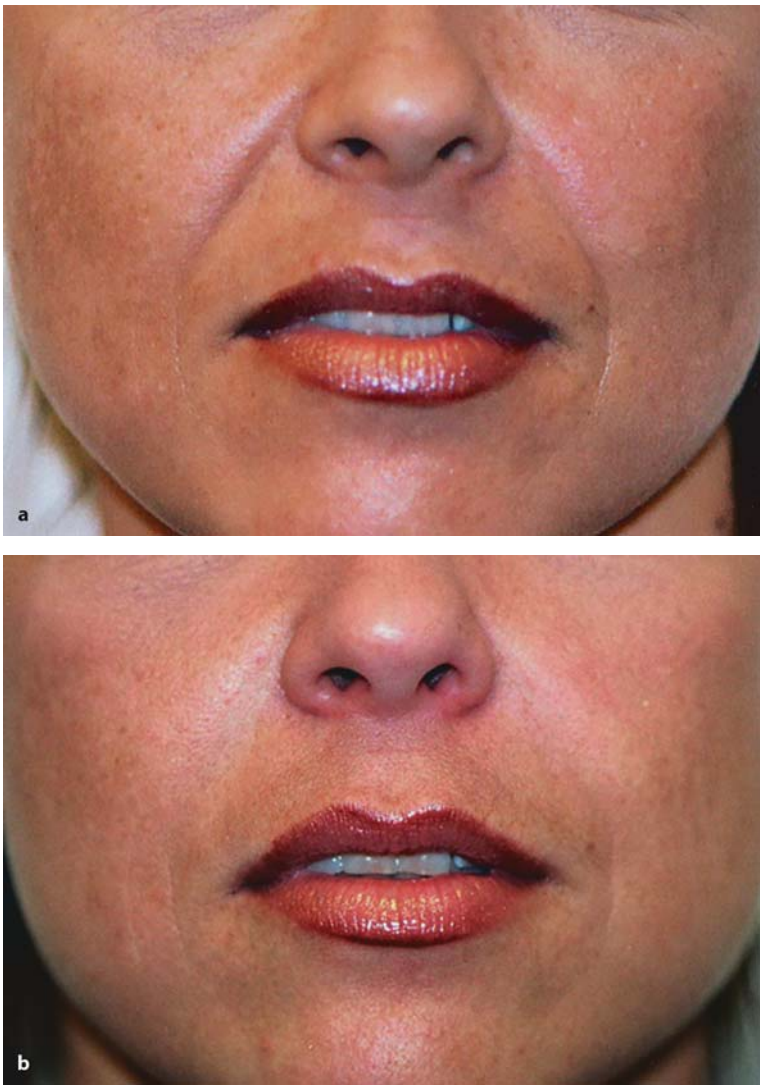

Fig. 6.1a,b.
Dermal enhancement using Restylane. **a** Before. **b** After (Courtesy of Z. Paul Lorenc, M.D., F.A.C.S.)

soft tissue augmentation is one of the few cosmetic procedures that can be used in all skin types (Fitzpatrick I–VI) [2, 3]. Figures 6.1a,b and 6.2a–d are before-and-after photos that demonstrate the results from soft tissue augmentation. This chapter focuses on procedures and products to ameliorate the fine lines, creases, and wrinkles associated with age and exposure to the elements as well as the process of revolumizing the face.

For the individual desiring to rejuvenate his or her face by treating perioral signs of aging, there are many options available, including use of botulinum toxin, injectable fillers, microimplants, and combination therapy. These include soft tissue fillers that may be synthetic, animal-derived, human-derived, or autologous–the latter harvested from the patient's own vein or fat. The primary action of these products and techniques is to induce collagen formation and/or occupy volume and space. The dermatologist or cosmetic surgeon can assess the patient's needs and desires and propose a course of treatment from among available products and techniques.

Fillers are categorized as permanent, semipermanent, and temporary. The majority of injectable fillers are temporary, lasting from several weeks to several months, although some reportedly last 9–12 months. Many of these processes require ongoing treatment to maintain the desired appearance. Injectable microimplants are, for the most part, semipermanent, although some newer products containing microspheres are temporary. Synthetic implants are permanent, remaining in place unless removed surgically; human-derived or cadaver-derived implants, while long lasting, do not ap-

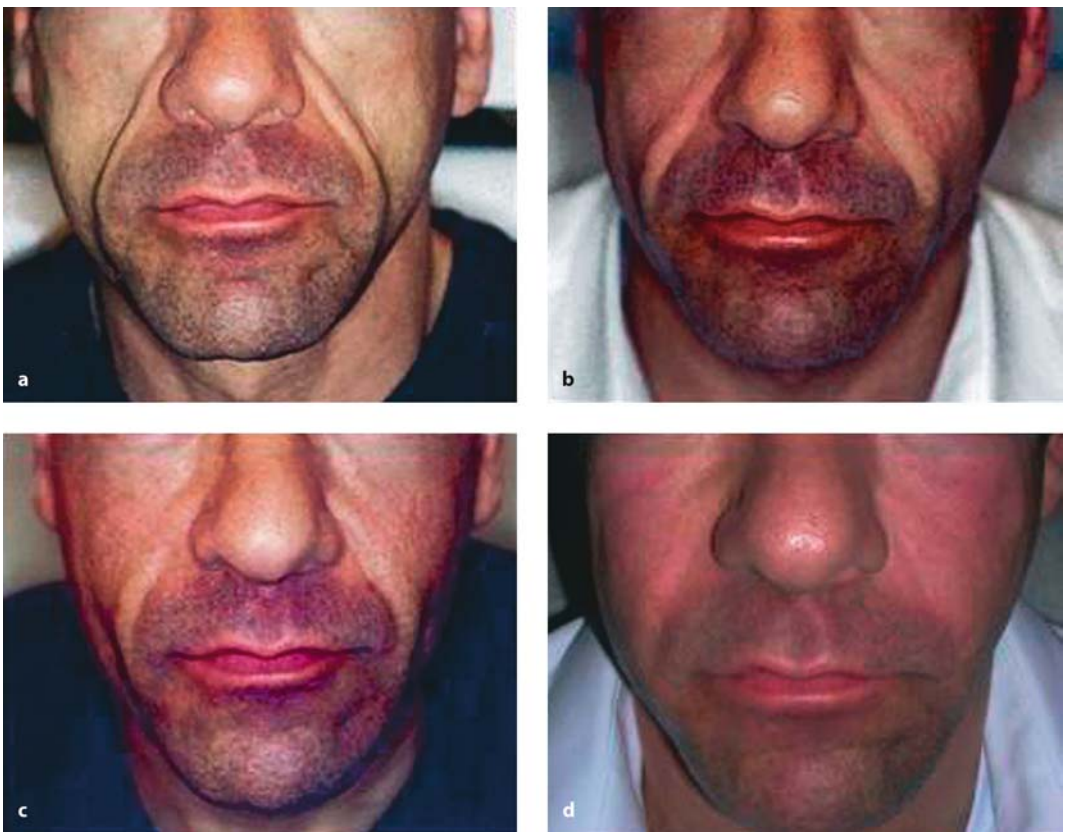

Fig. 6.2a–d. Lipoatrophy using Sculptra

pear to last indefinitely. Finally, autologous implants and injectables vary in their longevity.

Each type of soft tissue filler or implant has its own advantages and disadvantages. Candidates for treatment must consider factors such as product availability, treatment complexity (number of required serial treatment sessions), necessity for local anesthesia, longevity of augmentation, contraindications, allergy testing, potential complications, cost, and technical expertise required of clinicians.

General contraindications include any active disease (including diabetes) that may affect risk or outcome; disorders involving collagen, scarring, or connective tissue; lupus (dependent on type of treatment); recent treatment with isotretinoin; and clotting problems. Each type of treatment may have additional contraindications, and these are discussed in the appropriate section below.

New products and techniques are being developed at a rapid pace in numerous countries. Clinical trials are in progress for many products. Product availability varies widely, and a variety of products are being used off-label. Dermatologists and cosmetic surgeons should regularly review treatment options to provide the best care possible for patients.

6.1.1 Overview of Common Injectable Fillers

6.1.1.1 Fat

Fat transfer remains a popular treatment option because there is no cost for materials and no risk of rejection. The source of the fat is a metabolically resistant part of the body, usually the lateral hip, abdomen, or flank. The donor site is infused with tumescent local anesthesia for collection of the adipose tissue, which is aspirated or manually excised and placed in storage. At a later date, a saline suspension of this tissue is injected into the cutaneous layer for treating lipoatrophy, rhytids, and folds [4].

Fat autograft muscle injection (FAMI) is a modification of existing methods for fat transfer that creates a natural living graft that is long lasting or permanent [5]. Unlike traditional fat-grafting methods, in this procedure, fat is injected solely into the muscle and immediately adjacent tissues in the direction of the muscle fibers. This allows immediate incorporation into the atrophied space and subsequent hypertrophy of the muscle. Seven specifically sized cannulas are used for each area to be injected. Fat injected into the muscle has greater longevity than when it is injected into the cutaneous layer. Preliminary findings reported that 30% of patients followed for 5 years retained at least 80% of the FAMI graft [6].

6.1.1.2 Autologous

Autologous collagen is derived from the patient's own skin. The skin is usually removed during surgery that involves tissue excision, such as abdominoplasty. The collagen is processed in a laboratory and kept frozen until ready for injection, which occurs within 48 h of harvesting [7]. Because the collagen is autologous, no allergy test is required [4, 8].

6.1.1.3 Cadaver-Derived

These implants are derived from donor tissue obtained at the time of death. The cadaver's dermis, muscle fascia, or tissue-derived collagen is harvested and brought to a special laboratory for testing and processing where its immunogenic components removed.

6.1.1.4 Collagen

Injectable collagen has been used since the early 1980s to improve facial rhytids. Collagen is a naturally occurring fibrous protein found in humans and animals. Injection of collagen into rhytids will replenish collagen matrix and restore the face to a more youthful appearance. In general, the effect will last from several weeks to several months [9].

6.1.1.5 Hyaluronic Acid

Hyaluronic acid is a natural cosmetic dermal filler that restores volume to moderate to severe facial rhytids and folds in the skin. Hyaluronic acid is found in all tissues of human and animal species and is biodegradable and biocompatible. Hyaluronic acid is currently obtained from biofermentation or from the combs of roosters. Depending on the source, allergy testing may be required. Current studies show that hyaluronic acid products last twice as long as collagen-based filler products.

6.1.1.6 Poly-L-lactic Acid

Poly-L-lactic acid (PLA) is a sterile synthetic polymer that is biodegradable and biocompatible. Once injected into the deep dermis, the PLA microparticles stimulate the formation of collagen. It has been approved in Europe since 1999 for soft tissue augmentation and is currently approved in the United States for HIV-associated lipoatrophy.

6.1.1.7 Silicone Oil

Silicone in the form of purified, medical grade, polydimethylsiloxane oil is considered permanent filler. It is used for the correction of moderate-depth lines and depressions. Microdroplets of silicone oil are dispersed within the dermal tissues, and fibrosis around these droplets localizes the material and provides "bulk" [10].

6.2 Scientific Background

6.2.1 Autologous Material

Materials used in autologous implants and injections are generally obtained during the course of other procedures that involve tissue excision. These include abdominoplasty, facelift, breast reduction, breast lift, etc. The tissue is sterile-packed and frozen until it is processed for use. In theory, because the materials used in autologous implants and injectables are from the patient's own body, there should be no risk of rejection. In rare cases, however, problems arise. In addition, the patient's body absorbs these natural fillers over time [8] (Table 6.1).

6.2.1.1 Fat Transfer

The use of autologous fat in soft tissue augmentation dates back to 1893 when Neuber reported the harvesting of blocks of free fat from the arms to reconstruct depressed facial defects. The technique was further advanced in the early 1900s by Lexer, who treated a malar depression and receding chin using single large block grafts, and by Bruning, who was the first to use a syringe to inject small cubes of surgically harvested adipose tissue into the subcutaneous space. Although these methods had excellent short-term results, the inability to prevent significant resorption of the transplant led to the investigation of other techniques for soft tissue augmentation [8].

Currently, fat transfer is a temporary treatment that lasts from several months to several years. During injection, an overcorrection is made, as resorption of saline occurs [11]. Advances in methodology, including, for example, reinjection of fat suspended in the patient's plasma, have increased the longevity of the procedure.

6.2.1.2 Fat Autograft Muscle Injection

The FAMI technique uses specialized, anatomically curved cannulas. Donor sites of fat include the buttocks, lateral thighs, abdomen, or medial knees [5].

6.2.1.3 Cultured Human Fibroblasts

Cultured human fibroblasts (example: Autologen) from the patient's own body are reinjected into the patient where they work as a biocatalyst. The effect reportedly is indefinite, although the collagen is susceptible to natural aging. The use of cultured human fibroblasts is in

Table 6.1. Autologous fillers

Filler	Indications	Treatment	Complications and potential adverse reactions
Fat transfer		Fat transfer: Injected into the subcutaneous fat layer and/or muscle. Overcorrection is necessary	Prolonged edema, bruising, under-/ overcorrection, migration, clumping, irregularities, fat necrosis, and infection [10]
Fat autograft muscle injection (FAMI)		FAMI: The face requires anesthetizing with a series of nerve blocks. Tiny puncture wounds are made at the superior central forehead at the hairline, zygomatic arches, oral commissures, and lateral chin. Injections are made into the muscle and immediate surrounding planes. Monthly visits may be necessary as needed. The effect is permanent or long lasting [5]	Rare complications may include swelling, bruising, infection, scarring, and dyspigmentation [5]
Autologen-cultured human fibroblasts	Stimulates cutaneous collagen formation	Soft tissue defects should be overcorrected by at least 20–30%. Injections are more painful, and nerve blocks or local or topical anesthesia may be needed. A minimum of three injections are required over several weeks. Skin testing not required. Effect lasts 3–6 months [10]	No risk for disease transmission or allergic reaction because material is autologous [10]

the process of clinical trials in the United States [12].

6.2.2 Cadaver-derived Implants

A summary of cadaver-derived implants is provided in Table 6.2.

6.2.2.1 Acellular Allogeneic Dermis

An acellular allogeneic dermis (example: AlloDerm) is composed of cadaveric dermis and an extracellular cell matrix that has been processed to remove immunogenic components [13].

6.2.2.2 Injectable Microparticulate Acellular Allogeneic Dermis

Acellular allogeneic dermis is available in an injectable microparticulate form (example: Cymetra). This preparation of collagens and elastin provide structure for cell repopulation. Preserved proteoglycans and proteins direct the patient's own cells to initiate revascularization and cell repopulation, integrating into the patient's own tissue.

6.2.2.3 Lyophilized Human Particulate Fascia Lata

Another preparation contains lyophilized human particulate fascia lata (example: Fascian)

Table 6.2. Cadaver-derived implants

Implants	Indications	Treatment	Complications and potential adverse reactions
AlloDerm	FDA-approved for lip augmentation in the USA [14]. The allograft scaffold is also used for burn injuries and cancer excisions and to correct soft tissue defects [8]	Tiny incisions are made at both corners of the lip. An instrument is passed from one incision to the other to make a tunnel. The implant is passed from one end of the incision toward the other end [14]. Reports of longevity vary, ranging from 6–12 months to several years [4]	The major complication is overcorrection. The risk of this is minimized by the physicianfully understanding the patient's expectations [14]
Acellular allogeneic dermis Cymetra	FDA-approved for treatment of rhytids, nasolabial folds, and lips	Injection at the midreticular level is optimal until the majority of the gentian lines have been removed or the deepest plane has been reached [4]. Double allergy testing is recommended [15], and patients shown to be allergic to bovine collagen might find this preparation to be a feasible alternative. Its longevity is normally 3–6 months	Bruising, redness, swelling, and wrinkling of skin [8]
Injectable, microparticulate acellular allogenic dermis Human cadaver tissue		Augmentation reportedly lasts longer than does bovine collagen [16].	
Fascian Lyophilized human particulate fascia lata Human cadaver tissue	FDA-approved for stimulation of cutaneous collagen formation [17]	Reports claim the effect lasts 3–6 months while the manufacturer states 6–8 months [4]	Complications may include edema, erythema, and ecchymosis, and later complications may include postinflammatory hyperpigmentation. The larger particle sizes appear to be associated with side effects that are more persistent [4]. Painful to inject; bruising [17]

from donor cadavers. It is available in particulate and line-like sheets and must be rehydrated prior to use with saline or a saline/lidocaine mixture [8].

6.2.3 Temporary

Collagen serves to provide structural support for bones, skin, tendons, and blood vessels and lends stability to the body's tissues. With age, the body's collagen weakens and loses its elasticity, leading to, among other effects, the vari-

ous signs of aging. The main sources of collagen for this purpose are bovine, porcine, and human. Bovine collagen is very similar to the human molecule, with specific differences only in the end peptides (telopeptides). These regions can be removed in processing, leaving a core protein similar to that of a humans [9] (Table 6.3).

6.2.3.1 Animal-Based Collagen

Bovine Dermal Collagen Dispersed in Phosphate-Buffered Physiological Saline Containing 0.3% Lidocaine

These substances (example: Zyderm) are composed of highly purified bovine dermal colla-

Table 6.3. Temporary fillers

Implants	Indications	Treatment	Complications and potential adverse reactions
Zyderm Bovine dermal collagen dispersed in phosphate-buffered physiological saline containing 0.3% lidocaine	FDA-approved for the correction of facial rhytids, scars, and lip augmentation [10, 17]. The low-concentration filler is used to treat fine lines, rhytids, shallow scars, and thin-skinned areas, and the high-concentration filler is used to treat moderate lines, rhytids, and scars [15]	Injected intradermally. Infiltrated into the superficial papillary dermis. Requires second skin test on the contralateral arm [15]. Topical anesthesia may be required. Overcorrection is mandatory because water in the suspension is reabsorbed within 24 h after injection [10]. The average longevity of both fillers is 3–6 months [10, 18]	Bovine collagen may induce an allergic reaction [10]
Zyplast Bovine collagen cross-linked with glutaraldehyde and suspended in saline and 3 mg/ml lidocaine	FDA-approved for the correction of facial rhytids, scars, and lip augmentation [10, 17]. Often, this filler is used as a foundation in the nasolabial folds or oral commissure with non-cross-linked bovine collagen injected as an overlay. Cross-linked bovine collagen is also used to enhance the vermilion border, but it should be avoided in treatment of fine lines or in the glabella [18]	Placed into the midreticular or deep reticular dermis at the dermal subcutaneous interface. Requires second skin test on the contralateral arm. Topical anesthesia may be required. Overcorrection is mandatory because water in the suspension is reabsor bed within 24 h after injection [10]	Bovine collagen may induce an allergic reaction [10]
CosmoDerm Human-based collagen isolated from human fibroblas tcell cultures	Used for superficial skin defects [4]. FDA-approved for rhytids and scars [17]	May require pretreating with topical anesthetic cream [9]. Allergy test not required. Longevity is generally 3–6 months	Short-term complications may include mild swelling, erythema, bruising, and rarely, palpable lumps [9]
CosmoPlast Human-based collagen cross-linked with glutaraldehyde	Reserved for deeper lines but can be used off-label for the lips. FDA-approved for rhytids and scars [17]	May require pretreating with topical anesthetic cream [9]. Because of the low incidence of sensitivity, an allergy test is not required. Longevity is generally 3–6 months	Short-term complications may include mild swelling, erythema, bruising, and rarely, palpable lumps [9]

Table 6.3. Continued

Implants	Indications	Treatment	Complications and potential adverse reactions
Restylane Hyaluronic acid derived from bacterial biofermentation process	Perlane: 20 mg/ml stabilized hyaluronic acid with approximately 10,000 gel particles/ml is recommended for nasolabial folds and lips (fullness and pouting)	Perlane: Injected into the deep layer of the dermis and/or surface layer of the subcutis	Temporary skin reactions [23], including redness, swelling, localized granulomatous reactions, bacterial infection, acneiform, and cystic lesions. Hypersensitivity, although declining after introduction of more purified hyaluronic acid raw material [24]. However, no long-range problems [9]
	Restylane: 20 mg/ml stabilized hyaluronic acid with approximately 100,000 gel particles/ml is recommended for rhytids such as glabellar, oral commissures. Lips: fullness, pouting, and vermilion border	Restylane: Injected into the mid part of the dermis	
	Restylane fine lines: 20 mg/ml stabilized hyaluronic acid with approximately 200,000 gel particles/ml is recommended for thin superficial lines, such as worry lines, periorbital lines, perioral lines	Restylane fine lines: Injected into upper part of the dermis	
	FDA-approved [9]	None of the three should be overcorrected. Various injection techniques apply, depending on the type of correction and product used. These techniques include linear threading, serial puncture, fanning, and cross-hatching [23]	
Juvederm [18, 24, 30] Viscoelastic, nonanimal hyaluronic acid gel	18 mg/g, designed for the superficial dermis, specifically for fine lines and rhytids	The first is designed for injection in the superficial dermis, the second is designed for injection in the mid dermis, and the third is designed for injection in the mid to deep dermis. Not permanent. Eventually absorbs into the body; typically last 3–6 months.	Temporary skin reactions [23] including redness, swelling, localized granulomatous reactions, bacterial infection, acneiform, and cystic lesions. Hypersensitivity, although declining after introduction of more purified hyaluronic acid raw material [24]. However, no long-range problems [9]
	24 mg/g, designed for the mid dermis, specifically for deeper rhytids		
	30 mg/g, designed for the mid to deep dermis, specifically for deeper furrows such as nasolabials and for lip and cheek augmentation. Not available in the USA. Outside the USA, approved for a wide range of facial applications, from lip augmentation and superficial lines to frown lines and deep rhytids [25]		

Table 6.3. Continued

Implants	Indications	Treatment	Complications and potential adverse reactions
Hylaform Viscoelastic hyaluronic acid gel from rooster combs	FDA-approved for cosmetic use	May require local anesthetic or a regional block for pain. May require skin testing because of avian source. Immediate results, effect lasts 2–3 months [17]	Delayed inflammatory skin reactions have been reported [23]
Sculptra/New-Fill Poly-L-lactic acid	FDA-approved for use in absorbable suture material and treatment of HIV-associated lipoatrophy. FDA approval pending for the treatment of fine lines, rhytids, and more marked furrows or creases, as well as for the augmentation of the tissue volume in certain areas of the face (cheek bones, cheek depressions, chin, etc.) [17]	Correct placement in the deep dermal and/or deep dermal subcutaneous plane is important; too shallow and visible nodules and/or blanching of the skin occurs [26]. Takes effect in 4–6 weeks, lasts 12–18 weeks [17]	Infection, allergic reaction, and inflammatory granulomas [27]
Poly-L-lactic acid			Injection site reactions. Rare, nonvisible nodules [17]

gen that has been dispersed in phosphate-buffered physiological saline containing 0.3% lidocaine [10, 18]. Concentrations include 35 mg/ml and 65 mg/ml of purified bovine dermal collagen.

Bovine Collagen Cross-Linked with Glutaraldehyde and Suspended in Saline and 3 mg/ml Lidocaine

Another injectable bovine collagen (example: Zyplast) is cross-linked with glutaraldehyde and suspended in saline and 3 mg/ml lidocaine. Cross-linking with glutaraldehyde adds strength and makes the collagen more resistant to proteolytic degradation. The implant will retain its integrity and its inherent water content to a greater degree than is the case for non-cross-linked bovine collagen [18].

6.2.3.2 Non-Animal-Based Collagen

Human-Based Collagen Isolated from Human Fibroblast Cell Cultures

Highly purified human-based collagen (example: CosmoDerm) is dispersed in phosphate-buffered physiological saline containing 0.3% lidocaine. The source material is isolated from human fibroblast cells grown under controlled laboratory conditions. Two forms of this human-based collagen are available and differ by the amount of collagen contained in the preparation [4].

Human-Based Collagen Cross-Linked with Glutaraldehyde

Another highly purified human-based collagen (example: CosmoPlast) is cross-linked with

glutaraldehyde and dispersed in phosphate-buffered physiological saline containing 0.3% lidocaine and is used for deeper defects.

6.2.3.3 Hyaluronic Acid

Hyaluronic acid is a polysaccharide, glycosaminoglycan, that is chemically identical across all species and tissue types [19]. Hyaluronic acid was first used commercially in 1942 when Endre Balazs applied for a patent to use it as a substitute for egg white in bakery products [20]. It plays an important role in giving volume to the skin, shape to the eyes, and elasticity to the joints. As humans age, cells lose their ability to produce hyaluronic acid, and the skin becomes drier, thinner, and looser, leading eventually to wrinkling, among other changes.

Two main sources of hyaluronic acid have been developed to create a filling agent able to correct moderate rhytids and folds and augment lips: (1) nonanimal hyaluronic acid derived from bacteria in a biofermentation process, and (2) hyaluronic acid from the combs of roosters. Its ability to bind large volumes of water makes hyaluronic acid attractive for dermal implantation [21]. Although the effect of hyaluronic acid is temporary, it is very long lasting [8]. Hyaluronic acid is cross-linked with ester and ether linkages to stabilize the molecule for dermal purposes. The amount of cross-linking of the molecule affects biocompatibility of hyaluronic acid: Less cross-linking of the molecule achieves greater biocompatibility.

Hyaluronic Acid Derived from Bacterial Biofermentation Process

Several preparations of nonanimal hyaluronic acid (example: Restylane) are derived from *Streptococcus* bacteria in a biofermentation process. Three forms differ in terms of concentration, volume, needle size, and recommended usage [9]. Restylane contains hyaluronic acid particle size of 200 µm and 1% cross-linking; 20 mg/ml hyaluronic acid is cross-linked with ester and ether linkages to stabilize the molecule. Some theorize that the less cross-linking of molecules, the more biocompatible the hyaluronic acid.

In a randomized, double-blind, multicenter comparison of the efficacy and tolerability of nonanimal hyaluronic acid versus bovine collagen cross-linked with glutaraldehyde for the correction of nasolabial folds, it was shown that less injection volume was required for "optimal cosmetic result" with hyaluronic acid gel than with bovine collagen. Moreover, both patients and investigators judged hyaluronic acid more effective in maintaining cosmetic correction [22].

Viscoelastic, Nonanimal Hyaluronic Acid Gel Derived from Bacterial Biofermentation

Another family of products containing a viscoelastic nonanimal hyaluronic acid gel (example: Juvederm) is available in three different concentrations (18 mg/ml, 24 mg/ml, and 30 mg/ml) to address different correction needs. Hyaluronic acid gel is eventually absorbed into the body.

Viscoelastic Hyaluronic Acid Gel from Rooster Combs

Another hyaluronic viscoelastic gel contains hyaluronic acid derived from the combs of roosters (example: Hylaform). Hylaform contains 5.5 mg/ml hyaluronic acid with a particle size of 500 µm. It has 20% cross-linking as a result of using glutaraldehyde and vinyl sulfone for hyaluronic acid stabilization. According to the manufacturer, the product's high molecular weight makes it more viscous and longer lasting than the hyaluronic acid produced from bacteria.

6.2.3.4 Poly-L-lactic Acid

The vial of dry lactic acid monomers is reconstituted with bacteriostatic water to form the PLA (example: Sculptra/New-Fill). When in-

jected into the deep dermis or dermal-subcutaneous plane, PLA causes an immediate physical improvement to the appearance. The PLA hydrogel is slowly degraded into lactic acid microspheres and carbon dioxide, thus leaving behind the crystals to stimulate collagen and non-allergic granulomatous reaction leading to dermal thickening.

6.2.4 Semipermanent

A summary of semipermanent fillers is provided in Table 6.4.

6.2.4.1 Synthetic Calcium Hydroxylapatite Microspheres Suspended in Aqueous Polysaccharide Gel

Calcium hydroxylapatite has been safely used for many applications, including dental work, reconstruction, tissue-marking orthopedics, bone repair, and in block form for cosmetic applications such as cheek, jaw, cranial, and chin implants [4].

In general, calcium hydroxylapatite works by creating a stable scaffold in which soft tissue can grow. Calcium hydroxylapatite (example: Radiance) is injected by threading the solution into the deep dermis where the microspheres are held in place until the product is resorbed and collagenation occurs. In this process, fibroblasts build a non-scar-tissue type of collagen, thus creating volume in the area under treatment [4].

6.2.5 Permanent

A summary of permanent fillers is provided in Table 6.5.

6.2.5.1 Polymethylmethacrylate Microspheres in Denatured Bovine Collagen

This synthetic implant (example: Artecoll/Artefill) is composed of polymethylmethacrylate (PMMA) microspheres suspended in 3.5% denatured bovine collagen mixed with 0.3% lidocaine. PMMA has been used in medical implants for many years, and it is found in numerous products today. The PMMA is formulated into microspheres and mixed with denatured bovine collagen and lidocaine in a phosphate-buffered saline solution. PMMA is an inert substance, well tolerated by the body, and reports of allergic reactions to it are rare [18, 28].

Table 6.4. Semipermanent filler

Implants	Indications	Treatment	Complications and potential adverse reactions
Radiesse/ Radiance Synthetic calcium hydroxylapatite microspheres suspended in polysaccharide gel	FDA-approved only for vocal cord augmentation and urinary incontinence [17]	Injected into the subdermis. Intradermal placement can result in swelling, pain, persistent erythema, and visible or palpable granules. Slight overcorrection is recommended. Massage area once the injection is completed. Repeat injections 1–3 months after the initial treatment. Skin testing is mandatory [8, 10]	Pruritus or hypertrophic-scarring can occur and implantation site allergic reactions and granulomas aqueous may occur. Removal of calcium hydroxylapatite is not easy. If excessive collagen production is observed, it can be dealt with using corticosteroid injections [4]

Table 6.5. Permanent fillers

Implants	Indications	Treatment	Complications and potential adverse reactions
Artecoll/Artefill Polymethyl-methacrylate microspheres in denatured bovine collagen	Indicated for the correction of facial rhytids and scars and lip augmentation [10]. It is useful especially for correcting depressions and deeper creases [18, 28]. FDA approval pending US clinical testing	Injected into the junction of the dermis and the subcutaneous space using a tunneling technique in which the material is injected as the needle is withdrawn. Use of a small needle often gives a more even result. Overcorrection is not recommended, and it may take several sessions to obtain the desired correction [18, 28]. Repeat treatment every 6 weeks until adequate augmentation [10]. It is used for the correction of moderate-depth lines and depressions [4]. An allergy test is required because bovine collagen is used as a carrier [18, 28]	May cause inflammation, induration, discoloration, ulceration, migration, and formation of granulomas [10, 18, 28]
Silskin AdatoSil 5000 Silikon 1000 Silicone Oil	FDA-approved for ocular medical purposes. The FDA has not approved silicone oil for cosmetic use in the USA. However, it is used in Europe, Mexico, and some parts of Canada for cosmetic purposes, and off-label use within the USA does occur. It is used for the correction of moderate-depth lines and depressions. Silicone has been approved by the FDA for use in treatment of retinal detachment and/or hemorrhage [4]	Microdroplets of silicone oil are dispersed within the dermal tissues, and fibrosis around these droplets localizes the material and provides "bulk." No allergy testing is required as silicone oil in small amounts is well tolerated [4]	Risks of infection, generally due to granuloma formation as the silicone becomes encapsulated as a foreign body in a chronic inflammatory reaction. Several other disadvantages exist as well, including the risk of possible migration to other organs and the lymph nodes [4]

6.2.5.2 Silicone Oil

Silicone compounds must be synthesized because they do not naturally exist. Silicone oil varies in chemical structure, physical properties, purity, sterility, and biocompatibility. Silicone oils used for medical purposes (example: Silikon 1000) contain long polymers of dimethylsiloxanes. As opposed to use in manufacturing, etc., silicone oil used in medical applications should undergo several additional steps of purification and testing. Serious complications can result from the use of adulterated or impure silicone oils. In fact, impurities present in silicone oil can cause granulomas up to 11 years after implantation [8].

Viscosity of silicone oil is measured in centistokes (cs), a unit of kinematic viscosity. Higher viscosity is denoted by larger centistoke

values. For example, Silikon 1,000 has a viscoity of 1,000 cs. Two silicone oil formulations have been FDA-approved for ophthalmologic purposes but not for cutaneous use. In fact, in certain states in the United States, it is illegal to inject silicone oil into human skin. However, one formulation, PMS-350 (viscosity of 350 cs), has European approval for treatment of glabellar lines, nasolabial folds, perioral lines, lip augmentation, atrophic disorders, and scars [8].

Silicone in the form of purified, medical-grade polydimethylsiloxane oil is considered permanent filler. Silicone oil is chemically well tolerated in small amounts [4, 8].

6.2.6 Implants

A summary of implants is provided in (Table 6.6).

Numerous materials have been used in the development of injectable microimplants. These include calcium hydroxylapatite microspheres, hydrophilic polyacrylamide gel, PMMA microspheres, solid, vulcanized methylpolysiloxane microspheres suspended in polyvinylpyrrolidone, hydroxymethylmethacrylate, and ethylmethacrylate. These all share some element of providing a "structural" framework, usually involving microspheres in a carrier, and are generally considered permanent or semipermanent.

Table 6.6. Implants

Implants	Indications	Treatment	Complications and potential adverse reactions
UltraSoft, SoftForm Expanded polytetrafluoroethylene	Indicated for subdermal soft tissue augmentation. SoftForm is used for the lip border, smile lines (nasolabial fold), and frown lines; UltraSoft is used for cheek and temple. Implants made of ePTFE are most applicable in lip enhancement, although they can also be used to ameliorate perioral rhytids [29]	Under local anesthesia, the patient has the appropriate length and width of the implant inserted subdermally via a 14- to 16-guage angiocatheter	Appear to have a higher rate of infection than permanent injectable microimplants, but the problems can be corrected more easily [29]
Gore-Tex Dual-porosity expanded polytetrafluoroethylene	FDA-approved for vascular grafts, implant material, and soft tissue repair	Under local anesthesia, the patient has the appropriate length and width of the implant inserted subdermally via a 14- to 16-guage angiocatheter	Complications range from transient bruising and swelling to infection of the implant site, formation of fistula, and implant extrusion, among others. These more serious complications are considered less common
Advanta Facial Implant Dual-porosity expanded	FDA-approved to fill deep wrinkles or folds or to enhance, augment, or repair soft tissues of the facial area, such as the lips [25]	Requires local anesthesia [25]	Low incidence of complications [25]

6.2.6.1 Expanded Polytetrafluoroethylene

Synthetic implants are usually made from expanded ePTFE, a nonreactive, nontoxic polymer that has been safely used in medical implants for many years for vascular grafts and soft tissue reconstruction. Depending on its design (tubular or in sheets) and varying porosities, the implant can feel anywhere from slightly firm to quite soft. Such implants are permanent [29].

In a study comparing the biomechanical effects of ePTFE implant structure on the stability of a soft tissue implant, the authors used an in vivo porcine model to look at implant retention, fixation strength, and removability in both tubular and solid-strip ePTFE implants. They found that tubular implants facilitated growth of soft tissue through the tube's lumen, which increased the attachment to surrounding soft tissues, increasing fixation strength and decreasing extrusion rate but still allowing easy removal. The authors concluded that these properties might improve clinical applications in facial implantation [29].

6.2.6.2 Gore-Tex

Gore-Tex implants are composed of sterile, medical-grade ePTFE. The Gore-Tex implant has pores that are 10–30 μm in diameter that allow the body's own tissue to attach itself to the implant. Gore-Tex implants are available in both tubular form and in sheets. Gore-Tex implants are extremely strong and are not likely to tear or disintegrate. The implant is permanent but reversible. Gore-Tex implants are not widely used.

6.2.6.3 Dual-Porosity Expanded Polytetrafluoroethylene

One of the newer implants containing dual-porosity ePTFE (example: UltraSoft, SoftForm) consists of a soft, high-porosity center integrated with a smooth, medium-porosity outer surface layer, and it has the benefit of readily accepting a patient's collagen. As a result, a more natural tissue healing response may be achieved. This facial implant has a low incidence of complications. The implant is permanent but reversible.

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6.3 Indications

Soft tissue augmentation is indicated for use in rhytids, creases, scars, and lip augmentation. Many are approved for nasolabial folds. See Tables 6.1, 6.2, 6.3, 6.4, 6.5, and 6.6 for specific indications.

6.4 Patient Selection

Soft tissue augmentation is suitable for all skin types (Fitzpatrick I–VI). Patients should be counseled about temporary augmentation to manage expectations and maximize satisfaction. Additionally, recommendations of temporary soft tissue augmentation in regard to aging changes and consideration of permanent augmentation for scars should be addressed [30]. Common contraindications of dermal-enhancing procedures are listed below. Persons on certain medications or having the following conditions may not be good candidates for dermal enhancement.

6.4.1 Contraindications

Contraindications for soft tissue augmentation are:

- Isotretinoin for 6 months prior or following treatment because it may increase chances of keloid-like scarring
- Collagen/scarring/connective tissue disorders
- Lupus for patients seeking bovine or porcine collagen. Other products may cause flare-ups as well.
- Active diseases may affect outcome or increase risks
- Diabetes may affect outcome or increase risks
- Coagulation problems
- Excessive oral plaque or dental abscesses
- Herpes labialis
- Pregnant or lactating women
- Psychological conditions

6.4.2 Specific Product Contraindications

Following is a list of contraindications to specific products used for soft tissue augmentation:

- Bovine dermal collagen (Zyderm, Zyplast): adverse reaction to allergy test, the presence of severe allergies manifested by a history of anaphylaxis, or of multiple severe allergies. In addition, patients with known lidocaine hypersensitivity should not be injected with these fillers, nor should patients with a history of allergies to any bovine collagen product. Contraindicated for use in the glabellar region
- Injectable microparticulate acellular allogenic dermis (Cymetra): autoimmune connective-tissue disease, infected or nonvascular surgical sites unless specifically prescribed by a physician, patients sensitized to the specific antibiotics used in the manufacture of this preparation, and in periocular line correction or glabellar contouring
- Human-based collagen cross-linked with glutaraldehyde (CosmoPlast/CosmoDerm): severe allergies manifested by a history of anaphylaxis and in patients with known lidocaine hypersensitivity. Contraindicated for use in the glabellar region, breast augmentation, and for implantation into bone, tendon, ligament, or muscle
- Viscoelastic, nonanimal hyaluronic acid (Juvederm): autoimmune diseases, pregnancy, lactation, allergies to hyaluronic acid, and direct sunlight or intense heat on the treatment area for several days postinjection.
- Hyaluronic acid (Hylaform): poultry allergy

References

1. Donofrio L (2000) Fat distribution: a morphologic study of the aging face. Dermatol Surg 26:1107–1112
2. Guttman C (2004) A generation speaks: dermatology answers growing desire to fight aging skin. Dermatology Times p 56–60
3. Guttman C (2004) Advances in anti-aging: new techniques technology should match demand. Dermatology Times
4. Bisaccia D, Scarborough D (1992) The esthetic correction of the aging mouth. Cosmetic Dermatol (11):8–11
5. Schwanke J (2003) Emerging technique restores volume: Fat autograft muscle injection deemed long-lasting natural filler. Dermatology Times p 84
6. Fat Autograft Muscle Injection (FAMI) 2003 Draft (2003). In: Thompson advanced therapeutics communications
7. West TB, Alster TS (1998) Autologous human collagen and dermal fibroblasts for soft tissue augmentation. Dermatol Surg 24(5):510–512

8. Klein AW, Elson ML (2000) The history of substances for soft tissue augmentation. Dermatol Surg 26(12):1096–1105
9. Glogau R, Narins R, Weiss R (2004) Advances in cosmetic procedures. Fall Clinical Dermatology Conference Supplement Proceedings. Supplement to skin and aging 20–27
10. Cheng JT, Perkins SW, Hamilton MM (2002) Collagen and injectable fillers. Otolaryngol Clin North Am 35(1):73–85
11. Scarborough D, Bisaccia E (1997) CO_2 laser resurfacing with fat grafting for rhytids and acne scars. Cosmetic Dermatol (10):7–12
12. Isolagen anti-aging product scar tissue treatment for wrinkle scar treatment acne scar therapy–trials scar removal 2004
13. Rohrich RJ et al (2000) Early results of vermilion lip augmentation using acellular allogeneic dermis: an adjunct in facial rejuvenation Plast Reconstr Surg 105(1):409–418
14. AlloDerm lip augmentation: Complications 2004
15. Klein AW (1989) In favor of double testing. J Dermatol Surg Oncol 15(3):263
16. Warmuth L et al (1998) Correction of the aging mouth. Cosmetic Dermatol 11(12):9–12
17. Sculptra Advisory Board briefing document
18. Elson M (1999) Soft tissue augmentation techniques: Update on available materials. Cosmetic Dermatol (May):13–15
19. Larsen NE et al (1993) Hylan gel biomaterial: dermal and immunologic compatibility. J Biomed Mater Res 27(9):1129–1134
20. Uneet Co, Inc. (2002) Synthovial 7 with medical grade hyaluronic acid for joint lubrication
21. Lupton JR, Alster TS (2000) Cutaneous hypersensitivity reaction to injectable hyaluronic acid gel. Dermatol Surg 26(2):135–137
22. Narins RS et al (2003) A randomized double-blind multicenter comparison of the efficacy and tolerability of Restylane versus Zyplast for the correction of nasolabial folds. Dermatol Surg 29(6):588–595
23. Lowe NJ et al (2001) Hyaluronic acid skin fillers: adverse reactions and skin testing. J Am Acad Dermatol 45(6):930–933
24. Friedman PM et al (200) Safety data of injectable nonanimal stabilized hyaluronic acid gel for soft tissue augmentation, Dermatol Surg 28(6):491–494
25. Beautysurge.com (2004) Cosmetic plastic surgery information. http://www.beautysurge.com. Cited 18 Nov 2004
26. Valantin MA et al (2003) Polylactic acid implants (New-Fill) to correct facial lipoatrophy in HIV-infected patients: results of the open-label study VEGA. AIDS 17(17):2471–2477
27. Saylan Z (2003) Facial fillers and their complications Aesthetic Surg J 23(3):221–224
28. Lemperle G, Romano JJ, Busso M (2003) Soft tissue augmentation with Artecoll: 10-year history indications techniques and complications. Dermatol Surg 29(6):573–587
29. Greene D, Pruitt L, Maas CS (1997) Biomechanical effects of e-PTFE implant structure on soft tissue implantation stability: a study in the porcine model. Laryngoscope 107(7):957–962
30. Tolleth H (1985) Long-term efficacy of collagen. Aesthetic Plast Surg 9(2):155–158