Minimally invasive Procedures for Facial Rejuvenation

Edited by
Curinga Giuseppe
Rusciani Antonio

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Abstract

During the times several dermal fillers have been introduced in the market. Theoretically, the ideal soft-tissue filler substance for wrinkles and skin defects should be safe, biocompatible, stable after implantation, nonmigratory, resistant to phagocytosis, and pliable, and should persist and maintain its volume without being absorbed or degraded. It should induce minimal foreign body reaction, including granuloma formation; be nonteratogenic, noncarcinogenic, noninfectious, and nonallergenic; not require pretesting; painless, and inexpensive; and able to be stored at room temperature. Unlikely, this kind of filler still does not exist, however there are 2 products that are able to give a long lasting results, without the side effects, already known, of permanent fillers. In this chapter, use, mechanism of action, potential complications and the injection technique of Calcium Hydroxyapatite (CH) and Poly-L-Lactic Acid (PLLA) dermal filler’s are exposed.

Introduction

Beginning in the 1970s, dermal filler substances consisting of highly viscous fluids or polymer particle suspensions were injected beneath wrinkles and acne scars [1-3]. These substances are useful for the correction of congenital or traumatic facial, bony, and soft-tissue defects, etc.; and currently may be grouped according to the degree of degradability [4]. In general, fillers can be grouped as biodegradable and non-biodegradable (permanent) products. Biodegradable materials such as collagen, hyaluronic acid, hydroxyethyl methacrylate, dextran, and polylactic acid are removed by phagocytosis over a period of 3 to 24 months, depending on the amount and type of bulking agent implanted [5]. Permanent fillers such as paraffin, fluid silicone, Teflon, or silicone particles have an irregular surface that cannot be phagocytized and may eventually form foreign body granulomas because of the memory of macrophages and giant cells (so called frustrated macrophages) [6]. Particles and microspheres smaller than 15 micron are generally phagocytized and can be transported to local lymphnodes. Larger microspheres from non- resorbable polymers with a smooth surface are encapsulated with fibrous tissue and escape phagocytosis. Clinically, all injected fluids and particles have been shown to cause foreign body granuloma in a small percentage of patients [7-9]. Until the mechanism of granuloma formation is fully understood, the chance of its late development is not predictable. The ideal soft-tissue filler substance for wrinkles and skin defects should be safe,
biocompatible, stable after implantation, nonmigratory, resistant to phagocytosis, and pliable, and should persist and maintain its volume without being absorbed or degraded. It should induce minimal foreign body reaction, including granuloma formation; be nonteratogenic, noncarcinogenic, noninfectious, and nonallergenic; not require pretesting; painless, and inexpensive; and able to be stored at room temperature [10]. Although the ideal filler has not yet emerged, there is an ever-increasing body of data demonstrating the search for filler that meets these demanding criteria. The clinical persistence of an injectable material and its effect on facial volume restoration depends in part on the amount, depth, and shape of the implant. A thin strand applied beneath a constantly moving wrinkle is absorbed faster than a round depot in the skin of the forearm or a rat’s forehead. The carrier substance, whether fast or slowly resorbable, may play an important role on persistence as well. Host defense mechanisms react differently to the various filler materials, but all substances-resorbable or nonresorbable—appeared to be clinically and histologically safe, although all may exhibit undesirable rare clinical side effects [11]. Because the mechanism of late inflammation or granuloma formation is still unknown, early histologic findings are not useful in predicting possible late reactions to filler substances. These can only be verified in exact clinical long-term studies and in an independent centralized European and/or U.S. independent implant registry. Currently there are 2 fillers named as semi-permanent: one of calcium hydroxyapatite, and another of Poly-L-Lactic Acid.

**Calcium Hydroxyapatite**

Calcium Hydroxyapatite (CH), the main mineral component of bone and teeth, is a naturally occurring substance found in humans, making it compatible and contributing to its nonantigenic properties. Radiesse (Merz Aesthetics, Palo Alto, CA) is an injectable filler material composed of synthetic Calcium HydroxylApatite (CaHA) microspheres suspended in an aqueous carrier gel. Seventy percent of the composition of Radiesse is sodium carboxymethylcellulose carrier gel; the remaining 30 percent of the composition is CaHA microspheres. These uniform microspheres (25-45 microns) are identical in composition to the mineral portion of human bone and teeth [12-14]. It should be stored at room temperature (15°C to 32°C) and expires 2 years from the date of manufacture. The formulation allows 1:1 implant-to-tissue volume defect correction and minimizes the need for overcorrection. Results from extensive in vitro and in vivo safety studies, including toxicology assessments, standardized biocompatibility testing, and a three-year animal study, demonstrate that injectable CH is biocompatible, nontoxic, nonirritating, and nonantigenic [12]. Because CH contains no animal or human tissue derivatives, patient sensitivity testing is not required before use [15]. In the United States, injectable CaHA has been used for several years for correction of oral and maxillofacial defects, vocal fold augmentation, and as a radiographic tissue marker [16]. Treatment sites amenable to CH injection include the naso-labial folds, marionette lines, prejowl sulcus, zygoma and malar eminence, tear trough depressions, nose, chin, acne scars, and it is also FDA-approved for facial augmentation in HIV patients with facial lipoatrophy [17]. Lips augmentation with CH filler has been advocated by some authors, however the high percentage of nodules occurred in this site don’t make this filler suitable for this indication [18]. CH fillers provide immediate correction, and following injection, the gel carrier is absorbed over several months. The CH microspheres left behind from a scaffold for ingrowth of fibroblasts. New collagen fibers are formed, which anchor the microspheres in place and prevent the migration of the implant. The microspheres gradually dissolve and are broken down to its metabolites, calcium and phosphate ions, over a period of several months to years [19]. Usually less volume is required
with Radiesse to produce the desired correction as compared with hyaluronic acid fillers. The longevity of CH fillers seems to depend on several factors, including the site of injection, the injection technique, and the patient’s metabolism of the product; however the durability of the correction persist for 9 to 18 months and can last longer if deposited in areas of minimal facial mobility [17].

**Mechanism of Action**

After injection, the carrier gel is gradually absorbed, and the CaHA particles remain. A local fibrobroblastic response at the site results in collagen matrix encapsulation of the CH particles, similar to a grapevine growing through a garden trellis. The result is a highly biocompatible long-lasting implant with similar characteristics to adjacent tissue [19]. Thus, when CH is implanted in soft tissue, new soft tissue develops. No calcification or osteogenesis has been reported in the extensive literature describing the use of CH in a variety of soft tissue applications [20,21]. A study of dermal tissue biopsies after injection of Radiesse, light microscopy, and electron microscopy at one month postinjection revealed the presence of CH microspheres, with minimal or no inflammatory response or fibrosis. Histological and immunohistochemical analysis studies have shown a local histiocyctic and fibroblastic response resulting in new collagen production around the microspheres [19]. Primarily, type I collagen and a small amount of type III collagen were found within the infiltrating fibrovascular stroma, consistent with the process of remodeling. Electron microscopy studies demonstrated an increase in histiocytes and associated fibroblasts, which appear to anchor down the microspheres and encourage new collagen formation. The persistence of microspheres and new tissue formation observed was accompanied by evidence of clinical improvement at six months. From a safety perspective, it is important to note that there was no evidence of granuloma formation, ossification, or foreign body reactions at one or six months [17].

**Injection Technique**

Because of the relative viscosity of CH, a 27 or 28 gauge needles is recommended. It should be injected in a retrograde fashion using a linear, threading, fanning, and/or cross-hatching technique, depending on the area being treated. Injection volumes vary with the treatment site. Generally, a lesser volume of CH is required to provide the same degree of correction as hyaluronic acid.

CH should ordinarily be injected at the subdermal plane, especially when filling creases, wrinkles, and deep lines. Injection depth can be just in the subcutaneous space but superior to the periosteum. The injection can also be placed on the periosteum if the intent is to augment the facial bony skeleton. Placement on the periosteum will not stimulate bone growth in the area. Correction is approximately 1:1 and is apparent immediately upon injection. Overcorrection is not necessary, nor is there a need to build correction over multiple sessions. When injected, patients usually claim a bit of pain for a few, which can be reduced adding lidocaine to the filler before the injection. The injection can be made both with a needle or a micro-cannula, however more often, compared to other fillers, the needle can be occluded by CH, if this occurs, needle must be changed. At the end of the procedure, the injected area is quite hard to touch due to the product; this will be felt by the patient for about 3 days. Less oedema can be observed at the site of injections the day after, comparing to jaluronic acid filler. Immediately after injection, the site should be gently massaged and molded by the treating physician to help ensure a smoother implant. Patients can massage the injected area the first
days after the injection to quickly reduce the hardness of the product felt by the patient-self. Post-treatment care involves, as for the other fillers, application of ice over the injection areas to reduce and limit tissue edema and ecchymosis.

**Potential Complications**

CH filler enjoy an excellent safety, with adverse events reported typical of that observed with other short-acting fillers such as hyaluronic acid. The potential for serious adverse reactions with Radiesse appears to be low. There is no evidence of granuloma formation occurring with CaHA [17]. Although the presence of nodules visible through the skin has been reported, these nodules are technique related due to too superficial injection of CH or inappropriate use of CH. If such nodules occur, they can be easily reduced using aggressive massage techniques [17].

*Figure 1 & 2: Pre-op and post op of a patients treated for aging and zigomatic volume replacement with 1,5 mL of Radiesse.*
Poly-L-Lactid Acid (PLLA) Filler

Injectable PLLA is a new class of synthetic devices that provides a semipermanent option to correct facial volume loss. Filler based composed of PLLA is named Sculptra in the U.S.; Sculptra was approved with CE Mark certification under the trade name New-Fill in Europe. The stimulatory action of PLLA is one of the main characteristics that differentiate it from other fillers. Most other filler, such as hyaluronic acid, have a passive and direct effect on enhancing volume. Their augmentation is limited to the persistence of the filler material and, once degraded, further injection is required. Likewise, the augmentation effects of PLLA typically require multiple injections and are delayed in nature. But the new collagen deposition yields results that last long after the injected material is absorbed [22]. Sculptra obtained US Food and Drug Administration approval in 2004 for use as soft-tissue filler into lipoatrophy of cheeks and temples of human immunodeficiency virus patients who are under highly active antiretroviral therapy [22,23]. Polylactic acids do not occur naturally, but were synthesized by French chemists in 1954. Polylactic acid and polyglycolic acid have been used safely in suture materials (Vicryl, Ethicon, Inc., Piscataway, NJ); in resorbable plates and screws; in guided bone regeneration; in orthopedic, neurologic, and craniofacial surgery; and as drug delivery devices [22]. Sculptra is composed of microparticles of PLLA, a biocompatible, biodegradable, and synthetic polymer from the alpha-hydroxy-acid family. The final composition of Sculptra consists of 150 mg of PLLA, 90 mg of sodium carmellose, and 127.5 mg of apyrogenic mannitol in the freeze-dried form. The PLLA particles provide the durable attributes of sculptra treatment. Raw material is milled, sieved, and sterilized before manufacture. PLLA microparticles are irregular in shape and have an average particle diameter of 40-63 micron. Polylactic acid is synthesized by esterification and polymerization of lactide monomers where the material is immunologically inert [24]. The amorphous crystalline structure and high molecular weight (>100,000 Da) of the product are responsible for the slow absorption when injected into the tissue. Once injected, 75 percent of the PLLA is broken down into CO2 and H2O. No allergy testing is required before use since PLLA is a synthetic material of nonanimal origin [22].
Mechanism of Action

The mechanism of action of PLLA is based on its ability to stimulate fibroblast proliferation and neocollagenogenesis. However, his mechanism of action by which PLLA corrects facial volume deficiencies is not comprehensively understood. It is postulated that this is due to a foreign body reaction to the injected material, which stimulates a cellular inflammatory response. The resultant formation of a vascularized, connective tissue capsule ensues, which is eventually composed of fibroblasts and new collagen deposits. The breakdown of PLLA occurs by hydrolysis into lactate, which is eventually converted to pyruvate, and oxidized into carbon dioxide for release [22,24].

Several histological studies of PLLA injections in mice reported a pronounced tissue response. Investigators observed polylactides surrounded by vascularized connective tissue capsules, consisting of connective tissue cells with mononuclear macrophages, lymphocytes, foreign body cells, and mast cells after one month of implantation. Over time, the capsule surrounding the implants decreased in cell number, whereas thickness and collagen fibers increased. In general, PLLA was well tolerated by the tissue and no acute inflammation, abscess formation, or tissue necrosis was observed adjacent to the injection sites [25]. Sculptra induces an immediate, local reaction that is followed by a progressive increase in volume. Within a few days, water absorption and the reduction of edema will result in a return to the baseline depression. Within several weeks of the injection, a natural, soft increase in dermal thickness due to neocollagenogenesis will begin to take shape.

Reconstitution and Injection Technique

PLLA filler, before its use, must be reconstituted with sterile, bacteriostatic injectable water (5 to 8 mL; the more water is used, the less possibility of papules or nodules you have); sufficient time to reconstitution is paramount, usually 24/48 hours. Inadequate mixing of PLLA with water leads to inadvertent injections of clumps of dry micro-particles, increasing the risk of nodule formation when they hydrate in vivo.

For uniform hydration, do not agitate but allow the powder cake to absorb the sterile H2O slowly overnight. When the water is added, it will take about five minutes for the powder to dissolve. The mixture is then kept overnight for complete hydration. The now reconstituted product is stored at room temperature to achieve proper viscosity for injection. It is fine to swirl, agitate, or shake hard after hydration overnight. The vial is thoroughly agitated before use. It is optional to add 1 mL of 1 percent lidocaine or lidocaine with epinephrine immediately before injection, making it slowly drip through an 18-gauge needle. When added too quickly, lidocaine can precipitate the hydrogel suspension, leading to difficulty, such as clogging, while injecting. The suspension of PLLA is injected with a 1-cc Luer-lock syringe with a 25-gauge needle to provide less clogging, more clogging results with the use of a 26-gauge needle. It is important for the injector to assess the viscosity of the suspension before insertion of the needle into the skin to deliver the product. Injection of the material is performed while slowly withdrawing the needle. Most importantly, injection of product must be stopped before withdrawal of the needle so that no product is injected superficially. This will decrease the risk of papule formation. PLLA is injected in the deep dermis and subcutaneous junction in one of several injection techniques (linear, threading, fanning, depot and/or cross-hatching). A depot or small bolus injection can be used in the areas of the upper zygoma or temples. Massage of the product is performed at intervals during injection. No overcorrection is required. Final
outcomes with PLLA are delayed and require multiple sessions, spaced every 4 to 6 weeks apart, to allow adequate time for augmentation and avoid overcorrection. The principle should be one of serial application to achieve augmentation goals. Patients should be counseled on the length of the process and goals with each subsequent application. In addition it should be noted that areas treated with PLLA are likely to decrease in volume within the first 24 to 48 hours as the body reabsorb the sterile, bacteriostatic injectable water within the solution. Smooth massage will distribute the Sculptra evenly. Periodic massaging during all treatment sessions may help evenly distribute the product and reduce the risk for papule formation.

**Potential Complications**

Overall, device-related adverse reactions are rare, and those that do occur do so as a result of incorrect reconstitution, poor injection technique, overcorrection, and deficient injection technique [25,26]. Thus, it is essential that the injecting physician follow the proper guidelines laid out in the product information provided with each vial of PLLA to avoid these adverse events. It is important enough to repeat that the injector not overcorrect as is sometimes done with other injectable fillers [25]. The results from PLLA are gradual and progressive and must be tracked over time. Failure to follow these techniques and guidelines may result in SPs, which form from improper dilution of PLLA and improper injection technique [26]. These injection-related papules may be prevented with proper dilution, a properly mixed suspension, proper injection depth, and vigorous massage. If papules or nodules form and the patient is distressed, it may be necessary to consider treatment of excision of papules. It should be noted that although these bumps can be palpable to the patients, they are often invisible and nonpathological. A bump resulting from a foreign body reaction will respond to a dilute triamcinolone injection. A bump resulting from clumping of PLLA may require subcision (breaking up) of nodule with an 18-gauge needle followed by injection of sterile water to dilute the PLLA and massage or surgical excision. Granulomas have been noted in the past as with all fillers. Late-onset granulomas may be surgical excision. Granulomas have been noted in the past as with all fillers. Late-onset granulomas may be treated with triamcinolone, fluorouracil, or methylprednisolone. Systemic therapy with low-dose prednisolone, doxycycline, or tetracycline has also been reported [27]. Additionally, injections into infected or inflamed skin are to be avoided. Patients who are allergic to any ingredients in PLLA should not be treated with the product [25].

A patient affected by facial lipoatrophy HIV-related treated with poly-l-lactic acid. First picture on the left is the pre-op; the one in the middle is the result after one filling sit, once that the saline solution used to restore the poly-l-lactic acid is resorbed; on the right the result after six filling sessions.
Figure 5-7: Final outcomes with PLLA are delayed and require multiple sessions, spaced every 4 to 6 weeks apart, to allow adequate time for augmentation and avoid overcorrection. The principle should be one of serial application to achieve augmentation goals. Patients should be counseled on the length of the process and goals with each subsequent application. In addition it should be noted that areas treated with PLLA are likely to decrease in volume within the first 24 to 48 hours as the body reabsorb the sterile, bacteriostatic injectable water within the solution.

References


