REVIEW

Nonsurgical periocular rejuvenation: advanced cosmetic uses of neuromodulators and fillers

Kristina Y. Pao[a] and Ronald Mancini[b]

Purpose of review
To review the current literature regarding aesthetic enhancement using facial neuromodulators and fillers and to present advanced techniques using facial injectables for periocular rejuvenation.

Recent findings
The authors provide a summary of traditional periocular locations for the injection of neuromodulators and dermal fillers. The authors also present novel and advanced techniques utilizing injectables in the periocular region.

Summary
Minimally invasive procedures with little-to-no recovery time are continuing to increase in popularity. Neuromodulators and hyaluronic acid gel fillers have been shown to be well tolerated and efficacious nonsurgical alternatives in periocular rejuvenation.

Keywords
dermal fillers, hyaluronic acid gel, neuromodulators, nonsurgical periocular rejuvenation

INTRODUCTION

In 2013, over 11 million surgical and nonsurgical cosmetic procedures were performed in the USA equating to over US$12 billion [1]. Eighty-three percent were nonsurgical procedures accounting for 42% of total expenditures with onabotulinumtoxinA and hyaluronic acid gel (HAG) injections as the most common nonsurgical cosmetic procedures performed [1]. Several specialties offer minimally invasive procedures to patients seeking nonsurgical aesthetic enhancement. The periocular region continues to be an area that is difficult to treat. We present a review of the literature and detail advanced cosmetic uses of neuromodulators and dermal fillers for nonsurgical periocular rejuvenation.

NEUROMODULATORS

Prior to injection of neuromodulators, a complete patient history must be obtained including a thorough past medical history, history of prior facial injections and outcome, facial surgery or trauma, skin disorders, allergies, use of anticoagulants, pregnancy, or breast feeding [2]. The physician must discuss patient expectations, limitations, potential complications of chemodenervation, financial considerations, need for additional treatment, and off-label use. After informed consent is obtained, pretreatment photography should be documented.

The physician may opt to pretreat patients with topical anesthetic agents. The authors prefer topical eutectic mixture of lidocaine and prilocaine (EMLA) cream applied 20 min prior to injection. Other options include desensitization with ice packs or reconstitution of botulinum toxin with saline containing 0.9% benzyl alcohol preservative.

Types of neuromodulators

Botulinum toxin is produced by *Clostridium botulinum* resulting in seven serotypes. Serotypes A and B are used for clinical use. Botulinum toxin binds to receptor sites in the presynaptic autonomic nerve terminals blocking acetylcholine release reversibly

[a]Medical Eye Associates, Inc., Middleburg Heights, Ohio, USA and [b]Department of Ophthalmology, Oculoplastic and Orbital Surgery Service, University of Texas Southwestern Medical Center, Dallas, Texas, USA

Correspondence to Ronald Mancini, MD, FACS, Department of Ophthalmology, Oculoplastic and Orbital Surgery Service, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390, USA. Tel: +1 214 648 7688; fax: +1 214 648 2469; e-mail: Ronald.Mancini@UTSouthwestern.edu

Curr Opin Ophthalmol 2014, 25:461–469

DOI:10.1097/ICU.0000000000000074

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

KEY POINTS

- In-office aesthetic procedures are gaining in popularity, and a growing body of literature has reported the relative long-term safety and efficacy of facial injectables.
- Neuromodulators and dermal fillers provide a repeatable and adjustable, nonsurgical option in patients who decline traditional surgical intervention or are poor surgical candidates seeking periocular rejuvenation.
- We present a review of the literature and detail advanced cosmetic uses of neuromodulators and dermal fillers for nonsurgical periocular rejuvenation.

inhibiting focal muscle contraction. Generally, onset of activity occurs 2 days after injection with maximal efficacy apparent 2 weeks after injection.

BOTOX Cosmetic (Allergan, Inc.), onabotulinumtoxinA, was the first neuromodulator approved by the US Food and Drug Administration (FDA) for temporary improvement in moderate-to-severe glabellar rhytides associated with corrugator or procerus muscle activity or both in patients less than 65 years of age [3]. This was followed by Dysport (Medicis Pharmaceuticals), abobotulinumtoxinA, and Xeomin (Merz Pharmaceuticals), incobotulinumtoxinA, which gained US FDA approval for treatment of glabellar lines in 2009 and 2012, respectively. Properties of the commercially available neuromodulators are summarized in Table 1.

Preparation of neuromodulators varies depending on type of neuromodulator and clinician preference. Label preparations recommend reconstitution with 0.9% sterile nonpreserved saline. However, Alam *et al.* [9] showed decreased patient discomfort using preserved saline. Label preparations recommend use within 4–24 h of preparation; yet, in two separate trials, Alam *et al.* and Hexsel *et al.* [10] showed that reconstituted solutions can be stored for approximately 1 week without affecting product efficacy. Several studies have shown that one unit of BOTOX Cosmetic equates to two to four units of Dysport [11]. The authors' preferred neuromodulators are BOTOX Cosmetic and Xeomin reconstituted using sterile 0.9% nonpreserved saline to a concentration of 2.5 units per 0.1 ml. Particles of Xeomin may be displaced on the underside of the vial cap; thus, the vial should be inverted to ensure consistent concentration.

Traditional locations of periocular injection

The traditional locations of periocular injection using neuromodulators include the glabellar complex, forehead, lateral brow, lateral canthal rhytides, and orbicularis roll.

Glabella

The glabellar complex comprises the procerus, corrugator supercilii, and depressor supercilii muscles (Fig. 1a). The triangular procerus lies in the central midline functioning to lower the medial brows resulting in a horizontal line. The corrugator supercilii lies superolateral to the procerus pulling the brows medially resulting in two vertical rhytides in the central brow area. The depressor supercilii lies superior to the orbicularis oculi and is distinct from the corrugator supercilii and functions to lower the brow [12].

Patients with glabellar rhytides may appear angry or concerned. Intramuscular injection with botulinum toxin may soften glabellar furrows and is generally performed by injecting five sites: one injection into the central procerus (Fig. 1b, blue dot) and two injections into each of the medial and lateral corrugator supercilii (Fig. 1b, purple dots). The intended injection site of the medial corrugator supercilii lies vertical to the medial canthus, whereas the intended injection site of the lateral corrugator supercilii lies vertical to the medial limbus. Both injections into the corrugator supercilii should remain peripheral to the orbital rim. Approximately 20 U of onabotulinumtoxinA or incobotulinumtoxinA should be injected into the glabellar region with a range of 10–30 U [13]. The authors routinely inject a total of 15 U into the glabellar region, 5 U into the procerus and 2.5 U with each injection into the corrugator supercilii, with satisfactory aesthetic results.

Forehead

The frontalis muscle is a thin, rectangular muscle that elevates the brows giving rise to horizontal forehead lines. The goal of neuromodulation in this area is to weaken, but avoid completely paralyzing the frontalis. Injection consists of several subcutaneous injections along the frontalis with attention to the temporal portion of the frontalis muscle, lateral to the conjoint tendon (Fig. 1b, pink dots), to avoid the 'Spock's quizzical' brow appearance [14]. The authors typically treat five to seven areas on each side injecting a total of 10–30 U.

Lateral brow

Brow position is the result of the balance between the brow elevators (frontalis) and brow depressors (glabellar complex and orbicularis oculi). The lateral brow position can be modified by injecting 2–3 U at the lateral sub-brow orbicularis muscle (Fig. 1b, yellow dots), resulting in a 1-mm to 3-mm elevation of the lateral brow [14].

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

Table 1. Properties of commercially available neuromodulators [2–7,8■■]

	Botox Cosmetic (onabotulinumtoxinA)	Dysport (abobotulinumtoxinA)	Xeomin (incobotulinumtoxinA)	Myobloc (rimabotulinumtoxinB)
Serotype	A (hall strain)	A (hall strain)	A (hall strain)	B
Complex molecular weight	900 kDa	500–900 kDa	150 kDa	500–700 kDa
Total protein	~5 ng/vial	4.35 ng/vial	0.6 mg/vial	25/50/100 mg/vial
Preparation	Vacuum-dried	Lyophilized	Lyophilized	Solution
pH	~7	~7	~7	~5.6
Vial size	50 U 100 U	300 U	50 U 100 U	2500 U 5000 U 10 000 U
Storage (packaged product)	36–46°F for 36 months	36–46°F until vial expiration date	36–46°F for 36 months	36–46°F until vial expiration date
Storage (reconstituted)	Use within 24 h	Use within 4 h	Use within 24 h	Use within 4 h
US FDA approval for cosmetic use	2002	2009	2011	None
US FDA approval	Cervical dystonia, severe primary axillary hyperhidrosis, strabismus and blepharospasm	Cervical dystonia	Cervical dystonia, blepharospasm previously treated with onabotulinumtoxinA	Cervical dystonia
Dilutant volume	2.5 mL (100 U vial)	2.5 mL (300 U vial)	2.5 mL (100 U vial)	
Volume/site	0.1 mL	0.08 mL	0.1 mL	
Units/site	4 U	10 U	4 U	
Duration of effect	~3–4 months	~3–4 months	~3 months	

kDa, kilo Dalton; U, units; US FDA, U.S. Food and Drug Administration.

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

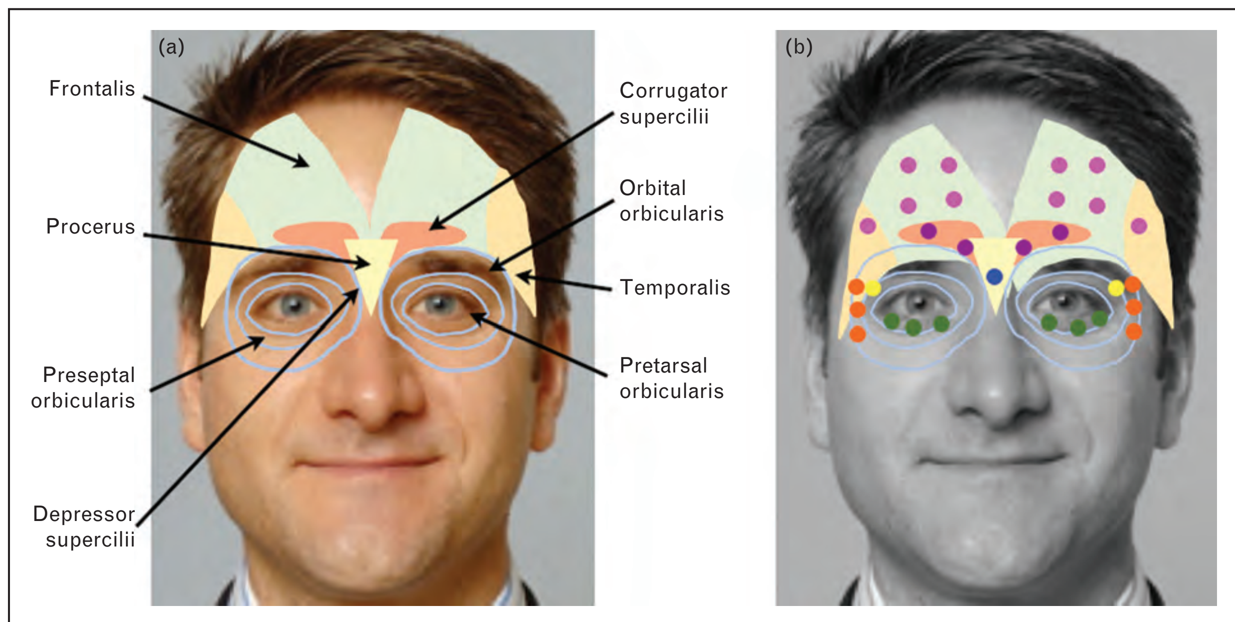

FIGURE 1. Periocular anatomy. (a) Periocular muscles. (b) Traditional locations for periocular rejuvenation using neuromodulators (glabellar complex, *blue and purple dots*; horizontal forehead lines, *pink dots*; lateral brow, *yellow dots*; lateral canthal rhytides, *orange dots*; orbicularis roll, *green dots*).

Lateral canthal rhytides

Lateral canthal rhytides or 'crows feet' can be softened by injecting the lateral orbicularis oculi at two to five injections sites approximately 1 cm outside the lateral orbital rim. Care should be taken to avoid injection below the zygomatic arch, which may result in upper lip ptosis. The authors typically inject three sites beginning at the temporal-most portion overlying the lateral canthal raphe and an additional injection 0.5–1 cm superior and inferior to the initial injection site injecting a total of 10–15 U (Fig. 1b, orange dots).

Orbicularis roll

Inferior orbicularis rolls are the result of contraction of the pretarsal orbicularis oculi muscle and commonly seen in healthy young adults. These folds can be improved by injecting 2–4 U of onabotulinumtoxinA into the orbicularis oculi along the lower eyelid widening the palpebral aperture [15]. The authors' preference is a subcutaneous injection at the junction of the pretarsal and preseptal orbicularis along the lateral and central lower eyelid (Fig. 1b, green dots). Care should be taken prior to injection to ensure adequate elasticity and absence of lower eyelid laxity prior to treatment.

Novel uses of neuromodulators

Alternative uses of neuromodulators in the periocular region can be used to address upper eyelid ptosis, asymmetric brow position and palpebral fissure asymmetry.

Ptosis

Unilateral upper eyelid ptosis can be improved by weakening the orbicularis oculi muscle. Depending on the amount of ptosis present, 0.5–1.5 U of onabotulinumtoxinA can be injected at one to two sites in the central and lateral pretarsal orbicularis of the upper eyelid [16]. The authors' preferred method is to inject 1–2 U of onabotulinumtoxinA subcutaneously at the junction of pretarsal and preseptal orbicularis oculi muscles along the upper eyelid at two sites, medial and lateral (Fig. 2a). Care should be taken to direct the needle away from the levator muscle during injection and to raise a superficial subcutaneous wheel to minimize the risk of worsening the ptosis. Alternatively, the contralateral upper eyelid may be treated with HAG to lower the eyelid, which can induce a reverse Herring effect and result in elevation of the ptotic eyelid [17].

Asymmetric brow position

Several factors including unilateral facial palsy, trauma, prior surgery, unilateral hyperkinesia of the frontalis, and/or orbicularis oculi muscles may lead to brow asymmetry [18]. Lateral brow ptosis can be addressed by injecting 2.5 U of onabotulinumtoxinA injected subcutaneously into the lateral orbicularis oculi beneath the lateral eyebrow (Fig. 2b, purple dots). Medial brow ptosis can be addressed by weakening the procerus, medial and lateral corrugator supercilii as described above (Fig. 2b, blue dots). Brow ptosis can be created in cases of frontalis

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

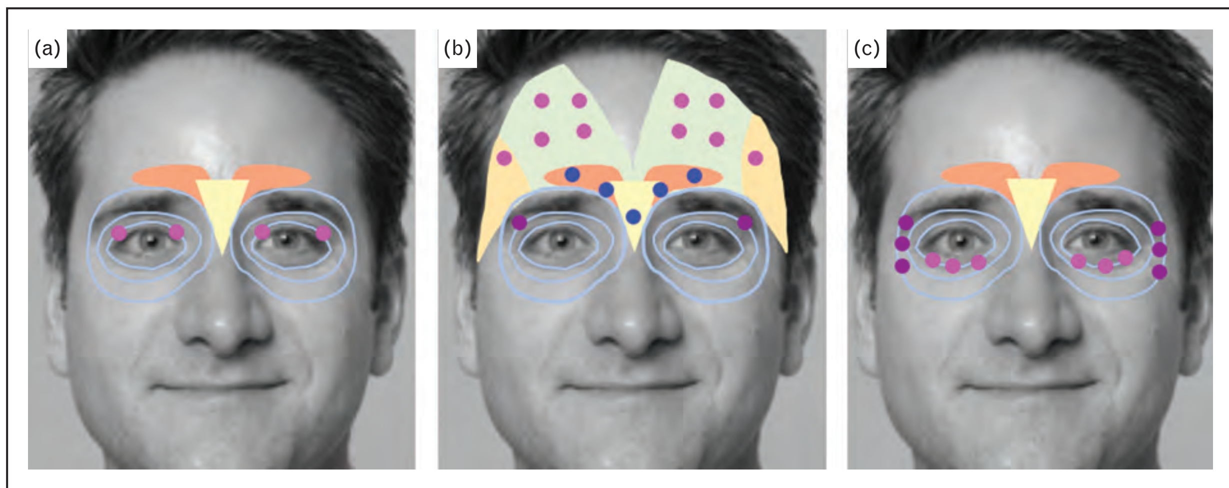

FIGURE 2. Novel uses of neuromodulators for periocular rejuvenation. (a) Ptosis, (b) asymmetric brow position, and (c) palpebral fissure asymmetry.

overaction with focal frontalis injection (Fig. 2b, pink dots). Aesthetic outcome and duration of effect are enhanced with dual injection of HAG filler into the deflated eyebrow fat pad in cases of lateral brow ptosis [17].

Palpebral fissure asymmetry

Lateral palpebral fissure asymmetry secondary to asymmetric lower eyelid position may be addressed nonsurgically by concomitantly injecting the lateral canthal rhytides (Fig. 2c, purple dots) and the lower eyelid of smaller fissure eye (Fig. 2c, pink dots). Flynn *et al.* [19] noted an increase of 2 mm in the palpebral fissure by injecting 2 U of onabotulinum-toxinA into the lower eyelid and 12 U into the lateral canthal rhytides.

Complications

Complications after botulinum toxin injection include ecchymosis, oedema, eyelid or brow ptosis, headache, worsening of dry eye, asymmetry, lagophthalmos, lower eyelid retraction, induction of the sternutatory reflex, diplopia, flu-like symptoms and cutaneous eruptions [20–22,23▪]. Eyelid ptosis may be temporized by topical apraclonidine 0.5% or naphazoline hydrochloride 0.025% drops administered in the affected eye.

DERMAL FILLERS

In addition to a detailed patient history, the physician should particularly discuss avoiding tobacco and anticoagulants prior to injection of dermal fillers. A history of herpes simplex virus (HSV) should be obtained [24]. The authors typically prescribe prophylactic oral valacyclovir 500 mg daily for 7 days beginning the day of injection in patients with a history of HSV. The patient is instructed to increase valacyclovir to 2000 mg every 12 h for 1 day should cold sores appear [25]. Patients are pretreated with local nerve blocks or topical anesthetic agents or both, such as EMLA cream, cryoesthetic agents, or vibratory counter-stimulation [26,27▪▪].

Types of dermal fillers

Several types of dermal fillers are commercially available and are summarized in Table 2. Given its availability, duration of effect, reversibility and favorable safety profile, the authors will limit their discussion to HAG fillers, which are their preferred agents in the periocular region.

Hyaluronic acid is a glycosaminoglycan biopolymer naturally present in the dermis and does not require preprocedural skin testing. The commercially available HAG products differ in their concentrations of hyaluronic acid, extent of hydration, consistency, viscosity and amount of cross-linking [44]. Fagien and Cassuto [45] found that reconstitution of dermal fillers with lidocaine and epinephrine decreases HAG concentration allowing injection through a smaller gauge needle and more superficial injection plane resulting in greater patient comfort. The authors' HAG of choice in the periorbital region is Restylane because of its availability, viscosity and limited capacity to create significant fluid accumulation in the periocular region.

Injection techniques

Table 3 summarizes the basic injection techniques for dermal fillers. The fanning technique is the authors' injection technique of choice using a

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

Table 2. Summary of commercially available facial fillers [3,28–42,43■]

HAG	HAG concentration	Type	Lidocaine	Needle size	FDA approval
Restylane	20 mg/mL	NASHA	No	30 G	2003
Restylane-L			Yes		2010
Juvederm Ultra	24 mg/mL	Hyalcross HAG	No	30 G	2006
Juvederm Ultra XC			Yes		2010
Juvederm Ultra Plus	24 mg/mL	Hylacross HAG	No	27 G	2006
Juvederm Ultra Plus XC			Yes		2010
Perlane	20 mg/mL	NASHA	No	27 or 29 G	2007
Perlane-L			Yes		2010
Prevelle Silk	5.5 mg/mL	NASHA	Yes	32 G	2008
Belotero Balance	22.5 mg/mL	CPM	No	27 or 30 G	2011
Calcium hydroxylapatite					
Radiesse	40–63 μm microspheres		No	26 G	2009
Poly-L-lactic acid					
Sculptra Aesthetic	25–45 μm microspheres		No	26 G	2006
Autologous fibroblasts					
laViv	10–15 μm microspheres		No	30 G	2011
Polymethylmethacrylate					
Artefill	30–50 μm microspheres		Yes	26 G	2006

CPM, cohesive polydensified matrix; G, gauge; HAG, hyaluronic acid gel; NASHA, nonanimal stabilized hyaluronic acid. Adapted from reference [42].

classic sharp 30-gauge needle injected perpendicular to the plane of the orbital rim through the thicker check tissues with a cotton-tipped applicator ready in the nondominant hand to apply immediate pressure should bleeding or bruising occur. Precise placement without overfilling is important, as there is very limited capacity to massage or smooth irregularities in the eyelid with the exception of areas over bone, where limited massage can be effective.

Periocular injection of hyaluronic acid gel filler

HAG fillers have been widely used for nonsurgical management of functional eyelid abnormalities, including lower eyelid retraction, cicatricial ectropion, paralytic lagophthalmos and congenital eyelid malpositions [48■■,49–53] (Figure 3). In this section, the authors describe uses of HAG fillers for nonsurgical management of aesthetic eyelid abnormalities. Concomitant use of neuromodulators and dermal fillers increases duration of effect compared with the use of dermal fillers alone [54].

Orbital rim hollow

The orbital rim hollow, also known as the tear trough or nasojugal groove, is the natural depression between the lower eyelid and cheek. Prominence of the orbital rim hollow can give the appearance of a 'tired' look. The plane of injection is deep to the orbicularis muscle, but anterior to the periosteum [46]. The authors prefer initiating the injection site in the thick upper cheek tissues and fanning the

Table 3. Basic injection techniques for dermal fillers [2,46,47]

Injection technique	Description of technique
Serial puncture	Filler is injected evenly and closely spaced punctures along fine lines or wrinkles
Linear threading	Filler is injected in 'threads' upon needle insertion or withdrawal along the length of the desired area
Serial threading	This technique combines serial puncture and linear threading techniques
Fanning	Filler is injected through one puncture site as the needle direction is constantly changed without complete withdrawal of the needle
Cross-hatching	Filler is injected in threads in a grid-like pattern 5–10 mm apart
Hyalurostructure	A reinforced, blunt microcannula is used to deliver filler to the desired area rather than classic sharp needles aiming to decrease the risk of tissue laceration, bruising and oedema

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

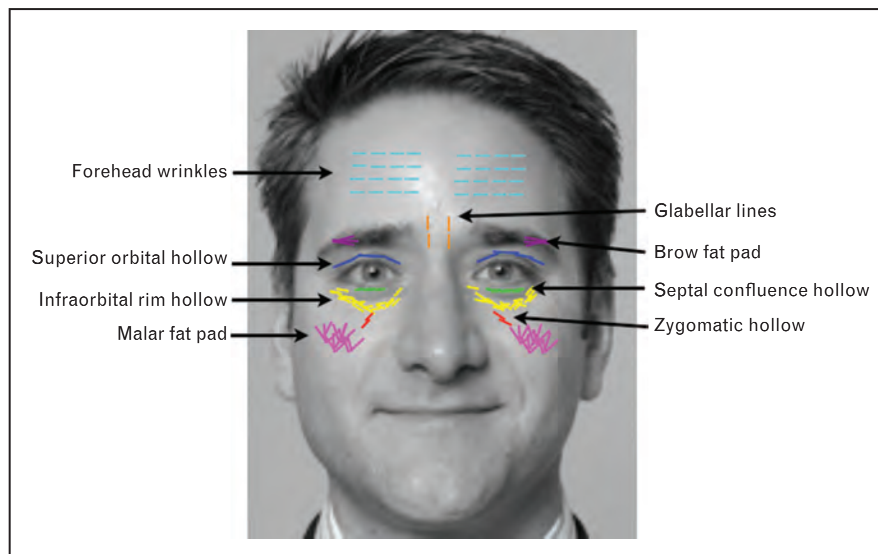

FIGURE 3. Periorbital hollows [55,56].

material perpendicular to the orbital rim hollow, in a suborbicularis plane. Superficial placement of HAG in this area may result in visible contour irregularities or bluish discoloration secondary to the Tyndall effect or both.

Goldberg and Fiaschetti [55] injected an average of 0.9 cm^3 of Restylane per session into the periorbital hollows as well as the eyebrow and malar fat pads with residual effect lasting for 6–12 months. Common complications included bruising, fluid accumulation and contour irregularities [55,56]. Goldberg and Fiaschetti proposed [55] screening patients for thin skin and preexisting malar and eyelid fluid as these patients likely have an anatomic propensity for fluid retention, often exacerbated by HAG injection. Tung *et al.* [57] demonstrated that augmenting the lower eyelid-upper cheek area utilizing two complementary dermal fillers resulted in a statistically significant improvement in aesthetic outcome. In the authors' anecdotal experience, Restylane has less propensity to collect fluid in the periocular area, as compared to Juvederm perhaps relating to the degree of cross-linking.

Upper eyelid margin asymmetry

Mancini *et al.* [17,49] injected an average volume of 0.2 cm^3 of HAG (Restylane) into the relatively retracted upper eyelid resulting in asymmetric upper eyelid margin position. The 'HAG goldweight' serves as a physical stent inhibiting the action of the levator muscle [48▪▪,49]. The technique involves administering topical anesthetic into the upper fornix, everting the upper eyelid over a Desmarres retractor exposing the supratarsal conjunctiva, while a 30-gauge needle is inserted into the subconjunctival levator plane as HAG slowly injected [17]. The technique can be used in combination with botulinum toxin to raise a relatively ptotic eyelid.

Eyebrow fat pad

A widely accepted concept of facial aging includes atrophy of the retro-orbicularis oculi fat pad causing deflation of the brow worsening the appearance of dermatochalasis. Additionally, an imbalance between the brow depressors and brow elevators, thinning skin and loss of skin elasticity result in brow ptosis. Volume restoration of the eyebrow fat pad with concomitant eyebrow recontouring and chemodenervation of the brow depressors rejuvenates the periocular region [58▪].

The eyebrow fat pad can be re-inflated by entering the lateral caudal end of the brow with a 30-gauge needle and injecting 0.4 cm^3 of HAG for each lateral brow or 0.6–0.8 cm^3 for the entire brow in the suborbicularis/preperiosteal plane taking care to feather the product laterally [59]. The product can then, to a limited degree, be moulded along the superior orbital rim to the desired contour.

Complications

The most common side-effects are often procedure-related and/or technique-related, such as contour irregularities, erythema, oedema, ecchymosis, injection site tenderness and implant visibility because of the Tyndall effect. Rare complications include angioedema, biofilm development, immediate or delayed hypersensitivity reactions, inflammatory nodule or granuloma formation, migration, tissue necrosis because of vascular compression or intra-arterial injection and vision loss because of retinal vessel occlusion [60–64,65▪▪]. Park *et al.* [64] proposed two 'danger zones': the glabella and nasal

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

ala as areas susceptible to tissue necrosis. If intra-arterial injection is suspected, immediate warm compresses, nitroglycerin paste and hyaluronidase should be administered. Hyaluronidase should be available at all times when injecting HAG. Fluctuant infectious collections may be treated with incision and drainage with culture and administration of antibiotics, typically a fluoroquinolone and third-generation macrolide for 2 weeks [2]. Intralesional steroids can be used to treat inflammatory nodules.

CONCLUSION

In-office aesthetic procedures are gaining in popularity, and a growing body of literature has reported the relative long-term safety and efficacy of facial injectables. The periocular region remains a difficult area to treat requiring exemplary knowledge of the periocular anatomy. Neuromodulators and HAG fillers provide a repeatable and adjustable, nonsurgical option in patients who decline traditional surgical intervention or are poor surgical candidates seeking periocular rejuvenation.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
■ of special interest
■■ of outstanding interest

1. American Society for Aesthetic Plastic Surgery. Cosmetic surgery national data bank: 2013 statistics. Available at: http://www.surgery.org/sites/default/files/Stats2013_3.pdf. Accessed March 31, 2014.
2. Nguyen AT, Ahmad J, Fagien S, Rohrick RJ. Cosmetic medicine: facial resurfacing and injectables. Plast Reconstr Surg 2012; 129:142e–153e.
3. Carruthers JDA, Glogau RG, Blitzer A; Facial Aesthetics Consensus Group Faculty. Advances in facial rejuvenation: botulinum toxin type A, hyaluronic acid dermal fillers, and combination therapies – consensus recommendations. Plast Reconstr Surg 2008; 121:5–30S.
4. Botox Cosmetic (onabotulinumtoxinA) [prescribing information]. Irvine, CA: Allergan, Inc.; November 2012. Available at: http://www.allergan.com/assets/pdf/botox_cosmetic_pi.pdf. Accessed July 9, 2013.
5. Dysport (abobotulinumtoxinA) [prescribing information]. Scottsdale, AZ: Medicis Aesthetics Inc.; 2012. Available at: http://pi.medicis.us/printer_friendly/dysport.pdf. Accessed July 9, 2013.
6. Xeomin (incobotulinumtoxinA) [prescribing information]. Greensboro, NC: Merz Pharmaceuticals, LLC; July 2011. Available at: http://www.xeominaesthetic.com/downloads/xeomin-prescribing-information.pdf#zoom=100. Accessed July 9, 2013.
7. Myobloc (rimabotulinumtoxinB) [prescribing information]. South San Francisco, CA: Solstice Neurosciences, Inc.; May 2010. Available at: http://www.myobloc.com/hp_about/PI_5-19-10.pdf. Accessed July 9, 2013.
8. ■■ Carruthers A, Kane MAC, Flynn TC, *et al.* The convergence of medicine and neurotoxins: a focus on botulinum toxin type A and its application in aesthetic medicine – a global, evidence-based botulinum toxin consensus education initiative. Part I: botulinum toxin in clinical and cosmetic practice. Dermatol Surg 2013; 39:493–509.

The authors review the history, science and safety of the three commercially available cosmetic neuromodulators detailing differences in product diffusion, spread, equivalency ratios, storage and immunoresistance.

9. Alam M, Dover JS, Arndt KA. Pain associated with injection of botulinum A exotoxin reconstituted using isotonic sodium chloride with and without preservative: a double-blind, randomized controlled trial. Arch Dermatol 2002; 138:510–514.
10. Hexsel DM, De Almeida AT, Rutowitsch M, *et al.* Multicenter, double-blind study of efficacy of injections with botulinum toxin type A reconstituted up to six consecutive weeks before application. Dermatol Surg 2003; 29:523–529.
11. Michaels BM, Csank GA, Ryb GE, *et al.* Prospective randomized comparison of onabotulinumtoxinA (Botox) and abobotulinumtoxinA (Dysport) in the treatment of forehead, glabellar, and periorbital wrinkles. Aesthet Surg J 2012; 32:96–102.
12. Cook BE, Lucarelli MJ, Lemke BN. Depressor supercilii muscle: anatomy, histology, and cosmetic implications. Ophthal Plast Reconstr Surg 2001; 17:404–411.
13. Hankins CL, Strimling R, Rogers GS. Botulinum A toxin for glabellar wrinkles: dose and response. Dermatol Surg 2003; 29:1181–1183.
14. Dayan SH, Bassichis BA. Evaluation of the patient for cosmetic Botox injection. Facial Plast Surg Clin N Am 2003; 11:349–358.
15. Flynn TC, Carruthers JA, Carruthers JA, Clark RE. Botulinum A toxin (BOTOX) in the lower eyelid: dose-finding study. Dermatol Surg 2003; 29:943–951.
16. Fagien S. Temporary management of upper lid ptosis, lid malposition, and eyelid fissure asymmetry with botulinum toxin type A. Plast Reconstr Surg 2004; 114:1892–1902.
17. Mancini R, Khadavi NM, Goldberg RA. Nonsurgical management of upper eyelid margin asymmetry using hyaluronic acid gel filler. Ophthal Plast Reconstr Surg 2011; 27:1–3.
18. Tiryaki T, Ciloglu SE. Eyebrow asymmetry: definition and symmetrical correction using botulinum toxin A. Aesthetic Surg J 2007; 27:513–517.
19. Flynn TC, Carruthers JA, Carruthers JA. Botulinum-A toxin treatment of the lower eyelid improves infraorbital rhytides and widens the eye. Dermatol Surg 2001; 27:703–708.
20. Kaltreider SA, Kennedy SH, Woog JJ, *et al.* Cosmetic oculofacial applications of botulinum toxin: a report by the American Academy of Ophthalmology. Ophthalmology 2005; 112:1159–1167.
21. Coté TR, Mohan AK, Polder JA, *et al.* Botulinum toxin type A injections: adverse events reported to the US Food and Drug Administration in therapeutic and cosmetic cases. J Am Acad Dermatol 2005; 53:407–415.
22. Levy LL, Emer JJ. Complications of minimally invasive cosmetic procedures: prevention and management. J Cutan Aesthet Surg 2012; 5:121–132.
23. ■ Kulkarni OC, Cox CA, Hedges TR 3rd, Tarsy D. Sternutatory reflex influenced by periocular needle insertion in patients receiving chronic botulinum toxin injections. Parkinsonism Relat Disord 2013; 19:770–771.

The sternutatory reflex or sneezing reflex is often triggered in 5% of patients receiving periocular anesthesia with i.v. sedation. The authors present two case reports in which the sneezing reflex was triggered in patients receiving chronic onabotulinumtoxinA after 5 and 8 years. The authors caution injectors of this possible side effect as stimulation of the sternutatory reflex may risk globe perforation.

24. McCracken MS, Khan JA, Wulc AE, *et al.* Hyaluronic acid gel (Restylane) filler for facial rhytids: lessons learned from American Society of Ophthalmic Plastic and Reconstructive Surgery member treatment of 286 patients. Ophthal Plast Reconstr Surg 2006; 22:188–191.
25. Valtrex (valacyclovir hydrochloride) [prescribing information]. Triangle Park, NC: GlaxoSmithKline; Jan 2013. Available at: http://us.gsk.com/products/assets/us_valtrex.pdf. Accessed March 31, 2014.
26. Monheit GD, Coleman KM. Hyaluronic acid fillers. Dermatol Ther 2006; 12:141–150.
27. ■■ Mally P, Czyz CN, Chan NJ, Wulc AE. Vibration anesthesia for the reduction of pain with facial dermal filler injections. Aesthetic Plast Surg 2014; 38:413–418.

Prospective study of 41 patients who received facial dermal fillers on both sides of the face, one side with vibration anesthesia and one side without. The tip of vibrator was positioned 1–2 cm from the injection site 2–3 s prior to injection and held in position until the needle was withdrawn. Patients experienced a statistically significant reduction in pain when receiving vibration anesthesia during facial dermal filler injection assessed by a post-treatment questionnaire.

28. Restylane [product information]. Scottsdale, AZ: Medicis Aesthetics Inc.; October 2011. Available at: http://pi.medicis.us/restylane.pdf. Accessed September 16, 2013.
29. Restylane-L [product information]. Scottsdale, AZ: Medicis Aesthetics Inc.; August 2012. Available at: http://pi.medicis.us/restylane_l.pdf. Accessed September 16, 2013.
30. Juvederm Ultra [directions for use]. Santa Barbara, CA: Allergan, Inc.; November 2012. Available at: http://www.allergan.com/assets/pdf/juvederm_ultra_dfu.pdf. Accessed September 16, 2013.
31. Juvederm Ultra XC [directions for use]. Santa Barbara, CA: Allergan, Inc.; 2011. Available at: http://www.allergan.com/assets/pdf/juvederm_ultra_xc_dfu.pdf. Accessed September 16, 2013.
32. Juvederm Ultra Plus [directions for use]. Santa Barbara, CA: Allergan, Inc.; 2011. Available at: http://www.allergan.com/assets/pdf/juvederm_ultra_plus_dfu.pdf. Accessed September 16, 2013.
33. Juvederm Ultra Plus XC [directions for use]. Santa Barbara, CA: Allergan, Inc.; 2011. Available at: http://www.allergan.com/assets/pdf/juvederm_ultra_plus_xc_dfu.pdf. Accessed September 16, 2013.

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

34. Perlane [product information]. Scottsdale, AZ: Medicis Aesthetics Inc.; August 2010. Available at: http://pi.medicis.us/perlane.pdf. Accessed September 16, 2013.
35. Perlane-L [product information]. Scottsdale, AZ: Medicis Aesthetics Inc.; August 2011. Available at: http://pi.medicis.us/perlane_l.pdf. Accessed September 16, 2013.
36. Prevelle Silk [product information]. Irving, TX: Mentor; 2007. Available at: http://www.ieaesthetics.com/files/product/product_56.pdf. Accessed September 16, 2013.
37. Belotero Balance [prescribing information]. Franksville, WI: Merz Aesthetics, Inc; 2012. Available at: http://www.belotero.com/prescribing-info.pdf. Accessed September 16, 2013.
38. Radiesse [instructions for use]. Franksville, WI: Merz Aesthetics, Inc.; March 2011. Available at: http://www.radiesse.eu/downloads/RADIESSE_Wrinkle_Filler_Instructions_for_Use.pdf. Accessed September 16, 2013.
39. Sculptra Aesthetic [prescribing information]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; May 2012. Available at: http://www.sculptraaesthetic.com/sculptra_aesthetic.pdf. Accessed September 16, 2013.
40. Artefill [instructions for use]. San Diego, CA: Suneva Medical, Inc.; February 2010. Available at: http://doctor.artefill.com/wp-content/uploads/2011/03/Artefill-IFU-7130REVO010210.pdf. Accessed September 16, 2013.
41. LaViv [product information]. Exton, PA: Fibrocell Technologies, Inc.; June 2011. Available at: http://mylaviv.com/pdf/LAVIV-prescribing-info.pdf. Accessed September 16, 2013.
42. Innovations in facial aesthetic medicine: a practical guide to the use of injectables in facial aesthetic medicine. Paradigm Communications, LLC, 2013. Print.
43. ▪ Bernardini FP, Cetinkaya A, Devoto MH, Zambelli. Calcium hydroxyl-apatite (Radiesse) for the correction of periorbital hollows, dark circles, and lower eyelid bags. Ophthal Plast Reconstr Surg 2014; 30:34–39.
Possibly because of its microparticulate nature, calcium hydroxyl-apatite is rarely used in the periorbital region. In their retrospective, unblinded study, the authors are the first to publish their results after injecting calcium hydroxyl-apatite to correct tear trough, infraorbital hollows, deep superior sulcus, dark circles and lower eyelid bags in 63 patients. Side-effects were temporary and included mild erythema, oedema, pseudoxanthalesma effect, product migration and overcorrection. The authors concluded that calcium hydroxyl-apatite is well tolerated and effective; however, the authors caution injectors to the use of calcium hydroxyl-apatite in the periorbital area as there is no anecdote as with HAG fillers.
44. Rzany B, Cartier H, Kestemont P, *et al.* Correction of tear troughs and periorbital lines with a range of customized hyaluronic acid fillers. J Drugs Dermatol 2012; 11:s27–s34.
45. Fagien S, Cassuto D. Reconstituted injectable hyaluronic acid: expanded applications in facial aesthetics and additional thoughts on the mechanism of action in cosmetic medicine. Plast Reconstr Surg 2012; 130:208–217.
46. Rohrich RJ, Ghavami A, Crosby MA. The role of hyaluronic acid fillers (Restylane) in facial cosmetic surgery: review and technical considerations. Plast Reconstr Surg 2007; 120:41S–54S.
47. Berros P. Periorbital contour abnormalities: hollow eye ring management with hyalurostructure. Orbit 2010; 29:119–125.
48. ▪▪ Mancini R. Managing eyelid malpositions with hyaluronic acid gel injections. Int Ophthalmol Clin 2013; 53:11–20.
The article reviews and describes injection techniques in the application of neuromodulators and dermal fillers in addressing functional eyelid issues such as lagophthalmos, eyelid retraction, cicatricial ectropion and congenital eyelid malpositions.
49. Mancini R, Taban M, Lowinger A, *et al.* Use of hyaluronic acid gel in the management of paralytic lagophthalmos: the hyaluronic acid gel 'gold weight'. Ophthal Plast Reconstr Surg 2009; 25:23–26.
50. Goldberg RA, Lee S, Jayasundera T, *et al.* Treatment of lower eyelid retraction by expansion of the lower eyelid with hyaluronic acid gel. Ophthal Plast Reconstr Surg 2007; 23:343–348.
51. Zamani M, Thyagarajan S, Olver JM. Functional use of hyaluronic acid gel in lower eyelid retraction. Arch Ophthalmol 2008; 126:1157–1159.
52. Zamani M, Thyagarajan S, Olver J. Adjunctive use of hyaluronic acid gel (Restylane Sub-Q) in anophthalmic volume deficient sockets and phthisical eyes. Ophthal Plast Reconstr Surg 2010; 26:250–253.
53. Fezza JP. Nonsurgical treatment of cicatricial ectropion with hyaluronic acid filler. Plast Reconstr Surg 2008; 121:1009–1014.
54. Carruthers J, Carruthers A. A prospective, randomized, parallel group study analyzing the effect of BTX-A (Botox) and nonanimal sourced hyaluronic acid (NASHA, Restylane) in combination compared with NASHA (Restylane) alone in severe glabellar rhytides in adult female subjects: treatment of severe glabellar rhytides with hyaluronic acid derivative compared with the derivative and BTX-A. Dermatol Surg 2003; 29:802–809.
55. Goldberg RA, Fiaschetti D. Filling the periorbital hollows with hyaluronic acid gel: initial experience with 244 injections. Ophthal Plast Reconstr Surg 2006; 22:335–343.
56. Goldberg RA. Nonsurgical filling of the periorbital hollows. Aesthetic Surg J 2006; 26:69–71.
57. Tung R, Ruiz de Luzuriaga AM, Park K, *et al.* Brighter eyes: combined upper cheek and tear trough augmentation: a systematic approach utilizing two complementary hyaluronic acid fillers. J Drugs Dermatol 2012; 11:1094–1097.
58. ▪ Sundaram H, Kiripolsky M. Nonsurgical rejuvenation of the upper eyelid and brow. Clin Plastic Surg 2013; 40:55–76.
This article reviews nonsurgical rejuvenation of the upper eyelid and brow by addressing the four pillars of rejuvenation: replacement of tissue volume, regeneration of tissue quality, rebalancing of facial vectors and proportions and improvement of skin reflectance. The authors recommend a tailored approach to each patient combining more than one treatment modality (e.g. neuromodulators, injectable fillers, resurfacing of skin with lasers or peels, lasers, or light energy-based devices) targeted within or outside the periorbital frame.
59. Kornstein AN. Soft-tissue reconstruction of the brow with Restylane. Plast Reconstr Surg 2005; 116:2017–2019.
60. Sclafani AP, Fagien S. Treatment of injectable soft tissue filer complications. Dermatol Surg 2009; 35:1672–1680.
61. Grossman K. Hyaluronic acid gel fillers: hypersensitivity reactions. Anesth Surg J 2005; 25:403–405.
62. Schanz S, Schippert W, Ulmer A, *et al.* Arterial embolization caused by injection of hyaluronic acid (Restylane). Br J Dermatol 2002; 146:928–929.
63. Apte RS, Solomon SD, Gehlbach P. Acute choroidal infarction following subcutaneous injection of micronized dermal matrix in the forehead region. Retina 2003; 23:552–554.
64. Park TH, Seo SW, Kim JK, Chang CH. Clinical experience with hyaluronic acid-filler complications. J Plast Reconstr Aesthet Surg 2011; 64:892–897.
65. ▪▪ Malik S, Mehta P, Adesanya O, Ahluwalia H. Migrated periocular filler masquerading as arteriovenous malformation: a diagnostic and therapeutic dilemma. Ophthal Plast Reconstr Surg 2013; 29:e18–e20.
Case report detailing an ill-defined mobile swelling involving the left brow and glabella with radiologic findings suggesting vascular malformation resulting in an unsuccessful attempted sclerotherapy. Surgical exploration revealed migrated permanent polyalkylimide filler with cicatrizing granuloma injected 10 years prior to presentation. This case report details the importance of a thorough history as cosmetic procedures become more commonplace.

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.