11 Technique-Related Complications

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Abstract

Soft tissue fillers are increasingly becoming more popular as a nonsurgical option for cosmetic enhancement. The growing number of versatile filler options, affordability, increasing public interest, and decreasing social stigma have all influenced their growing popularity. While Food and Drug Administration (FDA) approved fillers are regarded as a safe alternative to the more invasive surgical cosmetic procedures, adverse events are a statistical certainty with the increasing number of procedures. The most common side effects include mild injection reactions that are transient, including redness, swelling, bruising, tightness, and pain. Rarely, more serious adverse events such as infection, granuloma formation, intravascular injections leading to tissue necrosis, blindness, and even stroke have been reported. Hyaluronidase can be used to dissolve hyaluronic acid fillers and all providers injecting hyaluronic acid fillers should have a filler crash cart on standby if intravascular injection occurs. It is paramount that an injector have expert knowledge of facial anatomy before injecting soft tissue fillers into the face. Sterile technique will limit risk of infection and biofilms. This chapter focuses on technique-related complications and how to minimize adverse events through proper product selection, safe injection techniques, and how to treat appropriately if adverse events arise.

Keywords: Tyndall effect, delayed-onset nodules, vascular compromise, blindness, biofilms

11.1 Introduction

Nonsurgical cosmetic procedures have become increasingly more popular over the past two decades. According to the American Society of Plastic Surgeons, in 2023, over 25.4 million nonsurgical procedures were performed in the United States. More than 5.2 million hyaluronic acid filler procedures were performed, making it one of the top five nonsurgical procedures, second only to the more than 9.48 million botulinum toxin treatments performed.[1] Soft tissue fillers saw a 108% increase over the last 6 reported years.[1,2]

Soft tissue augmentation with fillers is a noninvasive procedure that offers instant and satisfying results with predictable longevity. The growing number of versatile filler options, affordability, increasing public interest, and decreasing social stigma have all influenced their growing popularity. Most cosmetic physicians regard soft tissue filler procedures as being very safe. The most common side effects include mild injection reactions that are transient, including redness, swelling, bruising, tightness, and pain. Rarely, more serious adverse events such as infection, granuloma formation, and intravascular injections leading to tissue necrosis and blindness have been reported.[3,4] With proper patient and product selection, as well as safe injection techniques, cosmetic physicians can prevent and treat appropriately if adverse events arise. Notably, due to the relative ease of entry into the industry and the expanding adoption of this cosmetic procedure by less experienced professionals, there is a concern for increasing number of reported serious adverse events. This chapter focuses on technique-related complications of soft tissue fillers as well as the prevention, recognition, and management using soft tissue fillers.

11.2 Fillers

Soft tissue fillers are categorized as either hyaluronic acid fillers or nonhyaluronic acid fillers (▶ Table 11.1). With the growing number of Food and Drug Administration (FDA) approved fillers on the market, it is important to understand how each filler behaves to achieve optimal results. Most of this understanding comes from expert experience; however, there are objective ways to test the physical properties of fillers. Rheology is the study of the deformation and flow of fluid materials. With regard to fillers, the rheometric settings and rheometers used in different

Table 11.1 FDA-approved fillers available in the United States

Brand name	Filler type	FDA indications
Juvederm Ultra XC	Hyaluronic acid	For injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (such as nasolabial folds). Injection into the lips and perioral area for lip augmentation in adults over the age of 21 y
Juvederm Ultra Plus XC	Hyaluronic acid	For injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (such as the nasolabial folds)
Juvederm Volbella XC	Hyaluronic acid	For injection into the lips for lip augmentation and for correction of perioral rhytids in adults over the age of 21 y
Juvederm Vollure XC	Hyaluronic acid	For injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (such as the nasolabial folds) in adults over the age of 21 y
Juvederm Voluma XC	Hyaluronic acid	For deep (subcutaneous and/or supraperiosteal) injection for cheek augmentation to correct age-related volume deficit in the midface in adults over the age of 21 y
Restylane Silk	Hyaluronic acid	For lip augmentation and dermal implantation for correction of perioral rhytids (wrinkles around the lips) in patients over the age of 21 y
Restylane L	Hyaluronic acid	For injection into the mid to deep dermis for correction of moderate to severe facial wrinkles/folds (such as the nasolabial folds) and for lip augmentation in those over the age of 21 y
Restylane Lyft	Hyaluronic acid	For deep implantation into the facial tissue for the correction of moderate to severe facial wrinkles and folds, such as the nasolabial folds and for cheek augmentation and for the correction of age-related midface contour deficiencies in patients over the age of 21 y For injection into the subcutaneous plane in the dorsal hand to correct volume deficit in patients over the age of 21 y
Restylane Refyne	Hyaluronic acid	For injection into the mid to deep dermis for the correction of moderate to severe facial wrinkles and folds (such as the nasolabial folds) in patients over the age of 21 y
Restylane Defyne	Hyaluronic acid	For injection into the mid to deep dermis for the correction of moderate to severe deep facial wrinkles and folds (such as the nasolabial folds) in patients over the age of 21 y
Belotero Balance	Hyaluronic acid	For injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds, such as the nasolabial folds
Revanesse Versa	Hyaluronic acid	For injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds, such as the nasolabial folds, in adults aged ≥ 22 y
Sculptra Aesthetic	Poly-L-lactic acid (PLLA)	For shallow to deep nasolabial fold contour deficiencies and other facial wrinkles For restoration and/or correction of the signs of facial fat loss (facial lipoatrophy) in people with human immunodeficiency virus (HIV)
Radiesse	Calcium hydroxylapatite (CaHA)	For subdermal implantation for the correction of moderate to severe facial wrinkles and folds, such as the nasolabial folds For hand augmentation to correct volume loss in the dorsum of the hands For restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with HIV

(Continued)

Table 11.1 (*Continued*) FDA-approved fillers available in the United States

Brand name	Filler type	FDA indications
Bellafill[a]	Polymethylmethacrylate (PMMA)	For the correction of nasolabial folds and moderate to severe atrophic, distensible facial acne scars on the cheeks in patients over the age of 21 y
RHA Redensity		For injection into the facial tissue for the correction of moderate to severe dynamic perioral rhytids
RHA 2 and RHA 4		For the correction of moderate to severe dynamic facial wrinkles and folds, such as nasolabial folds, in adults 22 or older
RHA 3		For the correction of moderate to severe dynamic facial wrinkles and folds, such as nasolabial folds, and also used to augment lip fullness in adults 22 or older

Abbreviation: FDA, Food and Drug Administration.
[a]Skin testing required before administration of filler.

studies make it difficult to compare viscoelastic values of the various FDA-approved fillers across studies.[5]

Viscoelasticity and cohesivity are two important properties that an injector should consider when selecting a filler for a specific treatment. Viscoelasticity (G* or viscoelastic modulus) is the ability of the gel to resist shearing forces. This property is often substituted with the value G' (elastic modulus) because today's current hyaluronic acid fillers behave more elastic than viscous (G''). Clinically, this relates to the firmness of the gel and means that a higher G' filler will recover its shape better when shearing forces are applied by facial movements. Cohesivity is the ability of the gel to resist compression and stretching forces. Clinically, this relates to the moldability and its internal desire to spread evenly when injected.[6] High cohesivity helps maintain vertical projection, medium cohesivity balances vertical projection with relatively easy moldability, and low cohesivity forms sheets by spreading evenly with easy moldability.[6] Generally, a high G' and highly cohesive filler is ideal for deep or preperiosteal injections that aim to lift the overlying soft tissue to achieve a more sculpted or contoured look. Deep placement reduces the palpability of the filler and is ideal for the cheeks and jawline. Low cohesive and low to medium G' fillers can be placed more superficially for fine lines and wrinkles because they are nonbulking and less likely to cause visible bumps.[6]

11.3 Injection Techniques

Six basic patterns have been described for injecting fillers using hypodermic needles (▶ Fig. 11.1).[7,8] The linear threading technique is a superficial injection that fills folds in a singular "thread-like" pattern. The serial puncture technique fills folds with multiple injections placed superficially in a row to provide linear volume. The fanning technique includes one puncture site from which linear threads can be placed in a "fan-like" pattern. The cross-hatch technique combines multiple injections of linear threads that crisscross, providing a "mesh-like" pattern. The fern pattern technique is a superficial technique where the needle is directed perpendicular to the skin fold and more product is injected upon withdrawal near the fold. This technique is repeated on the opposite side of the fold along the entire skin fold.[7] Depot injections are deeply placed supraperiosteal injections (0.1–0.2 mL) used to lift and sculpt the overlying soft tissue. A variant of this technique is the tower technique, where more product is injected deeply and as the needle is removed, less product is placed creating a cone pattern.[8]

Cannulation is a technique that uses a blunt-ended instrument instead of using the traditional

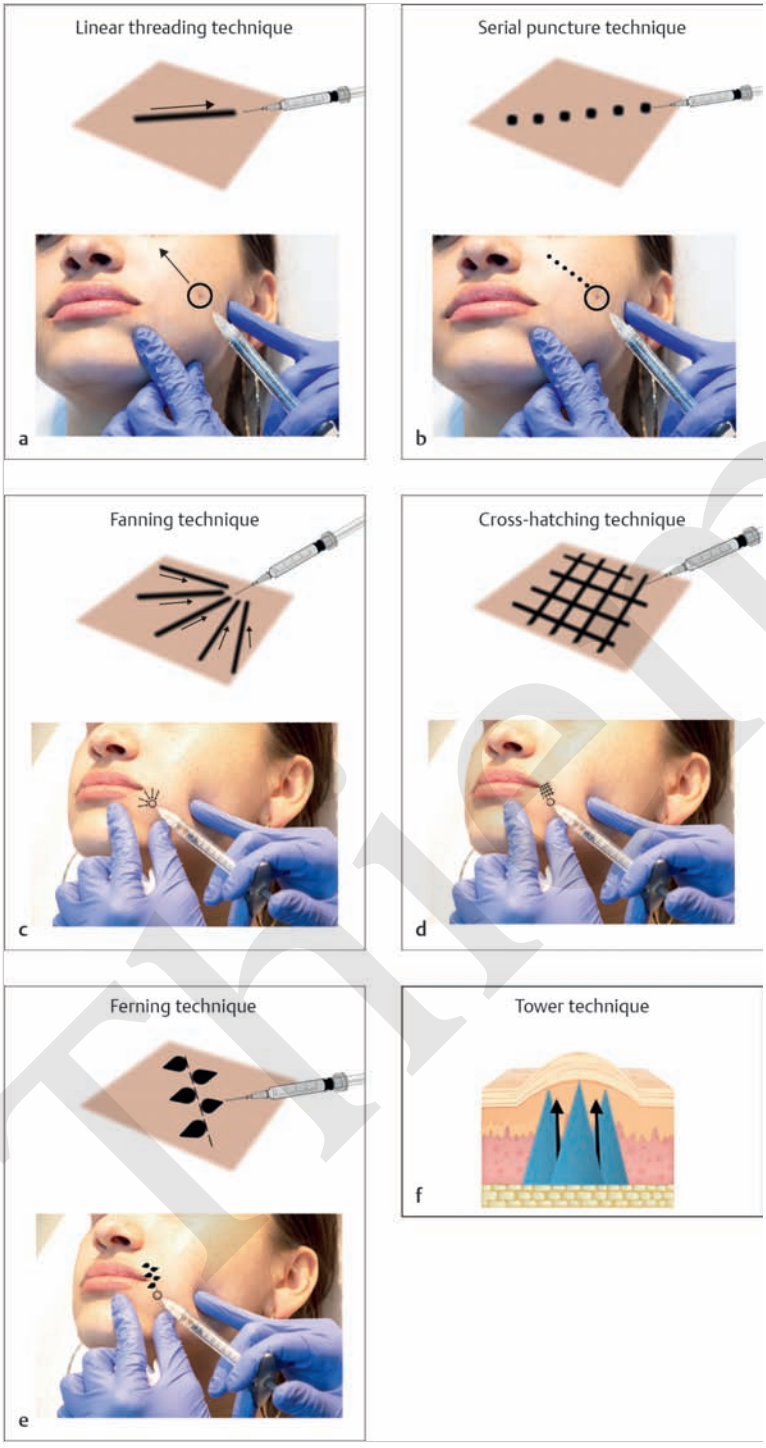

Fig. 11.1 **(a)** Linear threading technique. **(b)** Serial puncture technique. **(c)** Fanning technique. **(d)** Cross-hatching technique. **(e)** Fern pattern technique. **(f)** Tower technique.

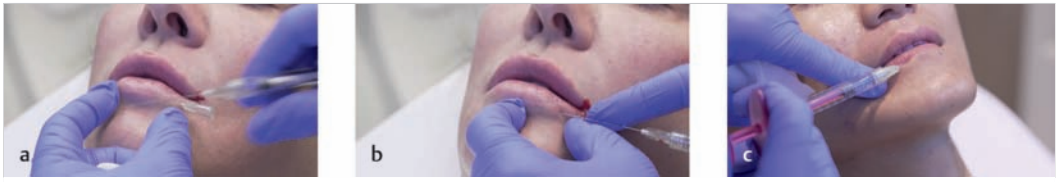

Fig. 11.2 **(a)** Creating a point of entrance using a 27-gauge needle. **(b)** Cannula advanced through the created entrance with a 27-gauge needle. Retrograde implantation of hyaluronic acid filler. **(c)** Hyaluronic acid filler placed in the lower lips using a needle.

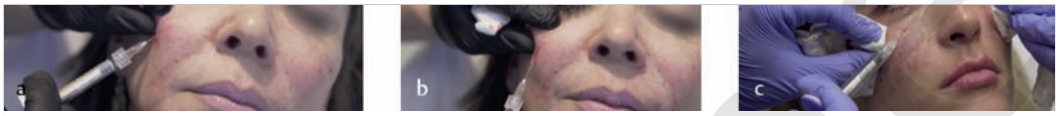

Fig. 11.3 **(a)** Hyaluronic acid filler treatment to the under eyes and midface. A major benefit of using the cannula technique is less needle sticks. The cannula can be maneuvered to treat the tear trough and lateral orbit. **(b)** Hyaluronic acid filler placed in the lateral orbit using the same entrance point as was used to treat the tear trough. **(c)** Hyaluronic acid filler placed in the infraorbital region. Multiple injection sites needed to achieve the desired effect.

hypodermic needle (▶ Fig. 11.2, ▶ Fig. 11.3, **Video 11.1**). The advantages of using this technique include less injection pain, swelling, bruising, and puncture sites. Cannulas are best suited for placement in the deep dermal or subdermal planes and require an "inflation" technique. This is in contrast to the micro-volume filling of individual wrinkles.[9] The use of cannulas for filler placement is still not without possible complications as it has been shown in cadaver models that intravascular perforations can occur.[10]

11.4 Technique-Related Complications

Although rare, at high enough volumes of procedures, it may be inevitable that a cosmetic provider will encounter a serious complication from injecting fillers. Therefore, having an organized approach and systematic protocol will help expedite recognition and management of these complications. Complications from fillers can be divided into early onset (occurring within several days to weeks posttreatment) and delayed onset (occurring months to years posttreatment).

Early complications include injections site reactions (i.e., erythema, edema, pain/tenderness, bruising, itching), infections (i.e., staphylococcal or streptococcal), hypersensitivity reactions (i.e., type I), noninflammatory nodules/contour irregularities caused by technique and placement errors, skin discolorations (i.e., hyperpigmentation, Tyndall effect), and vascular occlusion causing tissue necrosis and/or blindness.

Delayed-onset complications include malar edema, persistent discoloration, hypersensitivity reactions (i.e., type IV), infection (i.e., atypical mycobacterium and biofilm), migration, and inflammatory nodules/granulomatous reactions. This chapter focuses on technique-related complications in relation to the above categories and discusses their clinical presentations, management, and treatments. Not all the categories will be discussed, as some complications may be unpredictable and not directly related to injector technique. Additionally, practicing good techniques may not eliminate complications (i.e., bruising cannot be eliminated with good injection techniques, but may be reduced with skilled injection practices).

11.4.1 Bruising

Bruising is one of the most commonly encountered issues when it comes to injecting soft tissue fillers.

Although not life-threatening and seemingly relatively inconsequential, this can be a major matter of concern for patients because of fear of social stigma and downtime. The reputation of the physician injecting may be judged by this factor alone.

To minimize the risk of bruising and bleeding, the cosmetic provider should inquire about the use of anticoagulants (i.e., aspirin-containing products, nonsteroidal anti-inflammatory drugs [NSAIDs], warfarin, and clopidogrel) or supplements that have been shown to "thin" the blood. Supplements that have been shown to increase the risk of bleeding include but are not limited to vitamin E, fish oil, St John's wort, garlic, *Ginkgo biloba*, ginseng, ginger, and kava kava.[11] Patients who do not have a history of heart attack, stroke, or blood clots should discontinue aspirin and the above-listed vitamins and supplements 7 to 10 days prior to the procedure. Alcohol consumption should also be discontinued prior to treatment due to its vasodilatory properties and alteration of liver coagulation factors. Bromelaine and arnica supplementation may have benefit in speeding up bruise healing.[12]

Technique-related steps that may help reduce the chances of swelling include using the smallest gauge needle or a cannula when suitable, injecting slowly, and small aliquots, avoiding reinjections in the same areas. This will reduce the total amount of injections and statistically decrease the chances of injuring a vessel. If previously injected filler contained lidocaine, this can also cause vasodilatation and increase the risk of injuring a vessel.

Should an impending bruise be of concern, immediate application of pressure to the area and cold therapy are mainstays in progression. Pulsed dye laser, long-pulsed neodymium-doped yttrium aluminum garnet (Nd:YAG), and long-pulsed light (IPL) have also been suggested as adjunctive treatment to help speed recovery from bruising caused by soft tissue fillers.[13]

11.4.2 Inappropriate Placement of Soft Tissue Fillers

Clinicians injecting soft tissue fillers should be mindful of the rheologic properties (G' and cohesivity) of the product of choice in the context of the area of treatment and desired result. For example, the clinician should not be placing a high G' filler in a delicate area such as the tear trough. The clinician must also carefully consider injection techniques, depth, volume, speed, and accuracy of injection. A thorough understanding of facial anatomy is the essential foundation to these external factors. Placement of filler into muscles can result in migration and displacement causing nodules or pooling of product in unwanted areas (i.e., Tyndall effect in the tear trough). This is an excellent illustration of how inexperience, knowledge deficits, and incompatible technique can result in less-than-desired results. Lumps, bumps, and asymmetries may be treated early in the posttreatment period with massage. A benefit of using hyaluronic acid fillers compared to other soft tissue fillers (i.e., polymethylmethacrylate [PMMA] and calcium hydroxylapatite [CaHA]) is that it can be dissolved with hyaluronidase (▶ Fig. 11.4).

Tyndall Effect

The Tyndall effect, or Rayleigh scattering, is a blue-gray discoloration that occurs when previous injected hyaluronic acid filler had been placed or migrated. The Tyndall effect is due to the preferential scattering and reflection of blue light over red light by the hyaluronic acid filler. Similar principles govern why veins appear blue in the skin, despite the red color of blood.

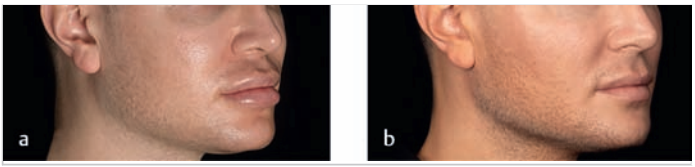

Fig. 11.4 **(a)** Accentuated facial features including the lips, cheeks, and chin with hyaluronic acid. **(b)** Post-hyaluronidase injection to reverse overdone facial filler injections.

One of the most common places to see the Tyndall effect is in the tear trough. One reason for this is the epidermis and subcutaneous tissues are much thinner than other areas of the face and are more conceivably prone to having visible pools of hyaluronic acid product. Extrinsic factors include the choice of hyaluronic acid filler and placement level of the product.

A patient who is exhibiting the Tyndall effect after having treatment of a hyaluronic acid filler in the tear trough region may present to the practice in distress because the "dark circles" under their eyes have gotten worse or the "bruise" has been persistent for months. First in the treatment algorithm is to listen to their concerns, evaluate the patient and reassure them that this issue can be fixed with injections of hyaluronidase enzyme that breaks down the hyaluronic acid filler. This dissolving procedure comes at the expense of having the "tear trough" return. However, retreatment of the tear trough with a hyaluronic acid filler at another time can be used for re-correction.

Hyaluronidase is an enzyme that hydrolyzes the hyaluronic acid by splitting the β-1,4-glucosaminidic bond between C1 of the glucosamine moiety and C4 of glucuronic acid.[14] Currently there are four FDA-approved hyaluronidase brands in the United States (Hylenex, Vitrase, Hydase, and Amphadase).[15] Amphadase and Hydase are bovine derived, Vitrase is ovine derived, and Hylenex is made of recombinant human DNA; thus, preliminary skin testing for hypersensitivity is officially recommended.[16,17] Patients with a history of allergic reactions to bee stings should warrant caution with hyaluronidase use, as it is one of at least eight biologically active components in bee venom.[14] Hyaluronidase allergies are well documented, but uncommon (< 0.1%), with most cases documented in the ophthalmologic literature.[14,18]

Once the patient is cleared from a hypersensitivity to hyaluronidase, a patient with the Tyndall effect can be injected with hyaluronidase by direct infiltration. Massage is recommended to mechanically mix the enzyme and hyaluronic acid together and promote degradation. A suggested rule of thumb is the following: for each 0.1 mL of hyaluronic acid filler needed to be digested, 5 to 10 units of hyaluronidase should be infiltrated in the area as a starting dose (▶ Fig. 11.5).[19]

Prevention of the Tyndall effect caused by hyaluronic acid fillers may be avoided if injected at the appropriate dermal level or deeper. When treating the tear trough, supraperiosteal injections just inferior along the orbital rim conceivably hides implanted filler below the overlying soft tissue, reducing the chances of light scattering and reflection caused by hyaluronic acid (▶ Fig. 11.5). The choice of filler may also play a role. For example, in a comparative study by Sundaram and Fagien, Belotero Balance distributed homogeneously throughout the reticular dermis, while Restylane distributed in large defined pools and Juvederm Ultra in small pools throughout the reticular dermis.[20] Although Restylane and Juvederm products are FDA indicated for mid to deep dermal injections, clinical experience has revealed them to be better as subcutaneous injections. The low elasticity (G') and high cohesivity properties of Belotero Balance predicts its soft and effective spreading

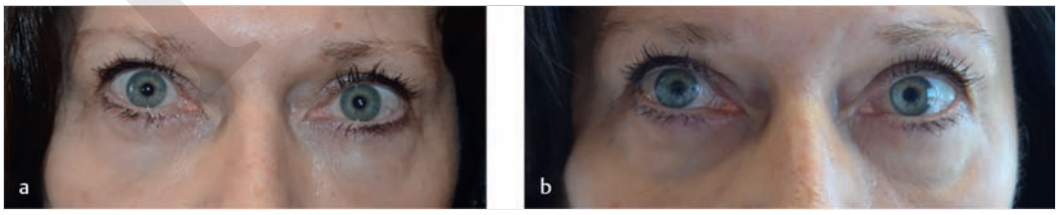

Fig. 11.5 **(a)** Tyndall effect (bluish hue) in the tear trough regions caused from a hyaluronic acid filler. **(b)** Tyndall effect reversed (i.e., decreased swelling and blue discoloration) after hyaluronidase was injected into the tear trough regions. Notice the substantial loss of volume and prominent eye bags now visible after filler reversal.

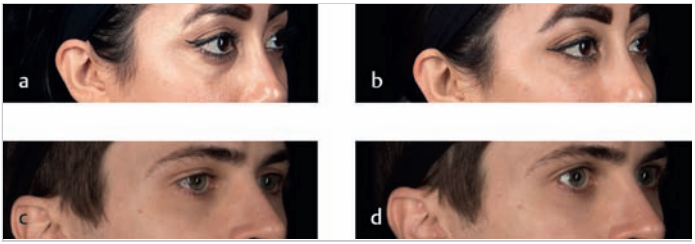

Fig. 11.6 **(a)** Tear trough before hyaluronic acid filler injected in a female. **(b)** Tear trough after hyaluronic acid filler injected in a female. **(c)** Tear trough before hyaluronic acid filler injected in a male. **(d)** Tear trough after hyaluronic acid filler injected in a male.

qualities, which allow it to integrate well into tissue and maintain its structure when mechanically stressed.[20] This makes it an appropriate product for superficial implantation and perhaps more ideal for minimizing Tyndall effect outcomes (▶ Fig. 11.6; **Video 11.2**).

11.4.3 Vascular Compromise

One of the most feared complications regarding aesthetic treatment with fillers is intravascular injection. With the increasing popularity of fillers used for cosmetic enhancement, the prevalence of rare complications (i.e., intravascular injection or external tamponade) will likely increase in proportion to the number of procedures. The true prevalence of vascular compromise caused by fillers is difficult to establish and it may likely be underreported by physicians for various reasons such as fear of embarrassment and scrutiny. However, even an experienced cosmetic physician who has performed thousands of injections is likely to see this complication as a statistical certainty. What is important to recognize are the signs of intravascular injection and impending skin necrosis and how to treat promptly. Some authors have advocated that all injectors should have a "filler crash kit" or "filler rescue kit" on standby for prompt treatment of impending necrosis analogous to crash carts found in hospitals.[21,22,23] A thorough understanding of risk reduction techniques and understanding of anatomy are paramount.

Skin Necrosis

The first step in the treatment of impending skin necrosis is recognition. Typically, skin blanching is the first phase, although this may not be obvious. It is usually seen upon injection and/or immediately after. Pain may or may not be present as local/regional anesthesia can augment the sensation. Another consideration is the use of epinephrine as it can cause vasoconstriction and mimic blanching.

The second phase is either a livedo pattern of violaceous mottled/reticulated discoloration or alternatively a reactive hyperemia. While the reactive hyperemia represents a restored circulation from insufficient occlusion usually leading to full recovery; the livedo pattern is a clear sign of impending necrosis. These phases are usually present within minutes after injection.

The final phases leading to necrosis include blue-black discoloration occurring within hours, followed by blisters or bullae in the following hours to days. Skin breakdown, sloughing, ulceration, and scarring occurring over days to weeks[22] (▶ Fig. 11.7).

Risk factors for vascular compromise leading to skin necrosis include injection site, volume, previous scarring, type of filler material, and sharp hypodermic needles versus blunt cannulation.[22] Extreme caution should be exercised when injecting in regions where named arteries run (i.e., facial artery, angular artery, etc.). High-risk regions include the midline regions of the face (i.e., nasolabial folds and glabella region).

As a safe rule, limit the volume injected into any one location to no greater than 0.1 to 0.2 mL. If more volume is needed in the region, the placement position should be adjusted. Intuitively, a larger volume injected in any one location can cause a proportionally greater degree of obstruction. If high resistance is perceived by the injector, attempting to clear the syringe with higher counterpressure should not be attempted, as this can lead to uncontrolled discharge of large volumes of filler.

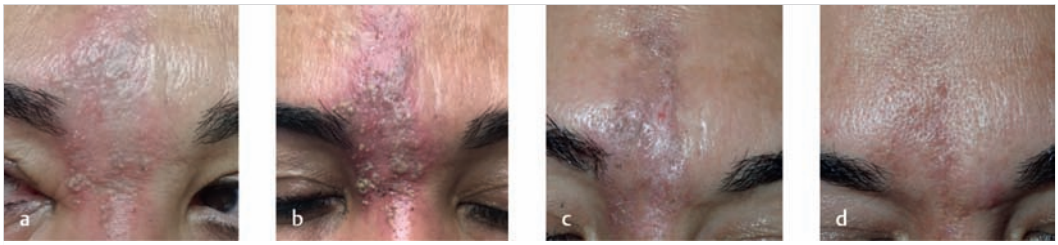

Fig. 11.7 **(a)** Progression photographs of a vascular occlusion. There is a dusky pallor with hyperemia surrounding the borders with vesicles. **(b)** Progression of skin necrosis with greater numbers of vesicles and erythema. **(c)** Skin breakdown with ulceration. **(d)** Healing phase with residual postinflammatory hyperpigmentation and scarring.

In the authors' opinion (J.E. and M.L.), a safe practice is to hold negative pressure for 6 to 10 seconds checking for a flash before injecting. Of note, the ability of the injector to perceive accidental intra-arterial penetration may be affected by the type of filler used. A highly viscous filler will be more difficult to aspirate. The use of non-hyaluronic acid fillers (i.e., calcium hydroxyapatite, PMMA) will also increase the risk of nonreversible ischemic damage as there are currently no available reversal agents on the market and highlight the importance of risk reducing techniques when injecting with these types of fillers. The use of blunt-tipped cannulas may reduce but not eliminate accidental intra-arterial injection.[10]

Expert consensus treatment recommendations regarding injection-induced necrosis caused by hyaluronic acid filler agree that prompt diagnosis and immediate treatment with high doses of hyaluronidase (at least 200 units) are critically important.[23,24] It was also felt that skin testing was not necessary, due to risk of impending necrosis. Dilution of the hyaluronidase with saline or lidocaine may be of benefit to help disperse the hyaluronidase. Additionally, lidocaine has the added benefit of vasodilation and may improve perfusion, as do warm compress. If no improvement is seen within 60 minutes, up to three to four cycles of hyaluronidase should be injected and massaged to help facilitate the spread of the enzyme. Topical nitroglycerine has vasodilatory affects and when massaged two to three times a day into the affected area may reduce necrotic spread, although this is a controversial topic.[25] Finally, two tablets of oral aspirin (325 mg) daily along with an antacid are recommended to prevent further clot formation due to vascular compromise and to prevent aspirin-associated gastritis, respectively. Other considerations include oral prednisone, hyperbaric oxygen, low-molecular-weight heparin, intravenous (IV) prostaglandin E, and sildenafil.[23]

Daily follow-up is highly recommended to monitor for signs of improvement or any signs of occlusion or necrosis. Topical nitroglycerin can be stopped with improvement, while repeat hyaluronidase and topical nitroglycerin regiments are recommended if no improvement is seen. Aftercare includes routine wound care ensuring adequate hydration, appropriate wound debridement of necrotic skin, and monitoring for secondary infections.

Blindness

The face has a rich vascular network that is a prime target for intravascular occlusion. In some cases, accidental intravascular injection can lead to permanent blindness or even stroke.[3,4,26,27] An expert understanding of the anastomosing network of the facial arteries is absolute for physicians who are injecting fillers.[21] It is generally accepted in the medical literature that vision can be restored if central retinal circulation is restored within 90 to 240 minutes, although some recent literature suggests that it may be as little as 12 to 15 minutes.[28] This is a true medical emergency and prompt recognition and immediate transport to an ophthalmologist or oculoplastic surgeon is recommended.[27]

The most common presentation of ophthalmic artery occlusion caused by retrograde injection of filler is complete or partial vision loss. Pain in the ocular, periocular, orbit, and periorbital regions may be described as a headache. Ophthalmoplegia (decreased extraocular movements) and ptosis have been described. Nausea, vomiting, and central nervous system (CNS) symptoms including unilateral weakness or evidence of infarction on imaging may also result. Impending skin necrosis may be seen in as much as 15 to 43% of patients who also have vision changes.[3,4]

Understanding the anastomosing arterial supply is key to understanding the high-risk areas of the face when injecting fillers. The glabella/forehead, nose, nasolabial folds, and medial periorbital areas are high-risk areas for blindness.[3,4] The facial artery is the root blood supply of the face provided by the external carotid system. Its connection to the internal carotid system is classically described as where the facial artery becomes the angular artery, anastomosing with the dorsal nasal artery and then the ophthalmic artery. Through this anastomosing arcade, it is conceivable that a high extrusion pressure could cause enough backflow of filler causing embolization into central retinal artery via the ophthalmic artery.

If accidental intravascular filler embolization to the ophthalmic artery occurs and the patient complains of ocular pain or vision loss, immediately stop injecting and urgently transfer care to an ophthalmologist, oculoplastic surgeon, or nearest stoke care center if CNS symptoms are present. If a hyaluronic acid filler is being used, injecting the area with hyaluronidase may help, as it has been shown that hyaluronidase can pass through intact arterial walls and hydrolyze embolized hyaluronic acid in cadaver models.[29] Retrobulbar injection with hyaluronidase (300–600 units) may also be considered by the injector or by immediate care by an ophthalmologist or oculoplastic surgeon.[30,31] Ocular massage can reduce intraocular pressure and may dislodge the embolus. Other treatments to reduce intraocular pressure include anterior chamber paracentesis, IV mannitol, and acetazolamide by physicians trained in these procedures and administration of these drugs.[3]

Danger Zones of the Face

Glabella and Brow

In the glabella, brow, and forehead regions with filler, the locations and patterns of the supraorbital and supratrochlear arteries must be considered and avoided. The supratrochlear artery travels superiorly from the medial canthal line starting deep in the superomedial orbit and becomes superficial approximately 2 cm above the orbital rim. The supraorbital artery exits the supraorbital notch in the medial limbus line and becomes superficial 2 cm above the orbital rim.[3,21] Both arteries are branches of the ophthalmic artery, and accident intravascular injection with enough pressure can cause retrograde embolism back to the ophthalmic artery.

When injecting fillers into the glabella, injections within 2 cm of the supraorbital rim should be placed superficially in the dermis, while fillers placed in the forehead should be placed in the supraperiosteal plane.[32] When injecting the "11's," a common complaint of the glabellar region, the preferred filler should be a low G' filler such as Belotero Balance or Restylane silk with serial puncture or ferning. Compression of the supratrochlear vessels at its base while injecting is another technique that may provide another level of safety.[21]

Nose

The major arteries of the nose that may be at risk when injecting fillers in the nose include the dorsal nasal, columellar, and lateral nasal arteries. This area is highly vascular with several anastomoses forming a vascular arcade. The dorsal nasal artery is the main blood supply for the upper base of the nose and is located approximately 5 mm above the medial canthal line.[32] The lateral nasal artery supplies blood to the tip of the nose and is a branch of the angular artery that runs within 2 to 3 mm along the alar groove in the subdermal plexus.[33] The main anastomosing arteries connecting the external and internal carotid systems of the nose are at the level of the subdermal plexus or superficial muscular aponeurotic system plane.[3,21,33,34] For this reason, the safest plane of inject for filler into the nose

for nonsurgical nose correction is the deep supraperiosteal or supraperichondrial plane. External compression of the dorsal nasal artery is recommended while injecting in the nasal region.[21] Patients who have had previous rhinoplasty should be injected with extreme caution due to normal anatomical plane alteration, scaring, and higher chance of intravascular injection.

The perpendicular bolus technique and the intralobular injection technique using a cannula are injection methods currently described in clinical practice.[35] The midline injection technique typically uses a 27- to 31-gauge needle and involves serial punctures, injecting small aliquots of a high G' filler deep onto the nasal dorsum using a perpendicular approach (▶ Fig. 11.8). This technique is still not without risk as it has been demonstrated that the dorsal nasal artery crosses midline approximately 20% of the time and that it can be found in the supraperiosteal layer 8% of the time[35] (▶ Fig. 11.9).

The infralobular injection technique has the advantage of only using one puncture and less risk of bruising. The cannula should be advanced between the columellar arteries gently and linear threads can be placed supraperichondrial or supraperiosteal along the midline (▶ Fig. 11.10; **Video 11.3**). External manipulation can be used to mold and fine-tune the shape the nose. It is important to balance the risk of the cannula size with the diameter of the relevant vasculature in the nasal region. Most studies on vasculature in the face are done on cadavers and most studies reference the dorsal nasal artery diameter as 1 mm.[32] However, the dorsal nasal artery diameter in a recent study on live patients using ultrasound showed that its diameter ranges from 0.5 to 2 mm with an average of 1.2 mm.[35] Thus, it is conceivable that smaller gauge cannulas may have a higher risk of intravascular cannulation. It is important for the injector to gently advance the cannula and use small aliquots of filler when placing filler. With proper knowledge of nasal anatomy and proper technique, nonsurgical liquid rhinoplasty can have a dramatic difference in appearance nasal profile (▶ Fig. 11.11).

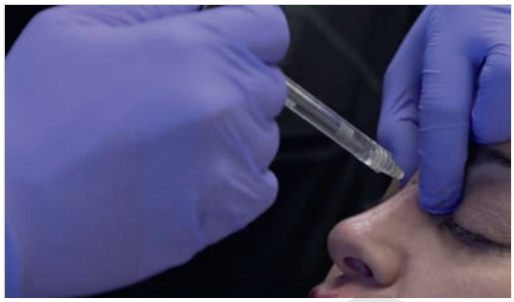

Fig. 11.8 Hyaluronic acid filler injected with a needle along the dorsal nose into the deep supraperiosteal or supraperichondrial plane with dorsal nasal artery compression.

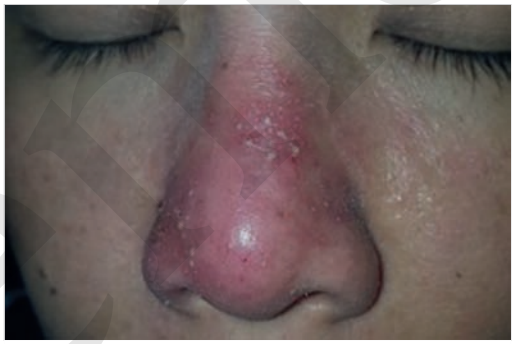

Fig. 11.9 Vascular occlusion of the nose from nonsurgical liquid rhinoplasty (nonsurgical liquid nose job) with hyaluronic acid filler.

Infraorbital

The infraorbital artery is a branch of the maxillary artery; however, its external connection to either the angular artery, supratrochlear artery, or dorsal nasal branch of the ophthalmic artery provides a potential to blindness.[36,37] The location of the infraorbital foramen has been reported with great variation in the literature. With regard to vertical lines, it has been documented in cadaver dissections to be in line with the first premolar 64% of the time, followed by the canine (17%) or second premolar (17%).[38] Multiple infraorbital foramens have also been documented.[39,40,41] The variation in distance between the orbital rim and infraorbital foramina ranges from 6.1 to 10.9 mm[42] and the

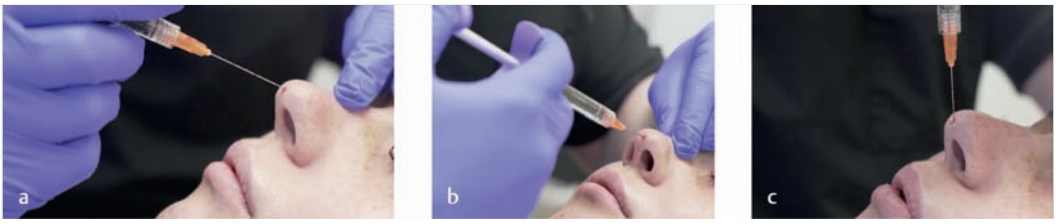

Fig. 11.10 **(a)** A single entry point is made at the tip of the nose for cannulation. Hyaluronic acid filler is placed along the dorsum of the nose in the deep supraperiosteal or supraperichondrial plane. **(b)** External compression of the dorsal nasal artery. Gentle advancement of the cannula with small aliquots of filler placed in a retrograde linear thread technique. **(c)** Injection within the columella between the columellar arteries is used to help lift and support the nose giving projection and shape to the nasal tip.

Fig. 11.11 **(a)** Nonsurgical liquid rhinoplasty (nonsurgical liquid nose job) after hyaluronic acid filler placement in a female. **(b)** Nonsurgical liquid rhinoplasty (nonsurgical liquid nose job) after hyaluronic acid filler placement in a female. **(c)** Nonsurgical liquid rhinoplasty (nonsurgical liquid nose job) before hyaluronic acid filler placement in a male. **(d)** Nonsurgical liquid rhinoplasty (nonsurgical liquid nose job) after hyaluronic acid filler placement in a male.

variation in distance from the facial midline ranges from 24.2 to 27.1 mm, with men averaging longer distances.[38,40,42,43,44] A good rule of thumb when trying to locate the infraorbital artery is to recall that it exits the infraorbital foramen in line with the medial border of the pupil or the first premolar approximately within 1 cm below the infraorbital rim.

There are two danger zones when injecting filler in the infraorbital region. The first danger zone lies between the vertical line of the medial border of the pupil and the lateral nasal sidewall. In this region, the nasal branch of the infraorbital artery runs along the periosteum before it anastomoses to one of the branches of the ophthalmic artery. For this reason, retromuscular injections are recommended.[37]

The second danger zone is lateral to the medial border of the pupil. In this region, the zygomaticomalar branch and its cutaneous perforators of the infraorbital artery supply the overlying skin. For this reason, injections should be deep and supraperiosteal to minimize risks of intravascular involvement of the zygomaticomalar artery and its cutaneous perforators leading to skin necrosis.[37]

Several techniques have been advocated when injecting fillers in the infraorbital hollow or tear trough region medial to the infraorbital foramen. (1) Injection using a blunt-ended cannula in the retromuscular or preorbital fat region at least 2 mm above the periosteum using small aliquots.[37] (2) Injecting on the infraorbital rim superior to infraorbital foramen on the supraperiosteum followed by gentle molding.[45] (3) Injecting lateral to the orbital foramen on the supraperiosteum, and gentle molding medially to fill tear trough defects.[21,46] Another factor to consider is a prior history of lower lid blepharoplasty, as altered anatomy and scarring from previous surgery can make it difficult to perceive the tissue layers and accidental intravascular cannulation (**Video 11.2**).

Nasolabial Fold

Filling the nasolabial fold is a common request of cosmetic patients. While completely eliminating this fold can look unnatural, softening this region can have instant rejuvenating and gratifying results. The major artery that runs along the nasolabial fold is the facial artery, a highly variable

and torturous vessel. Intravascular injection with filler in the facial artery is high risk for skin necrosis due to its tributaries (i.e., inferior and superior labial arteries and the lateral nasal artery) supplying the lips and nasal tip, respectively.[47] The facial artery is also a potential highway to blindness because it becomes the angular artery, as is classically described in textbooks. However, Kim et al described four types of various anastomosing paths of the angular artery where types I and II are the potential variations for blindness.[48] Type I (19.3%) and II (31.6%) have connections to the facial artery and are present 50.9% of the time, while type III (22.8%) has no connection to the facial artery and type IV (26.3%) has no angular artery.

Lee et al[49] described the various anastomosing patterns of the facial artery and found similar patterns to Kim et al.[48] Lee et al also described the variations in the depth of the facial artery in relation to the facial muscles. In 85.2% of the cadavers, the facial artery was superficial to the facial muscles at some point between the alar base and the modiolus. Further, in their dissections, Scheuer et al found that the facial artery becomes very superficial in the upper third of the nasolabial fold.[46] For this reason, they recommend deep supraperiosteal injection in the upper third of the nasolabial fold. Injections into the deep dermal and superficial subcutaneous plane are generally safe in the lower two-thirds of the nasolabial fold, because the facial artery courses beneath muscle, or above it in the deep planes.[21,46]

Lips

There is a risk of blindness regardless of the area of treatment, and the lips are no exception. Although most cases of intravascular injection in the lips lead to lip necrosis, there are case reports blindness following lip injections.[3] An understanding of the perioral vasculature is essential to minimize the risk of intravascular injection.

Near the oral commissure, the facial artery runs deep to the risorius and zygomaticus major muscles and superficial to the buccinators approximately. Classically, the facial artery supplies the perioral region with the superior labial and inferior labial arteries. The facial artery passes on average 15.5 mm (9.0–20.2 mm) lateral from the oral commissure.[50] Clinically, the superior labial artery can be estimated by placing the thumbnail beside the corner of the mouth.[51] The superior labial artery typically runs superior to the vermillion border, then courses inferiorly as it approaches the cupid's bow making this location high risk for intravascular injection.[51] The superior labial artery is usually found posterior to or within the orbicularis oris muscle.[52] In sagittal planes of cadaver dissections, the distance of the superior labial artery from the anterior surface of the red lip was 4 to 12 mm (mean: 7.6 mm). The distance of the superior labial artery from the inferior boarder of the red lip was 5 to 10 mm (mean: 6.7 mm). The distance of the superior labial artery from the posterior boarder of the red lip was 2 to 4 mm (mean: 3.2 mm).[53] The superior labial artery also gives off branches that anastomose with the inferior alar, columellar, and septal branches.

The inferior labial artery can run horizontally at the level of the vermillion border or lower near the labial mental crease, with vertically oriented branches supplying the lower lip.[50,54] This large distribution may be due to the lack of a universal definition defining the inferior labial and the mental arteries. In sagittal planes of cadaver dissections, the distance of the inferior labial artery from the anterior surface of the vermillion was 4 to 11 mm (mean: 6.4 mm). The distance of the inferior labial artery from the superior border of the vermillion was 3- to .5 mm (mean: 5.9 mm). The distance of the inferior labial artery from the posterior border of the vermillion was 3 to 6 mm (mean: 4.8 mm).[54]

Considering the depth of the artery is the most important factor to maximizing the safety when injecting the lips with filler; generally, injections should be kept to less than 3 mm deep along the mucosa–muscle interface, and an intermediate to low G' filler should be used with a superficial threading technique. The use of cannulation may also reduce the risk of intravascular injection and limit the amounts needle injections (▶ Fig. 11.2, ▶ Fig. 11.3; **Video 11.1**).

11.4.4 Delayed Nodules

Delayed-onset nodules can be organized into inflammatory nodules and noninflammatory nodules. These may appear months to years after injection and have variable etiologies. Early (within several weeks to months) nodules of delayed onset tend to be noninflammatory and noninfectious. Late (several months to years) nodules of delayed onset tend to be inflammatory, caused by biofilms or foreign body granulomas, and can be confirmed with cultures and biopsy, respectively. Biofilms (chronic indolent infections) are briefly discussed in the infection section with regard to techniques in the infection section. Foreign body granulomas are diagnosed from histologic evaluations and reveal dense granulomatous inflammation composed of histiocytes, giant cells (multinucleated histiocytes), lymphocytes, and, sometimes, foreign body material. Delayed noninflammatory nodules may be palpable or visible and tend to occur with particulate fillers (i.e., CaHA, poly-L-lactic acid [PLLA], PMMA) in highly mobile areas such as the periorbital hollows, lips, décolleté, and dorsal hands (▶ Fig. 11.12).

In the management of nodules, it is useful to differentiate them based on time of onset and type (i.e., noninflammatory vs. inflammatory). For earlier nodules that are noninflammatory, massage, aspiration, and intralesional sterile water or saline injections might be helpful in breaking up the implant. If the nodule is from a hyaluronic acid–based filler, hyaluronidase may be helpful. For persistent nodules and nodules of delayed onset, intralesional corticosteroids and 5-florouracil injections may help break apart palpable nodules. Surgical excision is a final option in persistent cases and may result in a poor cosmetic result. Delayed inflammatory nodules may present with edema, induration, tenderness with and without pus or filler material.[55] It is important to rule out underlying infection such as mycobacterium and biofilm and treat accordingly with adequate antibiotic coverage. If a hyaluronic acid filler was used, hyaluronidase may be used after appropriate antibiotic therapy is initiated, to not spread the infection. Once infection has been ruled out, inflammatory nodules may be treated similarly as described above. Systemic steroids may also be of consideration.

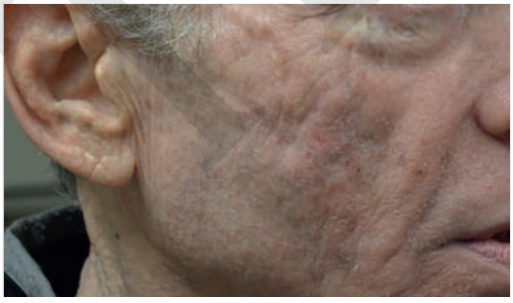

Fig. 11.12 Delayed-onset nodules in the cheek after calcium hydroxylapatite (CaHA) and polymethylmethacrylate (PMMA).

Sculptra Aesthetic/Poly-L-Lactic Acid

Sculptra (PLLA; Galderma Laboratories, L.P., Fort Worth, TX) is a nonhyaluronic acid biodegradable filler FDA approved for nasolabial folds and human immunodeficiency virus (HIV) associated lipoatrophy.[56] PLLA is the active ingredient used in the suture material Vicryl, and has been used in the medical field for over 30 years with excellent safety and biocompatibility.[57] The polymer is metabolized through the same pathway as lactic acid.[58] Nodule formation with PLLA was more common (6–44%) in the early clinical trials for FDA approval of HIV lipoatrophy[57,59,60,61] and is largely believed to be due to the reconstitution volumes. The first studies reconstituted the lyophilized milled powder with 3 to 5 mL of sterile water.[57] In the clinical trials for the aesthetic use of PLLA, 5 mL of a sterile water reconstituted was left to stand for at least 2 hours before injection was used.[56,62] Delayed papules and nodules for the 116 patients were reported to be 17.2% for the PLLA treatment arm, occurring 5 to 7 months postinjection and lasting for approximately 6 months.

Since then, the prevalent opinion in the medical literature suggests that higher reconstitution volumes, longer mixing times, and deeper injections correlate with lower incidences of nodule formation. This was demonstrated in one study with 819 treatments of PLLA in 300 patients over a 5-year period. Between the years 1999 and 2002, Woerle

et al treated patients using a protocol of 3 mL sterile water reconstitution, 2 to 12 hours standing time before injection. Nodule formation was observed in 10% of patients. In 2002, the treatment protocol was changed to a reconstitution of 5 mL (3 mL of sterile water, 36–48 hours mixing time before the addition of 2 mL of 1% lidocaine immediately before injection). Additionally, the injection plane was also changed from deep dermal to subcutaneous. A reduction of nodules formation (1%) was thought to be due to the described protocol changes by the authors.[63] Other authors have noted similar findings with reductions in nodule formation (0.13%) using 5-mL and occasionally 7-mL dilutions.[64] A 2015 survey of the average total reconstitution volume for PLLA use on the face by 87 aesthetic providers (dermatologists, facial plastic surgeons, plastic surgeons, oculoplastic surgeons, primary care physicians, nurse practitioners, physician assistants) found it to be 9 mL (7 mL of sterile water or saline plus 1.8 mL on average, of lidocaine postmixing time).[58] It is important to note that the package insert of PLLA for aesthetic use states 5-mL reconstitution and that the mix should sit for at least 2 hours.[56] In 2023, the package insert was changed to 8 mL sterile water and 1 mL of 2% lidocaine reconstitution for shallow to deep nasolabial fold contour deficiencies.

The authors (J.E. and M.L.) recommend injecting PLLA into deeper planes (i.e., supraperiosteal or deep subcutaneous fat) and avoiding superficial placement into dermal planes and facial muscles. Injections into the deep subcutaneous planes should be placed evenly with no more than 0.1 to 0.2 mL of product per thread of the needle. Treatment intervals 6 to 8 weeks apart, adequate reconstitution time (24–72 hours), higher reconstitution volumes (> 9 mL/vial), and vigilant posttreatment massage by the patient using the "5–5-5" rule (manual massage 5 minutes, 5 times a day, for 5 days) are highly recommended.

Radiesse/Calcium Hydroxylapatite

Radiesse (CaHA; Merz Pharmaceuticals GmbH, Frankfurt, Germany) is a nonhyaluronic acid filler that is biodegradable. It is composed of 30% CaHA in a 70% aqueous carboxymethylcellulose gel carrier.[65] CaHA is a mineral component of bone structures and, therefore, poses a low risk of being recognized as a foreign body by the immune system.[66] In 2006, Radiesse was FDA approved for HIV-associated facial lipoatrophy and facial soft tissue augmentation of moderate to severe nasolabial folds, and now has the indication for volume loss in the dorsum of the hands. Experienced injectors have shown excellent results with off-label applications, including the temples, cheeks, and mandible.[67,68]

The majority of nodule formation with CaHA has been with lip and perioral injections. Thus, lip injections have been mostly abandoned, and most injectors take caution when using this product in the perioral areas. In a 2015 review of 21 peer-reviewed articles published between 2004 and 2015, the highest adverse event with CaHA was nodules.[69] This review consisted of 5,081 treatments on 2,779 patients. Nodules ($n = 166$) represented 96% of all the 177 adverse events (3%). Of the reported nodules, 49% occurred in "dynamic areas" known for having a higher tendency to form nodules (lips 45%, perioral 4%). For this reason, the authors (J.E. and M.L.) do not recommend injection in dynamic regions of the face with CaHA.

Bellafill/Polymethylmethacrylate-Bovine Collagen

ArteFill (FDA approved in 2006), rebranded as Bellafill (Suneva Medical, San Diego, CA) in 2015, is a nonresorbable, long-lasting (5 years) polymer filler, composed of 20% PMMA microspheres (30–50 µm) that are smooth and round. It is suspended in an 80% bovine collagen solution, containing 3.5% bovine collagen, 2.7% phosphate buffer, 0.3% sodium chloride, 0.3% lidocaine hydrochloride, and 92.6% isotonic buffered water.[70] The bovine collagen carrier is absorbed after 1 to 3 months, allowing the PMMA microspheres to act as a scaffold for the patient's own connective tissue. In 2015, a 5-year safety and satisfaction study of PMMA for the correction of nasolabial folds was completed. As a required condition for approval in 2006, PMMA-collagen was tracked for the incidence of granuloma formation.[71] A total of 1,008 individuals were

enrolled, and 871 completed the full 5 years of the study. Granulomas were biopsy proven in 1.7% of the patients.[72] The granulomas were mostly treated with intralesional corticosteroids and none had surgical excision. By the end of the study, 0.9% of the patients had persistent granulomas, and were continuing treatment for them. With over 530,000 PMMA syringes distributed worldwide, postmarketing data from 2007 to 2016 on the safety of PMMA reported 11 confirmed granulomas (postmarketing data, excluding clinical trials), equating to a 0.002% incident report of granuloma formation.[71] It is hard to know if this represents the representation of granuloma formation as these reports are based on the clinician's willingness to report the adverse event.

Because Bellafill is made of bovine protein, skin testing is recommended prior to treatment. It is contraindicated in anyone who has a history of any allergies to bovine products or injectable collagen implants, those undergoing desensitization to meat products, or who have known sensitivity to keloid formation or hypertrophic scarring. It is contraindicated for the use of lip augmentation and injection into the vermilion or wet mucosa of the lip.[70]

11.4.5 Infections and Biofilms

Although uncommon, infections following filler injections can occur with *Staphylococcus*, *Streptococcus*, *Mycobacterium*, viruses, yeast, and polymicrobial species.[73] These usually present as inflammatory nodules or plaques, with or without abscess formation. Biofilms have been proposed as a cause of some delayed-onset inflammatory nodules, and should be ruled out along with atypical *Mycobacterium*.[74] Biofilms are composed of communities of bacteria that secrete a protective and adhesive matrix made of their own polymers and give rise to low-grade chronic infection that is resistant to antibiotics.[75,76] Prevention of infection is most useful, as identifying inflammatory lesions due to biofilms may be challenging and difficult to culture and treat.

Sterile technique should be of the highest priority when trying to minimize risks of infection when injecting fillers. Prior to injection, makeup should be completely removed, and injection sites should be sterilized with an antiseptic and re-sterilized if the patient touches the treatment area. There are numerous antiseptics on the market including, but not limited to, isopropyl alcohol, chlorhexidine, chloroxylenol, hexachlorophene, and hypochlorous acid. When applied to nonsterile gloves, chlorhexidine gluconate 0.4% has been shown to reduce potential exposures to infection.[77] It is also important to recall that with direct contact, chlorhexidine can cause corneal damage and ototoxicity, and should be used with caution when cleansing around the eyes and ears. Excess filler material from the needle tip should not be wiped off with nonsterile gauze.

11.5 Conclusion

Soft tissue fillers have quickly become one of the most popular and gratifying means for facial augmentation and rejuvenation. As such, it is critical for cosmetic providers to have the proper training and skills to reduce the risk of complications. A thorough understanding of facial anatomy, product characteristics, and injection techniques helps optimize results and reduce risk of complications. Also essential to safe practice and execution of these procedures is the ability to recognize adverse events and initiate the correct treatment algorithms in an appropriate manner. Proper patient selection and counseling will reduce unrealistic expectations by patients and result in more satisfying results.

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