

# Botulinum Neurotoxins and Injectable Fillers: Minimally Invasive Management of the Aging Upper Face

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For decades, the only available “off-the-shelf” injectable fillers available were Zyplast and Zyderm. Their impact on the upper face was relatively limited, primarily to the glabellar region. The thin-skinned regions of the periorbital and dynamic regions of the upper face also limited the durability of the product. The last few years have brought several new injectable soft tissue fillers to the market in the United States and a renewed interest in the use of autologous fat. These are being used not only as simple line fillers, but as volume replacement materials, and have provided new perspectives in the management of the aging face.

This article reviews the current injectable agents and techniques used in the management of the aging face and provide current concepts for their application.

## Botulinum neurotoxin

First used by Dr. Allen Scott of San Francisco in the 1980s, botulinum neurotoxin (BTX) showed promise in laboratory chick models for selective weakening of treated muscles and soon thereafter was used in the management of strabismus [1]. Under the trade name, Oculinum, this product was picked up by Allergan Inc (Irvine, CA), primarily an ophthalmic pharmaceutical company, for this and other neuromuscular disorders around the eye.

Botulinum toxin is found in nature in seven serotypes (A through G) defined by their specific biologic action in cleaving the particular proteins

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in the active transport of acetylcholine into the neurosynaptic cleft responsible for muscle contraction (and other autonomic functions) [2,3]. These naturally occurring proteins were described originally as toxins caused by the illness botulism, which is associated with ingestion of large amounts of *Clostridium botulinum*-contaminated food stuffs. They are better described, with respect to their now widespread medical use, as *neuromodulators*. Their distinct beneficial action is selective weakening, relaxation, or paralysis of treated muscles or muscle groups. By selective weakening of certain hypertrophic muscle groups in the face and neck, unwanted lines and facial expressions can be suppressed or even eliminated.

Although the B serotype (Myobloc; Solstice Neurosciences, San Francisco, CA) neuromodulator has shown benefit in the treatment of hyperfunctional frown lines, its benefit under current formulations is limited by the shorter duration of effect of the product [4,5]. This leaves the aesthetic practitioner with the A neurotoxin.

The A serotype has shown the longest duration of effect (90 to 120 days) and least discomfort with injection. The “Coca-Cola” of the available A serotype neuromodulators is Botox (Allergan, Inc). The techniques and dosages described herein are in reference to the use of this medicinally original botulinum neuromodulator, which now has a demonstrated safety and efficacy record of more than 15 years.

Reloxin (Inamed Inc, Santa Barbara, CA), known as *Dysport* in Europe, is in current phase III US Food and Drug Administration (FDA) clinical trials and shows promise as does Purtox (Mentor Corp, Santa Barbara CA), which is in early-phase FDA trials.

An understanding of how to use BTX relies on a clear understanding of the facial muscular anatomy (Fig. 1).

Although many techniques and surface points of injection have proven effective, it is clear that optimal response with minimal effective dosages requires precise placement in the selected muscle or muscle group.

The author has shown the upper facial anatomy in controlled large population anatomic studies [6]. The interest in lower facial applications reinforces the need for a fundamental understanding of this muscular anatomy [7]. It is clear, however, that because of diffusion effects and the relative safety of BTX, the variability in points of injection and dosages has not significantly reduced the product's overall satisfactory clinical results. In the author's opinion, required dosages for a given anatomic area can be reduced by precise localization and direct injection into the targeted muscle or muscle groups. Diffusion is helpful for those who lack a solid understanding of muscle location and general anatomy. In some cases, this has been perpetuated by inaccurate published anatomic drawings.

It is imperative to keep in mind not only the specific muscle locations when providing neuromodulator treatment, but also the functional interrelationships of the muscle action. Many of these act as antagonist-protagonists in the position of the brow (see Fig. 1). The use of BTX in general

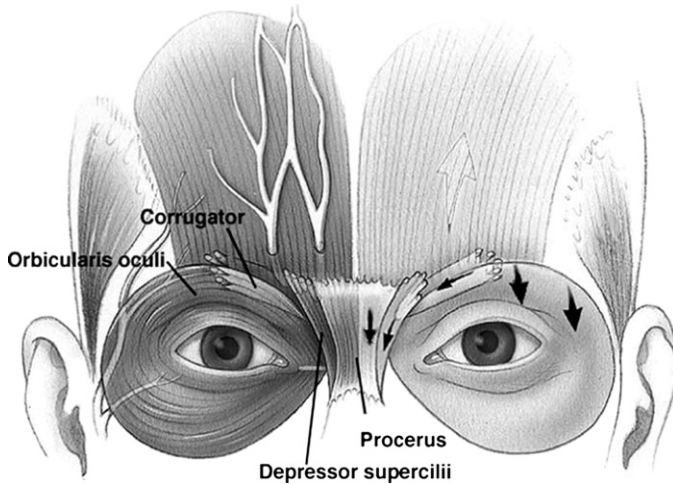


Fig. 1. Facial muscular anatomy.

has evolved with experienced and thoughtful injectors from a simple wrinkle treatment to means of reshaping, contouring, and softening the facial features associated with aging and the stigmata of the frowning, angry, or worried facial form.

### The glabellar complex

Furrows created at the base of the nose (radix) are created by the procerus muscle, which is statistically larger in women than men. Although this muscle has limited action as a brow depressor, it is a powerful “wrinkler” of the nose, which, with chronic activity, creates deep furrows. Many patients seeking treatment for vertical glabellar furrows have very limited procerus activity and do not require concurrent treatment. Not all patients are the same; thus, treatment formulas that are universal are wasteful and unnecessary. Three to five units placed in one or two aliquots in the area of radix are sufficient for most patients to achieve a satisfactory reduction in procerus activity (see Fig. 1).

The corrugator supercillii and its accompanying depressor orbicularis oculi muscle are clinically indistinguishable. Their anatomy is poorly understood as it relates to that position. In contrast to many schematic or figurative diagrams showing the tail (or insertion) of the corrugator muscle one centimeter above the brow, the corrugator in the majority of patients follows the course of the eyebrow and delicately interdigitates with the orbicularis oculi muscle laterally and the frontalis muscle superiorly. Thus, injections well above the midpupillary brow are of little value in targeting corrugator function and primarily disable lower portions of frontalis muscle. Such injections would be expected to result in medial brow ptosis.

Proper targeting requires the bulk of dosing for the corrugator at the clubhead of the eyebrow. At the author's institution, we use a minimum of 7.5 units in this area and 2.5 units in the scant muscle of the lateral brow to address "recruitment" of this lateral portion and some of the horizontally oriented orbicularis. These injections are directed at or slightly (within 1 or 2 mm) above the level of the eyebrow as the musculature descends with the aging ptotic brow (Fig. 2).

### *The lateral orbital region*

The orbicularis oculi (O.o.) muscle and the "crow's feet" are also seemingly poorly understood. Although primary emphasis is focused by many on the softening of lines in this area, the lateral O.o. is the most powerful depressor of the brow and, as such, has the greatest potential with neuromodulation to reshape the upper face. The emphasis on lateral orbicularis muscle is paramount because the muscle is a sphincter, and its superior and inferior portions create vectors of force that are in the horizontal plane. Treating these regions provides for softening vertically oriented supraorbital lines and "crepey" lines in the infraorbital region. Contrary to popular belief, in the author's opinion, the treatment of these areas has limited impact on horizontal brow position.

Treatment strategies, therefore, are stratified (although not mutually exclusive) around treatment of hypertrophic lines and reshaping the brow. Although single-point limited dosing at the lateral brow margin may provide some benefit in elevating brow position, it is advisable to keep in mind the entire lateral O.o. is responsible for brow depression, and, as shown in

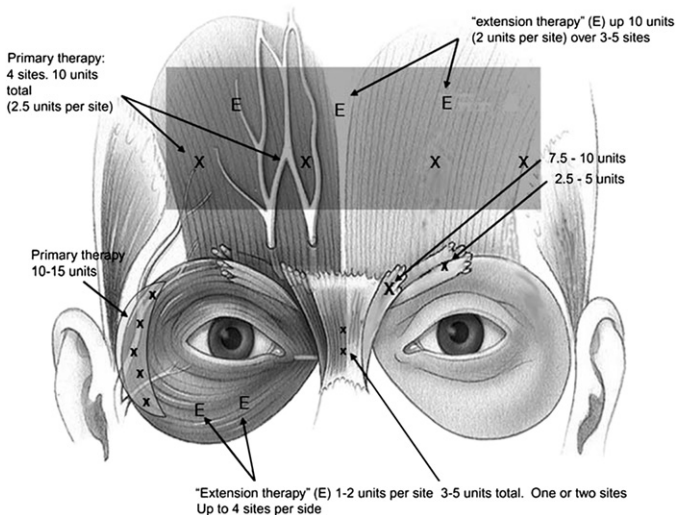


Fig. 2. Proper targeting for injections for the corrugator.

the author's previous work [8,9] treatment of this large and powerful depressor can have a profound impact on brow position. In contrast, the supra and infraorbital lines of expression can be substantively affected by small doses in these regions. Concerns about effects on extraocular movements and the elevators of the lip have not proven problematic in our experience in which lower eyelid injections are targeted outside the orbital rim and in the immediate subcutaneous plane.

Starting doses for the lateral orbital region are in the range of 10 units per side and can go quite comfortably as high as 20 units per side, in our experience, without impact on sphincteric function. Small 2.5-unit aliquots are placed at roughly 1-cm intervals in a "half-moon" configuration from the infralateral brow to the inferior extent of horizontally oriented lines (see Fig. 2). Extension for the crepey skin in the infraorbital region is easily done up to the area of the nasojugal groove.

### *The forehead*

The forehead is probably the most variably and poorly treated region of the upper face with neuromodulators. Injectors must balance the benefit of hyperfunctional line improvement with relaxation of the only brow elevator, the frontalis, and attendant ptosis of the brow that will occur. Dosages exceeding 20 units in the forehead are rarely warranted, in the author's opinion, because the trade of complete line effacement is not worth the side effect of noticeable brow ptosis.

In addition, many strategies for treating the forehead region leave lateral frontalis muscle action unattenuated, resulting in a "Dr. Spock-like" forehead deformity (Fig. 3) that is both a hallmark of treatment and unattractive. The key to success in forehead treatment is modest dosing (enough to soften the lines with minimal impact on brow position) and uniform distribution of injections to avoid asymmetries and an artificial appearance of brow position.

Typical starting doses are around 5 units per side in four or five 2.0- to 2.5-unit aliquots (see Fig. 2). Extension areas (E) may also be treated with similar dosing strategies deposited just through the galea aponeurosis.



Fig. 3. BTX brow deformity.

This layer can be “felt” as a gentle pop of the needle with insertion and is well above the frontal periosteum.

### *Soft tissue fillers*

Historically, soft tissue fillers, namely Zyderm (Inamed Corp), were the only available injectable agents for management of the aging face. This legacy has been supplanted by the use of BTX. There is still a role for the use of these materials in upper facial rejuvenation.

Although the list of fillers has grown dramatically over the last decade, their limited use in the upper third of the face limits the necessity for detailed description on all available fillers and their use. However, there remain shortcomings to the use of BTX alone in the upper face, namely, the inability to correct dermal resting lines, particularly deeper lines and those in older patients.

The predominant use of fillers in upper portions of the face is in the management of fine dermal lines, commonly in combination with BTX. Historically, Zyplast and, predominately, Zyderm were used to treat “crow’s feet,” horizontal forehead lines, and glabellar lines. The effectiveness of BTX in management of these regions has limited the use of fillers to deep dermal lines in the glabellar area refractory to the muscle atony induced by BTX. Although Zyderm is still used for this indication (Zyplast is contraindicated because of occlusion-related necrosis), Cosmoderm and Restylane (and to a lesser extent Hylaform and Captique) are more commonly used, because prior skin testing is not required.

The 2 techniques used for intradermal treatment of glabellar or other facial lines are linear threading and serial puncture techniques. Serial puncture is clearly the better choice for Cosmoderm, creating a wheal of product in the mid- to upper dermis that effaces lines (Fig. 4). This technique remains the author’s primary therapy for soft tissue filling in the upper face.

Restylane is more challenging to place correctly in the glabellar lines, or any fine line, because of its viscosity. Many providers place Restylane in the subcutaneous tissues, knowingly or unknowingly, where it may have long-term (approximately 6 months) benefit in volume restoration. This deep placement can provide long-term benefit for the patient, although it is not the optimal treatment for fine or dermal lines in the upper face. Proper placement for such lines will assure the best outcomes, and this can be quite challenging. Using a 30-gauge or 31-gauge needle, a combination of serial point and linear threading techniques are used. The difficulty with linear threading is remaining at uniform levels of dermis while passing a needle parallel to the skin surface. This technique seems to be the cause in most cases of the irregular blue-hued (Tindle effect) bumps on the skin surface that result from placement that is too superficial.

Intriguing work has been done in volume enhancement in and around the brows using fat and other longer-term fillers that generate the appearance of

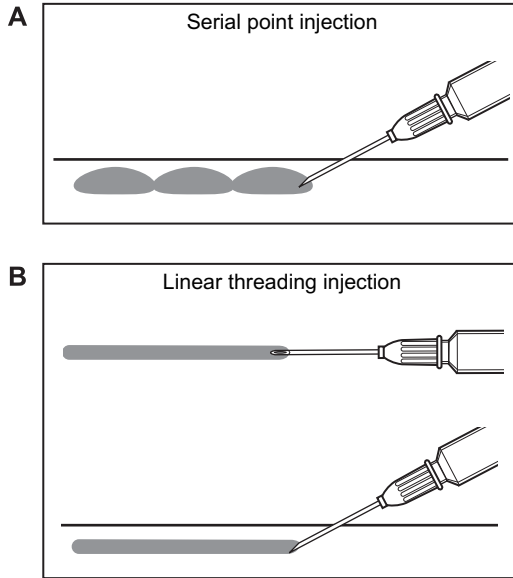


Fig. 4. (A, B) Injection techniques.

brow elevation and theoretically “replace lost volume” [10]. In addition, general volume loss associated with aging in the temporal region is evident in a subset of patients. In these patients, longer-term fillers such as autologous fat, hyaluronic acid and calcium hydroxyapatite, polylactic acid, and synthetic gel microparticulate products such as silicone are being used. For this application, most products are placed using a “cross-hatching” or “fanning” technique.

Radiesse (calcium hydroxyapatite) may be the most intriguing of the list. It had been proven in recent trials (Steve Basta, CEO, Bioform Inc. Palo Alto, CA, personal communication) to be preferred over an hyaluronic acid (HA) control in its subcutaneous placement in the nasolabial fold. It has, generally, 6 to 12 months’ duration. Radiesse is rarely any longer used in lips because of visible and palpable nodularity. However, in deeper soft tissue applications this has not been seen as a significant side effect.

Restylane and other HA fillers offer reasonable choices for volume restoration because they have a soft consistency, are reliable, and have a very good safety record. Their 6-month duration is suitable for many patients.

Sculptra is made of polylactic acid, a powder similar to Vicryl suture material, and has gained FDA clearance for marketing in HIV facial wasting. Temporal wasting is clearly evident in the temporal area of many HIV patients. Proper dilutions (now recommended at 6 mL of sterile water and left to stand overnight) are apparently helping diminish the high rate of needle and the nodularity that can be caused by bolus injection. The off-label use of this product for facial aging has also been described.

The author avoids the use of any permanent synthetic injectable filler. Early and late-term granulomas, draining fistulas, and severe reactions can occur with some frequency when using these products in other than the smallest amounts. These complications require wide local tissue resection as the only long-term solution. These are not acceptable risks for largely cosmetic indications.

## Summary

The advent of neuromodulation, injectable fillers, and other minimally invasive techniques has changed the treatment paradigm for upper facial aging. Although the products and technologies for these treatments are evolving rapidly, it is advisable to use conservative approaches. At the author's institution, we usually begin with BTX for our patients and add fillers for volume and line enhancement as rapport and needs are established with the patient.

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