

Tox Outside the Box: Off-Label Aesthetic Uses of Botulinum Toxin

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The FDA approves drugs and devices based on scientific data to prove efficacy with an acceptable safety profile. Double blinded, placebo controlled studies are conducted by pharmaceutical companies and are the gold standard to gain commercial release of their drug. Such studies are very rigorous and defined, with no variation allowed between test study sites, patients, or physicians. In other words, no creativity is allowed. When the drug or device is ultimately released with FDA approval, it is for a specific indication and exact dosage with strict adherence to the "label", which the company can promote to and educate physicians or advertise to patients via direct-to-consumer advertisements. Doctors, however, can legally recommend and utilize these approved and legally prescribed drugs and devices in any manner they deem safe and appropriate. Such use is called "off-label". The FDA controls the pharmaceutical industry, but not the free practice of medicine in the United States by licensed physicians, and in some cases, lower level medical care providers. Many creative and talented physicians use these drugs and devices in many ways quite different from the FDA label.

When onobotulinumtoxinA was FDA approved in 2002 for glabellar frown line improvement, it was already being used for quite some time in an aesthetic "off-label" manner, since it was originally intended for blepharospasm and strabismus. The new package insert called for 5 very specific injection points into the corrugator and procerus muscles, injecting a total of 20 units using a 2.5cc sterile, non-preserved, normal saline reconstitution. Many experienced doctors were already using 1cc or 2cc reconstitution volumes with good success and felt no need to alter their formula and as such, became the first to use the toxin in a manner technically beyond the package insert. Countless other changes and variations were to follow as experienced injectors began to think outside the box provided by the FDA. Soon after, besides injection volume variations, it was noted that substitution of sterile preserved saline for reconstitution provided a decrease in pain with no change in efficacy.[1] This too was technically "off label". The use of botulinum toxin in areas not approved for treatment led to the clinical trials that ultimately resulted in FDA approval for crow's feet in 2013. The advantage to the sponsoring company was the ability of sales people to promote this new indication and the ability for company-sponsored trainings to include a second area for injection in the teaching sessions. Many physicians choose competing botulinum toxins (abobotulinumtoxinA, which was FDA approved for only glabellar use in 2009 and IncobotulinumtoxinA received glabellar clearance in 2011) for the treatment of their patients' crow's feet with success even though those products have not undergone the stringent FDA approval process for this second area.

The real artistry of facial rejuvenation with injectable neuromodulators involves so much more than softening crow's feet and preventing frowning. Brow shaping, eyebrow lifting, opening the aperture of the eye, decreasing the mouth frown, defining a jaw line, increasing lip show, decreasing gummy smile, reducing the bar code lines around the mouth, lifting the nose tip, eliminating the "golf ball" chin, reducing platysma bands, and softening the squared, masculine jaw are all finesse treatments that turn us from aesthetic physicians into artists. To do this well, the physician needs to understand anatomy, the movement of muscles in isolation and in relation to other muscles, the concept of compensatory strengthening (as important sometimes as muscle weakening), and be observant evaluators of each individual patient's presentation at rest as well as with normal and exaggerated animation. There is no painting by numbers when it comes to artistry with injections. Every face is unique. I don't inject the same patient each time exactly the same, so the differences from patient to patient can be quite wide.

The Brows

The brows are critical to the unspoken messages females send to others. Low medial brows, even without furrowed wrinkles, signal hostility and anger. Neurotoxin injection into the glabellar complex can have significant impact on brow height and position sometimes resulting in a pleasing look and sometimes not (Figures 1 and 2).[2] This is why it is so critical to avoid the medial frontalis fibers that lie superficial to the corrugators when the frown complex is injected. Since I have been teaching toxin injections at Tulane since 1996, I can attest that this is the most common mistake novice injectors make. By the same token, lower lateral brows from injection of the lower lateral frontalis fibers (or by natural brow shape pattern) can signal uncertainty, concern, or distress. It is important for the female brow to be arced and arched in a feminine and

FIGURE 1. Browlift (before).

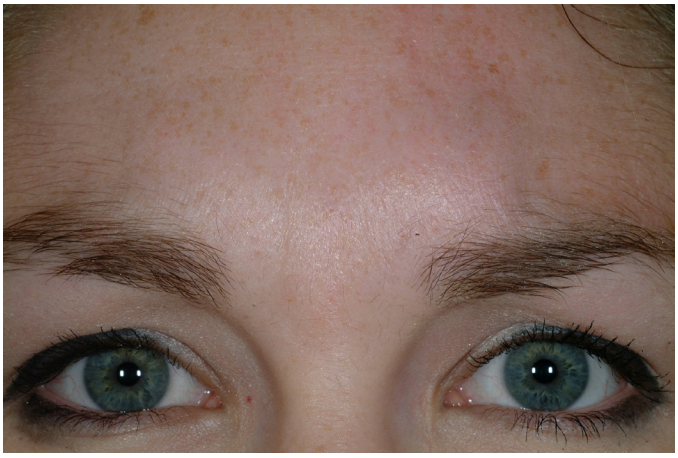
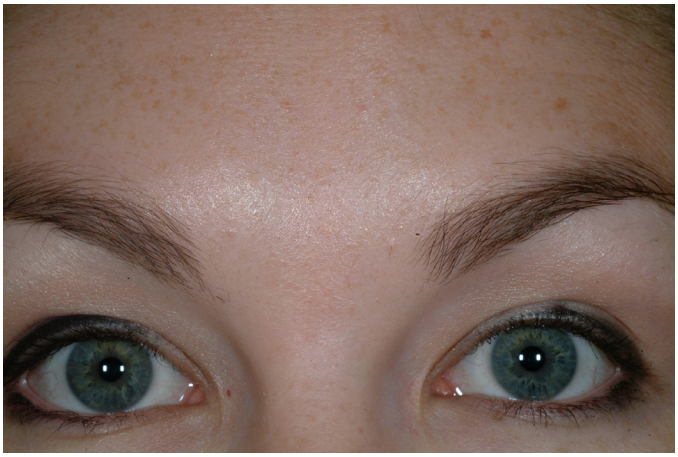


FIGURE 2. Browlift (after).



alluring manner to signal openness and mystery to a potential suitor. Male brows are optimally low and flat. For purposes of this discussion, it is sufficient advice to recommend avoiding injection into the frown complex in such a manner as to arch or "Spock" the male brow and to be very conservative when injecting the frontalis muscle to avoid a mannequin appearance that can be feminizing.

To raise the dropped medial brow, I usually inject a generous amount into the procerus (about 10 units) and 2-5 units to each brow tail where the lateral-superior orbicularis oculi depresses the lateral brow. At the same time, I also inject 2-5 units into the lateral frontalis to trigger compensatory strengthening of the medial frontalis and lift those scowling medial brows. Avoid injecting too close to the brow when injecting into the lateral frontalis as you do not want to drop the lateral brow. I might add I do a similar pattern in my patients with widely splayed medial brows. This "cow look" as I call it, can be natural anatomy from a wide nasal root, but is more often iatrogenically induced from too much toxin into the corrugators in a poor subject with an unobservant provider injecting by the cookie cutter pattern in the package insert.

To correct the concerned and distressed look of a low lateral brow, I usually do the following: 2-5 units into the lateral brow tail and 6-10 units into the central and superior fibers of the frontalis muscle (Figures 3 and 4). This results in compensatory strengthening of the lateral frontalis on each side to lift the lateral brows. It is important to understand that one must evaluate each patient as there is no cookbook to brow shaping. Sometimes nothing is better than a hyaluronic acid filler injected into the lateral eyebrow to give the best arch.

In addition to brow lift and shaping, use of neuromodulators can correct baseline brow asymmetry (Figures 5 and 6). Close examination often reveals that brow asymmetry is from lax skin or mild ptosis on one side and the resulting compensation of the

FIGURE 3. Concerned look (before).

FIGURE 4. Concerned look (after).

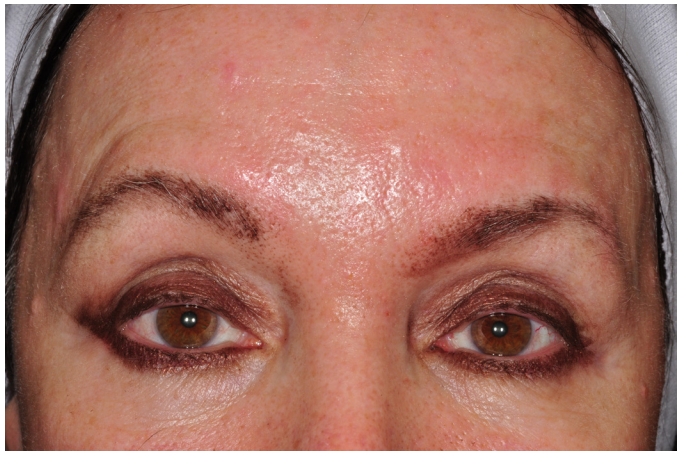


FIGURE 5. Crooked brow (before).

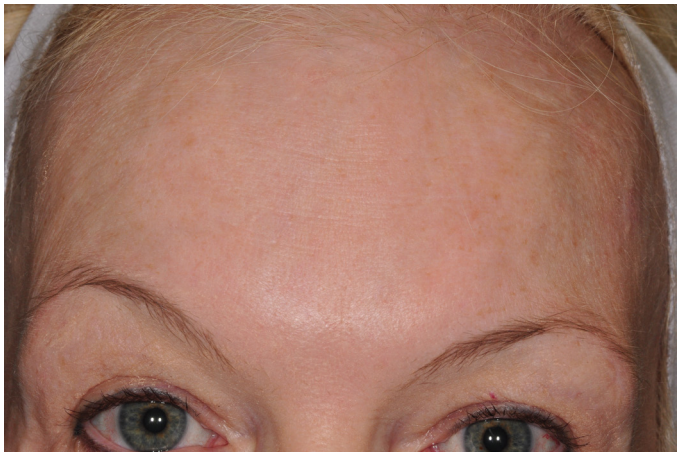
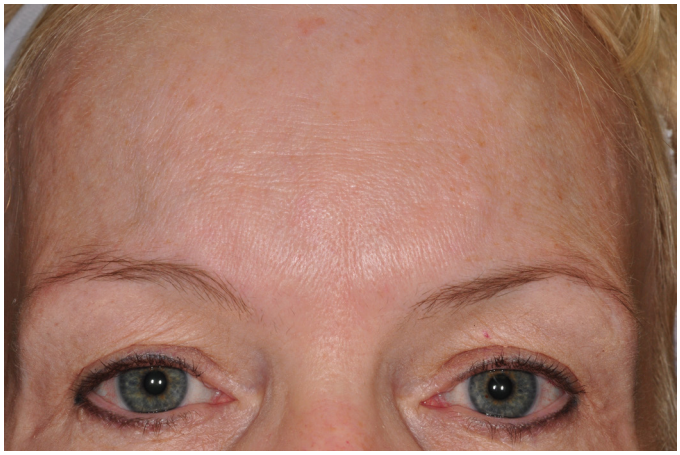


FIGURE 6. Crooked brow (after).



frontalis to lift the lower and sagging side. This side with the stronger frontalis from overuse will cause that brow to be higher. In some cases, patients are best served by a referral to an oculoplastic surgeon before proceeding because treating the frontalis will sometimes drop the brow and impede visual field. It is always important to verbally discuss the asymmetry, as well as document and photograph it, so that you are not blamed after injection for the imperfection if it is not corrected. In general, a small amount of 2-3 units above the stronger brow corrects the irregularity.

In certain ethnic groups, the injection of 1-3 units into a hypertrophic inferior orbicularis oculi muscle can open the eye and make it look more round. In general, this injection should never be done in older Caucasian females as it can result in accentuation of any laxity in the delicate skin in this area.

Lips, Chin, Nose, Jawline, and Beyond

There is nothing more unattractive than sausage or duck lips. Often, inexperience and/or the desire to please the female wishing to have larger lips prevent a doctor from stopping and actually looking at the patient. Ask them to smile. No good artist works on the dynamic and three dimensions that is the human face without first carefully observing and assessing it. If the upper lip rolls under and the red show diminishes with smiling, injection of filler alone will give you the duck or sausage look. Over active orbicularis oris must be treated prior to injecting volumizing fillers. Often when toxin is done first, there is more red lip "show" and the lips look larger without filler but at the very least, the filler result looks more natural with less material. This injection must be done deep into the upper orbicularis oris. 4-6 units are my usual starting dose. Here, it is so much easier to add than to subtract (Figures 7 and 8).

And if the duck isn't bad enough, who among us has not been horrified by the monkey roll? This occurs when injectors attempt to eradicate bar code lines with hyaluronic acid filler. Laser resurfacing or dermabrasion is often a

FIGURE 7. Lip roll (before).

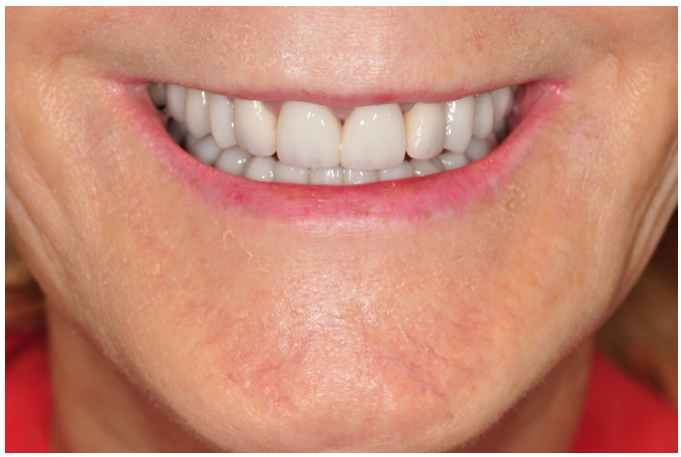


FIGURE 8. Lip roll (after).

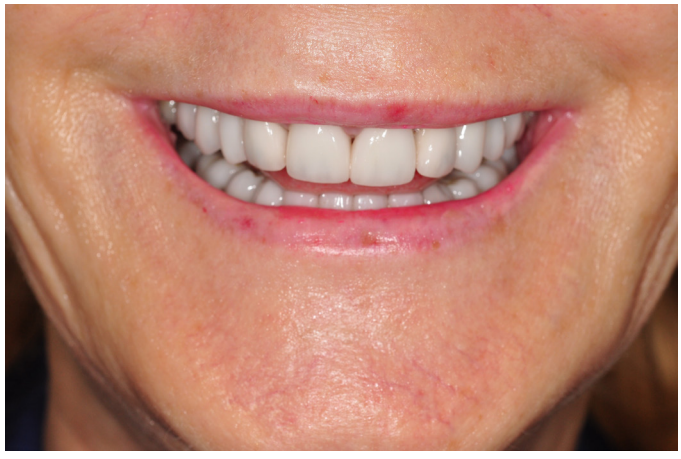


FIGURE 9. Lip line (before).

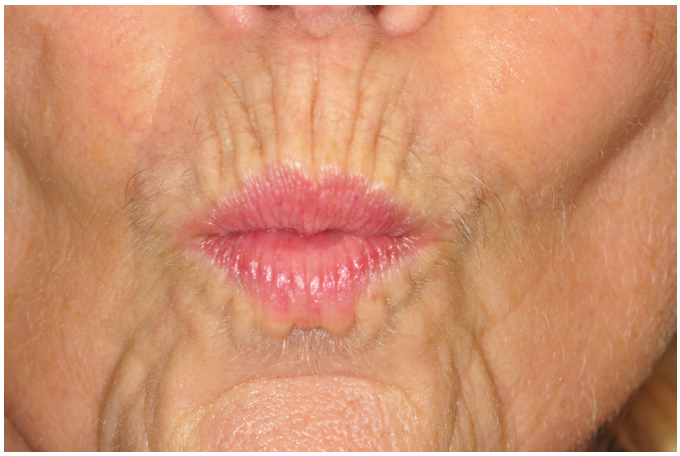
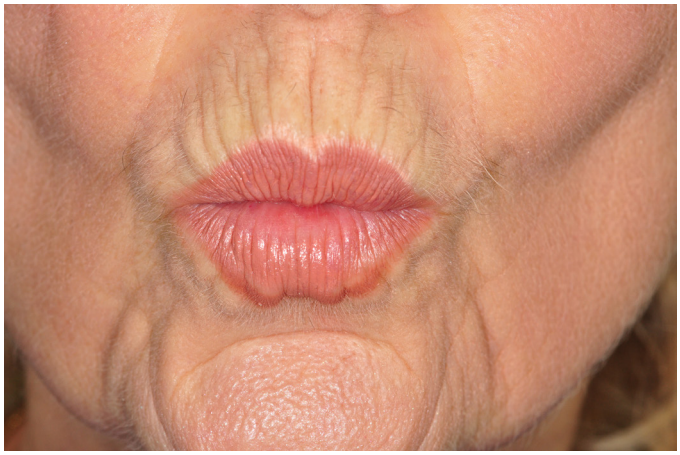


FIGURE 10. Lip line (after).



better idea than flooding the dermis and sub-q with filler. A no-downtime option here is toxin into the superficial fibers of the orbicularis oris to reduce constant lip pursing.[3] These patients can be identified with careful observation as they hold tension in their lips and seem to be in a state of constant pursed lips, looking stern and unfriendly. Here I typically start with superficial injections of 6-8 units (Figures 9 and 10).

If when the patient smiles, the tip of the nose dips, 2-3 units into the base of the columella can raise the tip and give it a youthful lift. Injection into the upper lateral nose weakens the nasalis "bunny lines" that can be strengthened from glabellar injections.

When the patient smiles and the gums show, that is called the "gummy smile". It is from excess action of the levator labii alaeque nasi muscles. I start with 2 units into the canine fossa-ala junction (Figures 11 and 12). Here again, better to under- than over-treat. Over-treatment here results in both a longer distance from nose to lip (which is very aging) and/or a Jimmy Carter -like frozen upper lip. This technique is never a good idea in someone with a pencil-thin upper lip.

Injections beyond the lips can also yield important results. Injection of neurotoxin into the depressor angularis oris (the DAO), is becoming a favored treatment to improve downturned oral commissures.[4,5,6]

The results work best when combined with filler for any volume loss in this area (Figures 13 and 14). Dimpled chins (golf-ball chin) can be softened by injection into the mentalis muscle (Figures 15 and 16).[5,7] When you combine toxin injections into the DAO with injections into the superior platysma insertion at the prejowl sulcus, a lifting effect can be seen at the jawline and a shrinking effect of the sub-mandibular salivary gland can be seen as well. Combining orbicularis oris injections with mentalis gives a rejuvenating effect to the entire mouth/chin complex (Figures 17 and 18).

FIGURE 11. Gummy smile (before).

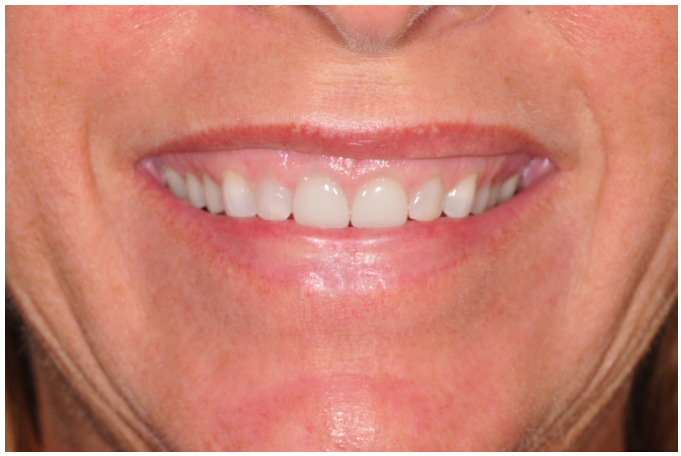


FIGURE 12. Gummy smile (after).

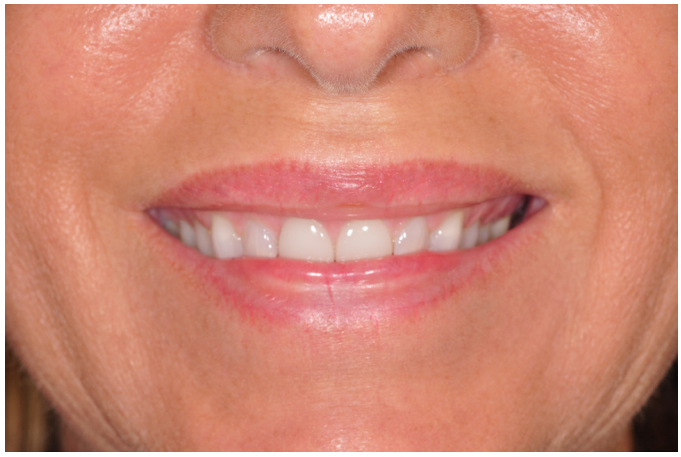


FIGURE 13. DAO (before).

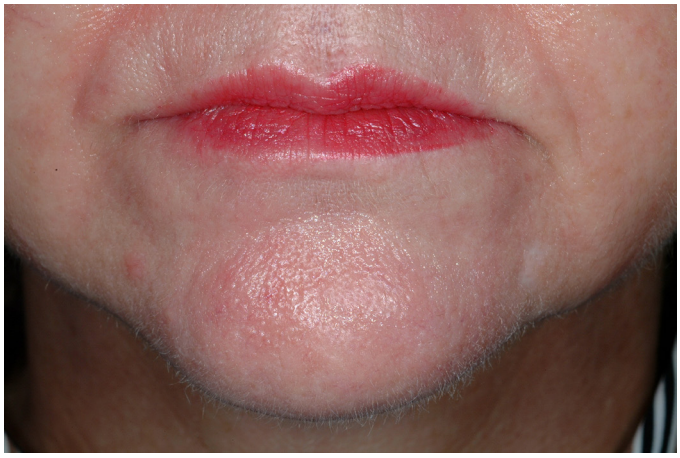
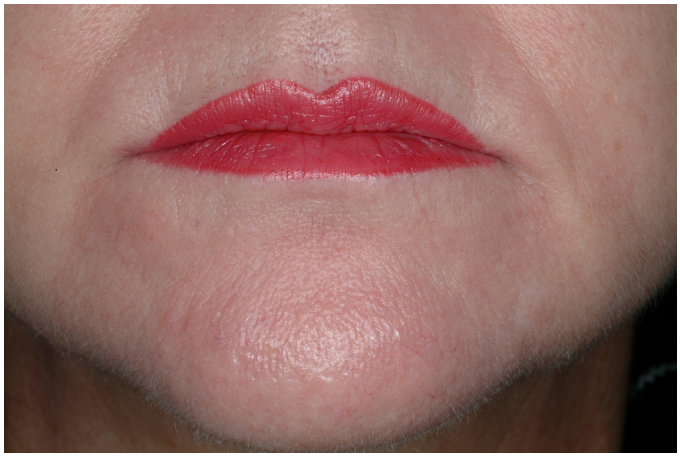


FIGURE 14. DAO (after).



Another important jawline treatment involves injection into the masseter muscles.[8] In females, an overly squared jaw can be masculinizing. In addition, the Asian face can have overly accentuated masseter muscles and they seek out this treatment to make their face more oval. Injection into this muscle results in a softening of the determined, clenched appearance of the face and a more feminine oval or heart shaped face (Figures 19 and 20). This injection is best saved for a younger patient where sagging at the jawline is not an issue. Patients will often report improvement in teeth grinding, temporal-mandibular joint symptoms, and headaches after treatment of an over-active masseter. I usually recommend a mouth guard in these patients to help retrain the masseter from being in constant tension. It may help reduce the need for constant injections into this area.

Platysma injections have been touted to improve the definition of the jaw line, decrease the downward pull of the lower face, reduce hyperactive platysmal banding (Figures 21 and 22), and soften the depth of horizontal neck lines.[5,9] In my experience, this use of neuromodulator should be reserved for younger patients who are not in need of surgical intervention, in some cases of residual banding post-surgery, and in those patients who have undergone treatment for submental chin fat, and newly exposed platysmal hypertrophy needs to be addressed to complete the non-surgical injectable neck rejuvenation. Moving further away from the face, the chest gains more attention for rejuvenation. Small aliquots of neurotoxin have been recommended to rejuvenate the aging décolletage area of women.[10] Results can be expected to be improved when combined with non-ablative resurfacing, vascular devices and ultrasound or radiofrequency devices to improve pigmentation, redness, and texture.

Botulinum toxins have known inhibitory effects on both acetylcholine and vasoactive intestinal polypeptide. These mechanisms of action have prompted many doctors to try using hyper-diluted product delivered into the dermal plane

FIGURE 15. Mentalis (before).

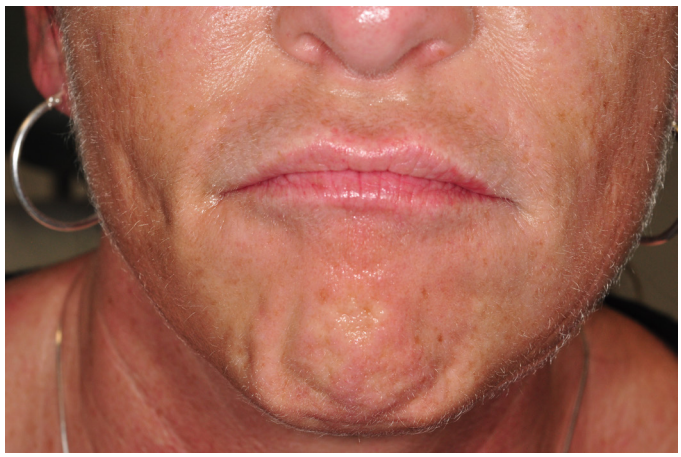


FIGURE 16. Mentalis (after).

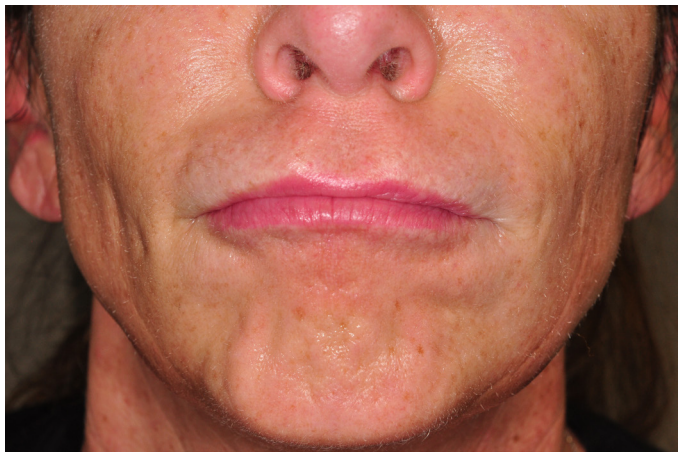


FIGURE 17. Mentalis and perioral (before).

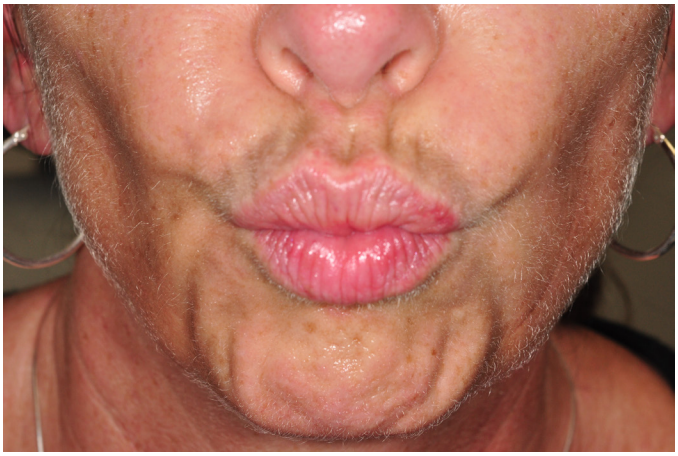
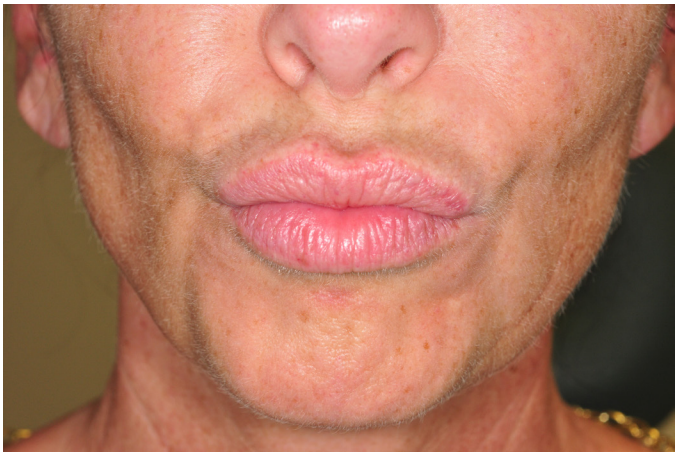


FIGURE 18. Mentalis and perioral (after).



to improve the appearance of pores, acne, rosacea, and flushing.[11,12,13] This is certainly yet another avenue for future exploration to make sure the results that are desired do not result in untoward changes in facial expression. Standardized dosages and uniform delivery mechanisms would best achieve safe and meaningful results.

Neuromodulator injections are a very important component of non-surgical rejuvenation. The science of the product injected and the anatomy of the face are important factors in the final result. The most important variable, however, is the injector and the skill, experience and the artistic eye of that person pushing on the plunger of the syringe.

DISCLOSURES

Dr. Lupo has the following disclosures: Researcher, advisory board, trainer, and speaker for Allergan; Advisory board, trainer, and speaker for Galderma; Advisory board, Merz.

FIGURE 19. Squared jaw (before).

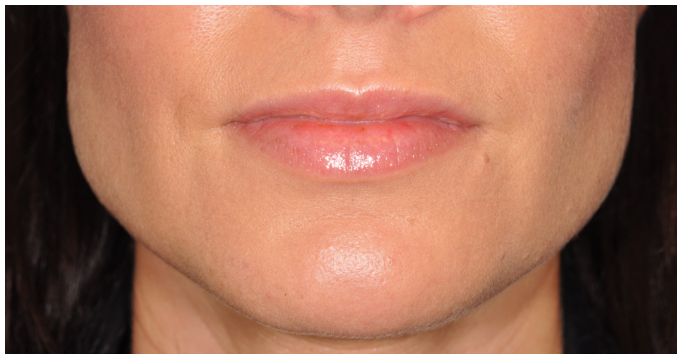


FIGURE 20. Squared jaw (after).

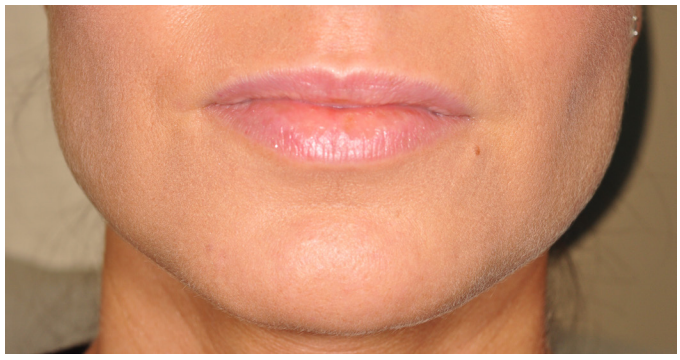


FIGURE 21. Neck banding (before).

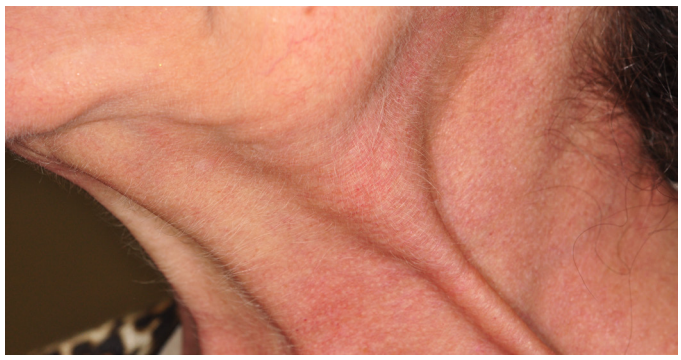
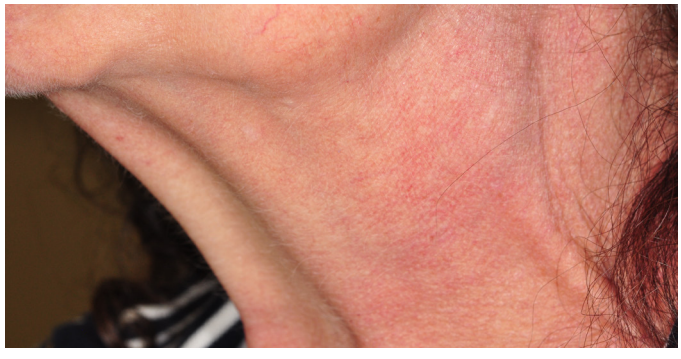


FIGURE 22. Neck banding (after).



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