

A PROTOCOL FOR FACIAL VOLUME RESTORATION WITH POLY-L-LACTIC ACID

Aimee L. Leonard MD, C. William Hanke MD

Laser and Skin Surgery Center of Indiana, Carmel, IN

Abstract

Poly-L-lactic acid is a biodegradable synthetic polymer used in an injectable form for subcutaneous volume restoration. Volumetric correction following subcutaneous and deep dermal injection of poly-L-lactic acid is thought to occur through a foreign body tissue response leading to increased production of fibroblasts and subsequent neocollagenesis. Despite the growing popularity and use of this material, there has been a scarcity of published information describing proper injection technique, and many practitioners remain unfamiliar with its use. Appropriate injection technique is critical since incorrect placement of the material can lead to long-lasting unintended results. We present a protocol for successful injection of poly-L-lactic acid into the submalar and buccal regions.

Introduction

Poly-L-lactic acid (PLLA) is a biodegradable, biocompatible synthetic polymer from the alpha-hydroxy-acid family derived from vegetable sources.^{1,2} An injectable form of this material has been available in Europe since 1999 for soft tissue augmentation and treatment of rhytides under the trade name New-Fill™. Injection of PLLA into the deep dermis and subcutis results in subcutaneous volume restoration, which is thought to occur through a foreign body tissue response resulting in increased fibroblasts and subsequent neocollagenesis. The efficacy of injectable PLLA for increasing mean skin thickness has been established in several studies.³⁻⁵ Since 1999, it has been estimated that over 150,000 patients have been treated with this material.⁶ In 2004, poly-L-lactic acid gained US FDA approval under the trade name Sculptra™ for the treatment of facial fat loss associated with human immunodeficiency virus (HIV) infection.

Although use of injectable PLLA is growing, there has been a scarcity of published information detailing proper injection technique, and many practitioners remain unfamiliar with its use. Appropriate injection technique is paramount as incorrect placement of the material can leave long-lasting unintended results. We present a protocol for successful injection of Sculptra into the cheeks and submalar regions.

Patient Selection

Patients most likely to derive a satisfactory response to treatment with injectable PLLA in the cheeks and submalar areas include those with marked hollowing of the buccal fat pads, as seen with HIV lipodystrophy, acquired and genetic lipodystrophies affecting the face, and those with pronounced loss of subcutaneous fat associated with the aging process (Figure 1). A proper evaluation includes visual and tactile assessment of facial volume, concavities, and tissue quality.

Although use of blood thinners is not a contraindication for injection with poly-L-lactic acid, patients who are anticoagulated are at greater risk of adverse events such as bruising, bleeding, and hematoma formation following injection. Use of PLLA should be avoided in anyone with active skin infection or inflammation in or near the treatment area, particularly in patients who are immunodeficient. Because the material is derived from a synthetic, nonanimal origin, no skin testing is required prior to use.

Material Packaging, Reconstitution, and Storage

Sculptra is supplied as a sterile, freeze-dried preparation composed of 24.5% sodium carboxymethylcellulose (an emulsifying agent), 34.7% nonpyrogenic mannitol (an agent which provides osmolarity), and 40.8% poly-L-lactic acid microparticles, contained in 2 glass vials.⁶ The microparticles range from 40 to 63 microns in diameter—small enough to allow passage through a 26-gauge needle, but large enough to avoid phagocytosis by dermal macrophages.

Figure 1. Candidate for poly-L-lactic acid injection demonstrating significant loss of subcutaneous volume.



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The manufacturer recommends reconstitution with 3 to 5 mL of sterile water. We prefer reconstitution with 3 mL of sterile water the night before the procedure. On the day of the procedure, an additional 2 mL of plain lidocaine is added for a total dilution of 5 mL. This upper limit of volume decreases needle blockages by reducing viscosity of the suspension and contributes to ease of injection.⁷ In addition, it has been suggested that a greater dilution decreases the risk of granuloma formation.^{8,9} If reconstitution occurs on the same day as treatment, vials should sit for at least 2 hours without shaking.⁶ Reconstitution for 24 hours may lead to more complete hydration of microparticles. The material is stored at room temperature prior to and following reconstitution. The freeze-dried product has a shelf-life of 2 years.⁶ Although the manufacturer states that reconstituted Sculptra should be discarded after 72 hours, a recent study demonstrated comparable efficacy in product reconstituted at 24 hours and 3 weeks prior to injection.¹⁰ No data exist regarding shelf-life of reconstituted PLLA greater than 3 weeks.

Prior to injection, the material is drawn into a 3-mL syringe with an 18-gauge needle, which is then changed to a 25-gauge needle prior to injection. Although the manufacturer recommends dermal injection with a standard 26-gauge needle, in our experience, a longer 25-gauge, 1.25-inch needle allows for treatment with fewer punctures. In addition, since the material has a tendency to settle out of suspension and clog the needle, the larger bore results in fewer blockages.

Pretreatment Planning

A pretreatment photograph as well as a photograph at each subsequent visit is critical in evaluating patient response. A consent form is reviewed with the patient, and informed consent is obtained. Prior to injection, the patient's cheeks are prepped with an antiseptic alcohol swab and the areas of concavity are outlined with a wax-based marking pencil (an eyeliner pencil works well for this purpose). When treating the cheeks, the outlined area is not extended above the inferior orbital rim. To avoid accentuation of the jowl region in some patients, the treatment area should not extend too far inferiorly. The patient is given a mirror to confirm agreement with the planned treatment area. Additional dots (typically 6-8 per side) are marked within the confines of the outlines to denote injection sites for anesthesia and PLLA (Figure 2). Several additional needles may be placed on the procedure tray to replace any blocked needles during the procedure.

Anesthesia

With the patient in the supine position, the areas to be treated are injected with 1% lidocaine with 1:100,000 epinephrine. One mL of lidocaine is injected into each designated site, marked by a dot, with 0.5 mL injected into the dermis and 0.5 mL injected into the subcutis for a total of approximately 6 to 8 mL per side. Local anesthesia in this manner results in constriction of small blood vessels leading to decreased risk of ecchymoses and bleeding. Sufficient anesthesia is demonstrable with blanching and swelling in the affected areas. Following injection of local anesthesia, there is mild distortion of facial topography. However, since the areas

to be filled have been outlined, accuracy of material placement is unaffected.

Anatomic Considerations

Injection into blood vessels can cause infarction or embolism, so care must be taken to insure accurate placement of the material at the correct layer of the skin. There are no major anatomical structures at the level of the upper subcutaneous fat in the submalar and buccal areas, so nerve damage or arterial injection is unlikely to occur. However, given that the subcutaneous fat layer can be markedly wasted in patients who are candidates for PLLA injection, knowledge of underlying anatomic structures is essential. The parotid duct is located in the lateral cheek region overlying the buccinator muscle and covered by the masseteric fascia. Muscles of facial expression in the mid-face region (levator labii superioris, zygomaticus minor and major, and the nasalis muscle) overlie and give coverage to the angular artery and vein. Nevertheless, it is prudent to draw back on the syringe prior to injecting near these anatomic structures, to minimize the risk of intravascular injection.

Technique

Prior to injection, the material is vigorously shaken to obtain a uniform translucent suspension. This should be done immediately prior to injection and at any point during the

Figure 2. Marked perimeter of treatment area and planned injection sites.



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procedure if the product appears to settle out of suspension. In our experience, the use of a laboratory vortex has been particularly useful. At the time of injection, the practitioner's non-dominant hand is used to stretch the skin, taking care to avoid the advancing needle (Figures 3 and 4). The suspension is injected into the outlined areas using several of the drawn dots as injection points. The needle is advanced in even, fan-like sweeps at the deep dermal-subcutaneous junction, and the material is injected as evenly as possible during needle withdrawal. Movements should be fluid and expeditious with constant motion until injection is complete to minimize needle blockage or uneven material dispersal. Although the manufacturer's package insert recommends injection of no more than 0.1 to 0.2 mL of material with each puncture,⁶ it is our preference to minimize the number of total injections by threading multiple tracks through one puncture with fanning dispersal of material in different directions (Figure 5). Of 6 to 8 marked anesthesia injection sites, only 3 to 4 are utilized for the injection of PLLA.

Figure 3. Incorrect hand placement for injection.



Figure 5. Poly-L-lactic acid injection technique with arrows depicting tunneling movements of needle.



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As injection of PLLA into the superficial dermis can result in formation of dermal nodules,^{9,11} injection should cease prior to pulling the needle upward from the dermal-subcutaneous junction into the mid to superficial dermis. Focal blanching and outpouching of the skin may be a marker for injection that is too superficial and should be followed by firm focal massage if observed. If the needle becomes blocked, it is withdrawn. The plunger can be pulled back to draw air in and then pushed forward. This introduction of air flow often results in unclogging the needle. If the needle remains plugged, it should be withdrawn and replaced, with strict attention to universal precautions.

Treatment volumes vary depending on the patient. In our experience, a patient with moderate to severe HIV lipoatrophy requires approximately one vial of Sculptra injected to each cheek per treatment session. A patient with minimal subcutaneous fat loss due to lipoatrophy of aging may only require one-half vial injected to each side. Injections should

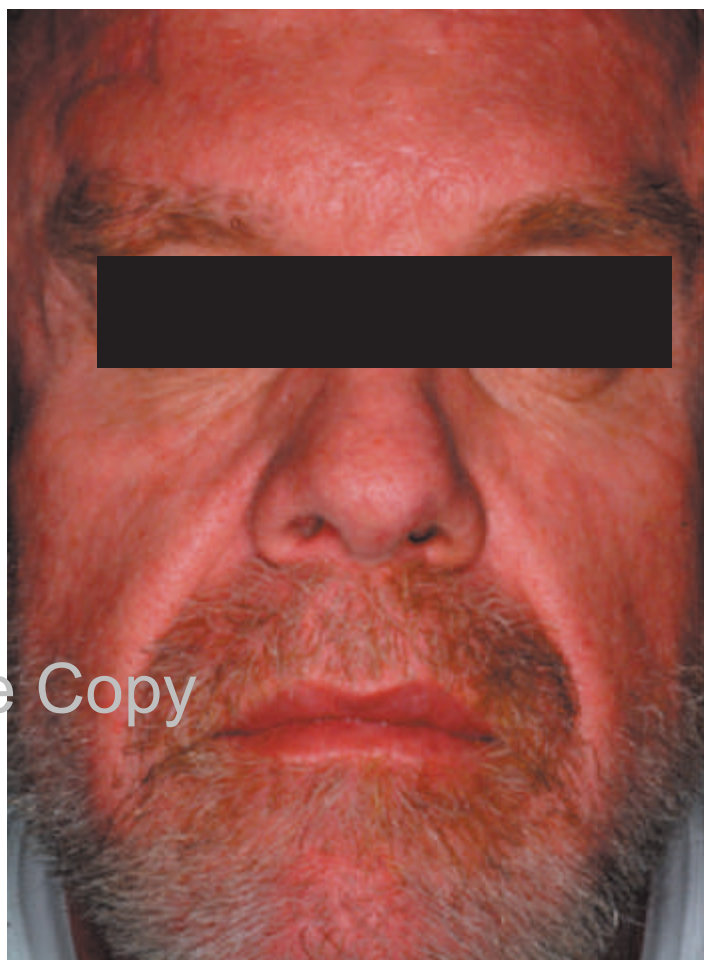
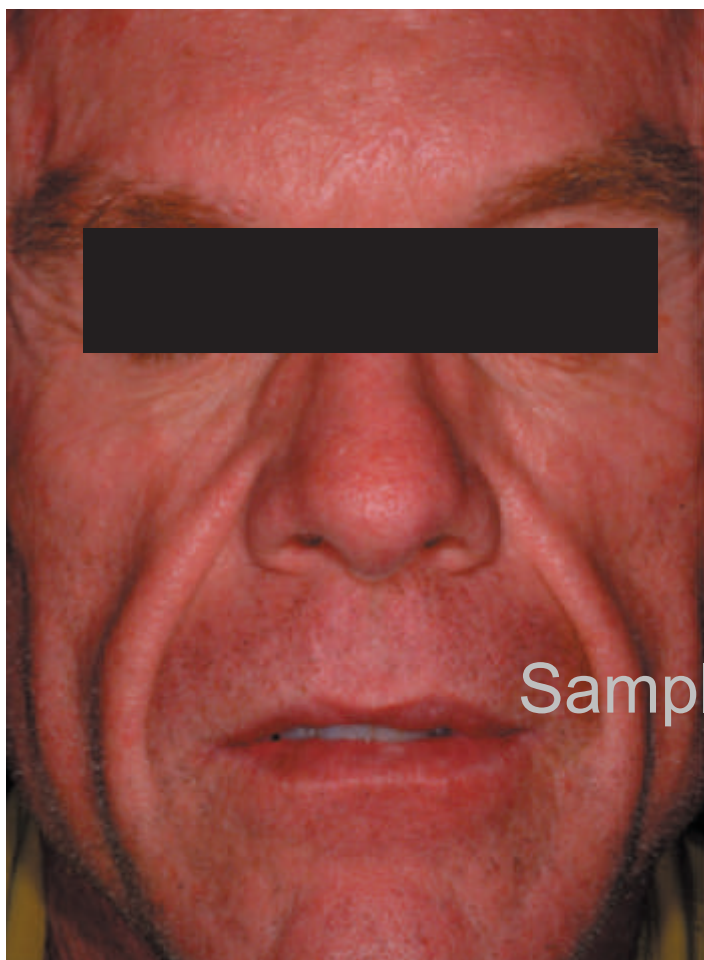
Figure 4. Correct hand placement for injection.



Figure 6. Post-injection sculpting massage.



Figures 7-8. Pretreatment and posttreatment with poly-L-lactic acid injections.



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be limited to a maximum of 2 total vials per treatment to avoid unintended overcorrection. Treatment intervals should be no sooner than 4 to 6 weeks to accurately determine the full response to prior treatments.

Posttreatment

One of the most important elements of injection with PLLA is the application of vigorous massage and manual sculpting to both cheeks to evenly distribute the material. We recommend that an assistant vigorously massage both cheeks simultaneously for 5 to 10 minutes to ensure a smooth and natural-appearing correction (Figure 6). Posttreatment instructions to patients include the application of ice packs to the injected areas for 15 minutes of every hour while awake over the next 12 to 24 hours to minimize the risk of bruising.

Patients should be counseled that the immediate posttreatment appearance is not lasting. Apparent correction is attributable to tissue edema and the mechanical volume effect of injected anesthesia and PLLA suspension. These transitory changes will dissipate within 3 or 4 days with return of the facial contour to baseline. However, these changes can provide the patient with a preview of the degree of correction

possible with continued treatment. Patients should be aware prior to initiating treatment that a series of injections will be necessary for stimulation of new collagen formation. Typically, 3 to 6 treatment sessions are required depending on the degree of severity, with a definite photographable difference occurring between the second and third treatments (Figures 7 and 8). Some patients may report a demonstrable difference after the first treatment.

Durability

Although the results seen with injectable PLLA are long lasting, the precise duration of volumetric correction is unknown. Gradual resorption is thought to occur over a 2- to 3-year period with eventual breakdown of the material to lactic acid, which is naturally found in the body.^{4,6} The protracted resorption of PLLA may be a result of its irregular crystalline structure and high molecular weight (140,000 daltons). Long-term efficacy data has not been published. Studies are currently underway to accurately determine the durability of treatment with poly-L-lactic acid over a 5-year period.

Complications

Tolerability of injectable PLLA has been well documented although the long-term safety beyond 2 years has not been investigated.^{3-5,8} No systemic complications from injection of PLLA have been reported in the literature.⁷ The most common treatment-related adverse effects are bruising, erythema, swelling, and hematoma occurring at the sites of injection. Pre-procedure screening for use of blood thinning medications and supplements and postprocedure application of icepacks can minimize these risks.

Asymmetry of volume can result when one vial is split between 2 sides and the product settles out of suspension prior to the procedure. This unintended effect is easily corrected with distribution favoring the undercorrected side at the next treatment and can be minimized with vigorous shaking of the vial(s) prior to drawing up into syringes. As results from treatment with PLLA injections are long lasting, overcorrection should be avoided.

Delayed occurrence of subcutaneous nodules in the sites of injection has been reported in treated patients.^{3,5} These papules tend to be asymptomatic and often visually imperceptible. The risk is likely technique-dependent and may be increased with superficial injection into the upper dermis.⁸ It should be emphasized that injection of this filler should only occur at the dermal-subcutaneous junction or subcutaneous fat, and not into the dermis. In addition, overcorrection, or differences in reconstitution are thought to increase the risk of dermal nodule formation.^{9,11} Vigorous post-procedure massage may reduce formation of nodules by optimizing distribution of the product. In a small pilot study, a decrease in the formation of subcutaneous nodules was observed when a deeper subcutaneous injection technique was utilized with an increased dilution of the material.¹¹ In a series of 100 immunocompetent patients treated with injectable PLLA, there were 12 cases of granuloma formation, 3 cases believed to be long-term allergic reaction, and 5 cases of infection.¹² These reports underscore the importance of proper technique in the injection of PLLA. Furthermore, they may suggest possible increased intrinsic reactivity to this material in some patients, particularly those with normal immune functioning.

Recently, a report of disfiguring linear granulomatous reactions developing at sites of tracked injections of PLLA in 3 immunocompetent patients was published.¹³ The granulomatous reactions developed over 12 months following treatment. Treatment of granulomas from injected foreign material is difficult, particularly when full resorption has not yet occurred. Therapeutic strategies that have been employed with variable results include surgical removal, intralesional corticosteroids, and imiquimod.¹³

As with any procedure involving puncture of the skin, infection is a risk, particularly in patients with compromised immune systems. With good aseptic technique, this risk remains low.

Finally, safety is paramount in dealing with elective injectable cosmetic procedures in patients infected with the human immunodeficiency virus to reduce the risk of needlestick injury. The practitioner injecting the material should be the only person working in the procedure field during injection. Care should be taken when changing and disposing of clogged needles, and strict attention should be given to universal precautions and disposal of biohazards.

Cost

Two vials of Sculptra, the typical dose required per treatment session, cost approximately \$980, not including the physician's injection fee. Full volumetric correction generally requires several treatments. The relatively high cost of Sculptra compared to other filling techniques, such as fat transfer, can be weighed against its extremely consistent results and high patient satisfaction.

A compassionate use program sponsored by Dermik Aesthetics, the Patient Access Program, has been instituted for qualified patients with the FDA-approved indication of HIV lipoatrophy. Eligibility is determined by income with those earning below \$80,000 qualifying for full or partial assistance. Under full assistance, the PLLA material is provided at no cost to the patient. The patient pays only an injection fee to the participating physician.

Integration into Practice

A busy practice may streamline procedures by designating and training a member of the clinical staff to be the PLLA "consultant." This person can act as a liaison for patients, ensure timely reconstitution of material, assist in pre- and post-procedure care, and coordinate patient participation in the compassion use program.

Summary

Poly-L-lactic acid is an effective treatment modality for the management of subcutaneous volume loss including that observed with HIV-associated facial lipoatrophy. Injection of PLLA at the dermal-subcutaneous junction or into the subcutaneous fat precipitates a host fibrotic response resulting in restoration of soft tissue volume. Results are long lasting and associated with high rates of patient satisfaction. Proper technique and patient selection are critical to achieving successful results and avoiding unintended complications.

Disclosure

Dr. Hanke is an investigator and Dr. Leonard is a co-investigator for a 5-year Sculptra clinical trial.

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ADDRESS FOR CORRESPONDENCE

C. William Hanke MD
Laser and Skin Surgery Center of Indiana
13450 N. Meridian Street, Suite 355
Carmel, IN 46032
Phone: 317-582-8484



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