

The Impact of Upper Face Botulinum Toxin Injections on Eyebrow Height and Forehead Lines: A Randomized Controlled Trial and an Algorithmic Approach to Forehead Injection

Samer F. Jabbour, M.D.
Cyril J. Awaïda, M.D.
Joseph S. ElKhouri, M.D.
Youssef A. Rayess, M.D.
Rani B. Makhoul, M.D.
Elio G. Kechichian, M.D.
Marwan W. Nasr, M.D.
Beirut, Lebanon; and Paris, France



Summary: No previous study has objectively evaluated the effect of different forehead injection patterns on the eyebrow height and forehead lines. The patients were divided into three groups. Botulinum toxin was injected into both the lateral and medial eyebrow depressors in all groups. The frontalis was injected using either a V-pattern (group 1), a middle horizontal pattern (group 2), or a high horizontal pattern (group 3). Objective eyebrow measurements were performed using standardized preinjection and postinjection photographs. Validated photonic scales were used to assess the forehead lines. Fifteen patients (30 eyebrows) were included in each group. In all of the groups, 2 weeks after injection, the brow was lower at all the measured positions, with the exception of the lateral brow edge, which was higher in the three injection patterns. No difference was found when comparing group 1 to groups 2 and 3. The middle forehead injection pattern lowered the eyebrow more than the upper forehead injection pattern. The three techniques improved the forehead lines at rest and with contraction. The forehead lines with contraction were more improved in group 1 compared with both groups 2 and 3. Each forehead injection pattern yielded different results on forehead lines and eyebrow position. Upper forehead injections were less effective on forehead lines but prevented eyebrow ptosis. (*Plast. Reconstr. Surg.* 2018;142:1212)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, II.

Currently, botulinum toxin injection is the most common noninvasive procedure for forehead rejuvenation.¹ Although frontalis botulinum toxin injection effectively effaces forehead lines, a proportion of patients experience some degree of brow ptosis caused by the unopposed action of the medial and lateral brow depressors.¹⁻⁵ Although brow elevation is aesthetically appealing, brow descent remains highly

unpleasing for patients.^{6,7} No previous study has objectively evaluated the effect of concomitant eyebrow depressor and forehead injections on brow height and morphology. The objective of this prospective randomized trial was to compare the effect of three different forehead injection patterns on the eyebrow height and the forehead lines using objective measurements and validated region-specific scores.

From the Departments of Plastic and Reconstructive Surgery and Dermatology, Faculty of Medicine Saint-Joseph University; and Policlinique Esthétique Marigny Vincennes.

Received for publication October 19, 2017; accepted April 12, 2018.

This trial is registered under the name "Frontalis Botulinum Toxin," ClinicalTrials.gov identification number NCT03186001 (<https://clinicaltrials.gov/ct2/show/NCT03186001?term=botulinum+forehead&entry1=ME%3ALB&rank=1>).

Copyright © 2018 by the American Society of Plastic Surgeons

DOI: 10.1097/PRS.0000000000004836

Disclosure: All the authors have no financial information to disclose. No funding was received for the article.

Supplemental digital content is available for this article. Direct URL citations appear in the text; simply type the URL address into any Web browser to access this content. Clickable links to the material are provided in the HTML text of this article on the *Journal's* website (www.PRSJournal.com).

PATIENTS AND METHODS

Design

This prospective, randomized, controlled trial was approved by the institutional review board of Hotel Dieu de France Hospital, Beirut, Lebanon. The patients were divided randomly into three groups. A 500-U vial of abobotulinumtoxinA (Dysport; Ipsen Ltd, Berks, United Kingdom) was reconstituted with 2.5 cc of saline. Botulinum toxin was injected in both the lateral (five injections) and medial (two injections) eyebrow depressors in all groups at the dose of 5 U of abobotulinumtoxinA per injection point. The frontalis was injected at five injection points using either a V pattern (group 1), a middle horizontal pattern (group 2), or a high horizontal pattern (group 3) (Fig. 1).

Evaluation of Results

Patient photographs were taken before and 2 weeks after the injections, at rest and on maximal brow elevation. Objective brow height measurements were obtained using Adobe Photoshop (Adobe Systems, Inc., San Jose, Calif.). Three independent blinded raters measured the distance from the midpupillary plane to the upper eyebrow border at seven points: the medial edge of the brow, the medial canthus, the medial limbus, the mid pupil, the lateral limbus, the lateral canthus, and the lateral edge of the eyebrow. [See **Figure, Supplemental Digital Content 1**, which shows the measurement technique. The midpupillary horizontal plane was used as a reference. The vertical distance (*arrow*) from the midpupillary horizontal plane to the upper brow margin was measured at seven points: the medial edge of the brow, the

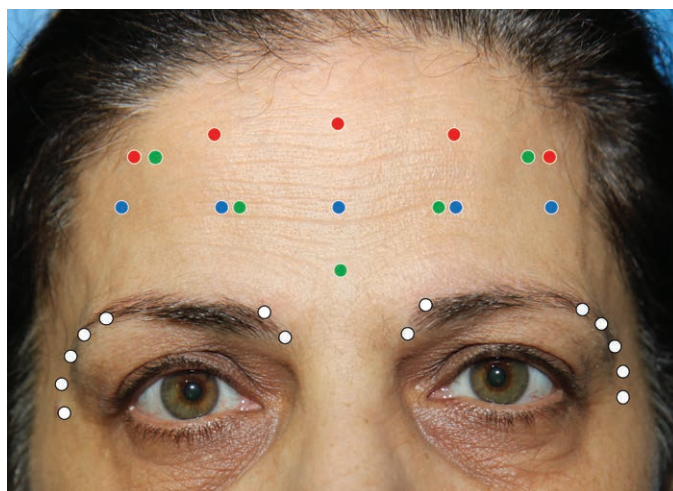


Fig. 1. Injection techniques. In all patients, botulinum toxin was injected superficially into the orbicularis oculi muscle with five equally spaced injection points from the lateral limbus to the inferior orbital rim, with two additional intramuscular injections into the medial eyebrow depressors. The first injection was performed at the medial edge of the brow and the second injection was performed 1 cm lateral to the first injection just above the eyebrow (*white dots*). In addition to the eyebrow depressor injections, group 1 received five equally spaced subcutaneous injections, in a V pattern. The first injection was placed at the midline of the forehead just above the eyebrows, two lateral injections were placed 1 cm below the hairline at the level of the lateral canthus, and the last two injections were placed between the medial and lateral injections (*green dots*). Group 2 received five equally spaced horizontal injections in the middle part of the forehead (*blue dots*). Group 3 received five equally spaced horizontal injections in the upper part of the forehead, 1 cm below the anterior hairline (*red dots*). Each site was injected with 0.05 ml (5 U) of abobotulinumtoxinA.

medial canthus, the medial limbus, the mid pupil, the lateral limbus, the lateral canthus, and the lateral edge of the eyebrow (*red dots*). A 4-cm forehead tag was used as a measurement scale (*dotted arrow*), <http://links.lww.com/PRS/D52>.]

Two weeks after the injection, each patient completed a four-scale satisfaction questionnaire ranging from 1 (very satisfied) to 4 (very dissatisfied). Validated photonumeric scales were used to assess the forehead lines at rest and with contraction.⁸ The patients' photographs were cropped to match the pictures of the photographic scales. Each preinjection and postinjection photograph was deidentified, randomized, and placed on a separate scoring sheet. Each scoring sheet was then independently assessed by three blinded raters (two plastic surgeons and one dermatologist).

RESULTS

In total, 15 patients (30 eyebrows) were included in each group. All patients were women with a mean age of 42, 39.6, and 40.6 years in groups 1, 2, and 3 respectively ($p = 0.382$). Two patients in each group were smokers.

In all groups, 2 weeks after the injection, the brow was lower at all of the measured positions, with the exception of the lateral brow edge, which was higher in the three injection patterns (Table 1 and Fig. 2). The difference between the preinjection and postinjection measurements

(postinjection height minus preinjection height) was not significantly different when comparing group 1 to groups 2 and 3. However, in group 2, the eyebrows were lower when compared to group 3 in most of the measured positions (Table 1).

The three techniques improved significantly the forehead line scores at rest and with contraction (Table 2). The comparison of the differences of the preinjection and postinjection region-specific scores (postinjection scores minus preinjection scores) among the three groups showed that the forehead lines with contraction were more improved in group 1 compared with both groups 2 and 3. Although the V-pattern injections improved the forehead lines more than the upper forehead injection pattern at rest, the improvement of the forehead lines at rest was comparable in both group 1 and group 2. The middle forehead injections did not improve the forehead lines more than the upper injection pattern either at rest or with contraction (Table 3). All of the patients in groups 1 and 3 were very satisfied with their results, whereas in group 2, nine patients were very satisfied, and six patients were only satisfied because of the low position of their middle eyebrows but were willing to repeat the same procedure. [See **Figure, Supplemental Digital Content 2**, which shows results for groups 1, 2, and 3. From *left to right*: Preinjection frontal photograph at rest; preinjection frontal photograph with frontalis contraction; frontal photograph at rest 2 weeks after injection; and

Table 1. Objective Measurements Results*

	Eyebrow Height Position above the Midpupillary Plane (cm)						
	Medial Brow	Medial Canthus	Medial Limbus	Mid Pupil	Lateral Limbus	Lateral Canthus	Lateral Brow
Group 1: V-pattern injections							
Preinjection	1.783	1.943	2.063	2.092	2.128	2.075	1.081
Postinjection	1.651	1.815	1.936	1.969	2.007	1.957	1.152
Group 2: Middle forehead horizontal injections							
Preinjection	1.623	1.809	1.978	2.067	2.131	2.077	1.038
Postinjection	1.465	1.667	1.827	1.902	1.976	1.925	1.119
Group 3: Upper forehead horizontal injections							
Preinjection	1.517	1.695	1.869	1.974	2.074	2.076	1.243
Postinjection	1.471	1.643	1.847	1.94	2.016	1.959	1.256
Postinjection and preinjection eyebrow height differences for each group							
Group 1 (postinjection – preinjection)	–0.132	–0.128	–0.127	–0.123	–0.121	–0.118	0.071
Group 2 (postinjection – preinjection)	–0.158	–0.142	–0.151	–0.165	–0.155	–0.152	0.081
Group 3 (postinjection – preinjection)	–0.046	–0.052	–0.022	–0.034	–0.058	–0.117	0.013
Comparison of the postinjection and preinjection eyebrow height differences between the three groups (p values)							
Groups 1 and 2	0.667	0.837	0.701	0.449	0.474	0.446	0.758
Groups 1 and 3	0.084	0.179	0.056	0.077	0.141	0.982	0.051
Groups 2 and 3	0.021†	0.067	0.005†	0.003†	0.026†	0.387	0.029†

*Displayed values are the mean of both the right and left eyes. Statistical analysis was performed with IBM SPSS Advanced Statistical Software Version 22.0 (IBM Corp., Armonk, N.Y.). Preinjection and postinjection eyebrow height differences were compared using an independent t test. Statistical significance was set at $p < 0.05$.

†Statistically significant.

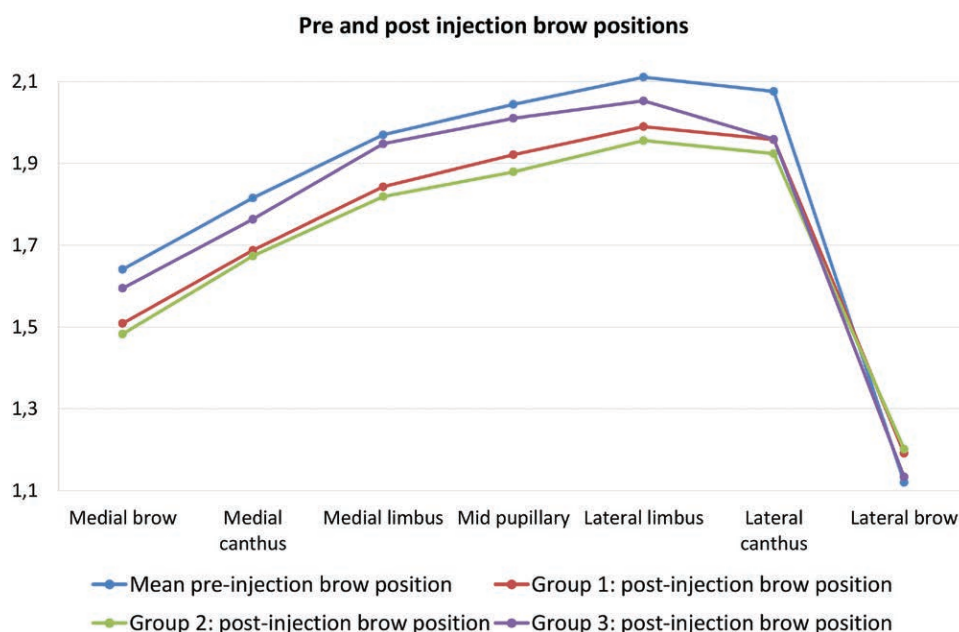


Fig. 2. Scaled eyebrow morphology, with vertical heights measured from the horizontal midpupillary plane. Dots represent the mean vertical distance between the upper border of the eyebrow and midpupillary plane at seven different locations: the medial brow, the medial canthus, the medial limbus, the mid pupil, the lateral limbus, the lateral canthus, and the lateral brow (in centimeters). Group 1, V-pattern injections; group 2, middle forehead horizontal injections; group 3, upper forehead horizontal injections.

Table 2. Region-Specific Score Results*

	Preinjection Score	Postinjection Score	Score Improvement	<i>p</i>
Forehead lines at rest				
Group 1	1.2	0.4	0.8	<0.001†
Group 2	0.8	0.2	0.6	<0.001†
Group 3	0.8	0.4	0.4	<0.001†
Forehead lines with contraction				
Group 1	3.2	1	2.2	<0.001†
Group 2	2.2	0.8	1.4	<0.001†
Group 3	2	1.2	0.8	<0.001†

*Group 1: V-shaped injections; group 2, middle forehead injections; group 3, upper forehead injections. Statistical analysis was performed with SPSS Advanced Statistical Software Version 22.0. Preinjection and postinjection scores were compared using a paired *t* test. Statistical significance was set as *p* < 0.05.

†Statistically significant.

Table 3. Comparison of the Postinjection and Preinjection Region-Specific Score Differences among the Three Groups*

	Group 1 (<i>p</i>)	Group 2 (<i>p</i>)	Group 3 (<i>p</i>)
Forehead lines at rest			
Group 1		0.246	0.025†
Group 2	0.246		0.289
Group 3	0.025†	0.289	
Forehead lines with contraction			
Group 1		0.043†	<0.001†
Group 2	0.043†		0.086
Group 3	<0.001†	0.086	

*Group 1, V-shaped injections; group 2, middle forehead injections; group 3, upper forehead injections. Statistical analysis was performed with SPSS Advanced Statistical Software Version 22.0. Preinjection and postinjection scores were compared using a paired *t* test. Statistical significance was set as *p* < 0.05.

†Statistically significant.

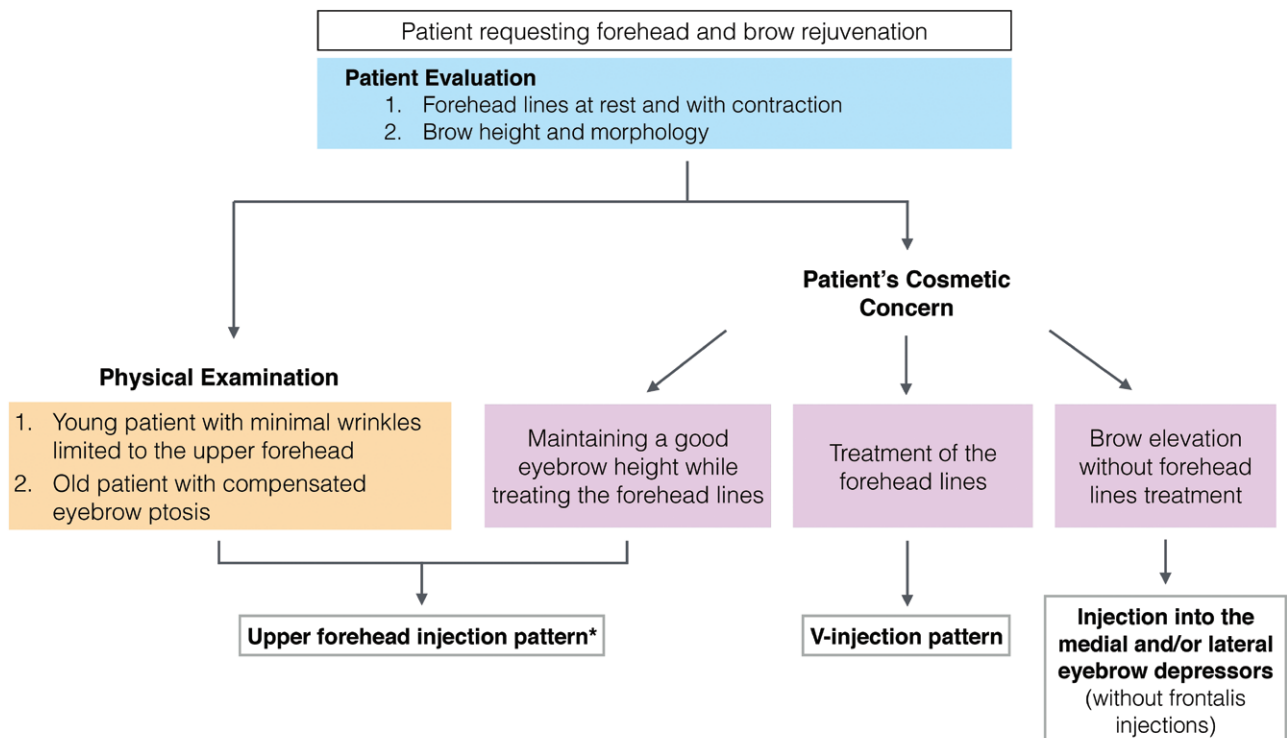
frontal photograph with frontalis contraction 2 weeks after injection. (*Above*) A 52-year-old patient that was treated with V-pattern injections. (*Center*) A 42-year-old patient that was treated with middle forehead horizontal injection pattern. (*Below*) A 35-year-old patient that was treated with an upper forehead horizontal injection pattern, <http://links.lww.com/PRS/D53>.]

DISCUSSION

Each forehead injection pattern affected the forehead lines and eyebrow position differently. A V-shaped injection pattern was the most effective treatment for the forehead lines, whereas middle forehead horizontal injections resulted in the most important eyebrow ptosis compared with the upper forehead injection pattern. Thus, when the patient's main concern is the treatment of the forehead lines, we use a V-shaped injection pattern because it is the most effective treatment of the forehead lines and yields less eyebrow ptosis than the middle forehead horizontal injections. When the patient's main concern is to maintain a good eyebrow height while treating the forehead lines, we use an upper forehead injection pattern and avoid any injections into the middle and

lower forehead. In these cases, the patient should be notified that although this pattern affects the eyebrow height the least, it is not the most effective treatment for the forehead lines. Therefore, the upper forehead horizontal injection pattern is mainly indicated in two specific clinical scenarios: (1) a young patient with minimal wrinkles limited to the upper forehead, in whom high horizontal injections will result in a complete resolution of the forehead lines and maintain a good position and mobility of the eyebrows (see **Figure, Supplemental Digital Content 2**, <http://links.lww.com/PRS/D53>); and (2) an old patient with senile eyebrow ptosis compensated by an active contraction of the frontalis muscles, in whom forehead injections should be prohibited or reduced to small doses injected in the most cephalic part of the forehead. Finally, when the patient's main concern is to elevate the eyebrows without treating the forehead lines, we inject only the medial and/or lateral eyebrow depressors without injecting the frontalis⁹ (Fig. 3).

The lateral eyebrow was higher after the injections in the three groups. We hypothesize that most of the botulinum toxin was injected into the medial frontalis, leading to an increased compensatory resting tone of the lateral fibers and an elevation



* The patient should be notified that although this pattern is the least to affect the eyebrow height, it is not the most effective treatment for the forehead lines.

Fig. 3. Algorithmic approach to upper face botulinum toxin injection.

of the lateral eyebrow. The elevation of the lateral eyebrow was more important in groups 1 and 2 when compared to group 3, in which the medial frontalis fibers were the least paralyzed. This lateral elevation is clearly illustrated in the photographs of groups 1 and 2 (see Figure, Supplemental Digital Content 2, <http://links.lww.com/PRS/D53>).

In general, the treatment of forehead lines with botulinum toxin yields a high level of satisfaction regardless of the injection pattern. However, when the treatment is adapted to each patient's demand, it will produce the optimal aesthetic result and avoid common complaints about low, medial, and middle eyebrow positions.

It has been known that different forehead injection patterns yielded different results. In previous trials, the majority of authors avoided overinjection of the forehead to prevent eyebrow ptosis.^{1,2,10,11} De Maio et al. injected the upper forehead at five sites with two additional lateral sites to avoid the Mephisto effect.¹ Jaspers et al. used a V-pattern injection to achieve an additional lateral eyebrow lift.² Prevot et al. injected the upper forehead at six to 12 points while avoiding the lower 3 cm of the forehead.¹¹ However, other authors injected the lower and middle forehead, depending on the patient's wrinkle pattern.^{12–14} We were the first to objectively demonstrate the impact of different forehead injection patterns, establishing an algorithmic approach combining the physician's objective assessment and the patient's aesthetic concern.

In a previous article, we hypothesized that elevation of the eyebrows is mainly caused by the frontalis contraction and not by the paralysis of the eyebrow depressors.⁹ In this study, we confirmed this hypothesis by demonstrating that higher forehead injections allowed a residual lower frontalis contraction that prevented the severe eyebrow depression observed with lower forehead injections.

The main limitation of this trial is the small sample sizes. However, each injection pattern resulted in the same eyebrow and forehead modifications in all of the patients. Therefore, small samples were enough to statistically prove differences among the three different techniques. Another limitation to this study is the randomization process, as the prescribed injection pattern was randomly assigned to each patient, and it may not have been the best treatment in each individual case.

CONCLUSIONS

Each forehead injection pattern yielded different results on forehead lines and eyebrow

position. Upper face botulinum toxin injections should be adapted to the patient's expectations and clinical examination.

Samer F. Jabbour, M.D.

Faculty of Medicine
Saint-Joseph University
Damascus Street
BP 17-5208 - Mar Mikhaël
Beirut, Lebanon 1104 2020
samermed@gmail.com

PATIENT CONSENT

Patient provided written consent for the use of patient's image.

REFERENCES

1. de Maio M, Wu WTL, Goodman GJ, Monheit G. Facial assessment and injection guide for botulinum toxin and injectable hyaluronic acid fillers. *Plast Reconstr Surg*. 2017;140:393e–404e.
2. Jaspers GW, Pijpe J, Jansma J. The use of botulinum toxin type A in cosmetic facial procedures. *Int J Oral Maxillofac Surg*. 2011;40:127–133.
3. Ahn MS, Catten M, Maas CS. Temporal brow lift using botulinum toxin A. *Plast Reconstr Surg*. 2000;105:1129–1135; discussion 1136–1139.
4. Carruthers A, Carruthers J. Eyebrow height after botulinum toxin type A to the glabella. *Dermatol Surg*. 2007;33:S26–S31.
5. Maas CS, Kim EJ. Temporal brow lift using botulinum toxin A: An update. *Plast Reconstr Surg*. 2003;112(Suppl):109S–112S; discussion 113S–114S.
6. Jones BM, Lo SJ. The impact of endoscopic brow lift on eyebrow morphology, aesthetics, and longevity: Objective and subjective measurements over a 5-year period. *Plast Reconstr Surg*. 2013;132:226e–238e.
7. Lazarus D. Changes in eyebrow position and shape with aging and brow lifting. *Plast Reconstr Surg*. 2010;125:1291–1292.
8. Flynn TC, Carruthers A, Carruthers J, et al. Validated assessment scales for the upper face. *Dermatol Surg*. 2012;38:309–319.
9. ElKhouri JS, Jabbour SF, Awaida CJ, Rayess YA, Kechichian EG, Nasr MW. The impact of botulinum toxin on brow height and morphology: A randomized controlled trial. *Plast Reconstr Surg*. 2018;141:75–78.
10. Qaqish C. Botulinum toxin use in the upper face. *Atlas Oral Maxillofac Surg Clin North Am*. 2016;24:95–103.
11. Prevot M, Thomet C, Cornette De Saint-Cyr B, Marchac A, Delay E. Forehead rejuvenation (in French). *Ann Chir Plast Esthet*. 2017;62:406–423.
12. Susmita A, Kolli NN, Meka S, et al. An evaluation of use of botulinum toxin type A in the management of dynamic forehead wrinkles: A clinical study. *J Clin Diagn Res*. 2016;10:ZC127–ZC131.
13. Uygur S, Eryilmaz T, Bulam H, Yavuzer R, Latifoglu O. The quantitative effect of botulinum toxin A over brow height. *J Craniofac Surg*. 2013;24:1285–1287.
14. Carruthers A, Carruthers J, Cohen J. A prospective, double-blind, randomized, parallel-group, dose-ranging study of botulinum toxin type a in female subjects with horizontal forehead rhytides. *Dermatol Surg*. 2003;29:461–467.