Microbotulinum: A Quantitative Evaluation of Aesthetic Skin Improvement in 62 Patients

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Background: Microbotulinum refers to the systematic injection of tiny blebs of diluted botulinum toxin at repeated intervals into the skin. This targets the superficial fibers of the facial muscles, and weakens their insertion into the undersurface of the skin, which is responsible for the fine lines and wrinkles on the face. The authors present a pilot study based on quantitative evaluation, by means of a skin-scanning technology, of the aesthetic improvement of skin texture, microroughness, and enlarged pore size in a patient group treated with microbotulinum injections for cosmetic purposes.
Methods: The treatment was performed using a 32-gauge needle to deliver injections on a regular 1-cm grid from the forehead to the cheek and down to the jawline.
Results: Sixty of the 62 patients completed the study. All analyzed parameters improved significantly ($p < 0.0001$) at 90 days with respect to the pretreatment time point (skin texture, -1.93 ± 0.51; microroughness, -2.48 ± 0.79; and pore diameter, 2.1 ± 0.43). Best results have been obtained in patients aged between 42.7 and 46.8 years, and standard deviation calculation allows us to recommend it in patients aged between 36.5 and 53 years.
Conclusions: The results of this pilot study suggest that intradermal botulinum toxin injection, or so-called microbotulinum, is a safe and effective method to treat skin flaws. Because of the high satisfaction rate among both physicians and patients, further studies are indeed mandatory to determine the optimal number of units needed for a longer and lasting effect with this particular novel dilution. (*Plast. Reconstr. Surg.* 146: 987, 2020.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

Botulinum toxin can be used to treat cosmetically sensitive areas of the face by improving the appearance of dynamic rhytides caused by muscle contraction. Several areas are commonly treated with botulinum toxin in the upper face (glabella, forehead, eyebrows), midface (bunny lines, crow's feet), and lower face (gummy smile, masseter, mentalis, nasolabial folds, and neck).

Regardless of the treated area, the typical frozen nonmovement is undesirable for most patients today. Following the euphoric satisfaction of the 1990s given by the possibility of inducing muscle paralysis and reducing the appearance of wrinkles through injections alone, a time came when patients started to complain about the stiff and unnatural appearance. To achieve more natural and less dramatic results, clinicians began experimenting by reducing the dose and increasing the dilution to obtain optimal results in small aesthetic flaws and skin conditions.

With the aim of granting a more natural appearance on the face, small blebs with lower doses are injected into the dermis—or the interface between dermis and the superficial facial muscles—and this leads to decreased muscle activity where facial muscles are attached to the skin. The appearance of the wrinkles and fine

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lines would be decreased, yet sufficient movement of the underlying muscles would be maintained. In the forehead or undereye regions, microbotulinum allows avoidance of the stiff and motionless appearance often secondary to traditional dosage and droplet size.

In the lower face and neck, botulinum toxin can be successfully used to improve neck skin texture and to decrease the activity of the superficial fibers of the platysma muscle, which results in a better cervicomental contouring of mild neck laxity and jowling.[1] In addition, the smooth lustrous appearance of the skin caused by decreased sweating and sebaceous gland activity—secondary to the neurochemically induced bulk atrophy of sweat and sebaceous glands—is an aesthetic bonus.[2–6]

Microbotulinum refers to the systematic injection of multiple tiny blebs of diluted botulinum toxin at repeated intervals into the skin.[1] This targets the superficial fibers of the facial muscles and weakens their insertion into the undersurface of the skin, which is responsible for the fine lines and wrinkles on the face and neck.

Less invasive techniques are constantly being pursued with the aim of correcting aesthetic flaws, in a safe and reliable way, and with this in mind, the authors present a pilot study based on quantitative evaluation—by means of a skin-scanning technology—of the aesthetic improvement of a large group of patients treated with microbotulinum injections of the face and neck for cosmetic purposes.

MATERIALS AND METHODS

Between January of 2017 and December of 2017, 62 patients were enrolled in this study, 54 women and eight men. Men were aged between 34 and 47 years (mean, 35.1 years), and women were aged between 28 and 64 years (mean, 45.2 years).

The assessment was focused on skin texture (compactness and homogeneity), skin microroughness, and pore diameter before and 90 days after the microbotulinum injection. [**See Figure, Supplemental Digital Content 1**, which demonstrates a patient treated for skin texture: DermoPrime scan image shows skin texture before (*left*) the microbotulinum injections and the improvement after 30 days (*right*), *http://links.lww.com/PRS/E204*. **See Figure, Supplemental Digital Content 2**, which demonstrates a patient treated for microroughness: DermoPrime scan image shows microroughness before (*left*) the microbotulinum injections and the improvement after 30 days (*right*), *http://links.lww.com/PRS/E205*.]

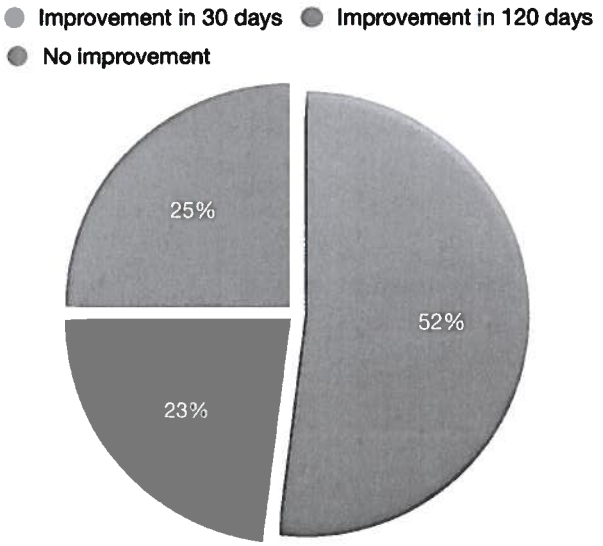

Fig. 1. Investigator Global Aesthetic Improvement Scale–Allergan Skin Roughness Scale.

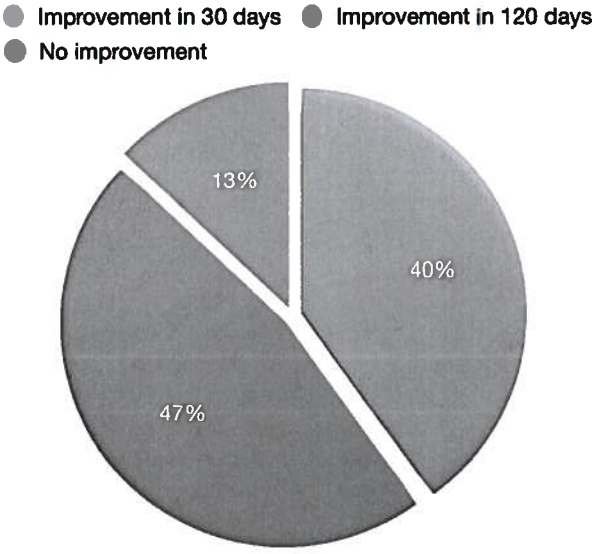

Fig. 2. Investigator Global Aesthetic Improvement Scale–Allergan Fine Lines Scale.

In addition, the Investigator Global Aesthetic Improvement Scale for "skin roughness" (Fig. 1) and "fine lines" (Fig. 2) photonumeric scale was used to assess the improvement in the overall appearance of the skin[7,8] before and 90 and 120 days after the treatment.

Also, each patient was provided with a questionnaire including a Subject Global Aesthetic Improvement Score at 30 (Fig. 3) and 120 days (Fig. 4) after the treatment.

Participants were asked to maintain the same skin-care regimen throughout the study and 4 weeks before treatment. The study protocol

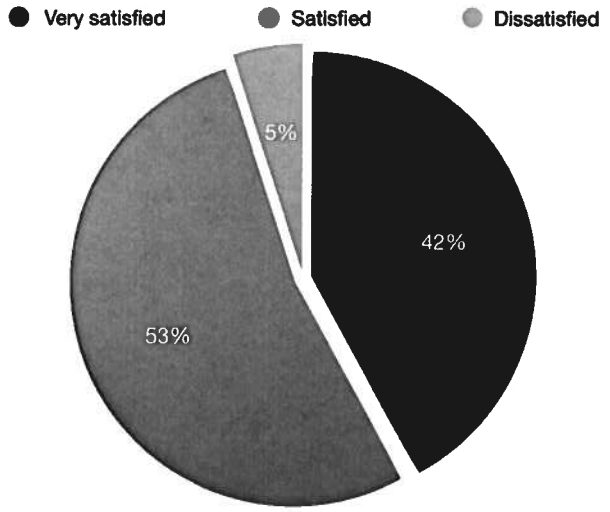

Fig. 3. Subject Global Aesthetic Improvement Scale: 1, very satisfied; 2, satisfied; 3, dissatisfied; and 4, very dissatisfied at 30 days.

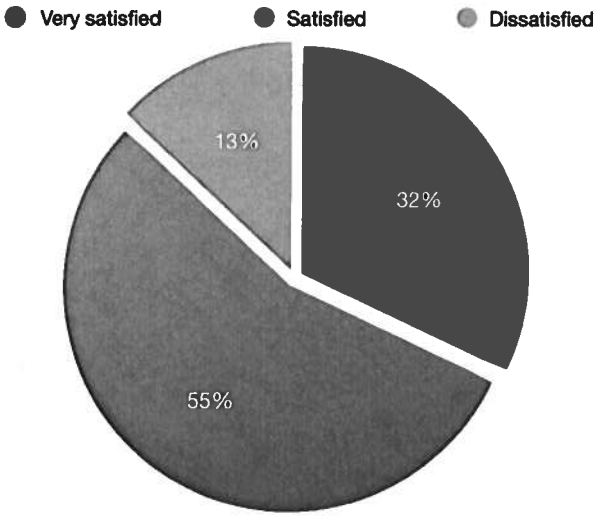

Fig. 4. Subject Global Aesthetic Improvement Scale: 1, very satisfied; 2, satisfied; 3, dissatisfied; and 4, very dissatisfied at 120 days.

followed the ethical guidelines of the Declaration of Helsinki and the participants were asked to give their informed consent before any study procedure.

Exclusion criteria included known allergy to cow's milk protein, active use of antiaging products containing retinol, and any treatment 6 months before baseline, including botulinum toxin type A injections in the face or neck; facial soft-tissue filler; laser, ultrasound technology, and/or radiofrequency on the face or neck; and treatment with isotretinoin or oral acne medications. The treatment was performed with the patient placed in a semireclined position, using a 32-gauge needle with the bevel pointed downward.

To treat the face, a 125-US (Speywood units) vial of abobotulinum toxin A (Azzalure; Ipsen S.p.a., Milano, Italy) was reconstituted with 1.25 ml saline solution. Then, 0.5 ml (50 US) was drawn into a 1-ml syringe and a further 0.5 ml of lidocaine (0.5%), or saline if the patient reported allergy to lidocaine, was added to the syringe to make it a 1-ml volume. This would give a concentration of 50 US/ml. During the injection procedure, the skin was kept taut by additional finger pressure and the injections were given in a regular 1-cm^2 grid. (**See Figure, Supplemental Digital Content 3**, which shows the forehead and cheek 1-cm^2 grid used to deliver the injections, ***http://links.lww.com/PRS/E206.***)

Approximately 150 injections were delivered into the superficial dermis using 32-gauge needles over the entire area, from the forehead to the cheek and down to the jawline. Care was taken to penetrate the needle into the skin as superficially as possible: a resistance was to be felt on pressing the plunger, and a small, raised, blanched bleb in the skin would be seen. In contrast, if the solution was easily injected, the needle had probably been inserted too deeply into the subdermal or intramuscular layer, which offers less resistance to diffusion of the injected liquid.

Patient photographs were obtained using a Nikon digital SLR D90 12.3 megapixel (Nikon Corp., Tokyo, Japan) camera. Skin photographs were taken in the center of the forehead and of the cheeks, and computerized analysis were carried out before and 3 months after treatment, using a skin scanner DPLite2 (DAVI&CIA, Barcelona, Spain) equipped with a three-dimensional processing lens, and skin analysis was performed with DermoPrime software (DAVI&CIA).

The high-resolution microcamera (410,000 pixels) was equipped with a 1.0-lux illuminating system with polarized light analysis[9] to assess skin homogeneity and pore characteristics through the dedicated software.[10] Once the angle of incidence of light is identified, microwrinkle depth can therefore be calculated accordingly. Ultrasounds are emitted by the handpiece, and they produce small waves on the skin so that its compactness can be inferred by the time necessary for the wave to return to the handpiece.

This tool therefore allows evaluation of skin texture, the presence of microwrinkles, and pore diameter.[11] Skin texture was evaluated on an inverted scale from 10 to 0 (10, very bad texture; 0, best texture), the microroughness was evaluated

on an inverted scale from 10 to 0 (10, maximum presence of microroughness; 0, no microroughness) and pore diameter on an inverted scale from 10 to 0 (10, minimum diameter; 0, maximum diameter).

Statistical Analysis

Statistical analysis was performed with GraphPad Prism software (GraphPad Software, Inc., La Jolla, Calif.). The D'Agostino-Pearson normality test was performed to verify data distribution. Descriptive statistics and *t* test for paired samples were performed for each considered value (i.e., skin texture, microroughness, and pore diameter). The statistically significant level was fixed at $p < 0.05$.

RESULTS

Sixty of the 62 patients completed the study, and two were lost to follow-up. Descriptive statistics are shown in Figures 5 and 6 and *t*-test results are reported in Tables 1 through 3. [**See Table, Supplemental Digital Content 4**, which shows skin scanner results. Skin texture before (*t0*) and 90 days after (*t90*) the microbotulinum injections, *http://links.lww.com/PRS/E207*.]

All analyzed parameters improved significantly ($p < 0.0001$) at 90 days after treatment with respect to before treatment (skin texture, −1.93 ± 0.51; microroughness, −2.48 ± 0.79; and pore diameter, 2.1 ± 0.43). When comparing their own before-and-after photographs and using the Subject Global Aesthetic Improvement Scale, 100 percent of the 60 patients rated themselves as improved in skin texture, microroughness, and pore size. Five patients had injection-point ecchymosis; no patients reported muscle weakness or facial asymmetries.

Blind evaluation performed by the authors (Investigator Global Aesthetic Improvement Scale) using the Allergan Skin Roughness Scale (Fig. 1)[7] before, 30 days after, and 120 days after treatment showed an overall 75 percent improvement at 30 days and 23 percent at 120 days. Fourteen patients (23 percent) showed improvement lasting up to 120 days after the treatment, 31 (52 percent) went back to baseline after reaching an improvement at 30 days, and the remaining 15 patients (25 percent) did not show any improvement. The 14 patients who experienced skin roughness improvement lasting up to 120 days were aged between 36 and 61 years (mean age ± SD, 46.8 ± 8.03 years).

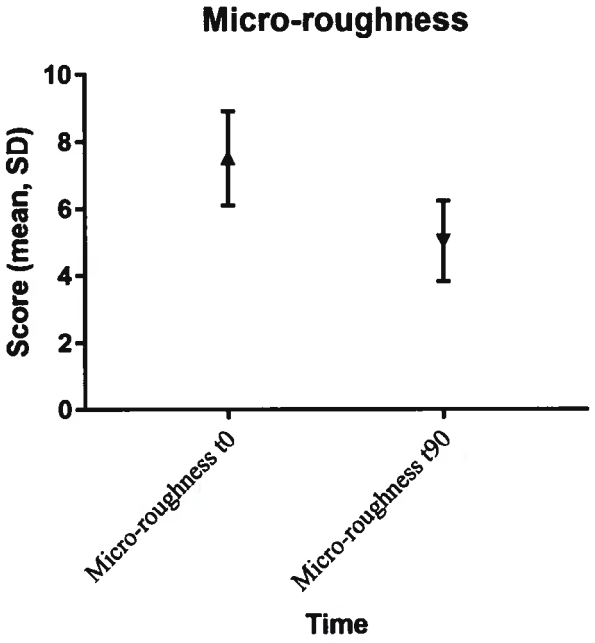

Fig. 5. Skin scanner results. Microroughness before (*t0*) and 90 days after (*t90*) the microbotulinum injections.

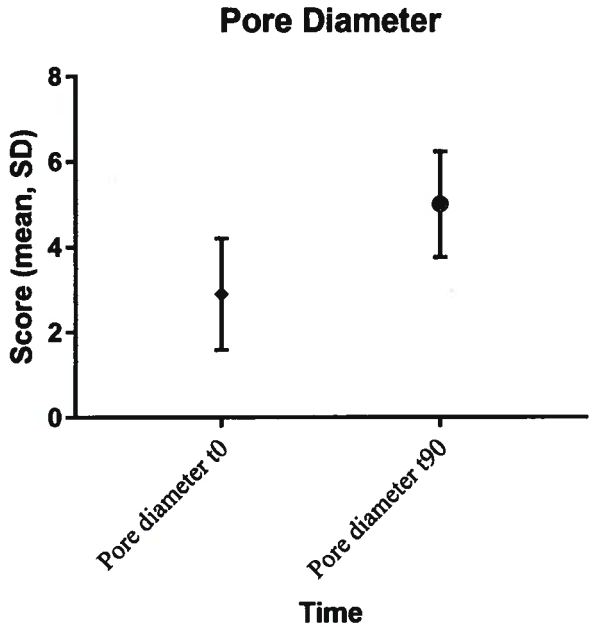

Fig. 6. Skin scanner results. Pore diameter before (*t0*) and 90 days after (*t90*) the microbotulinum injections.

Blind evaluation performed by the authors (Investigator Global Aesthetic Improvement Scale) using the Allergan Fine Lines Scale (Fig. 2)[8] before, 30 days after, and 120 days after treatment showed an overall 87 percent improvement at 30 days and 40 percent at 120 days. Twenty-four patients (40 percent) showed improvement

Table 1. Skin Scanner *t*-Test Results*

	Skin Texture		
	t0	t90	t90
Skin texture t0″ no. of values	60	60	60
Minimum	2	0	−2
25th percentile	4.25	2.25	−2
Median	6	4	−2
75th percentile	8	6	−2
Maximum	10	8	2
Mean	6	4.067	−1.933
SD	2.456	2.51	0.5164
SEM	0.3171	0.3241	0.06667
Lower 95% CI	5.365	3.418	−2.067
Upper 95% CI	6.635	4.715	−1.8

*Skin texture before (t0) and 90 days after (t90) the injection.

Table 2. Skin Scanner Results, *t*-Test Results*

	Microroughness		
	t0	t90	t90
Microroughness t0″ no. of values	60	60	60
Minimum	5	3	−5
25th percentile	7	5	−3
Median	7	5	−2
75th percentile	8	5.75	−2
Minimum	10	8	−2
Mean	7.517	5.033	−2.483
SD	1.408	1.207	0.7917
SEM	0.1818	0.1558	0.1022
Lower 95% CI	7.153	4.722	−2.688
Upper 95% CI	7.88	5.345	−2.279

*Microroughness before (t0) and 90 days later (t90) the injection.

lasting up to 120 days after the treatment, 28 (47 percent) went back to baseline after an improvement at 30 days, and the remaining eight patients (13 percent) did not show any improvement. The 24 patients who experienced improvement of fine lines lasting up to 120 days were aged between 30 and 61 years (mean age ± SD, 42.7 ± 8.54 years).

Patient self-assessment (Subject Global Aesthetic Improvement Scale) at 30 days (Fig. 3) showed that 26 patients (42 percent) were "very satisfied," 33 patients (53 percent) were "satisfied," and three (5 percent) were "dissatisfied." At 120 days (Fig. 4), 19 patients (32 percent) were "very satisfied," 33 (55 percent) were "satisfied," and eight (13 percent) were "dissatisfied."

DISCUSSION

Botulinum toxin type A is produced by various strains of *Clostridium botulinum*, a Gram-positive, anaerobic, spore-forming rod. Botulinum toxin type A has many beneficial applications in medicine: in the 1980s, Dr. Alan Scott published

Table 3. Skin Scanner Results, *t*-Test Results*

Column F vs. column E	Pore diameter t90 vs. t0	*df*
Paired *t* test		
p value	<0.0001	
p value summary	****	
Significantly different ($p < 0.05$)?	Yes	
One- or two-tailed *p* value?	Two-tailed	
t	*df t* = 37.01	59
No. of pairs	60	
How big is the difference?		
Mean of differences	2.1	
SD of differences	0.4396	
SEM of differences	0.05675	
95% CI	1.986–2.214	
R^2 (partial eta squared)	0.9587	
How effective was the pairing?		
Correlation coefficient *r*	0.9421	
p value (one tailed)	<0.0001	
p value summary	****	
Was the pairing significantly effective?	Yes	

*Pore diameter before (t0) and 90 days later (t90) the injection.

articles on the use of purified botulinum toxin for the treatment of strabismus.[12]

In 1989, the U.S. Food and Drug Administration first approved botulinum toxin for the treatment of blepharospasm.[13] Although Carruthers and Carruthers published their first clinical study of botulinum toxin type A for glabellar lines in 1992,[14] it would take another decade to achieve U.S. Food and Drug Administration approval for this limited indication, and in 2002 botulinum toxin type A received its first cosmetic indication for the treatment of dynamic rhytides of the glabella. Nowadays, botulinum toxin type A injection is the most common cosmetic procedure globally, and its aesthetic use is supported by a broad literature base.[15]

North American consensus recommendations for botulinum toxin type A were revised and updated in 2008.[16] European (French) guidelines were further published in 2011.[17,18] Comparative guidelines for onabotulinumtoxinA, abobotulinumtoxinA, and incobotulinumtoxinA were provided by five experts from Canada, Europe, and South America in 2013.[19]

All of the U.S. Food and Drug Administration–approved botulinum toxin type A formulations are now used successfully for the treatment of the upper face, including onabotulinum toxin [Botox (Allergan, Inc., Dublin, Ireland) or Vistabex (Allergan)], abobotulinum toxin [Dysport (Galderma Laboratories, Fort Worth, Texas) or Azzalure (Ipsen, Paris, France)], and incobotulinum toxin [Xeomin (Merz Pharmaceuticals, Frankfurt am Main, Germany) or Bocouture (Merz)].

Although the traditional injection points and the standardized dosage are still commonly used and should be the teaching tool for novice injectors, most cosmetic physicians have evolved to tailor dosage and injection points on an individual basis. This includes taking into account differences in the anatomy of the muscles, muscle strength, baseline asymmetries, and relationships to other aesthetic units, along with the most important factor of all, the patient-desired outcome.

Although clinical trials have emphasized the efficacy of the drug with full doses, the frozen and nonmovement of the glabella and upper face and eyebrows is undesirable for most of our patients today. The most common single-unit treatment sought for upper face nonsurgical rejuvenation is that for the glabella, along with forehead and periorbital lines, but cosmetic application of neuromodulators to the lower face can lead to dramatic aesthetic improvement.[20,21] To achieve more natural results, clinicians carried out dose-reduction strategies and increased the dilution to reach optimal results in small aesthetic flaws.

Among the factors that determine sebum production and pore size, the activity of the arrector pili muscle and the acetylcholine-mediated activation of local muscarinic receptors in the pilosebaceous unit are strongly related, as previously published,[5,22] and these anecdotal reports have motivated authors to investigate this topic. Even if the role of the nervous system and acetylcholine in sebum production is not well defined, the improvement of skin condition is dramatic, both self-assessed and as measured by instrumental analysis.[6]

A quantitative instrumental evaluation of intradermal injection of botulinum to reduce the flaws of facial aging has already been published,[23,24] but to the best of our knowledge, this is the first study that analyzes the cosmetic effect of microbotulinum injection technique on skin quality by means of instrumental and thus objective assessment. A skin scanner technology analysis has been coupled with a blind evaluation of the results by the authors and a self-assessment score performed by the patients themselves, to determine the effectiveness of intradermal botulinum toxin injection in improving skin texture, decreasing microwrinkles, and reducing pore size by means of quantitative analysis.

This pilot study has been designed and carried out pushed by the common assumption that cosmetic medicine is very subjective and that there needs to be a method for determining the true outcome of treatments besides the mere judgment of patients and clinicians. Photography has been chosen as the method to overcome this; therefore, standardized photographs of the results of the forehead (Fig. 7) and of the cheeks and jawline regions are presented (Fig. 8). However, as one photographs smaller things, the relationship of the light against the surface of the subject becomes more determining and difficult to control. [**See Figure, Supplemental Digital Content 5**, which shows a patient's right cheek and jawline before (*left*) and 30 days after (*right*) microbotulinum injection, ***http://links.lww.com/PRS/E208***. **See Figure, Supplemental Digital Content 6**, which show a patient's right cheek before (*left*) and 30 days after (*right*) microbotulinum injection, ***http://links.lww.com/PRS/E209***. **See Figure, Supplemental Digital Content 7**, which shows a patient's left cheek 30 days (*right*) after microbotulinum injection, ***http://links.lww.com/PRS/E210***.] When studying tissue texture, fine wrinkles, and pores, reproducibility of photographs becomes exponentially more difficult because tiny variations of light can easily cause major changes in appearance.[25]

This is the largest case series that shows that intradermal injection of botulinum toxin can temporarily improve skin texture (**see Figure, Supplemental Digital Content 1**, ***http://links.lww.com/PRS/E204***), decrease microwrinkles (**see Figure, Supplemental Digital Content 2**, ***http://links.lww.com/PRS/E205***), and control sebum production (as shown by the decrease in pore size), with statistically significant results in the first 3 months, together with a high degree of patient satisfaction (95.1 percent). From our results, we can state that the best results have been obtained in patients aged between 42.7 and 46.8 years, and calculation of the standard deviations allows us to recommend this treatment, for better results, in patients aged between 36.5 and 53 years (average of the standard deviation). Moreover, given the decrease in patient satisfaction at 120 days after the peak at 90 days, it has to be pointed out that, to maintain skin results and a high satisfaction level, retreatment should be considered after 120 days.

The length of efficacy of this intradermal toxin use is shorter than for the intramuscular one. The authors believe this must be attributable to the amount of injected material which, compared to the published literature, is one-half.

The authors believe that the reported 5 percent lack of patient satisfaction at 30 days is attributable to a lack of effect secondary to an undetected loss of toxin solution while delivered, regardless of whether lost on the skin or because

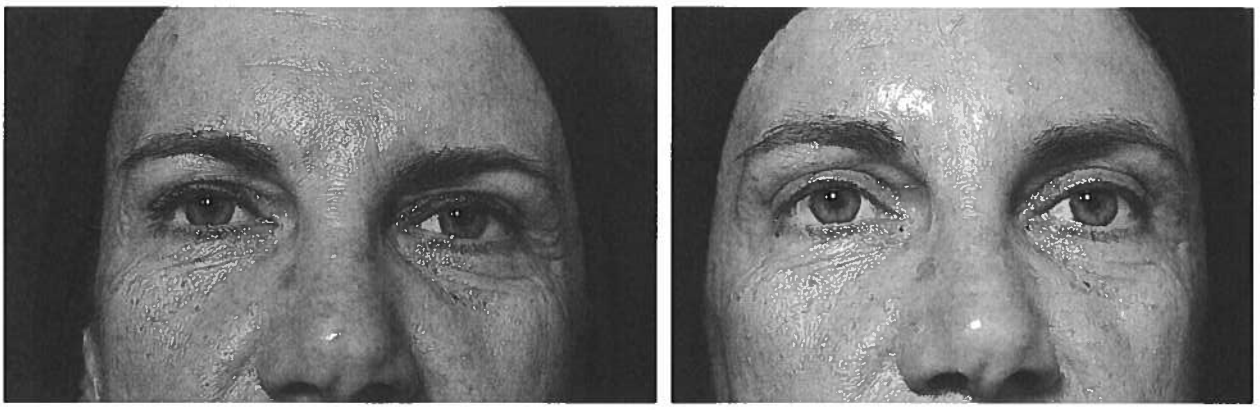

Fig. 7. Patient forehead before (*left*) and 30 days after (*right*) microbotulinum injection.

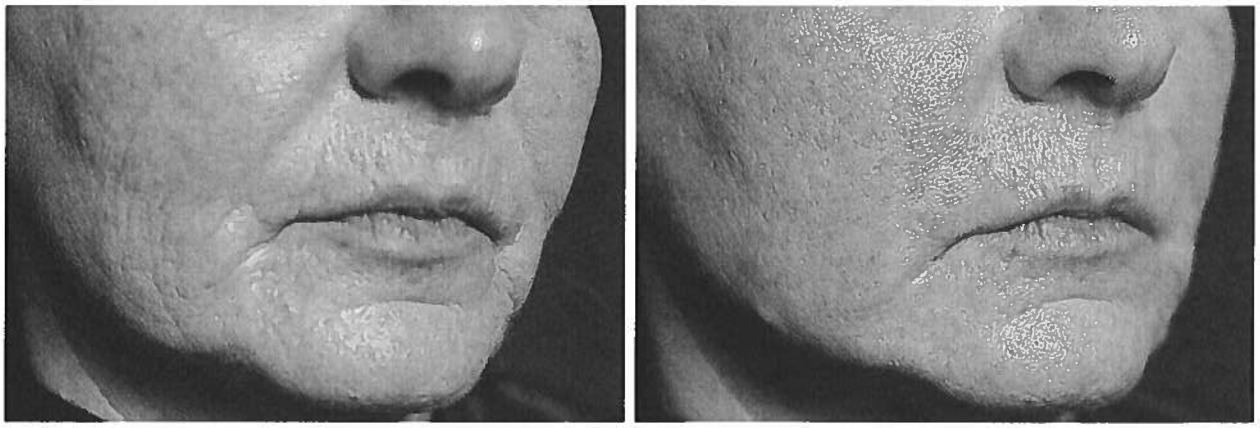

Fig. 8. Patient cheek and jawline before (*left*) and 30 days after (*right*) microbotulinum injection.

of being injected too deep and thus ineffectively: this injection technique, as reported in the literature, is technically dependent on injector skills.[1–24]

The intradermal use of larger amounts could result in muscle weakness or lack of mimic activity of the muscles at the treated sites, because of the deeper level of diffusion. Despite over 100 injections being delivered, patients are comfortable and tolerant of the procedure: this is largely because of the lidocaine that has been mixed into the microbotulinum solution. The initial prick may be painful, but within 1 or 2 seconds, the injection point becomes anesthetized and no longer bothers the patients, as the rest of the injections are completed in the remaining areas.[21]

If contraindicated because of a referred allergy or other systemic illness, lidocaine can be avoided and the dilution can be made with saline only. If this is the case, patients could experience some pain along with the injection procedure. Nevertheless, it is the authors' opinion that the use of topical anesthetic could improve patient compliance to the treatment, as reported with different intradermal injection techniques.[26–28]

Proper localization of injection points on the cheeks or the perioral region is mandatory, because inadvertent paralysis in these areas can significantly affect function. In this series, five patients had injection-point ecchymosis, and no patients reported muscle weakness or facial asymmetries during the follow-up period. Moreover, the possibility of delivering an intramuscular injection and causing subsequent paralysis also becomes relevant in the design of future studies concerning intradermal botulinum toxin, as it has the potential to unblind the treated subject and the investigator.

CONCLUSIONS

The results of this pilot study suggest that intradermal botulinum toxin injection, or so-called microbotulinum, is a safe and effective method to treat skin flaws affecting texture and microroughness and to reduce enlarged pore size. It is to be

preferred in middle-aged patients, between 36.5 and 53 years, looking for middle-term results, as the here-considered follow-up period does not extend beyond 120 days. Because of the high satisfaction rate among both physicians and patients, further studies are indeed mandatory to determine the optimal number of units needed for a longer and lasting effect with this particular novel dilution.

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PATIENT CONSENT

Patients provided written consent for the use of their images.

REFERENCES

1. Wu WTL. Microbotox of the lower face and neck: Evolution of a personal technique and its clinical effects. *Plast Reconstr Surg.* 2015;136(Suppl):92S–100S.
2. Bushara KO, Park DM, Jones JC, Schutta HS. Botulinum toxin: A possible new treatment for axillary hyperhidrosis. *Clin Exp Dermatol.* 1996;21:276–278.
3. Glogau RG. Botulinum A neurotoxin for axillary hyperhidrosis: No sweat Botox. *Dermatol Surg.* 1998;24:817–819.
4. Naumann M, Lowe NJ. Botulinum toxin type A in treatment of bilateral primary axillary hyperhidrosis: Randomised, parallel group, double blind, placebo controlled trial. *BMJ* 2001;323:596–599.
5. Shah AR. Use of intradermal botulinum toxin to reduce sebum production and facial pore size. *J Drugs Dermatol.* 2008;7:847–850.
6. Rose AE, Goldberg DJ. Safety and efficacy of intradermal injection of botulinum toxin for the treatment of oily skin. *Dermatol Surg.* 2013;39:443–448.
7. Donofrio L, Carruthers A, Hardas B, et al. Development and validation of a photonumeric scale for evaluation of facial skin texture. *Dermatol Surg.* 2016;42(Suppl 1):S219–S226.
8. Carruthers J, Donofrio L, Hardas B, et al. Development and validation of a photonumeric scale for evaluation of facial fine lines. *Dermatol Surg.* 2016;42(Suppl 1):S227–S234.
9. Matsubara A, Liang Z, Sato Y, Uchikawa K. Analysis of human perception of facial skin radiance by means of image histogram parameters of surface and subsurface reflections from the skin. *Skin Res Technol.* 2012;18:265–271.
10. Koprowski R, Wilczyński S, Samojedny A, Wróbel Z, Deda A. Image analysis and processing methods in verifying the correctness of performing low-invasive esthetic medical procedures. *Biomed Eng Online.* 2013;12:51.
11. Korotkov K, Garcia R. Computerized analysis of pigmented skin lesions: A review. *Artif Intell Med.* 2012;56:69–90.
12. Scott AB. Botulinum toxin injection into extraocular muscles as an alternative to strabismus surgery. *J Pediatr Ophthalmol Strabismus* 1980;17:21–25.
13. Gendler E, Nagler A. Aesthetic use of BoNT: Options and outcomes. *Toxicon* 2015;107:120–128.
14. Carruthers JD, Carruthers JA. Treatment of glabellar frown lines with *C. botulinum*-A exotoxin. *J Dermatol Surg Oncol.* 1992;18:17–21.
15. Sundaram H, Signorini M, Liew S, et al. Global aesthetics consensus: Botulinum toxin type A. Evidence-based review, emerging concepts, and consensus recommendations for aesthetic use, including updates on complications. *Plast Reconstr Surg.* 2016;137:518e–529e.
16. 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(Suppl):5S–30S; quiz 31S–36S.
17. Raspaldo H, Baspeyras M, Bellity P, et al.; Consensus Group. Upper- and mid-face anti-aging treatment and prevention using onabotulinumtoxin A: The 2010 multidisciplinary French consensus. Part 1. *J Cosmet Dermatol.* 2011;10:36–50.
18. Raspaldo H, Niforos FR, Gassia V, et al.; Consensus Group. Lower-face and neck antiaging treatment and prevention using onabotulinumtoxin A: The 2010 multidisciplinary French consensus. Part 2. *J Cosmet Dermatol.* 2011;10:131–149.
19. Carruthers J, Fournier N, Kerscher M, Ruiz-Avila J, Trindade de Almeida AR, Kaeuper G. 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 II—Incorporating botulinum toxin into aesthetic clinical practice. *Dermatol Surg.* 2013;39:510–525.
20. Monheit G. Neurotoxins: Current concepts in cosmetic use on the face and neck. Upper face (glabella, forehead, and crow's feet). *Plast Reconstr Surg.* 2015;136(Suppl):72S–75S.
21. Wu DC, Fabi SG, Goldman MP. Neurotoxins: Current concepts in cosmetic use on the face and neck. Lower face. *Plast Reconstr Surg.* 2015;136(Suppl):76S–79S.
22. Roh M, Han M, Kim D, Chung K. Sebum output as a factor contributing to the size of facial pores. *Br J Dermatol.* 2006;155:890–894.
23. Sapra P, Demay S, Sapra S, Khanna J, Mraud K, Bonadonna J. A single-blind, split-face, randomized, pilot study comparing the effects of intradermal and intramuscular injection of two commercially available botulinum toxin A formulas to reduce signs of facial aging. *J Clin Aesthet Dermatol.* 2017;10:34–44.
24. Awaida CJ, Jabbour SF, Rayess YA, El Khoury JS, Kechichian EG, Nasr MW. Evaluation of the microbotox technique: An algorithmic approach for lower face and neck rejuvenation and a crossover clinical trial. *Plast Reconstr Surg.* 2018;142:640–649.
25. Lambros V. Discussion: Evaluation of the microbotox technique: An algorithmic approach for lower face and neck rejuvenation and a crossover clinical trial. *Plast Reconstr Surg.* 2018;142:650–651.
26. Kim J. Clinical effects on skin texture and hydration of the face using microbotox and microhyaluronic acid. *Plast Reconstr Surg Glob Open* 2018;6:e1935.
27. Bertossi D, Giampaoli G, Lucchese A, et al. The skin rejuvenation associated treatment-Fraxel laser, microbotox, and low G prime hyaluronic acid: Preliminary results. *Lasers Med Sci.* 2019;34:1449–1455.
28. Calvani F, Santini S, Bartoletti E, Alhadeff A. Personal technique of microinfiltration with botulin toxin: The SINB technique (superficial injection needling botulinum). *Plast Surg (Oakv.)* 2019;27:156–161.