Radiesse: Advanced Techniques and Applications for a Unique and Versatile Implant

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Background: Radiesse is a well-tolerated facial injectable with unique filling and lifting capabilities. Although initially approved for facial volumizing in HIV-related lipodystrophy patients, it quickly gained wide acceptance for aesthetic facial rejuvenation. In the USA, the Food and Drug Administration has approved several new indications for its use. This synopsis presents the experience and injection techniques currently favored by the primary author after many years of use in thousands of patients.
Methods: The anecdotal practice of an experienced injector is presented along with the current Food and Drug Administration–approved standards of Radiesse injection.
Results: Radiesse has many on- and off-label applications that can be thoughtfully incorporated into clinical practice. Its unique chemical composition allows for immediate lifting and filling with long-term collagen stimulation. The product can be reconstituted to increase its versatility and minimize adverse events. Injections can be performed in the supraperiosteal space and the subcutaneous layer and are best administered in small, calculated doses to prevent nodules or vascular occlusion. Various techniques for Radiesse injection in specific areas are discussed in detail.
Conclusions: Radiesse is a versatile injectable implant and a valuable tool for short- and long-term cosmetic and reconstructive treatments. In addition to various off-label uses, this injectable is often used in conjunction with botox, other injectables, collagen stimulators and tightening devices. A customized reconstitution of product increases its versatility for natural appearing and long lasting results that are both economical and effective for full facial rejuvenation. (*Plast. Reconstr. Surg.* 136: 164S, 2015.)

Radiesse, first launched in the United States as Radiance, is a long-lasting synthetic injectable implant. Although first approved for its reconstructive and surgical applications, it has gained popularity with facial rejuvenation because of its elasticity, longevity, excellent biocompatibility, and low incidence of allergenicity.[1] As the first volumizing filler, it was originally approved for treatment of HIV-related facial lipodystrophy.[2] Much of our understanding and early knowledge of nonsurgical reshaping and lifting was learned in this patient cohort.

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The original Food and Drug Administration (FDA) studies for aesthetic approval looked at correction of the nasolabial fold by direct injection of Radiesse and graded improvement based on a global standardized aesthetic scale.[3,4] It was only in subsequent years that studies of the aging face began to unveil the remarkable and complex changes of the bone, fat compartments and other anatomic markers. The advent of newly available volumizing agents supplanted fat injection, allowed for a more nuanced approach to facial rejuvenation that helped move us away from only filling folds or cutting and lifting soft tissue and skin for natural appearing and long-lasting results that are both effective for full face rejuvenation.[5–7]

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RADIESSE

Radiesse is an admixture of calcium hydroxylapatite microspheres suspended in a gel structure that is composed of sterile water, glycerin, and carboxymethylcellulose. This unique chemical composition initially allows for direct filling and lifting due to its cohesive, space occupying properties. The product is considered a semipermanent tool in facial rejuvenation because as the carboxymethylcellulose is resorbed, it creates a foreign body reaction that stimulates elastin and type 1 collagen replacement in the injected soft tissue to maintain long-term correction.[8–11] Although the gel carrier is absorbed during the first few weeks, the subsequent secondary biostimulatory tissue swelling creates a net neutral filling effect.

Radiesse's characteristically high G-prime, a measure of elasticity, makes it suitable for lifting soft tissue and contouring.[12] Its high density, viscosity, and cohesiveness make it an ideal agent for deep supraperiosteal injections along the malar eminence and zygomatic arch to replenish bone resorption in an aged face. These properties also make it an excellent filler to replenish fat loss in the deep fat compartments of the midface or submental area. These same qualities require that it be used with caution and in small amounts, generally with retrograde injection technique of 0.1-cc aliquots, when injected into deep dermis or the subcutaneous plane, in patients with thin skin, or in locations such as the temples and periorbital region where the benefits of collagen stimulation and activation of fibroblasts are felt to outweigh the possibility of a nodule.

Unlike with hyaluronic acid fillers, which can be quickly dissolved with hyaluronidase when needed to treat a nodule, overcorrection, or other adverse event, there is no "reversing agent" for Radiesse. Smaller nodules that are generally nonvisible respond well to conservative treatment with digital massage. Large nodules, which are rare in experienced hands, can be treated by breaking up the overaccumulation of product with an injection of normal saline and lidocaine. Up to 0.3 cc of 5-fluorouracil can be mixed with an equal amount of lidocaine or lidocaine with epinephrine and injected directly into the nodule to reduce fibroblastic activity in these sites while breaking up the nodule. This technique mechanically disrupts the nodule and prevents further volume creation by inhibiting its biostimulatory properties. Injection of steroid into these noninflammatory nodules has been largely abandoned due to its potential for permanent skin thinning and depigmentation, which may result in a potentially more visible contour problem for the patient. Finally, the most rare but feared adverse event with injectable fillers is arterial vascular occlusion, leading to tissue necrosis or blindness. Although exceedingly rare with all products, this complication becomes a larger treatment challenge without the ability to immediately dissolve the implanted product. For occlusion, the same protocols are advised as with other agents (including the use of hyaluronidase) to release the occlusion.

Another important consideration in the "real world" is the cost of the treatment. Radiesse is an ideal agent for pan-facial volumization because it is available in a large 1.5-cc syringe with a base cost that is competitive with products distributed in smaller volumes per syringe. When one looks at the ideal full correction achieved in FDA trials, multiple syringes are required for panfacial treatment compared with the amount required in nasolabial fold correction. There are various ways to address this issue in patients who are financial unable to achieve the "full" or ideal correction. A provider could choose to treat a single area to full correction to the neglect of other areas, which would result in an odd or unbalanced appearance. Alternatively, the provider could undertreat the entire face, which would result in a dissatisfied patient. Radiesse often allows for more complete facial volumization for patients whom caost is an issue. In addition, by adding 0.4, 0.6 or 0.8 cc of lidocaine to customize the Radiesse syringes (to the needs of the patient), they benefit from the collaborative efforts of immediate space occupying correction with long-term collagen stimulatory properties of the product.

ALTERNATE VOLUMIZERS

In addition to Radiesse, we now have other volumizing fillers, each with distinct properties, to formulate an optimal treatment plan for each patient. Properties that differentiate these products and their usage in the clinical setting include particle size and shape, cohesiveness and the degree of cross-linking, G-prime, flow characteristics, varying thickness, and the ability to lift rather than spread.[13]

Injectable grade silicone, approved in the United States for intraocular injection during retinal detachment repair, was historically used off-label to create volume in the area of injection by a similar biostimulatory process. Nonpermanent hyaluronic acid fillers are the most widely used and marketed for facial implantation. Finally, L-polylactic acid (Sculptra) is a unique injectable that also has a biostimulatory mode of action. This treatment is FDA approved for both aesthetic treatments and HIV-associated facial lipodystrophy as

is Radiesse and both companies offer compassionate-use pricing for eligible patients.

PREPARATION

Historically, when "dermal fillers" such as collagen and then Restylane were injected into the dermis, topical anesthetic was applied prior to injection. Nerve blocks were used for especially sensitive areas, such as the lips. When injecting Radiesse during the HIV lipodystrophy trial, it became obvious that the injections couldn't anesthetize the entire face, were, uncomfortable for the patient, and there was also lasting discomfort for more than 30 minutes post treatment. Despite discomfort, these young disfigured patients were very motivated to correct what exposed their illness.

With advances in knowledge of facial aging and the use of products for off-label aesthetic corrections, experienced injectors have found that supraperiosteal injections created a more physiologic correction that resulted in a more natural appearance. Subsequently, Lidocaine was also added to the product via a sterile connector for more comfortable injections without the need for nerve blocks. Subsequent studies established that the slightly reduced viscosity allowed for use of a 27-gauge 1¼-inch needle (rather than a 25-gauge needle) without diminishing the aesthetic result or longevity of the product. Although this connector is now "on-label" and provided with the product, some advanced injectors will add more lidocaine or normal saline to lower the G-prime when needed to allow the product to be used in areas such as the temples, the hands, periorbital area, and dermis. With this diluted formulation, small 0.1-cc aliquots can now be injected in a layered fashion subdermally or in the deep dermis to add volume by skin thickening, improving tone, texture, and reducing rhytids.

Both needles and cannulas can be used in the injection of Radiesse. Although there are no controlled studies comparing needles and cannulas, one may claim that the blunt tip of cannulas prevents trauma to the tissue. However, if an artery is entered, the cannula with a larger diameter potentially could inject larger volumes of product with more devastating complications. Needles are a popular choice because of the ease of treating various tissue compartments through the same puncture site.

TECHNIQUE

In-depth knowledge regarding facial anatomy is imperative to safely achieving an optimal aesthetic outcome. Facial asymmetry at varying degrees is the norm and needs to be recognized, documented, and communicated with the patient as is facial balance and harmony. Digital photography and assessment of facial photographs with the patient should be performed during each session to highlight subtle changes and clarify the goals of each treatment session. Symmetry can be achieved between the 2 sides of the face by injecting varying amounts in different locations and the patients' gender, ethnicity, age and degree of skin laxity and sun damage all play a role in setting expectations and establishing a long term treatment plan.

Injections in the subdermal or supraperiosteal plane with volumes kept below 0.2 cc under low pressure and always injected in a retrograde fashion significantly minimizes any risk of arterial occlusion should an artery be pierced. The infraorbital foramen is palpated and identified prior to tear trough injections. If a patient complains of increased or radiating pain, the needle should be immediately repositioned.

There have been studies looking at the technique of midface, chin, and cheek volumization through an intraoral approach. Although this technique has the advantage of less bruising due to implant placement directly over the periosteum instead of through muscle, the theoretical increased risk of late onset biofilm infection and the inability to fully sterilize the injection points in the mucosa have greatly reduced this, otherwise well accepted, technique by many injectors. Pretreatment with hydrogen peroxide is one option when using this technique.

Advanced injectors treat structural deficits with deep volumetric correction in small aliquots using a retrograde fanning or linear threading technique. This is followed by a customized lower G-prime product injected with the same 27-gauge needle in the subdermal plane or in areas such as temples where more spread and less lift is desired.

Lidocaine 2% with epinephrine 1:100,000 can be used during product reconstitution if an injector's technique involves injecting segmentally in the face from side-to-side and returning to the previous area of injection for refinement. Studies that look at the effectiveness of adding lidocaine with epinephrine to fillers with varying techniques are still lacking. However, anecdotally, less bruising and discomfort are noted in areas well anesthetized by previous product injection as this author's technique involves partial treatment of one side of the face and then returning to refine the correction after treating the contralateral face.

A combination of injectable products can be used in a staged fashion to evaluate the patients'

physical and mental response to treatment and minimize soft-tissue swelling and the short-term appearance of overcorrection. Gradual improvements over several treatment sessions are believed to result in better tissue integration, collagen stimulation, and longer-lasting results.

Patients are advised that although the product has been shown to last histologically in the body for years, this duration varies based on the targeted location of injections.[14] Furthermore, the longevity of the product is different from the duration of correction. In managing the patient's expectation, treatment every 6–12 months of a small volume is generally recommended, depending on the patients' goals, metabolism of the product, and lifestyle.

What follows is a brief outline of general principles of Radiesse use in commonly injected facial regions.

PERIORBITAL REJUVENATION

Loss of volume in the periorbital region due to a combination of bone remodeling, deep fat pad, and subcutaneous fat loss can result in the appearance of "bags" and "dark circles" due to exposed contours of underlying structures. The use of injectable fillers in this region can produce natural and long-lasting results in patients where the underlying pathophysiology lends itself to volumetric correction.[15] Experienced injectors often use Radiesse in this area in a more dilute reconstitution. Due to the complex anatomy of the region, careful slow injections in the deep supraperiosteal plane are advised. Inexperienced injectors are recommended to choose more forgiving reversible hyaluronic acid–based products in this region.

Temples/Lateral Brow

As with many other aesthetic procedures, there are different approaches with the goal of achieving similar results. A layered approach with deep supraperiosteal injections can be useful for correcting large volumetric deficiencies, while subtler contour and skin changes can be targeted with injections in the subcutaneous plane. Neurotoxin is often used during the same or in prior treatment sessions to contour the brows. Hyaluronic acid products can be used in a more superficial plane or other segments of the face, such as subgaleal injections, to improve the forehead contour and support the brows when there is bony contour deficiency. Radiesse can be injected with a thinner reconstitution of 0.9 cc of 2% lidocaine with epinephrine, up to and beyond the hair line to lift the lateral brow and lateral canthus if descent is felt to be secondary to volume loss and soft-tissue laxity.

Zygomatic Arch/Cheek

Age-related descent of the cheek associated with aging or lipodystrophy can create a visible defect at the lid and cheek junction as a prominent tear trough and accentuate the nasolabial fold. Radiesse injections can restore volume to

Fig. 1. A 55-year-old woman with periorbital volume loss and shadowing from the resultant contour causing prominent skin discoloration. Patient also has lower face soft-tissue and bony loss and a hyperactive mentalis.

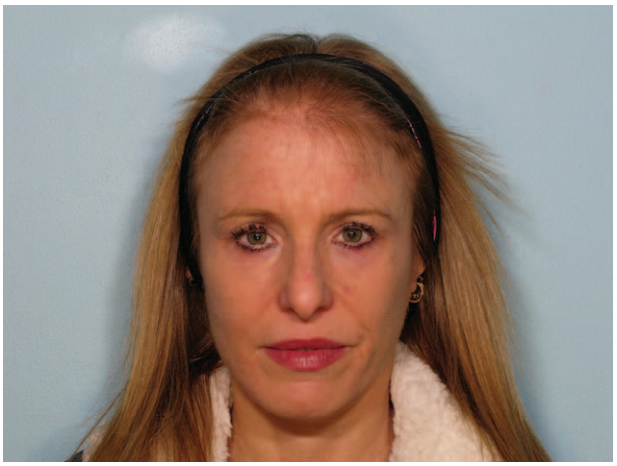

Fig. 2. After treatment, the patient had improved overall facial symmetry and increased midface and lower face volumization 6 months after 2 treatments with 2 Radiesse syringes in each session (6 cc), with emphasis placed on volumization of the periorbital region to reduce the appearance of "bags" and "dark circles." Each syringe was reconstituted with 0.9 cc of 2% lidocaine with epinephrine 1:100,000. The patient also received Botox to the chin. Further possible nonsurgical treatments include Botox or filler to the superolateral aspect of the brow to create a lateral brow lift and improve facial contour.

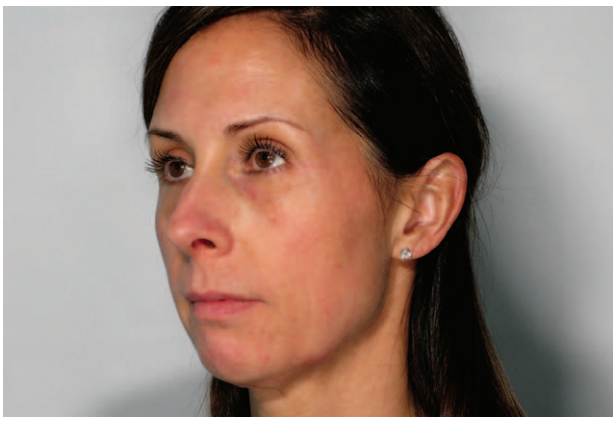

Fig. 3. Pretreatment view of a 47-year-old woman with weak architecture of the chin and jawline area that creates unbalanced facial proportions.

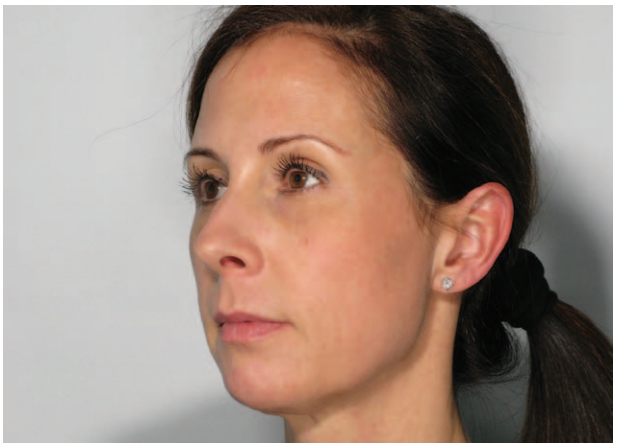

Fig. 4. After treatment, the patient had improved lower face and chin contouring 1 month after injection of 5 Radiesse syringes (7.5 cc), with each syringe reconstituted with 0.9 cc of 2% lidocaine with epinephrine 1:100,000. Radiesse was first administered to the supraperiosteal region and then to the subcutaneous tissue. Botox was also administered to the depressor anguli oris and the mentalis. Future correction should be performed in a staged fashion to improve the longevity of the jawline volume.

this region, minimizing tear trough deformity and a deep nasolabial fold. Volumetric or structural contouring is performed first to lift and shape the area of correction. Improvement of nasolabial folds or marionette lines is usually left for the end of the session to refine the final appearance with an injection in the deep dermal or subdermal plane. Care is taken to identify and avoid the neuromuscular bundles hen product is injected in a retrograde fashion (Figs. 1 and 2).

Lower Face Rejuvenation

After treatment of the upper face, attention should then be directed at the lower facial structures and jowling. Radiesse is currently the only FDA-approved filler with a jawline indication. Radiesse is a preferred injection for the jawline because it can define and correct volume through periosteal and subcutaneous injections. Revolumization of the chin can be accomplished in a layered fashion with deeper volume restoring injections in the supraperiosteal plane using the slow retrograde linear threading technique with care to avoid the neurovascular structures in this sensitive region. The parotid gland and vasculature prevent deep implantation in this area by most injectors.

Depending on the patient's skin quality and amount of correction necessary, the product can be customized with 0.3 cc or more for a full correction. After volume of the chin is corrected, the rest of the jaw line is defined in a subcutaneous fashion. Gender considerations and the underlying facial architecture are essential for Jawline improvement. In general, women require smaller amounts of product in this region, whereas the male jaw aesthetically favors larger volume injections (Figs. 3 and 4).

Other Commonly Injected Areas

Although treatment of the nose, glabella, horizontal forehead lines, and crow's-feet are commonly performed with fillers, extra caution is advised when using Radiesse in these areas due to its high viscosity and the challenging nature of treating adverse events, such as nodules or vascular occlusion. Diluted small aliquots and meticulous, slow retrograde injection technique must be used for these areas if Radiesse is used in other regions of the face. If these areas are targeted in isolation, a hyaluronic acid substitute would be the preferred first-line injection.

Neck rejuvenation can be performed in selected patients with narrow, thin necks and skin laxity with 1.5 cc of Radiesse reconstituted with 2 cc of normal saline and 0.3 cc of 2% lidocaine in a fanning technique. The effect can be augmented by soft-tissue tightening treatment such as Ulthera or ThermiSmooth 250. Further studies are needed to evaluate the synergistic effect of combination therapy and the dilution of Radiesse beyond the current FDA recommendation, which limits dilution to less than 2.5 cc of lidocaine or normal saline.

Radiesse has been shown to be unpredictable for lip filling or contouring and is considered to be contraindicated for use in this region[16,17] (Figs. 5 and 6).

Fig. 5. A 50-year-old woman presented for facial rejuvenation. She had pan-facial volume loss with good underlying bone structure and skin representing predominant soft-tissue loss.

Fig. 6. After treatment, the patient had improved periorbital, midface, and lower face volume 1 month after injection with 2 Radiesse syringes (3 cc). Each syringe was reconstituted with 0.6 cc of 2% lidocaine with epinephrine 1:100,000. Additional future treatments could include Restylane injection to the upper lid and nonsurgical brow lift with Radiesse or Botox.

Hands

Although hand rejuvenation has just now been approved with the standard FDA-reconstituted product, many injectors have an extensive experience using a less viscous admixture with good patient satisfaction and minimal adverse events. An ideal candidate may include an individual with loss of volume in the subcutaneous dorsum of the hand with prominent veins and tendons. This author uses a 1.5 cc of Radiesse is mixed with 1.0 cc of 2% lidocaine with epinepherine. The skin on the dorsum of the hand is pinched for ease of injection into the immediate subcutaneous plane. Injections are performed in a linear threading fashion of up to 0.4 cc with massage to the site after each injection. Injections are strategically placed in the deepest troughs to smoothen the transitions between tendons and veins. This author limits treatment to 1.5 cc syringes per hand and prefers to repeat the treatment 2-4 weeks later to achieve full correction if needed. Intense pulsed light (IPL) or V-beam (Vascular) laser are excellent adjunctive treatment.

HIV-RELATED LIPODYSTROPHY

Treatment of this condition is different from aesthetic facial rejuvenation because these, often young, patients have significant volume loss without the bony, structural changes of their older counterparts. Less attention is needed to correct deep volumetric changes attributed to bone remodeling and deep fat pad atrophy. Moreover, there is often an intact dermal "envelope" within which to fill. A less viscous reconstitution can be used for the superficial subdermal injections required in the midface. A severely fat depleted patient would be treated over 2 or more sessions to allow collagen stimulation to contribute to a more natural appearing result. Just 6–9 cc of total product is not unusual to sufficiently achieve full correction in a patient with grade 4 lipodystrophy over a 3- to 6-month period. Maintenance with 1–2 additional vials is generally necessary at 3- to 6-month intervals to maintain this full correction.

POSTENUCLEATION/EVISCERATION SOCKET SYNDROME

Postoperative volume insufficiency is a common issue after enucleation or evisceration of an eye with intraoperative placement of an orbital implant and subsequent fabrication of an ocular prosthesis. This can lead to enophthalmos, a deep superior sulcus, blepharoptosis, and lower lid laxity. Enlarging the prosthesis and altering its shape can often mitigate some of these problems; however, the increased weight of the prosthesis can lead to excess lower lid laxity, ectropion, and poor overall fit of the prosthetic device. Surgical options for augmentation of orbital volume include implant exchange, autologous tissue placement, or tissue expanders. Each of these procedures carries the potential risk of anesthesia and operative complications.

As a nonsurgical, off-label option for orbital augmentation, Radiesse has been used with good results and minimal adverse events and other fillers are being similarly used for such indications.[18] The product is mixed with 0.2 cc of 2% lidocaine, with or without epinephrine, and delivered via 27-gauge needle in a bolus retrobulbar injection technique along the orbital floor in an extraconal, preperiosteal position. It is critical to pass the needle posterior to the orbital implant before injection to create an anterior displacement of the implant. If needed, balancing injections can also be made along the lateral and/or medial orbital walls, again in the extraconal preperiosteal position. Immediate reduction in enophthalmos and sulcus deformity is usually seen, and the amount of injected filler can be titrated to reach the desired symmetry.

Complications of anophthalmic injection of Radiesse may include hemorrhage, orbital pain/discomfort, and anterior migration of the calcium hydroxylapatite into the lower lid. Migration of injected product may be due to prior postsurgical scarring leading to tracks for injected material through anterior paths of less resistance. Eyelid massage or nodule injection can often lead to resolution, although surgical removal of the displaced product also remains an option.

CONCLUSIONS

Radiesse is a useful and versatile tool for facial rejuvenation due to its high G-prime, robust filling, and lifting capabilities. Although there are now more and more FDA-approved applications, there remain are many effective off-label uses for Radiesse. The collagen-stimulating properties of Radiesse allow for potential long-term benefits that could be coupled with other injectables and minimally invasive skin and soft-tissue tightening devices. Optimal treatment is often achieved by considering each product and device as a unique tool to be used toward the creation of a desired result. The combination of treatments with fillers, toxins, and devices is the norm, rather than single-product treatment for most patients. Further studies are required to truly determine the synergistic value or potential negative effects of using these products in combination with tissue tightening devices (i.e. Ulthera, Thermage, ThermiTight, etc).

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PATIENT CONSENT

Patients provided written consent for the use of their images.

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