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# ABOUT FACE: Navigating Neuromodulators and Injection Techniques for Optimal Results

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# ABOUT FACE: Navigating Neuromodulators and Injection Techniques for Optimal Results

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## Faculty Credentials

**Steve G. Yoelin, MD (Chair)**
Ophthalmologist
Steve Yoelin, MD, Medical Associates
Newport Beach, California

**Shino Bay Aguilera, DO, FAAD**
Medical Director
Shino Bay Cosmetic Dermatology and Laser Institute
Fort Lauderdale, Florida

**Joel L. Cohen, MD**
Director, AboutSkin Dermatology and DermSurgery
Director, AboutSkin Research
Greenwood Village and Lone Tree, Colorado
Associate Clinical Professor
University of California, Irvine
Irvine, California

**Michael H. Gold, MD, FAAD**
Medical Director
Gold Skin Care Center
Tennessee Clinical Research Center
Nashville, Tennessee

**Joely Kaufman, MD, FAAD**
Medical Director
Skin Associates of South Florida
Associate Professor of Dermatology
University of Miami Miller School of Medicine
Coral Gables, Florida

**Corey S. Maas, MD, FACS**
The Maas Clinic Facial Plastic and Aesthetic Surgery
San Francisco and Lake Tahoe, California
Associate Clinical Professor
University of California, San Francisco
San Francisco, California

## Statement of Need

This activity provides a review of the properties and aesthetic uses of currently available neuromodulators (botulinum neurotoxin type A products) through a review of the literature, real-world cases, and expert clinical perspectives. The desired results of this activity are for health care practitioners to improve their ability to provide neuromodulators appropriately to their patients for optimal patient outcomes.

## Educational Objectives

Upon completion of this activity, participants will be better able to:

- Explain the conversion ratios needed for individual neuromodulators based on clinical practice
- Use appropriate reconstitution procedures for the different neuromodulators
- Explain how to switch between neuromodulators to achieve optimal clinical outcomes
- Employ appropriate strategies for the management of complications to improve patient satisfaction
- Illustrate the most appropriate injection strategies for a variety of patients treated with neuromodulators
- Describe the anatomy of the face and neck that is relevant to ensure safe and effective treatment outcomes

## Target Audience

This educational activity is intended for health care practitioners, including physicians, physician assistants, nurses, and nurse practitioners, with an interest in facial aesthetics.

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*Consultant*: Allergan; Dermira, Inc; Galderma Laboratories, LP; Merz, Inc; and SkinCeuticals

**Joel L. Cohen, MD**
*Consultant:* Allergan; Biofrontera, AG; Biopelle, Inc; Endo Pharmaceuticals Inc; Evolus, Inc; Galderma Laboratories, LP; Lutronic; Merz, Inc; Revance Therapeutics, Inc; Sciton, Inc; SENTÉ Inc; Sonoma Pharmaceuticals, Inc; and Swiss-American CDMO, LLC
*Speaker:* Galderma Laboratories, LP; and Sciton, Inc
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**Michael H. Gold, MD**
*Consultant:* Aclaris Therapeutics, Inc; Aerolase Corp; ALASTIN Skincare, Inc; Allergan; Alma Lasers; Almirall, SA; Aquavitpharma; Bayer Corporation; Biofrontera AG; Brickell Biotech, Inc; Candela Corporation; Celgene Corporation; Clarisonic; Croma-Pharma GmbH; Cutanea Life Sciences, Inc; Dermata Therapeutics, LLC; Dermira, Inc; DUSA Pharmaceuticals, Inc; EndyMed Medical; Erchonia Corporation; Essence Novel; Exeltis; Galderma Laboratories, LP; Invasix; Johnson & Johnson Services, Inc; Joylux, Inc; Kadmon Holdings, Inc; L'Oréal; Lumenis; Merz, Inc; MTF Biologics; Novartis Pharmaceuticals Corporation; Pierre Fabre; Progenitor Biologics, LLC; Prollenium Medical Technologies; Promius Pharma, LLC; Revision Skincare; Sensus Healthcare; SENTÉ Inc; Sinclair Pharma; SkinCeuticals; Sonoma Pharmaceuticals, Inc; Stratpharma AG; Sun Pharmaceutical Industries Ltd; Suneva Medical, Inc; ThermiGen, LLC; Valeant; Viviscal Limited; XBiotech; and Zimmer Aesthetics
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**Joely Kaufman, MD**
*Speaker:* Allergan; and Galderma Laboratories, LP
*Contracted Research:* Allergan; Croma-Pharma GmbH; Cutera; Endo Pharmaceuticals Inc; Evolus, Inc; Galderma Laboratories, LP; Merz, Inc; and Revance Therapeutics, Inc

**Corey S. Maas, MD**
*Consultant:* Allergan; Galderma Laboratories, LP; and Merz, Inc
*Speaker:* Allergan; Galderma Laboratories, LP; Merz, Inc; and Valeant
*Advisory Board:* Allergan; Evolus, Inc; Galderma Laboratories, LP; and Merz, Inc
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**Steve G. Yoelin, MD**
*Consultant:* Allergan; and Evolus, Inc
*Speaker:* Allergan
*Contracted Research:* Allergan; Merz, Inc; and Revance Therapeutics, Inc

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 ORIGINAL ARTICLE Journal of Drugs in Dermatology

# About Face: Navigating Neuromodulators and Injection Techniques for Optimal Results

Steve G. Yoelin MD,[a] Shino Bay Aguilera DO FAAD,[b] Joel L. Cohen MD,[c] Michael H. Gold MD FAAD,[d] Joely Kaufman MD FAAD,[e] Corey S. Maas MD FACS[f]

[a]Steve Yoelin, MD, Medical Associates, Newport Beach, CA
[b]Shino Bay Cosmetic Dermatology and Laser Institute, Fort Lauderdale, FL
[c]AboutSkin Dermatology and DermSurgery, AboutSkin Research, Greenwood Village and Lone Tree, CO; University of California, Irvine, Irvine, CA
[d]Gold Skin Care Center, Tennessee Clinical Research Center, Nashville, TN
[e]Skin Associates of South Florida; University of Miami Miller School of Medicine, Coral Gables, FL
[f]The Maas Clinic Facial Plastic and Aesthetic Surgery, San Francisco and Lake Tahoe, CA; University of California, San Francisco, San Francisco, CA

## ABSTRACT

Interest in the cosmetic use of neuromodulators for facial rejuvenation is increasing among physicians, other practitioners, and patients alike, and an expanding array of formulations and reported applications might be helping to drive this trend. Safety, efficacy, and a high level of patient satisfaction can be achieved with all the available botulinum neurotoxin type A (BTXA) products. With any of the formulations, optimal results require knowledge of the individual product's unique properties and dosing, along with an understanding of the patient's goals, relevant anatomy, and proper injection technique. This educational activity reviews these topics on the basis of the published literature and expert opinion. A series of case narratives is also included that provides readers with information and insights for achieving success in clinical practice.

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## INTRODUCTION

### Botulinum Neurotoxin Type A Composition

Four BTXA products are commercially available in the United States with approval for cosmetic use, but they vary in their approved indications **(Table 1)**.[1-6] Listed in order of date of first approval for cosmetic use are the products onabotulinumtoxinA (onaBTXA), abobotulinumtoxinA (aboBTXA), incobotulinumtoxinA (incoBTXA), and prabotulinumtoxinA-xvfs (praBTXA).

The BTXA products are all derived from *Clostridium botulinum* type A, which produces a protein complex containing the core neurotoxin, BTXA, with ≥ 1 nontoxic accessory (or neurotoxin-associated) protein (NAP).[7,8] The core neurotoxin has a molecular weight of approximately 150 kDa and is responsible for the therapeutic action of the BTXA product. The total molecular weight of the available BTXA products varies given differences in NAP content. NAPs can be removed during the manufacturing process and are absent in incoBTXA.[5] Although NAPs are present in the other BTXA products, they dissociate from the core protein when saline is added to the vial for reconstitution.[9] NAPs are believed to protect the core protein against harsh environments such as the gut and intestinal tract, and they aid in the movement of BTXA across epithelial barriers.[10] Whether NAPs have an effect on clinical outcomes is still unknown and quite controversial.

### Conversion Ratios/Dose Equivalence

In real-world practice, clinicians might vary their injection of each BTXA product, as well as among BTXA products, at different anatomic sites to achieve optimal results for individual patients. The potency units of the different BTXA products are not interchangeable.[2,11] The potency of each product is determined using the manufacturer's proprietary assay and reference standard. Therefore, potency units are specific to each product.[2,11] Because the potencies of BTXA products cannot be directly compared, there are no universally accepted conversion ratios for making dose-equivalence comparisons among products.[2] Published reports suggest that the conversion ratio for aboBTXA:onaBTXA is between 2:1 and 3:1 and that for incoBTXA:onaBTXA is between 1:1 and 1.25:1; these ratios are frequently used in clinical practice.[11-15]

**TABLE 1.**

**BTXA Products With Cosmetic Indications**

| | OnaBTXA[1,2] | AboBTXA[3,4] | IncoBTXA[2,5] | PraBTXA[6] |
|---|---|---|---|---|
| Year of FDA approval | 2002* | 2009 | 2010 | 2019 |
| Active substance (molecular weight) | BTXA + NAPs (900 kDa) | BTXA + NAPs (500-900 kDa) | BTXA (150 kDa) | BTXA + NAPs (900 kDa) |
| Excipients | HSA, NaCl | HSA, lactose | HSA, sucrose | HSA, NaCl |
| Units per vial | 50 or 100 | 300 or 500 | 50 or 100 | 100 |
| Approved indications for cosmetic use† | Temporary improvement in the appearance of moderate-to-severe glabellar lines, moderate-to-severe lateral canthal lines, and moderate-to-severe forehead lines | Temporary improvement in the appearance of moderate-to-severe glabellar lines in adults aged < 65 years | Temporary improvement in the appearance of moderate-to-severe glabellar lines | Temporary improvement in the appearance of moderate-to-severe glabellar lines in adult patients |

Abbreviations: aboBTXA, abobotulinumtoxinA; BTXA, botulinum neurotoxin type A; FDA, US Food and Drug Administration; HSA, human serum albumin; incoBTXA, incobotulinumtoxinA; NAP, neurotoxin-associated protein; onaBTXA, onabotulinumtoxinA; praBTXA, prabotulinumtoxinA-xvfs.
*Year of approval for cosmetic use
†AboBTXA, incoBTXA, and onaBTXA have both cosmetic and medical indications

## DISCUSSION

**Dr Yoelin:** What conversion ratios do you use for switching among the BTXA products?

**Dr Gold:** I was an investigator in the US Food and Drug Administration clinical trials for incoBTXA and aboBTXA and have always used the ratios of 1:1 for incoBTXA:onaBTXA and 2.5:1 for aboBTXA:onaBTXA that were used to determine dosing for aboBTXA and incoBTXA in the clinical trials.

The 1:1 ratio for incoBTXA:onaBTXA is supported by the results of a multicenter, randomized, blinded clinical trial in which I participated.[16] In this 4-month trial, we compared the 2 neuromodulators for treating glabellar frown lines. We used a 20-U dose of both products and found they had similar efficacy at 1 month, which was the primary end point, and at subsequent monthly follow-up visits.

**Dr Kaufman:** I use a conversion ratio of between 2:1 and 3:1 for aboBTXA:onaBTXA and 1.5:1 for incoBTXA:onaBTXA.

**Dr Aguilera:** My conversion ratios are the same as Dr Kaufman's.

**Dr Maas:** I use a conversion ratio of 3:1 for aboBTXA:onaBTXA and 1.2:1 or 1.25:1 for incoBTXA:onaBTXA. I think it is important to emphasize that although the use of these conversion ratios results in a higher dose of incoBTXA or aboBTXA than onaBTXA, the difference in total dose does not mean that incoBTXA or aboBTXA is weaker or less effective than onaBTXA.

## RECONSTITUTION

**Table 2** lists the recommended diluent volumes for BTXA product reconstitution.[1,3,5,6,17,18] **Table 3** lists reconstitution

**TABLE 2.**

**Recommended Reconstitution Methods for BTXA Products**

| | Units per Vial | Diluent, mL | Concentration |
|---|---|---|---|
| OnaBTXA[1,17] | 100 | 2.5 | 4 U/0.1 mL |
| AboBTXA[3,18] | 300 | 1.5 | 10 U/0.05 mL |
| | | 2.5 | 10 U/0.08 mL |
| IncoBTXA[5] | 100 | 2.5 | 4 U/0.1 mL |
| PraBTXA[6] | 100 | 2.5 | 4 U/0.1 mL |

Abbreviations: aboBTXA, abobotulinumtoxinA; BTXA, botulinum neurotoxin type A; incoBTXA, incobotulinumtoxinA; onaBTXA, onabotulinumtoxinA; praBTXA, prabotulinumtoxinA-xvfs.

**TABLE 3.**

| Reconstitution Methods for BTXA Doses per 0.1 mL | | | |
|---|---|---|---|
| | Units per Vial | Diluent, mL | Dose per 0.1 mL, U |
| OnaBTXA[1,17] | 100 | 2.5 | 4 |
| AboBTXA[3,18] | 300 | 3.0 | 10 |
| IncoBTXA[5] | 100 | 2.5 | 4 |
| PraBTXA[6] | 100 | 2.5 | 4 |

Abbreviations: aboBTXA, abobotulinumtoxinA; BTXA, botulinum neurotoxin type A; incoBTXA, incobotulinumtoxinA; onaBTXA, onabotulinumtoxinA; praBTXA, prabotulinumtoxinA-xvfs.

methods that achieve doses based on conversion ratios of 2.5:1 for onaBTXA:aboBTXA and 1:1 for onaBTXA:incoBTXA per 0.1 mL in a volume of 0.1 mL.[1,3,5,6,17,18]

As clinicians gain experience using the various BTXA products for both on- and off-label indications, they can refine their approaches for reconstitution. In addition, reconstitution methods could change, depending on a variety of factors, including injection sites, treatment goals, patient-specific characteristics (eg, previous response), and clinician experience. For example, when wanting to create a global relaxation effect, clinicians might choose to inject a higher total volume. Therefore, they are adding a higher volume of diluent to create a less concentrated solution. In contrast, when precise control of the affected area is particularly critical, less diluent would be added for reconstitution to produce a more concentrated solution that would deliver the total dose in a smaller volume.

Sterile preservative-free, 0.9%, normal saline is the recommended diluent for reconstitution of all BTXA products according to manufacturers' directions.[1,3,5,6] However, off-label use of bacteriostatic saline for reconstitution improves comfort with injection and can then enhance overall patient satisfaction.[19]

## DISCUSSION

**Dr Yoelin:** What are your approaches and recommendations regarding reconstitution?

**Dr Cohen:** During my fellowship, Alastair Carruthers, MD, used to always say, "Dilution is for the convenience of the injector, whereas dose determines efficacy for the patient." I think this concept holds true, specifically when injecting small muscle groups such as the glabellar complex. This is supported by the results of glabellar studies in which I participated. In one study, we reconstituted 300 U of aboBTXA with a volume of 1.5 or 2.5 mL of saline and treated patients with a total dose of 50 U.[20] In an earlier study, we injected 20 U of onaBTXA and compared results when the 100-U vial was reconstituted with 1, 3, 5, or 10 mL of saline.[21] Efficacy was the same in each study, regardless of BTXA concentration when the dose was kept constant.[20,21]

With convenience in mind, I use 1 mL of preserved saline to reconstitute a 300-U vial of aboBTXA. This approach results in a final concentration of 30 U/0.1 mL, which makes calculating the injection volume very easy with any given dose. When injecting larger muscle areas, such as the frontalis or platysma (and for hyperhidrosis), I double the reconstitution volume for all the neuromodulators I use in my practice.

**Dr Aguilera:** I choose my diluent volume for each product so that the total injection volume for a specific indication will be the same regardless of the product used. When reconstituting onaBTXA and incoBTXA, I add 2.0 mL of diluent to a 100-U vial. For aboBTXA, I add 2.5 mL to a 300-U vial. This approach eliminates performing mathematical calculations each time to determine volume.

**Dr Kaufman:** I usually add 2.0 mL of diluent to the 100-U onaBTXA vial and 300-U aboBTX vial and 1.5 or 1.6 mL of diluent to the 100-U incoBTXA vial. For varying reasons for certain procedures, however, I will double the diluent volume to create a less concentrated solution. For example, to avoid an unnatural-looking result, I might inject a hyperdiluted toxin into a very large forehead to achieve an even distribution of the drug without completely paralyzing the muscle.

For new users, I recommend using the same volume of diluent for whatever product they are using because that will help mitigate confusion and avoid potential dosing errors when using different products.

**Dr Yoelin:** What is your advice to clinicians about choosing or switching among the BTXA products?

**Dr Gold:** I recommend focusing on the use of one product—it could be any of the 4 that are available—and then developing expertise with that one BTXA before adopting another product.

**Dr Cohen:** I agree that it is easier to start using just one product or perhaps 2. In reality, we now have 4 good products that are more similar than they are different.

**Dr Maas:** I also think it is best for new users to stick to one product. Speaking as someone who has experience with all these products, however, I encourage clinicians to begin trying other BTXA products once they feel they have reached a comfort level because some patients respond differently to different products.

## ABOUT CASE 1

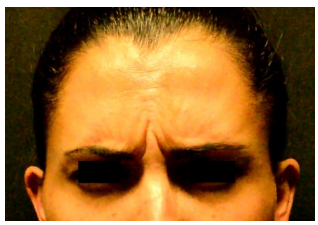
**Treatment of Glabellar Lines**
***From the Files of Joely Kaufman, MD, FAAD***

*A 41-year-old white female presented complaining about lines between her brows that she believed made her look tired. Evaluation with animation showed depression of the medial brow, which was greater on the right side than on the left, and a U pattern of glabellar contraction, with minimal recruitment of the lateral corrugator* ***(Figure 1A)****.*

*A 100-U vial of praBTXA was reconstituted with 2.0 mL of bacteriostatic saline. Using a 32G needle, a total of 25 U was injected at 5 sites: 7.5 U into each medial corrugator, 5 U into the procerus, and 2.5 U into the midfrontalis on each side* ***(Figure 1B)****. Alternative treatments (total dose administered) would be 75 U of aboBTXA, 32.5 U of incoBTXA, and 25 U of onaBTXA. When the patient returned 10 days postinjection, her glabellar lines were effaced and she had lifting of her medial brows, which helped to open up the eyes so that she looked less tired* ***(Figure 1C)****.*

**FIGURE 1.** Before (1A [at maximum frown] and 1B) and after (1C) photographs of the patient described in Case 1. The units of prabotulinumtoxinA-xvfs injected are indicated in the legend.

(1A)



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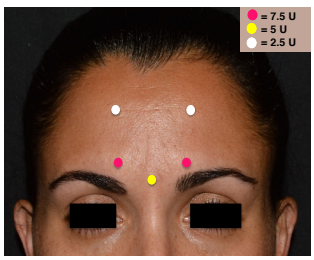
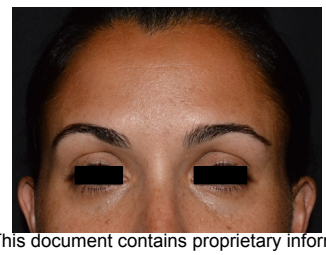



(1C)



## Discussion

**Dr Kaufman:** The patient in this case is relatively young, and her glabellar lines are subtle. Early treatment with BTXA can be very effective for eliminating these lines. BTXA might also help prevent them from becoming deeper and ingrained over time.

In this patient, a 3-point injection technique was used, along with 2 midfrontalis injections to lift the medial brow. I find that aboBTXA might have a larger field of action than the other products, which would make aboBTXA particularly useful for a 3-point injection technique. When I see a patient with little or no use of the lateral portion of the corrugator muscle, I use a 3-point glabellar injection instead of a 5-point injection. This usually keeps the midline arch of the brow intact.

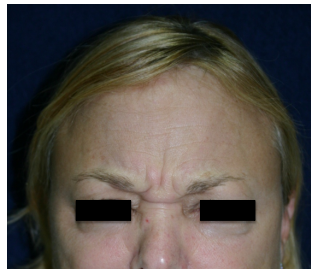
A 5-point injection pattern for treating glabellar lines with equal doses distributed across all sites is recommended by all BTXA manufacturers. This one-size-fits-all approach, however, does not account for interindividual variation in the use of upper face muscles to contract the glabella.

Five different glabellar contraction patterns have been described: converging arrows **(Figure 2A)**, U **(Figure 2B)**, V, omega, and inverted omega **(Figure 2C)**.[22,23] Individualizing the injection technique on the basis of the contraction pattern will optimize results.

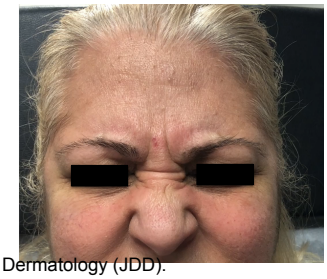
**FIGURE 2.** Examples of glabellar contraction patterns: converging (2A), U (2B), and inverted omega (2C).

(2A)

(2B)



(2C)



For example, the converging arrows pattern, which was reported to be most common in Asian patients, creates more of a flat frown, without brow depression or elevation.[23] A 5-point injection technique using a lower BTXA dose at the 2 lateral corrugator sites might work well for patients with this pattern.

With the U pattern, there is medial brow depression, which is caused by corrugator contraction. I find that patients with this pattern have a short corrugator muscle and require little or even no injection into the distal/lateral end of the corrugator. Injecting BTXA at 3 sites concentrated in the center would probably lift the medial brow.

The inverted-omega pattern has a deep nasal root crease as a distinguishing feature. Treatment of patients with this pattern would include a standard 5-point injection plus a nasalis injection to address the deep nasal crease, thereby resulting in a 7-point injection pattern.

**Dr Yoelin:** Achieving the best results for each patient requires individualizing the approach to BTXA injection. In addition, assessing individuals on animation is critical because this will guide injection placement. Lastly, the doses used take into account muscle mass or strength.

**Dr Cohen:** Data from cadaveric studies show that the medial corrugator is much thicker than the lateral corrugator.[24] This information argues against injecting equal doses medially and laterally into the corrugators when treating glabellar lines.

**Dr Gold:** The informed consent that patients sign should mention all possible complications because health care practitioners who perform enough BTXA injections can expect to encounter every potential complication at some time. Bruising is the most common complication after a BTXA injection, and it can be persistent. Treating bruising with energy-based devices, including ultrashort-pulse Nd:Yag (neodymium-doped yttrium aluminum garnet) lasers and pulsed-dye lasers, has been widely accepted as an option to make posttoxin bruising diminish faster than time alone.[25] I use a short-pulsed 1064-nm laser to reduce postbruising time, and have observed nice results in my patients.

**Dr Yoelin:** I try to use a 33G needle for my injections because I think the thinner needle reduces the risk for bruising.

**Dr Cohen:** Eyelid ptosis is an uncommon complication after treatment of glabellar lines. It is thought to result from BTXA diffusion from the lateral corrugator injection site through the orbital septum to the levator palpebrae superioris, which elevates the upper lid. The ptosis typically appears 3 to 7 days postinjection, lasting 2 to 4 weeks.[26]

Eyelid ptosis can be managed with an ophthalmic alpha-adrenergic agonist drop to contract the Müller muscle.[27,28] Products are available over the counter (naphazoline) or by prescription (apraclonidine). The prescription medication can be more effective, but not all pharmacies stock it. Having a supply of the over-the-counter drop in the office provides a convenience for patients who might need treatment for eyelid ptosis.

Avoiding BTXA injections below the orbital septum or at or under the midbrow can help minimize the risk for eyelid ptosis. Care should be taken if there is concern about integrity of the orbital septum in older patients, those with a history of lid surgery or traumatic injury, and patients who experienced lid ptosis after previous BTXA treatment.

Brow ptosis can also occur. Preventive measures include being conservative in frontalis dosing when treating older patients and avoiding treatment of the frontalis altogether in patients with more advanced degrees of dermatochalasis (brow-lid redundancy, in which the lid is literally touching the lashes at baseline). Another instance is in those with prior brow ptosis who have experienced neuromodulator therapy.

With descent of the medial brow and lifting of the lateral brow, a "Spock-like", Mephisto, or devil-like appearance might also occur, especially when using the standard 5-point injection in men, who tend to have strong frontalis muscles. The problem could be prevented by treating these men with a 7-point injection technique that includes lateral frontalis injections. Undesired or excessive lateral-brow lift can be corrected by injecting a small dose of BTXA (eg, ≤ 1 U of onaBTXA) into the lateral frontalis.

Widening of the interbrow distance is another possible complication of corrugator muscle weakening after glabellar-line treatment. There is no known therapy for this problem, and its potential should be discussed with patients, particularly those who already have wide spacing between their eyebrows.

To minimize the risk of potential unwanted migration of neuromodulators, which can lead to complications such as eyelid ptosis, I instruct patients to avoid yoga or other activities in which they would invert the head during the first couple of hours after their injection.

**Dr Yoelin:** When recommending an alpha-adrenergic agonist to treat lid ptosis, I tell patients to put a drop of the medication in the affected eye(s), gently close the lids, and keep them closed for approximately 15 seconds without blinking. This promotes contact of the medication with the Müller muscle and minimizes drainage through the lacrimal duct, which can

lead to systemic absorption and side effects. The treatment does not accelerate ptosis resolution, and the benefit is only temporary. I tell patients that they can use the drop once every 3 to 4 hours as needed while they are awake if they are concerned about their appearance in public. This is in line with the reported dosing regimen of 1 to 2 drops 3 times a day.[27] I do not consider development of lid ptosis to be an absolute contraindication to future BTXA injections. In patients with this history, though, I will use a lower dose in the lateral corrugator and perhaps inject with a threading technique.

## ABOUT CASE 2

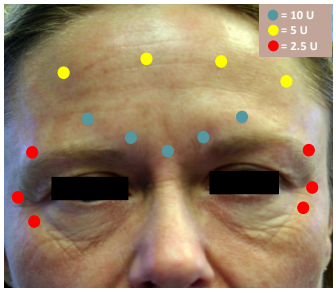
**Rejuvenating the Upper Face**
***From the Files of Michael H. Gold, MD, FAAD***

*A 60-year-old white female wanted treatment for her glabellar, forehead, and lateral canthal lines. The patient stated that she was interested only in a BTXA injection and did not desire treatment with any energy-based devices or fillers.*

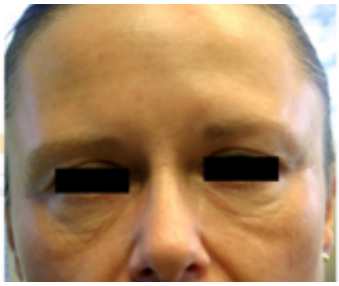
*AboBTXA was used. A total of 85 U was delivered using a 30G needle: 10 U into each of 5 sites for the glabellar complex; 5 U into each of 4 frontalis sites, and 2.5 U into 3 sites on each side of the face (crow's feet and lateral brow)* ***(Figure 3A)****. Alternative treatments would be 32 U of incoBTXA, onaBTXA, or praBTXA, with 20 U/glabellar site in the glabella, 8 U/frontalis site, and 4 U/site in the crow's feet/lateral canthal lines. Remarkable improvement was seen at 2 weeks posttreatment* ***(Figure 3B)****.*

**FIGURE 3.** Before (3A) and after (3B) photographs of the patient described in Case 2. The units of abobotulinumtoxinA injected are indicated in the legend.

(3A)




(3B)



**Discussion**

**Dr Gold:** Optimal rejuvenation of the aging face often requires multimodal treatment. I complied with this patient's request to use only BTXA because I sensed she feared cosmetic surgery. I also thought that a good result with BTXA might alleviate her concerns and make her more willing to consider other procedures.

In the United States, only onaBTXA is approved for treating lateral canthal and forehead lines in addition to glabellar lines.[1] The other BTXA products might effectively treat lateral canthal and forehead lines, but patients should be told that the treatment is off-label.

**Dr Yoelin:** Do you perform BTXA injections on the same day as you do another cosmetic procedure?

**Dr Cohen:** I typically avoid injecting BTXA on the same day that I do procedures that cause a lot of swelling, such as nonablative fractional treatments, chemical peels, full-field laser resurfacing, and fractional ablative resurfacing.

**Dr Yoelin:** In some patients with horizontal forehead rhytids, frontalis muscle contraction is also compensating for preexisting brow and lid ptosis, which can be unmasked by BTXA treatment of the forehead lines. Preinjection evaluation is important to guide the treatment so that you avoid the situation in which you have addressed one problem but created another.

**Dr Cohen:** Evaluating patients for brow shape, positioning, symmetry, and dermatochalasis is essential for success with the nuances of treating the upper face. Exercising care with BTXA forehead injections in people with severe upper lid dermatochalasis is especially important because they might be using the frontalis muscle to lift the brow and, in turn, depend on that muscle to lift the lid as well.

Another fine point is that when treating crow's feet, I often administer the neuromodulator with a medial needle insertion and then lateral advancement of the needle. For this approach, I point the needle toward the temporal hairline at entry and direct it laterally and inferiorly, staying away from the inferior aspect of the orbicularis oculi, which is where the zygomaticus minor inserts. In short, clinicians injecting BTXA must consider where the needle tip *ends* and not just where it *enters*.

**Dr Kaufman:** Lid edema can also occur when treating the upper third of the face. I believe that its cause is decreased fluid movement to the lymphatics as a result of reduced muscle function. The risk for lid edema might be greater when several areas of the upper face are treated at the same time.[29]

**Dr Aguilera:** If a patient develops swelling around the eyes, I prescribe hydrochlorothiazide to help eliminate the excess fluid.

**Dr Yoelin:** I advise patients with swelling to sleep with the head elevated on 2 or 3 pillows and to actively contract the muscles around the eyes. In my experience, the problem is usually transient and can be worse in those who have filler injections deep in the midface simultaneously with BTXA injection in the orbicularis oculi.

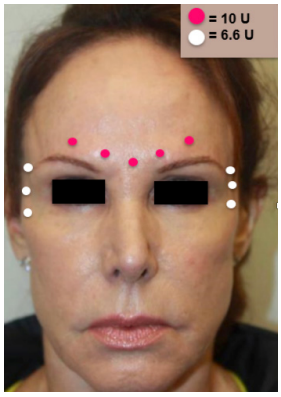
## ABOUT CASE 3

**Treatment of the Upper Face**
***From the Files of Shino Bay Aguilera, DO, FAAD***

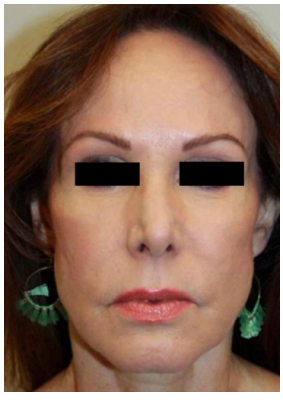
*A 59-year-old white female desired lifting of her brow and forehead. Using a 31G needle, she was treated with a total of 90 U of aboBTXA, with 50 U distributed evenly across 5 sites in the glabellar complex and 40 U in total injected in the lateral canthal and brow regions across 3 sites on each side* ***(Figure 4A)****. Dosing using incoBTXA, onaBTXA, or praBTXA instead of aboBTXA would be 20 U in total for the glabellar complex and 8 U per side for the lateral canthal/brow injections.* ***Figure 4B*** *shows her appearance 2 weeks later.*

**FIGURE 4.** Before (4A) and after (4B) photographs of the patient described in Case 3. The units of abobotulinumtoxinA injected are indicated in the legend.

(4A)




(4B)



**Discussion**

**Dr Aguilera:** The combined effects of aging and repeated BTXA injections can also cause changes in facial appearance over time, so the treatment approach should be modified accordingly. There are distinct differences between the upper third of the face of a female and that of a male due to sexual dysmorphism. Females have a more dominant upper third of the face because of a more convex frontal bone and additional fat, which causes the brows to arch to a greater extent and at an elevated position. In addition, females tend to have larger eyes than do males.

Certain races/ethnic groups, such as Asian and Latinos of Native American descent, tend to have a weaker upper third of the face compared with other groups. They have less bone and soft tissue, and the position of the brows is lower. This is a disadvantage when the aging process begins.

Previously, this patient was getting BTXA injections in the glabellar complex, lateral canthus, and frontalis. Over time, however, she developed widening of the area over her nose from the repeated frontalis injections. As mentioned previously, women have a more dominant upper third of the face compared with men. As the aging process takes place, there is a progressive loss of bone and soft tissue (fat and collagen). With the loss of these deeper tissues, there is a natural descent of the frontalis muscle, causing it to collapse at the bridge of the nose. The patient was told that she could either continue BTXA without the frontalis injections or have a frontoplasty to extend the use of BTXA frontalis injections.

I prefer to use aboBTXA in the glabellar complex and lateral canthus, but onaBTXA for frontalis injections. I find that onaBTXA in the frontalis provides a more natural relaxation of the muscle, whereas aboBTXA can give a more exaggerated relaxation, perhaps because of a greater diameter spread of the toxin.

**Dr Yoelin:** Would you use different BTXA products together on the same day?

**Dr Cohen:** I commonly use 2 different neuromodulators on the same day; for instance, onaBTXA in the glabella and aboBTXA in the lateral canthal area. In clinical trials and over many years of lots of treatments, immunogenicity has not been a problem with either product.

**Dr Maas:** I know clinicians who combine the use of products without any problems, but I prefer not to do that. Although there is no indication that blocking antibodies or tachyphylaxis develops at the low doses we use for cosmetic treatments, I think those events are theoretically possible.

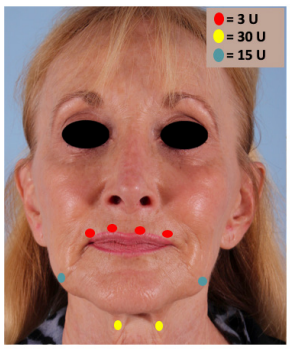
## ABOUT CASE 4

**Treatment of the Lower Face**
***From the Files of Corey S. Maas, MD, FACS***

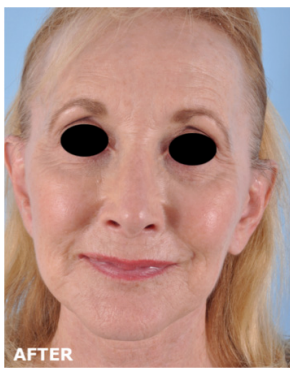
*A 65-year-old white female presented complaining about the aged appearance of her lower face and neck, including prominent platysmal bands, perioral lines, and a downturned mouth. A total of 102 U of aboBTXA was injected at 4 sites over the upper lip into each depressor anguli oris and the vertical platysmal bands* ***(Figure 5A)****. Alternative treatments would be 34 total units of onaBTXA and praBTXA or 42 total units of incoBTXA.* ***Figure 5B*** *shows her appearance after treatment.*

**FIGURE 5.** Before (5A) and after (5B) photographs of the patient described in Case 4. The units of abobotulinumtoxinA injected are indicated in the legend.

(5A)




(5B)




**Discussion**

**Dr Maas:** Injection of BTXA is very effective for improving the appearance of prominent vertical platysmal bands and the cervicomental angle. Lateral platysmal bands do not affect the cervicomental angle and typically do not have to be injected unless the patient is bothered by their appearance.

Injection into the vertical platysmal bands is generally quite safe. Excessively high doses and injecting too deep might risk creating problems with swallowing and neck flexion.[30]

BTXA injection into the depressor anguli oris addresses downward turn of the oral commissures. Clinicians can avoid complications, such as problems with lip function and symmetry, by injecting lateral to the oral commissure and along the jawline.

Low doses of BTXA are used when treating radial lip lines to avoid causing oral incompetence. For rejuvenation of the lower face, I generally consider BTXA as an adjunct to fillers rather than as a substitute. In patients with subtle defects, however, BTXA by itself can provide a nice improvement.

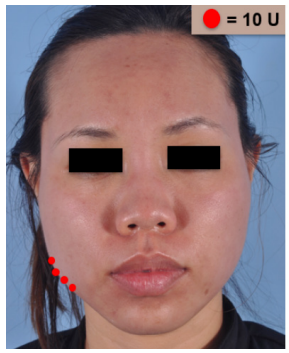
## ABOUT CASE 5

**Lower Face Contouring With Masseter Injections**
***From the Files of Corey S. Maas, MD, FACS***

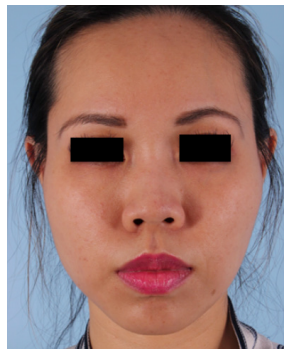
*A 31-year-old Asian female sought contouring of her lower face to lessen its broad appearance. She was treated with 80 U of onaBTXA administered as 10 U/site into 4 sites on each side of the face* ***(Figure 6A)****. Alternative treatments would be 240 U of aboBTXA, 100 U of incoBTXA, and 80 U of praBTXA.* ***Figure 6B*** *shows the outcome after treatment.*

**FIGURE 6.** Before (6A) and after (6B) photographs of the patient described in Case 5. The units of onabotulinumtoxinA injected are indicated in the legend.

(6A)




(6B)



**Discussion**

**Dr Maas:** Masseteric hypertrophy broadens the lower face and can be seen in people of Asian descent and those with bruxism. BTXA injection to reduce masseteric mass alters the shape of the lower face, thereby creating a narrower contour that is more aesthetically pleasing in women and can also treat bruxism. I believe that some benefit might be due to a reduction in parotid gland size, although imaging studies are required to confirm this idea. Because bruxism can lead to dental trauma, pain, and temporomandibular joint dysfunction, patients with masseteric hypertrophy suspected to be related to bruxism should be referred for dental evaluation if they are not already under a dentist's care.

The patient in this case was treated with a high dose of onaBTXA because I knew her well and was comfortable starting at this dose. Typically, I will use just 20 U per side for initial therapy. Then, I will increase the dose by 10-U increments to a maximum of 40 U when the patient returns for repeat treatment after the benefit has disappeared. I use a 31G short needle and keep the delivery posterior, staying away from the anterior border of the masseter to avoid hitting the facial nerve.

**Dr Yoelin:** Injections for masseteric hypertrophy should be kept posterior to avoid weakening of the risorius, zygomaticus major, and zygomaticus minor muscles, which could result in an asymmetric smile or the appearance of facial paresis. Weakening of the masseter itself usually does not interfere with the ability to chew because several other muscles are also used for mastication.

Older patients, in particular, might be at risk for developing skin laxity after BTXA injections that reduce the space-occupying masseter muscle mass. Filler injections along the ramus, angle of the mandible, and even the lateral portion of the mandible can correct this issue.

## ABOUT CASE 6

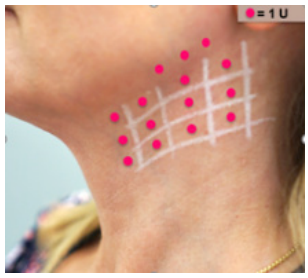
**Neck Rejuvenation**

***From the Files of Shino Bay Aguilera, DO, FAAD***

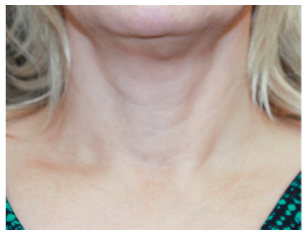
*A 55-year-old white female requested neck-skin rejuvenation and lifting **(Figure 7A)**. She was treated with 30 U of incoBTXA, with 15 U per side distributed evenly across 15 sites **(Figure 7B)**. The injection was delivered deeper on the jawline and with a microinjection technique into the dermis on the neck. With this technique, the first 3 injection sites are along the medial fibers of the lower border of the mandible. Then, the patient was asked to grimace to expose the platysmal bands, and a total of 3 U was injected down along the bands 1 cm apart for a total of 9 injection sites along the lateral fibers of the platysma. Each injection site received 1 U separated by 1 cm, as illustrated in **Figure 7A**. Alternative treatments would be 30 U of onaBTXA or praBTXA-xvfs and 75 U of aboBTXA. **Figure 7C** shows the patient's appearance after treatment.*

**FIGURE 7.** Before (7A and 7B) and after (7C) photographs of the patient described in Case 6. The units of incobotulinumtoxinA injected are indicated in the legend.

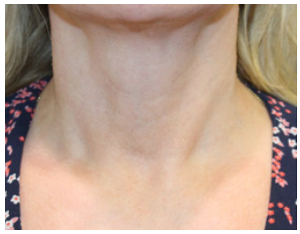
(7A)




(7B)



(7C)



**Discussion**

**Dr Aguilera:** The Nefertiti lift redefines the jawline using deep injections into the platysmal bands and intradermally along the mandibular border and upper neck.[31] This patient was treated with a variation of the Nefertiti lift, one that I find provides more enhanced lifting by relaxing the posterior lateral fibers of the platysma.

**Dr Cohen:** The Nefertiti lift was quite popular in 2007 for a few years after Phil Levy, MD, described it. In my experience, it is rarely a standalone success along the jawline. I think BTXA can soften platysmal bands that are present at rest quite nicely (particularly in people who have had a neck lift or recent submental fat minimization treatment). However, I find jawline contouring to be especially enhanced with the use of a lifting filler (such as a calcium hydroxylapatite or hyaluronic acid dermal filler) in the prejowl sulcus as well as along the postjowl jawline. In addition, some patients show a nice added improvement to the jawline with the use of microfocused ultrasound or radiofrequency in the lateral jawline.

## ABOUT FACE SUMMARY POINTS

Four BTXA products are commercially available for cosmetic use

- Their potency units are not interchangeable and cannot be directly compared
- All are good products, but some patients respond differently to different BTXA products

There is no universally accepted conversion ratio among BTXA products

- Several reviews and experts suggest the ratio for aboBTXA:onaBTXA is between 2:1 and 3:1
- Several reviews suggest the ratio for incoBTXA:onaBTXA is 1:1, but some experts believe it is higher (between 1.2:1 and 1.5:1)

Practitioners who are new to BTXA use should consider gaining expertise with one product before adopting another.

Practitioners might vary the diluent volume used to reconstitute BTXA products, depending on site of injection, treatment goals, patient-specific characteristics, and mathematical ease of dose conversion among products.

An individualized approach to BTXA injection is important for achieving the best results.

- Dose selection and placement of BTXA injections should consider muscle size, strength, and recruitment along with facial asymmetry and sex differences in anatomy and facial aesthetics
- Optimal rejuvenation of the aging face may require multimodal treatment

Proper injection technique and knowledge of facial anatomy are necessary for minimizing the risk of complications with BTXA treatments.

- Interventions can be offered to patients bothered by post-treatment bruising, eyelid ptosis, and lid edema

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1. Which BTXA product does NOT contain NAPs?
   a. aboBTXA
   b. incoBTXA
   c. onaBTXA
   d. praBTXA

2. Which BTXA product is approved for the treatment of lateral canthal lines?
   a. aboBTXA
   b. incoBTXA
   c. onaBTXA
   d. All the above

3. According to reviews of available study data, the conversion ratio of aboBTXA to onaBTXA ranges between _____.
   a. 1.2:1 and 1.5:1
   b. 1:1 and 2:1
   c. 1.5:1 and 3:1
   d. 2:1 and 3:1

4. According to reviews of available study data, what is the conversion ratio of incoBTXA to onaBTXA?
   a. 1:1
   b. 1.5:1
   c. 2:1
   d. 3:1

5. Which of the following is *NOT* a factor affecting the amount of diluent used for BTXA reconstitution?
   a. Injection site
   b. Planned storage of reconstituted solution
   c. Treatment goals
   d. Patient-specific characteristics

6. Why is bacteriostatic saline used for BTXA reconstitution?
   a. It improves injection comfort
   b. It minimizes infection risk
   c. It is recommended to prolong storage time
   d. It increases field of effect

7. Which of the following strategies should be employed to avoid/manage complications?
   a. Obtain an informed consent and explain possible complications prior to treatment
   b. Consider modifying treatment as the result of changes due to the aging process
   c. Avoid injecting under the midbrow to minimize the risk for eyelid ptosis
   d. All the above

8. Males can be at increased risk for developing a Mephisto appearance of the eyebrows after BTXA injection for the treatment of glabellar lines using a standard 5-point pattern. Compared with females, this condition is caused by males having:
   a. More subcutaneous fat
   b. Stronger frontalis muscles
   c. Stronger medial corrugator muscles
   d. Stronger procerus muscles

9. When treating glabellar lines, BTXA injection into the nasalis muscle might be considered in a patient with a/an _____ glabellar contraction pattern.
   a. Vertical converging
   b. U
   c. Omega
   d. Inverted omega

10. Which is the most common complication after cosmetic BTXA injections?
    a. Bruising
    b. Headache
    c. Itching
    d. Swelling

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