

Advances in Nonsurgical Periocular Rejuvenation



Jeffrey Desmond Markey, MD^{a,*}, William Matthew White, MD^b

KEYWORDS

- Tear trough • Periocular • Hyaluronic acid • Platelet-rich plasma • Calcium hydroxyapatite
- Poly-L-lactic acid • Injectable

KEY POINTS

- Aging of the periocular region includes changes to the periocular skin, orbicularis oculi, ligamentous attachments, and fat.
- Injectable hyaluronic acid (HA) may include a variety of products administered with both cannula and/or needle techniques.
- New study protocols describe more dilute poly-L-lactic acid formulations with combined administration algorithms.
- Periocular platelet-rich plasma (PRP) injections and topical applications are increasingly studied with mixed results.
- Calcium hydroxyapatite administration provides both benefits and detractions when compared with other periocular rejuvenation agents.

INTRODUCTION

Rejuvenation of the periocular region can be a challenging endeavor for any facial plastic surgeon. However, treatment of lower eyelid “bags,” a “tired appearance,” or “tear trough” deformities are common requests from patients. Increasingly, nonsurgical treatment options are used by both surgeons and nonsurgeons alike to provide a refreshed result. Modern facial plastic surgeons must make the nuanced decision to decide whether surgery is the better option or to use a dermal filler or volumizing agent. This summary aims to provide an updated review of injectable options available to rejuvenate the lower eyelid – cheek junction. Please see other articles in this issue for the treatment of periocular pigmentation and vascularity and use of resurfacing and tightening devices.

ANATOMY

Aging of the lower eyelid–cheek junction is a predictable process that involves the skin, muscle, fat, and ligaments. Each anatomic structure must be considered when rejuvenating this delicate area.¹

The lower eyelid skin overlying the infraorbital rim continues to thin with time, loses elasticity, suffers sun-related dyschromias, and develops increased laxity and redundancy, or dermatochalasis. Subciliary horizontal rhytids and the more lateral “crow’s feet” contribute to an aged appearance. Further, as the epidermal rete ridges decrease in height and number and dermal collagen loses density the skin thins and fails to adequately camouflage the loss of volume along the infraorbital rim.

Attenuation of the orbicularis oculi muscle, divided into the pretarsal, preseptal, and preorbital

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^a Ascentist Plastic Surgery, 4801 College Boulevard, Leawood, KS 66211, USA; ^b Dr. Matthew White Facial Plastic Surgery, 800A 5th Ave #502a, New York, NY 10065, USA

* Corresponding author. 6815 E. Frontage Rd, Merriam, KS 66208.

E-mail address: Jeff.markey@ascentist.com

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divisions, leads to decreased lower lid dynamic and static support and further reveals the lid-cheek junction. Also, festoons can form over the malar eminence due to the laxity of the inferior orbicularis oculi muscle draped over the bony orbital rim or edema within the overlying skin.

Ligamentous laxity over time also leads to clear signs of aging (Fig. 1). The inferior orbital septum lies deep to the orbicularis oculi muscle and superficial to the 3 inferior orbital fat pads. The superior margin of the septum is suspended by the tarsus from the medial to lateral canthi, with the inferior border attaching to the orbital rim. With progressive laxity of the orbital septum, the orbital fat pads settle anteriorly, leading to “pseudoherniation” and eye “bags.” The orbitomalar ligament is an osteocutaneous ligament originating immediately anterior to the orbital septum along the infraorbital rim extending anteriorly to the skin at the lid-cheek junction. It traverses the orbicularis oculi muscle and lies superior to the SOOF (suborbicularis oculi fat). Nasal to the medial limbus, the orbitomalar ligament attenuates as the orbicularis oculi become tightly adherent to the medial infraorbital rim.

Age-related changes to orbital and superior cheek fat of the lower periocular complex also lead to common patient concerns. The 3 aforementioned lower orbital fat pads are separated by the inferior oblique muscle (medially and centrally) and the arcuate expansion of Lockwood’s ligament (centrally and laterally). As the orbital septum becomes laxer with time an unwanted lower lid convexity becomes visible. Further, with the descent and deflation of the SOOF, the infraorbital rim is revealed, forming a “tear trough” deformity. Ligamentous laxity and deflation of the fat lead to the classic double convexity deformity (Fig. 2). The superior convexity refers to the aforementioned pseudoherniation of the orbital fat pads. The inferior convexity refers to the settling of the SOOF inferior to the orbitomalar ligament. The convexities are separated by the infraorbital rim.

Understanding the “ideal,” youthful anatomy of the lower eyelid–cheek junction is essential, as is understanding the changes associated with aging in the region when considering injectable options in one’s practice. A rejuvenated, refreshed lower eyelid and lid–cheek junction involves the anatomic position of the lateral canthus, the tarsus, the orbital fat pads, the orbital septum, the orbitomalar ligament, and the SOOF. The lateral canthus should provide a positive tilt and be positioned 1–2 mm higher than the medial canthus.² The tarsus should remain moderately taut against the globe without exposing the inferior

limbus to allow for proper lateral-to-medial tear conduction but be elastic enough to allow digital displacement from the infraorbital rim on examination. The orbital septum should support the 3 inferior orbital fat pads to allow a seamless transition from the lash line through the lid–cheek junction. Finally, the orbitomalar ligament and SOOF should be positioned to enable a smooth contour to the lower eyelid–cheek junction and not expose the infraorbital rim. Injectable fillers can be used to camouflage anatomic changes related to the aging process to restore a youthful appearance.

HYALURONIC ACID

Hyaluronic acid (HA) injectables were first FDA-approved to correct facial contour deformities with the approval of Restylane in 2003. Since this time, the FDA approved additional HA fillers including, chronologically, Juvéderm® (Allergan Pharmaceuticals, Irvine, CA), Belotero® (Merz Aesthetics, Raleigh, NC), RHA® 2, 3, and 4 (Revanche Therapeutics, Nashville, TN), among others.³ The duration of each product’s effect and viscosity differ based on the degree of cross-linking, HA concentration, and molecular weight.^{4,5} HA fillers are also characterized by a quantitative descriptor G' (G prime). G' refers to the elasticity of the filler, or how well the product retains its shape after a force is applied. Higher G' products are firmer, more easily palpated, and are often placed by injectors in deeper planes to lift tissues. Lower G' products are softer, more easily spread within a tissue plane, and are often placed by injectors in more superficial planes to contour tissues.

Acknowledgment of the wide variability in tear trough correction techniques led to a literature review by Trinh and colleagues⁶ The review identified needle injection techniques via aliquots placed in the preperiosteal plane as the most commonly used technique. Restylane was the most commonly used HA product among the reports that met the study criteria.

As the HA product options continue to grow each year, with varying viscosities, durations, and marketing strategies, the injector must strive to stay current to provide the most efficacious results. More specifically, the challenging anatomy of the lower lid–cheek junction forces the modern injector to choose carefully. For example, a high level of cross-linking and larger particle size likely extend product duration but may increase water absorption and subsequent edema.⁷ When administering HA products, the ideal endpoint is to slightly underfill the volume deficit to account for their hydrophilic nature.

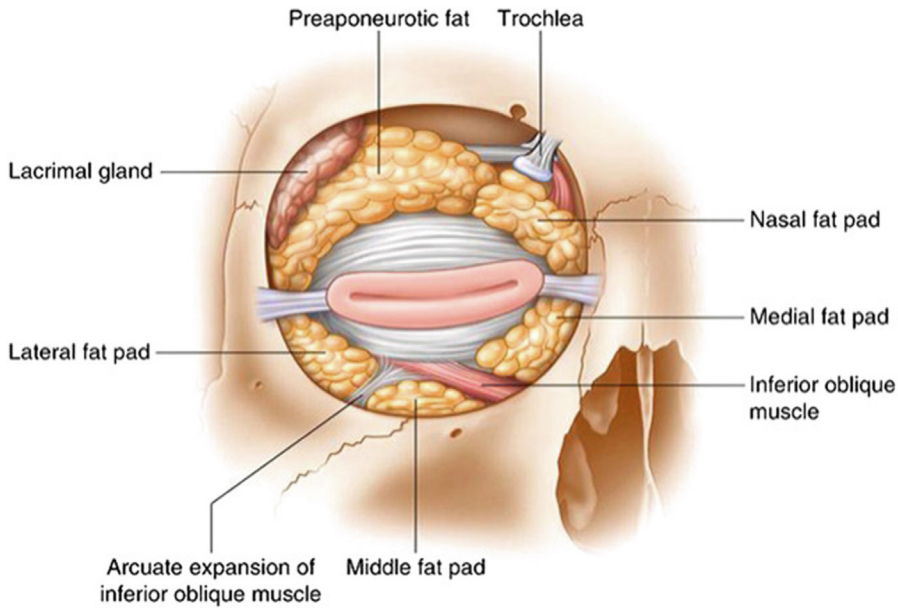


Fig. 1. The nasal and middle fat pads are separated anteriorly by the inferior oblique muscle. The lateral fat pad is separated anteriorly from the middle fat pad by the arcuate expansion. (Reprinted by permission from Tan, K.S., Oh, SR., Priel, A., Korn, B.S., Kikkawa, D.O. (2011). Surgical Anatomy of the Forehead, Eyelids, and Midface for the Aesthetic Surgeon. In: Massry, G., Murphy, M., Azizzadeh, B. (eds) Master Techniques in Blepharoplasty and Peri-orbital Rejuvenation. Springer, New York, NY. https://doi.org/10.1007/978-1-4614-0067-7_2.)

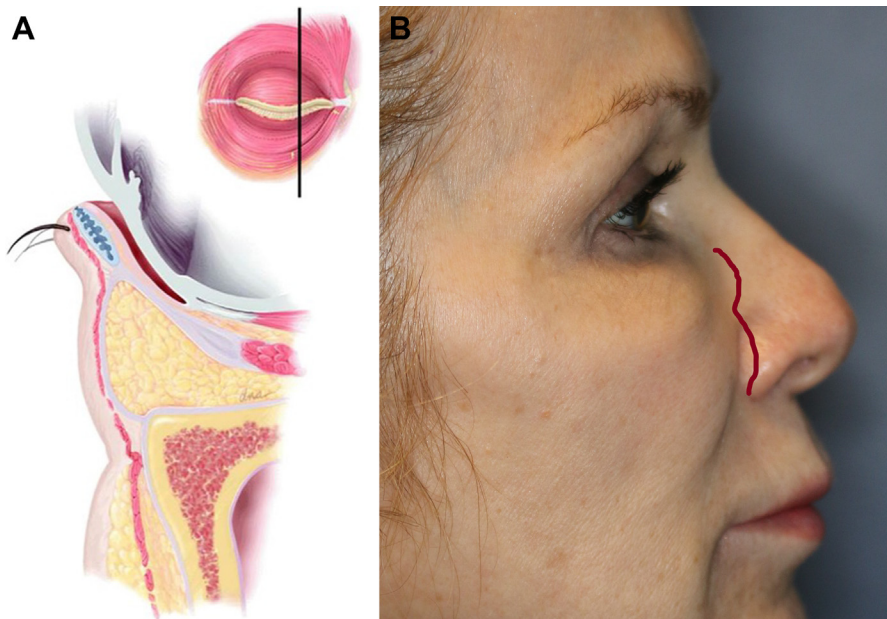


Fig. 2. (A) Sagittal view of the double convexity deformity. Increased laxity of the orbital septum allows for anterior displacement of the lower orbital fat pads. Descent of the malar fat exposes the infraorbital rim and forms second convexity in the superior cheek. (B) Clinical photo of a double-convexity deformity. ([A] Haddock, Nicholas T. M.D.; Saadeh, Pierre B. M.D.; Boutros, Sean M.D.; Thorne, Charles H. M.D. The Tear Trough and Lid/Cheek Junction: Anatomy and Implications for Surgical Correction, Plastic and Reconstructive Surgery: April 2009 - Volume 123 - Issue 4 - p 1332-1340 doi: 10.1097/PRS.0b013e31819f2b36; [B] photos courtesy of Dr Jessyka Lighthall.)

Juvéderm® Voluma XC (Allergan Pharmaceuticals, Irvine, CA) is a tightly cross-linked, less hygroscopic HA filler that retains contour improvements for up to 2 years.⁸ Common usage for higher G' products such as Juvéderm® Voluma XC, RHA 4, Restylane Lyft, among others, involves placement in deeper anatomic planes such as preperiosteal or submuscular to treat anatomic regions such as the malar eminences, temples, chin, and mandibular angles. However, Hall and colleagues reported high rates of patient satisfaction with Juvéderm® Voluma XC administered to the infraorbital hollows.⁹ The authors divide the infraorbital hollow into 3 anatomically distinct regions: the medial tear trough, the central nasojugal fold, and the lateral palpebromalar groove. They placed 0.5 cc of filler on each side using a 27g 1.5-inch Dermasculpt Microcannula® (Cosmo-France Inc., Miami, FL) in the preperiosteal or submuscular planes. Before injection, an infraorbital nerve block was performed via an intraoral approach. Follow-up showed 18 of the 52 patients required touch-up procedures defined as additional filler placed within 3 months of the initial injection. Most patients completing the postprocedure FACE-Q Satisfaction with Eyes Questionnaire reported significant satisfaction with the injections.

Hussain and colleagues reported a needle technique involving Juvéderm® Ultra Plus XC aliquots to the undereye.¹⁰ The authors describe an algorithmic volume predetermination based on Hirman's three grades of tear trough deformity. The authors call this the "tick" method as the 3 anatomic points of filler deposition resemble a checkmark. Zone "A" was located at a point between the inferolateral aspect of the tear trough and the nasojugal groove aligned with the mid-pupillary line (Fig. 3). Zone "B" was medial, 1–2 cm inferolateral to the medial canthus along the infraorbital rim. Zone "C" is lateral, 1 cm lateral to the lateral limbus at the lid–cheek junction. Subjects with Hirman classes 1, 2, and 3 received 0.3 mL, 0.4 mL, and 0.5 mL, respectively, on each side, spread across the 3 zones as mentioned above. Juvéderm® Ultra Plus XC was backfilled into BD U-40 insulin syringes with 6 mm 31g needles—one for each side. 15% of subjects required additional filler for optimal results at the time of the initial injection. 92% of subjects reported "exceptional improvement" or "very improved" 1 year after the procedure.

Regardless of the specific HA administration technique for the undereye, the injector must understand the risks of HA injection in this region and the most effective management strategies for possible adverse outcomes. These

complications can be classified as either acute or long term. Acute complications, including bruising and contour deformities, are normally associated with the injection technique and makeup 90% of the total adverse events.¹¹ Another acute complication, vascular compromise with or without vision loss, is very rare but a devastating adverse event. Bruising most often occurs secondary to direct vascular injury with either needle or cannula. Avoidance strategies include holding antithrombotic and antiplatelet medications or supplements before injection, applying ice immediately before and after injection, minimizing travel distances of the needle or cannula subdermally, and ensuring injection are placed in an avascular plane such as preperiosteally. Contour deformities include palpable boluses of HA that are inadequately camouflaged, as well as overfilled tear troughs. Management of filler "nodules" is often treated with firm massage alone, or dispersal with hyaluronidase if persistent. Overfilled tear troughs may appear in the first few days to a few weeks following injection and may be related to the hydrophilic nature of HA fillers. Management of these contour deformities includes watchful waiting for 3 weeks to allow swelling resolution or dispersal with hyaluronidase if persistent.¹² Finally, intravascular injection and downstream occlusion with HA particulate can result in vascular occlusion and periocular soft tissue necrosis. When identified in the acute setting one must set out to restore perfusion by flooding the region with hyaluronidase, applying nitropaste topically, local massage and heat application, and oral administration of aspirin 325 mg.¹³ Vision loss may result from retrograde passage of HA filler to occlude the ophthalmic and central retinal arteries. This is treated in the acute setting with the aforementioned treatments as well as supratrochlear and supraorbital hyaluronidase injection, rebreathing into a bag, and ocular massage. A recent consensus statement recommended against retrobulbar hyaluronidase injection.^{14,15}

Long-term adverse events include the Tyndall effect and delayed onset nodules. The Tyndall effect occurs when a bluish-gray tint is evident in the tear trough following superficial HA injection. This has been described as occurring anywhere from a few weeks following injection to months or years.¹¹ To treat the Tyndall effect deformity one may perform dermal treatments to thicken the skin and reduce its transparency, or disperse the filler with hyaluronidase. Delayed onset nodules can occur any time after the acute setting and may follow local trauma to the undereye, filler migration, or infection. When identified, accurately diagnosing the inciting event is essential. If

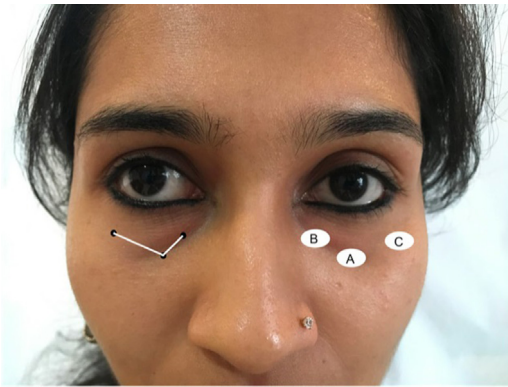


Fig. 3. Patient illustrating “Tick” technique points of injection. (From: Hussain SN, Mangal S, Goodman GJ. The Tick technique: A method to simplify and quantify treatment of the tear trough region. *J Cosmet Dermatol.* 2019 Dec;18(6):1642-1647; reprinted with permission.)

following local trauma, injection with an intraleisional steroid such as triamcinolone or 5-fluorouracil may be helpful. If a delayed nodule forms following filler migration dispersal with hyaluronidase should be performed.¹³ Finally, if concerned about infection one should treat empirically with broad-spectrum antibiotics including macrolides or tetracyclines following a culture, if possible.

POLY-L-LACTIC ACID

Injectable poly-L-lactic acid (PLLA) (Sculptra®, Galderma, Lausanne, Switzerland) is a biodegradable, immunologically inert, synthetic polymer that provides facial volumization through the stimulation of an inflammatory tissue response with subsequent collagen deposition with dermal fibroplasia. Sculptra initially received FDA approval for the restoration and correction of HIV-associated facial lipoatrophy in August 2004 and has received approval for broader aesthetic indications.¹⁶

The distinctive mechanism of action of PLLA compared with other facial fillers provides both benefits and detractors regarding the rejuvenation of the periocular region. HA fillers are largely predictable, lead to an immediate result for real-time feedback, and are able to precisely treat specific facial deficiencies (eg, lines, folds, attenuated lips) with low rates of adverse reactions. In comparison, PLLA is designed to provide volumetric expansion more broadly in volume-deficient areas.¹⁷ PLLA injection leads to delayed results, albeit longer lasting, and usually requires multiple injection sessions spaced 4 to 6 weeks apart for optimal results. PLLA, however, can provide

substantial volumization when placed in a supra-periosteal plane and can treat medium to deeply etched lines and wrinkles via collagen deposition when placed in a subcutaneous plane.¹⁸ PLLA boasts an improvement in skin texture and firmness as well.¹⁶

Various techniques and dilution strategies have been published without consistent protocols among authors. These technical disparities reflect the pursuit of PLLA injectors to minimize the medium and long-term adverse events associated with PLLA administration, without one gold standard approach. The most common complications include contour irregularities or nodules shortly after injection, or delayed granulomatous reactions months to years after injection.¹⁰ Lam and colleagues described injecting 1 to 2 vials per rejuvenation session when applied to the full face.¹⁷ The authors suggest diluting each vial with 6.5 cc of sterile water and 2 cc of a lidocaine mixture for patient comfort for a total dilution of 8.5 cc for each vial. This additional volume is more diluted than former administration techniques, which often called for as little as 2 cc diluent per vial. The authors also recommended diluting each vial at least 12 hours before injection to allow for more even distribution. Injections to the tear trough area included 0.1 cc preperiosteal depot injections, 0.5 cc on each side in total spread across 5 sites. Circular massage was recommended for each participant for 3 minutes, three times daily, for 3 days. The authors noted the immediate aesthetic changes in facial volume that resulted after the injection of the 8 cc volume of diluted Sculptra approximated the long-term results, with collagen deposition and dermal fibroplasia, after 3 total injection sessions.

Scheirle and Casas performed a similar dilution to study malar augmentation, effacement of the orbitomalar groove, and undereye correction.¹⁶ The authors describe the administration of depot injections, 0.05 cc to 1 cc of product per cm² of the surface area to be injected. The injections were placed in the immediate subdermal plane across the malar region and undereye rather than preperiosteally. The authors emphasize the importance of a concurrent topical regimen as well. The study protocol involved the administration of 0.025% tretinoin QHS until tolerated, gradually increasing to 0.05% tretinoin. A portion of the subjects included a hydroquinone-based product to ease distribution and help reduce the incidence of hyperpigmentation. The authors state the beneficial effects of tretinoin—improved skin quality, vascularity, and collagen synthesis—have a synergistic effect with the collagen deposition found with Sculptra Aesthetic. The study reported

99.1% patient satisfaction with a 4.7% incidence of nodule formation at the injection site, with all but one resolving spontaneously.

PLATELET-RICH PLASMA

Platelet-rich plasma (PRP) is also commonly used by facial plastic surgeons to improve skin texture and undereye contours. PRP is a derivative of autologous whole blood with 4 to 7 times the physiologic concentration of platelets. The clinical benefit of PRP injection or topical administration results from activated platelets' release of multiple growth factors, including platelet-derived growth factor, transforming growth factor- β , fibroblast growth factor, epidermal growth factor, keratinocyte growth factor, and vascular endothelium growth factor.^{19,20} PRP has been administered both topically and via injection for multiple indications including wound healing, orthopedic indications, dermatologic conditions, and hair restoration.

A review performed by Frautschi and colleagues highlights the multiple current aesthetic uses of PRP, as well as the lack of consistency regarding techniques, preparation processes, and platelet concentration.²¹ The authors identified 38 studies meeting the criteria. The studies described injection into aging skin (29%), scalp alopecia (26%), lipofilling (21%), fractional laser uses (13%), and facial surgery (11%). They note that 95% of these studies report clinical benefits to PRP usage. However, only 47% of the studies used objective measures to evaluate these benefits. Despite this lack of consistent efficacy measures the clinical benefit of PRP for aesthetic purposes, including undereye applications, is well described, but further randomized clinical trials or meta-analyses are needed.²² To better aggregate PRP research moving forward, Frautschi and colleagues recommended a description of the PRP studied to be categorized within the FITPAAW system—centrifugation Force, Iteration (sequence), Time, Platelet concentration, Anticoagulation, Activation, and White Blood Cells. Future reviews may be improved when able to more directly compare PRP harvest, preparation, and administration techniques with objective, quantifiable methods.

Split-face trials serve as some of the best comparisons regarding aesthetic PRP outcomes. Alam and colleagues performed a split-face trial that assessed 19 subjects undergoing mid-dermal PRP serial punctures with a 25g needle spaced 1 cm apart to the cheek and undereye.²³ The contralateral side received saline injections and only one treatment was performed. Both the patient and the dermatologists that served as

objective reviewers posttreatment were masked. Photos were taken, and subject self-assessment scores were gathered at 2 weeks, 3 months, and 6 months after the treatment. Two blinded dermatologists reviewed each photo and noted no statistically significant difference regarding fine lines, mottled pigmentation, roughness, and sallowness between halves. However, the subjects' self-assessment scores noted significant improvement regarding pigmentation, texture, wrinkles, and telangiectasias favoring the PRP half. This significant improvement was not detected until the 6-month posttreatment questionnaire and was not noted at 2 weeks or 3 months. The authors' concluded that the improvements may be subtle and thus were not identified by the blinded dermatologists using two-dimensional photography; while the subjects might have been more easily able to scrutinize differences in the mirror. The study also highlights that a much longer time was needed to appreciate improvements following undereye PRP intradermal injections, as the beneficial changes were delayed until the 6-month questionnaire.

Topical PRP application to the periorbital region performed concurrently with resurfacing or microneedling treatments is also a commonly performed modality. Microneedling uses multiple intradermal, small punctures to facilitate the absorption of topical serums or medications. Even without topical application of PRP, microneedling alone has been shown to increase collagen production, skin tightening, and subjective improvement in skin quality.²⁴ The microneedling depth and technique are chosen by the practitioner to achieve an endpoint of erythema with or without pinpoint bleeding. PRP can be applied topically during or after microneedling sessions.

Asif and colleagues performed a split-face study to assess the effect of microneedling, with or without PRP, on facial atrophic scarring.²⁵ The study included 50 subjects. The treatment involved injecting 1 cc of PRP, mixed with 0.1 mL of 10% calcium chloride, with a density of 0.1 mL/cm². An additional 1 cc of PRP, again mixed with 0.1 mL of 10% calcium chloride, was applied topically. The contralateral side underwent microneedling with intradermal injection of distilled water. A total of 3 sessions were performed at monthly intervals. Using Goodman's Qualitative Scale, the PRP treated side showed a 62.20% improvement compared with 45.84% for the contralateral side, a statistically significant benefit. Both self-reported subject scores and independent dermatologist reviewers further confirmed a statistically significant improvement.

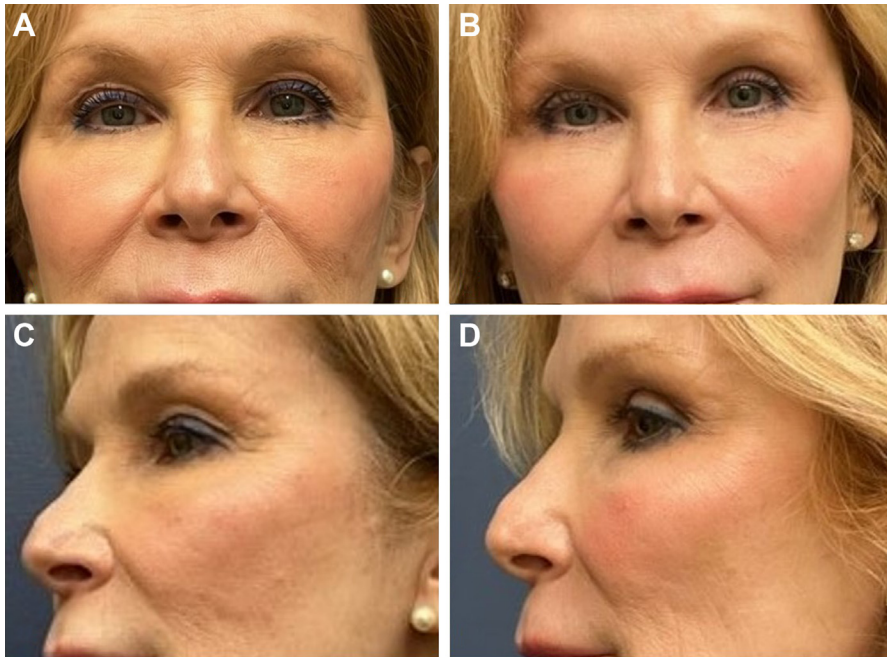


Fig. 4. A/C. Pre and B/D 2-weeks postinjection with calcium hydroxylapatite (Radiesse) in the cheek to treat the double-convexity deformity. (Photos courtesy of Dr Jessyka Lighthall).

CALCIUM HYDROXYLAPATITE

Lastly, calcium hydroxylapatite (Radiesse®, Merz, Raleigh, NC) is less often used to treat infraorbital volume deficits than other modalities listed in this summary. CaHA was initially FDA approved in 2006 for subdermal administration to correct moderate to severe facial wrinkles such as the nasolabial folds. A review performed by Emer and Sundaram found that CaHA has a good safety profile compared with HA fillers and boasts an immediate volume replacement when applied to the deep dermis in the nasolabial folds which may persist up to 12 months after injection, followed by a longer term deficit improvement secondary to collagenesis.²⁶ Studies mentioned in the review illustrate the longevity of 30 months or more regarding nasolabial fold injection. However, CaHA is not fully reversible like HA fillers. The injectable implant is also more viscous than HA fillers and is thus often avoided by facial plastic surgeons in the lid-cheek junction region due to concern for contour deformities.

However, CaHA continues to serve in the armamentarium of facial plastic surgeons seeking to rejuvenate the lid-cheek junction. The viscosity of the product provides substantial lift to ptotic soft tissues such as the superior cheek (**Fig. 4**). Also, while both HA and CaHA when placed in the tear trough can result in adverse events such

as blindness, CaHA may be chosen to reduce complication risk.²⁷ For these reasons and others CaHA administration to the periorbital complex continues to be an area of active study.

Bernadini and colleagues followed 63 patients undergoing tear trough deformity correction with Radiesse.²⁸ The technique described involved adding 0.5 cc 2% lidocaine to the 1.5 cc Radiesse vials. Most patients received 1 cc of this mixture in each side. Via a 25g cannula, the product was threaded in a retrograde fashion deep to the orbicularis oculi muscle to achieve the desired effect. As opposed to the slight under correction that is ideal with HA periorbital injections, the authors describe the ideal endpoint as a slight overfill of the volume deficit. The study notes a 92% improvement rate, with 36.5% of patients requiring an additional treatment at 1 month. No patient reported irregular contours, palpable lumpiness, or unevenness. However, 17.4% of patients noted a yellowish discoloration of the skin, which regressed in all cases within 6 weeks. Other non-randomized case series document similar satisfaction rates with minimal adverse events.^{29,30}

SUMMARY

Nonsurgical rejuvenation of the undereye region remains an evolving topic. Each year new volumizing injectables, resurfacing and skin-tightening

treatments, and topicals are introduced. The modern facial plastic surgeon must understand the risks, benefits, and alternatives to both the established treatment protocols and the recently developed options.

Hyaluronic acid fillers, poly-L-lactic acid, PRP, and calcium hydroxylapatite are all established rejuvenation options with prior studies documenting reasonable safety profiles. However, each treatment modality varies according to patient expense, risk of adverse events, the longevity of volume deficit improvement, overlying skin changes, and method of administration. It is up to the individual practitioner to identify which products, if any, provide the most efficacious results in their hands.

While there may be a lack of general consensus regarding the ideal technique or product, practitioners can agree that the rejuvenation of the lower lid–cheek junction is a challenging procedure with a steep learning curve and serious complication risk. Before attempting the rejuvenation of this area, injectors should have intimate knowledge of the periorbital anatomy, practical experience with various injection techniques, and an understanding of how to manage complications should they arise.

CLINICS CARE POINTS

- Choosing specific non-surgical modalities to rejuvenate the periocular complex requires in-depth knowledge of the delicate anatomy.
- Each modality - HA, PLLA, PRP, CaHa - has various advantages and disadvantages and should be used with distinct clinical endpoints in mind.

DISCLOSURE

The authors report no commercial or financial conflicts of interest and report no funding sources for this article.

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