A Quantitative Analysis of OnabotulinumtoxinA, AbobotulinumtoxinA, and IncobotulinumtoxinA: A Randomized, Double-Blind, Prospective Clinical Trial of Comparative Dynamic Strain Reduction

Anthony J. Wilson, M.D.
Brian Chang, B.S.
Anthony J. Taglienti, M.D.
Bianca C. Chin, M.D.
Catherine S. Chang, M.D.
Nancy Folsom, R.N.
Ivona Percec, M.D., Ph.D.

Philadelphia, Pa.

Background: U.S. Food and Drug Administration–approved formulations of botulinum toxin include onabotulinumtoxinA (Botox; Allergan, Inc., Irvine, Calif.), abobotulinumtoxinA (Dysport; Galderma Pharma S.A., Lausanne, Switzerland), and incobotulinumtoxinA (Xeomin; Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany). This study uses digital image correlation to compare dynamic strain reduction between available neurotoxins.

Methods: Seventy-three treatment-naive female patients aged were randomized to injection with onabotulinumtoxinA (20 units), abobotulinumtoxinA (60 units), or incobotulinumtoxinA (20 units) in the glabella. Imaging was conducted at 4, 14, and 90 days after injection. Change in average dynamic strain of the glabella was compared using ANOVA.

Results: At day 4, there was a 42.1 percent strain reduction in the onabotulinumtoxinA group, a 39.4 percent strain reduction in the abobotulinumtoxinA group, and a 19.8 percent strain reduction in the incobotulinumtoxinA group (onabotulinumtoxinA versus abobotulinumtoxinA, $p = 0.77$; onabotulinumtoxinA versus incobotulinumtoxinA, $p = 0.02$; and abobotulinumtoxinA versus incobotulinumtoxinA, $p = 0.04$). At day 14, there was a 66.1 percent strain reduction in the onabotulinumtoxinA group, a 51.4 percent strain reduction in the abobotulinumtoxinA group, and a 42.8 percent strain reduction in the incobotulinumtoxinA group (onabotulinumtoxinA versus abobotulinumtoxinA, $p = 0.14$; onabotulinumtoxinA versus incobotulinumtoxinA, $p = 0.02$; and abobotulinumtoxinA versus incobotulinumtoxinA, $p = 0.36$). At day 90, there was a 43.5 percent strain reduction in the onabotulinumtoxinA group, a 38.4 percent strain reduction in the abobotulinumtoxinA group, and a 25.3 percent strain reduction in the incobotulinumtoxinA group (onabotulinumtoxinA versus abobotulinumtoxinA, $p = 0.66$; onabotulinumtoxinA versus incobotulinumtoxinA, $p = 0.12$; and abobotulinumtoxinA versus incobotulinumtoxinA, $p = 0.24$).

Conclusions: Using digital image correlation, the tested neuromodulators do not have equivalent strain reduction in the glabella at the doses used. These results confirm assertions of noninterchangeability. (*Plast. Reconstr. Surg.* 137: 1424, 2016.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, II.

With more than 6.1 million procedures conducted in 2012, and an annual growth of 8 percent, neuromodulation with botulinum toxin type A is the most commonly performed aesthetic intervention (both nonsurgical and surgical) in the United States.[1] Although the U.S. Food and Drug Administration–approved

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botulinum toxin type A injection sites remain limited to the glabella and lateral canthal rhytides, aesthetic neuromodulation applications have broadly expanded and commonly include treatment of the forehead rhytides, perioral rhytides, masseter hypertrophy, and platysmal banding, among others. Despite the widespread use of botulinum toxin type A, there remains a paucity of objective, reproducible, and quantifiable data for comparative toxin analysis. Previous clinical evaluations of toxins, on both individual and comparative bases, have relied on static photography in conjunction with potentially subjective although validated scores (e.g., Facial Wrinkle Scale, Modified Fitzpatrick Wrinkle Scale, Glabellar Line Severity Score), field of anhidrosis analyses, or even electromyography.[2–7] Although these various methodologies have yielded important data on the efficacy and safety of toxins for static rhytide improvement, they do not accurately capture and evaluate the true dynamic rhytide alteration following a given dose of toxin.

Currently, there are three U.S. Food and Drug Administration–approved botulinum toxin type A formulations: onabotulinumtoxinA (Botox; Allergan, Inc., Irvine, Calif.), abobotulinumtoxinA (Dysport; Galderma Pharma S.A., Lausanne, Switzerland), and incobotulinumtoxinA (Xeomin; Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany) (Table 1).[8–10] Each neurotoxin is formulated differently and demonstrates unique characteristics that distinguish it from its competitors. Consequently, these products are not and should not be considered interchangeable. Following pivotal studies by Carruthers et al., onabotulinumtoxinA (Botox) was initially approved in 2002 and rapidly became the branded "gold standard" for neuromodulation.[11,12] Since its initial approval for glabellar lines, onabotulinumtoxinA has also garnered approval for lateral canthal line modulation.[13] It is formulated with hemagglutinin complexing proteins, stabilized by means of vacuum drying, and requires both dilution and refrigeration before use. AbobotulinumtoxinA (Dysport) was approved in 2009. Like onabotulinumtoxinA, abobotulinumtoxinA is formulated with hemagglutinin complexing proteins, and although it differs in its stabilization by means of lyophilization, it also requires dilution and refrigeration before injection. AbobotulinumtoxinA is clinically and colloquially considered to have the fastest onset of effect with the greatest local spread, despite limited comparative and quantitative evidence supporting this characterization.[6,14–20] IncobotulinumtoxinA (Xeomin) was approved in 2011.[5,21–23] Unlike other toxins, incobotulinumtoxinA is not formulated with complexing proteins and therefore does not require refrigeration before dilution. The absence of these binding proteins is associated with a theoretically decreased immunogenicity of the toxin.[24–27] Similar to abobotulinumtoxinA, incobotulinumtoxinA is stabilized by means of lyophilization. Since its introduction, there have been anecdotal reports of variability in incobotulinumtoxinA efficacy and duration of effect compared with the other two formulations, although there are no direct data to support these observations.

Table 1. The Three Currently U.S. Food and Drug Administration–Approved Botulinum Toxin Type A Formulations with Comparative Pharmacologic Information*

	Botox Cosmetic (OnabotulinumtoxinA)	Dysport (AbobotulinumtoxinA)	Xeomin (IncobotulinumtoxinA)
Manufacturer	Allergan, Inc.	Galderma Pharma S.A.	Merz Pharmaceuticals GmBH
Composition	*Clostridium botulinum* toxin type A ATCC 3502 (Hall strain) hemagglutinin complex; 0.5 mg of human serum albumin; 0.9 mg of NaCl	*Clostridium botulinum* toxin type A ATCC 3502 (Hall strain) hemagglutinin complex; 0.125 mg of human serum albumin; 2.5 mg of lactulose	*Clostridium botulinum* toxin type A ATCC 3502 (Hall strain); 1.0 mg of human serum albumin; 4.7 mg of sucrose
Toxin per 100 units, ng	0.73	0.65	0.44
FDA approval	2002	2009	2011
FDA aesthetic indications	Glabellar rhytides; lateral canthal rhytides	Glabellar rhytides	Glabellar rhytides
Storage	36°–46°F	36°–46°F	68°–77°F
Dilution preservative-free NaCl	2.5 ml	2.5 or 1.5 ml	Variable
Purported benefits	Branded gold standard	Faster onset; greater spread	No required refrigeration; decreased immunogenicity; decreased spread

ATCC, American Type Culture Collection; FDA, U.S. Food and Drug Administration; NaCl, sodium chloride.
*Data are from package inserts.

Multiple variables likely contribute to subtle differences in toxin activity. These include number of units administered, dilution technique, dilution volume, product storage, and injection technique, among others. Although some injectors elect to work with a single neurotoxin for reproducibility and cost-effectiveness, many prefer to take advantage of the differences in neurotoxin behavior to optimize patient outcomes. Unfortunately, there are limited data obtained using techniques that accurately capture and evaluate the true dynamic rhytide alteration following toxin administration. Expanding our understanding of the therapeutic differences between botulinum toxin type A formulations will optimize patient neuromodulation outcomes.

Digital image correlation with speckle-tracking photogrammetry is a state-of-the-art technology that our group has previously validated for precise and reproducible evaluation of dynamic tissue strain of the face.[28] Prior medical investigations using the digital image correlation technology have focused on characterizing tissue strain in tendons and bone and for deformational cardiac imaging.[29,30] We recently expanded the application of digital image correlation to the study of aesthetic interventions of the face, specifically, to precisely quantify the effect of onabotulinumtoxinA on dynamic glabellar rhytide reduction. We propose here that the application of the digital image correlation technology in a comparative analysis of botulinum toxin type A formulations will provide novel insights into their putative therapeutic differences. Accordingly, in this work, we directly compare the effects of onabotulinumtoxinA, abobotulinumtoxinA, and incobotulinumtoxinA on dynamic glabellar rhytide reduction using digital image correlation technology.

PATIENTS AND METHODS

After approval by the University of Pennsylvania Institutional Review Board, 75 neurotoxin-naive female patients were prospectively recruited. Inclusion criteria included any female patient between the ages of 21 and 75 years with any Fitzpatrick skin type, Glogau score, or degree of rhytide etching. Exclusion criteria included male sex, prior neuromodulation, prior facial surgical rejuvenation, facial paralysis and significant facial asymmetry, known contraindication to neuromodulation, or open wound. Recruited patients were randomized into treatment with onabotulinumtoxinA, abobotulinumtoxinA, or incobotulinumtoxinA.

Randomized patients underwent baseline imaging of the glabella using digital image correlation. Each patient was placed a standard distance of 5 feet from a dual camera. Using a white foundation and black facial paint, speckles were placed on the upper face (Fig. 1) in a random pattern. Patients were instructed to furrow their brow following demonstration by technician. Each patient held the position for 5 seconds at a rate of seven frames per second for a total of 35 frames. As the patients furrow their brows, the digital image correlation software, ARAMIS (Trilion Quality Systems, Plymouth Meeting, Pa.), tracks and calculates the movement of the black paint speckles, subsequently translating their movement into tissue strain. Strain is defined as the percentage change in distance between any two black speckles and is further subdefined as positive for stretch and negative for compression. The software calculates the strain between all of the black speckles as total strain. In addition, a specific target area can be manually selected to determine the average strain in the desired region. This study focused on the analysis of horizontal strain as the major vector of soft-tissue deformation during brow furrowing. Although brow furrowing also results in a small amount of vertical motion, the excessive variability in vertical strain between and within patients precluded analysis of the vertical component of brow furrowing in this study.

Once baseline imaging was completed, each patient underwent treatment with randomized toxin. Treatment was blinded to both subject and injector. Consistent dilution was used and all dilution occurred on the day of injection according to the manufacturer's suggested technique. For onabotulinumtoxinA, 100 units was diluted in 2.5 cc of preservative-free saline. For abobotulinumtoxinA, 300 units was diluted in 2.5 cc of preservative-free saline. For incobotulinumtoxinA, 100 units was diluted in 2.5 cc of preservative-free saline and inverted for a minimum of 10 minutes before use, according to the manufacturer's instructions. Individual syringes with either 20 units of onabotulinumtoxinA, 20 units of incobotulinumtoxinA, or 60 units of abobotulinumtoxinA were prepared. All patients were injected by a single trained and blinded injector (I.P.) into five separate and consistent injection points in their corrugator and procerus muscles (Fig. 2).

Patients were instructed to return for repeated imaging at 4, 14, and 90 days after baseline imaging and treatment. At each subsequent visit, digital image correlation was performed consistently as described previously. After each imaging session,

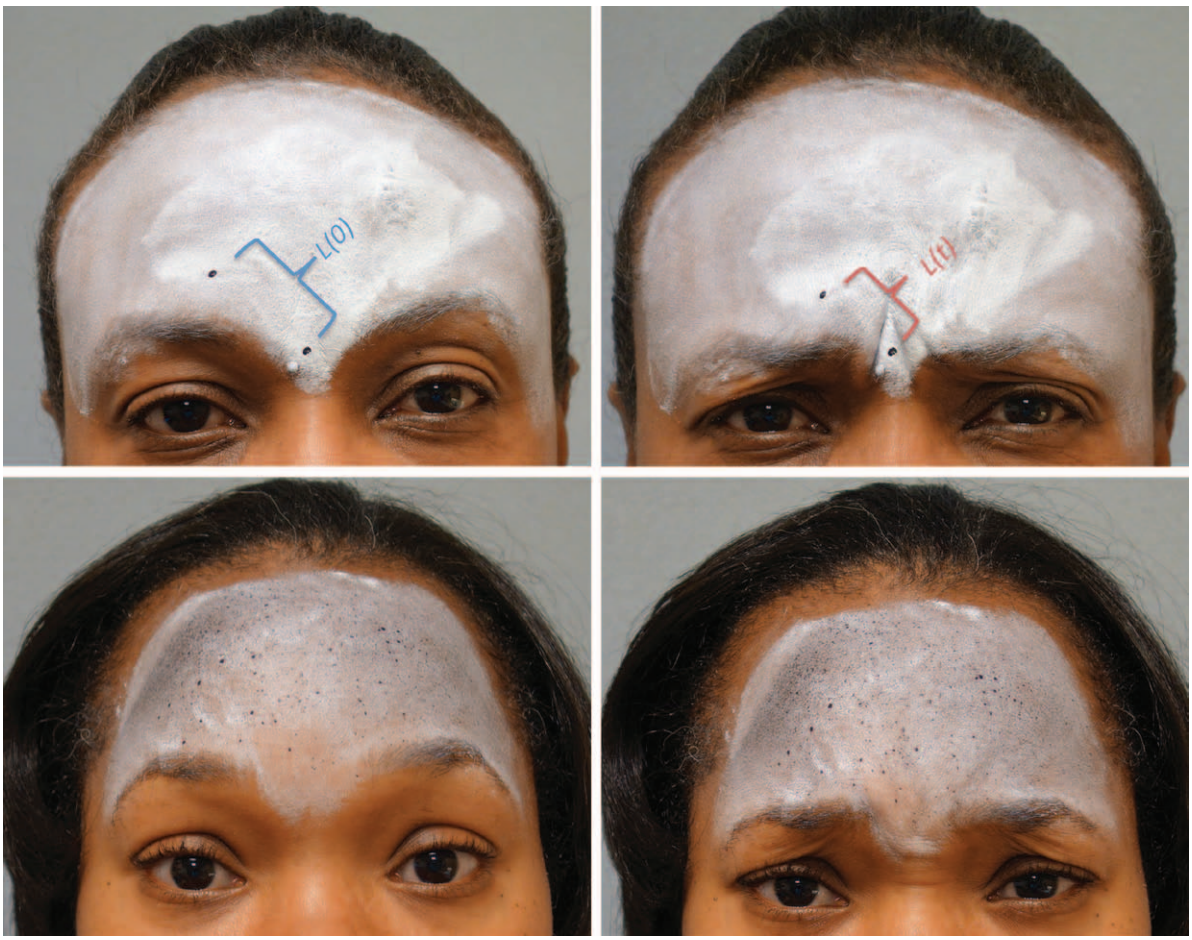

Fig. 1. The concept of speckle tracking with digital image correlation is illustrated here. Digital image correlation precisely captures the change in dynamic tissue strain through speckle displacement. (*Above*, *left*) A patient is illustrated with the white foundation makeup and two speckles. At rest, there is a set length between the two speckles, *L(0)*. (*Above*, *right*) Following corrugator activation, the distance between the two speckles changes with a new length, *L(t)*. The strain of this tissue is the percentage change between *L(0)* and *L(t)*. (*Below*, *left*) This patient, following application of the white foundation and black speckle makeup, has the complete complement of potential data points. (*Below*, *right*) Now, with corrugator activation, strain between all the speckles relative to each other is determined over all 35 frames. These data are uploaded into ARAMIS software, where average strain is calculated.

data were exported to the ARAMIS software. A single trained individual then defined the area of the glabella for each patient during each imaging session (Fig. 3). The glabella was determined as the box outlined by the midpupillary lines between the nasion and one-third above the brow. Average horizontal strain in the indicated region was tabulated by the ARAMIS software and exported to Microsoft Excel (Microsoft Corp., Redmond, Wash.) and JMP (SAS Institute, Inc., Cary, N.C.), where statistical analysis was performed. Differences in strain reduction among the toxins were assessed with one-way analysis of variance, followed by multiple comparison tests for each of the toxin comparisons. Differences with a value of $p < 0.05$ were considered statistically significant.

RESULTS

A total of 75 patients were initially recruited into the study, with 25 patients randomized to each category. After randomization, two patients were excluded, both from the onabotulinumtoxinA group: one for history of myasthenia gravis and another for open wound on the face. There were no statistically significant differences between groups with respect to age, sex (all female), Fitzpatrick skin type, Glogau score, or baseline glabellar strain (Table 2).

At day 4 after injection, a total of 71 patients returned for follow-up imaging: 22 from the onabotulinumtoxinA group, 24 from the abobotulinumtoxinA group, and 25 from the incobotulinumtoxinA group (Table 3). At this time

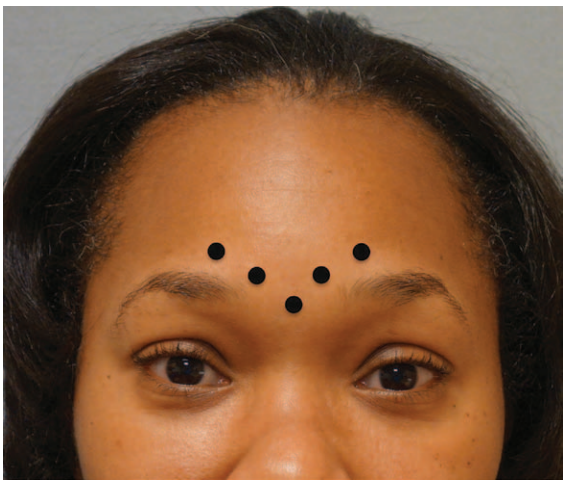

Fig. 2. Each patient underwent standardized injection of the corrugator and procerus muscles by a single trained injector. There was no variation of dose or injection location.

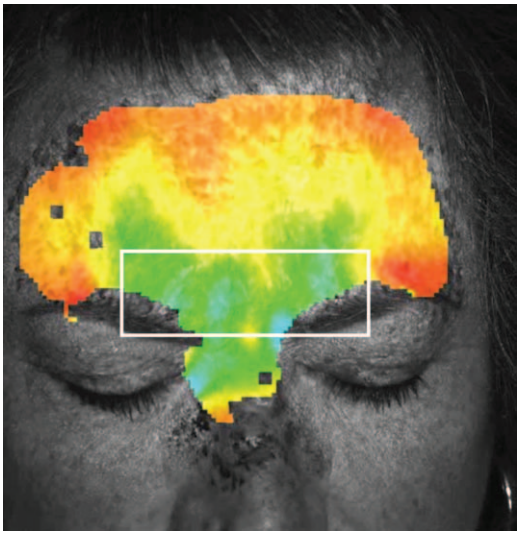

Fig. 3. After imaging, data are uploaded into the ARAMIS software, where average strain is calculated over the entire painted region and through all dynamic motion (35 frames). A single investigator then identifies the anatomical region of interest (i.e., the glabella). This region was defined as a box, outlined by the midpupillary lines between the nasion and one-third above the brow as illustrated here.

point, which was selected to evaluate the onset of toxin efficacy, we observed a 42.1 percent decrease of strain in the onabotulinumtoxinA group, a 39.4 percent decrease in the abobotulinumtoxinA group, and a 19.8 percent decrease in the incobotulinumtoxinA group. There were significant differences in strain reduction at day 4 among the three toxin groups ($p = 0.04$). When the three groups were compared directly to one another, the onabotulinumtoxinA group demonstrated

Table 2. Baseline Characteristics of Each Randomized Group*

	ONA-A	ABO-A	INCO-A	*p*
Total no.	23	25	25	
Age, yr	44.5	48.2	44.1	0.42
Glogau classification	2.3	2.7	2.4	0.24
Fitzpatrick scale	3.0	3.1	3.1	0.50
Baseline strain	16.4%	14.1%	14.4%	0.21

ONA-A, onabotulinumtoxinA; ABO-S, abobotulinumtoxinA; INCO-A, incobotulinumtoxinA.
*Initially, 25 patients were randomized to each treatment group; however, two patients were excluded from the onabotulinumtoxinA group for a history neuromuscular disorder and an open wound of the face.

significantly more strain reduction relative to the incobotulinumtoxinA group ($p = 0.02$) (Table 4). The abobotulinumtoxinA group also demonstrated significantly more strain reduction relative to the incobotulinumtoxinA group ($p = 0.04$). There was no significant difference between the onabotulinumtoxinA and abobotulinumtoxinA groups ($p = 0.77$) (Fig. 4, *above*).

At day 14, which was selected to evaluate the full effect of neuromodulation, a total of 68 patients returned for follow-up imaging: 21 from the onabotulinumtoxinA group, 24 from the abobotulinumtoxinA group and 23 from the incobotulinumtoxinA group. At this time point, we observed a 66.1 percent decrease of strain in the onabotulinumtoxinA group, a 51.4 percent decrease of strain in the abobotulinumtoxinA group, and a 42.8 percent decrease of strain in the incobotulinumtoxinA group. The differences in strain reduction at day 14 among the three toxin groups trended toward significance ($p = 0.06$). When the groups were directly compared, the onabotulinumtoxinA group continued to demonstrate significantly more strain reduction relative to incobotulinumtoxinA ($p = 0.02$). There were no significant differences between the onabotulinumtoxinA and abobotulinumtoxinA groups ($p = 0.14$), or the abobotulinumtoxinA and incobotulinumtoxinA groups ($p = 0.36$) (Fig. 4, *center*).

At day 90, which was selected to evaluate the longevity of neuromodulation, a total of 66 patients returned for follow-up imaging: 19 from the onabotulinumtoxinA group, 24 from the abobotulinumtoxinA group, and 23 from the incobotulinumtoxinA group. At this time point, we observed a 43.5 percent decrease of strain in the onabotulinumtoxinA group, a 38.4 percent decrease of strain in the abobotulinumtoxinA group, and a 25.3 percent decrease of strain in the incobotulinumtoxinA group relative to baseline patient glabellar strain (before treatment).

Table 3. Absolute Strain and Percentage Change of Strain at Initial Imaging and at Days 4, 14, and 90

	Day 0		Day 4				Day 14				Day 90			
	No.	Strain (%)	No.	Strain (%)	Strain Reduction (%)	*p*	No.	Strain (%)	Strain Reduction (%)	*p*	No.	Strain (%)	Strain Reduction (%)	*p*
ONA-A	23	16.4	22	9.4	42.1	<0.01	21	5.7	66.1	<0.01	19	9.3	43.5	<0.01
ABO-A	25	14.1	24	8.7	39.4	<0.01	24	7.0	51.4	<0.01	24	8.6	38.4	<0.01
INCO-A	25	14.4	25	10.0	19.8	0.04	23	7.7	42.8	<0.01	23	9.2	25.3	0.02

ONA-A, onabotulinumtoxinA; ABO-S, abobotulinumtoxinA; INCO-A, incobotulinumtoxinA.

Table 4. Statistical Values for Intertoxin Efficacy Comparison of Strain Reduction at Days 4, 14, and 90

	p		
	Day 4	Day 14	Day 90
ONA-A vs. ABO-A	0.77	0.14	0.66
ONA-A vs. INCO-A	0.02	0.02	0.12
ABO-A vs. INCO-A	0.04	0.36	0.24

ONA-A, onabotulinumtoxinA; ABO-S, abobotulinumtoxinA; INCO-A, incobotulinumtoxinA.

There were no statistically significant differences between any of the toxins at this time point ($p = 0.27$) (Fig. 4, *below*). There were no significant differences between the onabotulinumtoxinA and abobotulinumtoxinA groups ($p = 0.66$), onabotulinumtoxinA and incobotulinumtoxinA groups ($p = 0.12$), or abobotulinumtoxinA and incobotulinumtoxinA groups ($p = 0.24$).

At each time point, the percentage of patients in each group with a less than 10 percent reduction in strain was determined (Table 5 and Fig. 5). This degree of response represents a limited responder. At the 4-day time point, 4.5 percent of the onabotulinumtoxinA group were in this category, as compared with 8.3 percent of the abobotulinumtoxinA group and 28.0 percent of the incobotulinumtoxinA group. There were significant differences in the limited responder percentage among the toxin groups ($p = 0.04$) (Table 6). There was a significant difference between the onabotulinumtoxinA group and the incobotulinumtoxinA group ($p = 0.02$) and between the abobotulinumtoxinA group and the incobotulinumtoxinA group ($p = 0.05$). There was no significant difference between the onabotulinumtoxinA and abobotulinumtoxinA groups ($p = 0.71$).

At the 14-day time point, 4.8 percent of the onabotulinumtoxinA group, 20.8 percent of the abobotulinumtoxinA, and 17.4 percent of the incobotulinumtoxinA group had less than 10 percent reduction in strain. At this point, two patients in the incobotulinumtoxinA group and two patients in the abobotulinumtoxinA group were deemed complete nonresponders, with an actual increase in strain. There were no complete nonresponders in the onabotulinumtoxinA group. There were no significant differences between the toxin groups with respect to limited responders at this time point ($p = 0.30$). There were no significant differences between the onabotulinumtoxinA and abobotulinumtoxinA groups ($p = 0.14$), onabotulinumtoxinA and incobotulinumtoxinA groups ($p = 0.24$), or abobotulinumtoxinA and incobotulinumtoxinA groups ($p = 0.74$).

At the 90-day time point, 21.1 percent of the onabotulinumtoxinA group, 20.8 percent of the abobotulinumtoxinA group, and 34.8 percent of the incobotulinumtoxinA group demonstrated less than 10 percent reduction of strain. There were no significant differences between the toxin groups with respect to limited responder groups at this time point ($p = 0.48$). There were no significant differences between the onabotulinumtoxinA and abobotulinumtoxinA groups ($p = 0.99$), onabotulinumtoxinA and incobotulinumtoxinA groups ($p = 0.32$), or abobotulinumtoxinA and incobotulinumtoxinA groups ($p = 0.28$).

DISCUSSION

Digital image correlation provides a precise, quantitative, and reproducible means of directly characterizing the effects of neuromodulation on facial strain. Consequently, our application of the digital image correlation technology in a comparative analysis of botulinum toxin type A activity in this study differs from prior comparative and noncomparative trials of available toxins that have relied on static photography and potentially subjective scoring parameters to evaluate toxin behavior. This study argues here that this precise means of characterizing toxin performance, including onset, maximal strain reduction effect, and longevity, allows for an improved understanding of prior assessments of comparative botulinum toxin type A efficacy. Notably, the current study was performed without industry bias, including sponsorship and interpretation, thereby minimizing potential conflicts of interest.

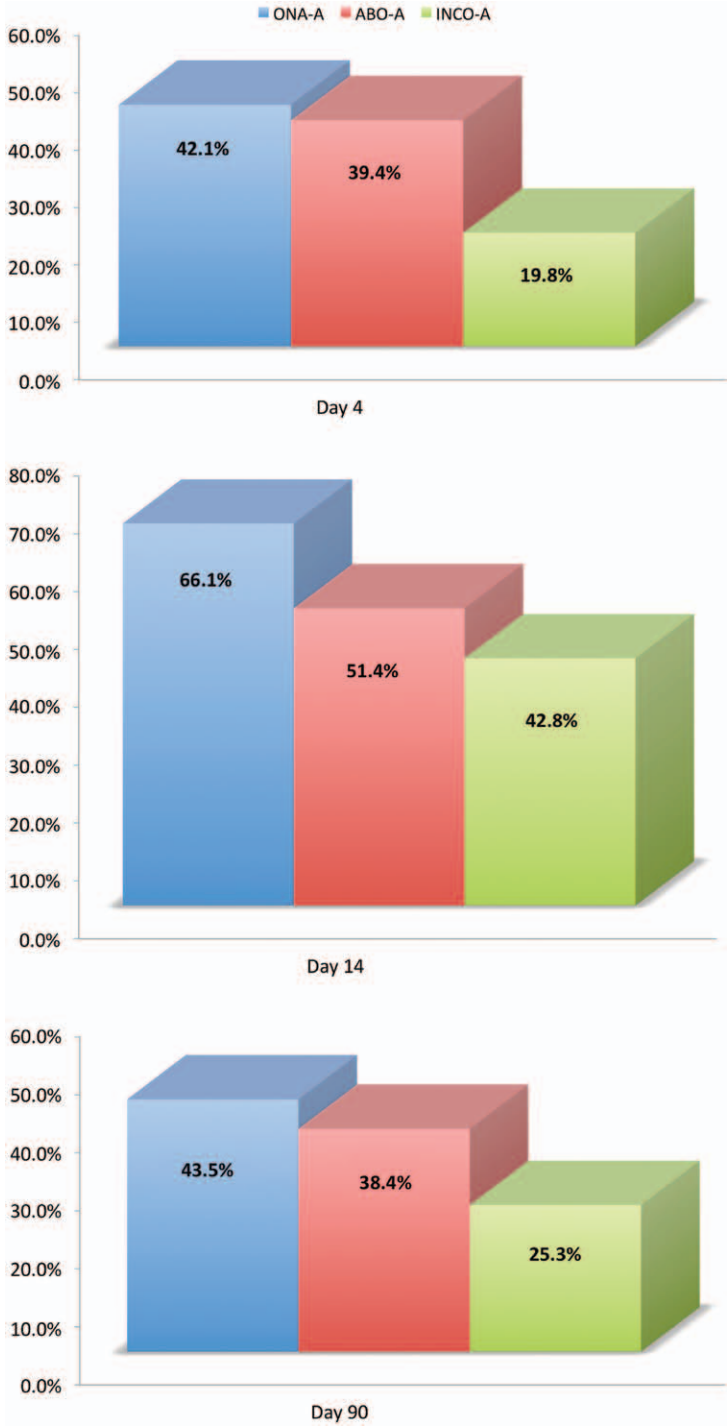

Fig. 4. (*Above*) Percentage reduction of strain is illustrated for each toxin at the 4-day time point. (*Center*) Percentage reduction of strain is illustrated for each toxin at the 14-day time point. (*Below*) Percentage reduction of strain is illustrated for each toxin at the 90-day time point. *ONA-A*, onabotulinumtoxinA; *ABO-S*, abobotulinumtoxinA; *INCO-A*, incobotulinumtoxinA.

The data demonstrate that all three botulinum toxin type A formulations available in the United States are effective in reducing glabellar strain. This is evidenced by significant strain reduction and a low percentage of patients demonstrating a less than 10 percent reduction in strain for all formulations at day 14 after injection. This observation is consistent with

Table 5. Percentage of Limited Responders, Defined as <10 Percent Strain Reduction, at Days 4, 14, and 90

	Day 4			Day 14			Day 90		
	No.	Limited Responders (%)	*p*	No.	Limited Responders (%)	*p*	No.	Limited Responders (%)	*p*
ONA-A	22	4.5	0.33	21	4.8	0.33	19	21.1	0.04
ABO-A	24	8.3	0.16	24	20.8	0.02	24	20.8	0.02
INCO-A	25	28.0	0.01	23	17.4	0.04	23	34.8	<0.01

ONA-A, onabotulinumtoxinA; ABO-S, abobotulinumtoxinA; INCO-A, incobotulinumtoxinA.

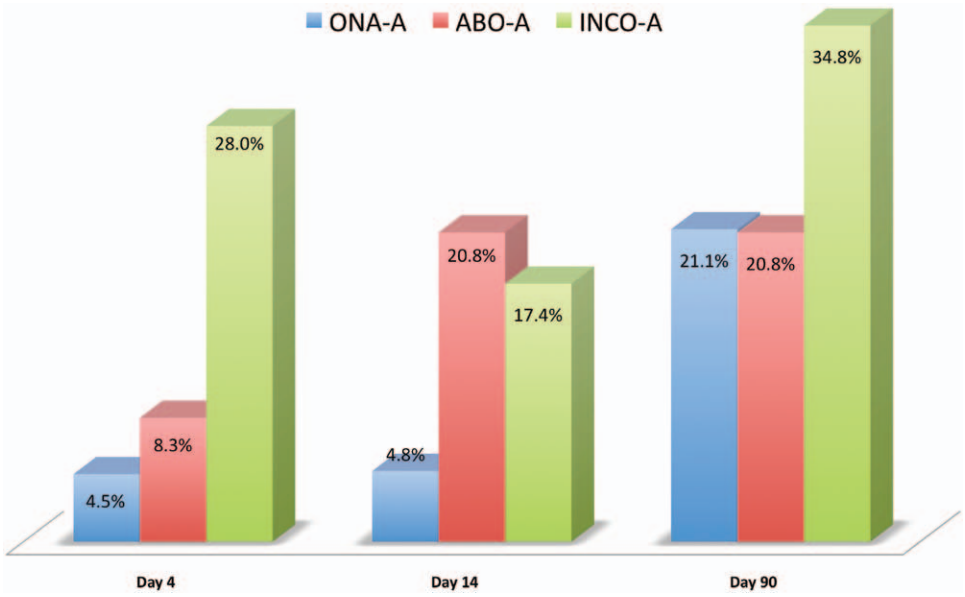

Fig. 5. Patients with strain of 10 percent or less were identified for each group at each time point. Here, the percentage of these "limited responders" is illustrated graphically. *ONA-A*, onabotulinumtoxinA; *ABO-S*, abobotulinumtoxinA; *INCO-A*, incobotulinumtoxinA.

prior comparative toxin evaluations that have suggested similar maximal efficacy among onabotulinumtoxinA, abobotulinumtoxinA, and incobotulinumtoxinA in dynamic rhytide reduction. Although this finding is not surprising in and of itself, it does not account for the persistent anecdotal reports of variability in the performance of different botulinum toxin type A formulations from experienced injectors. Toward this end, important insights into observed toxin variability are provided by the comparative data at the time points examined in this study, specifically, days 4, 14, and 90 after injection.

Table 6. Statistical Values for Intertoxin Comparison of Percentage of Limited Responders at Days 4, 14, and 90

	p		
	Day 4	Day 14	Day 90
ONA-A vs. ABO-A	0.71	0.14	0.99
ONA-A vs. INCO-A	0.02	0.24	0.32
ABO-A vs. INCO-A	0.05	0.74	0.28

ONA-A, onabotulinumtoxinA; ABO-S, abobotulinumtoxinA; INCO-A, incobotulinumtoxinA.

At day 4 after injection, the greatest and most consistent strain reduction was observed with onabotulinumtoxinA, as demonstrated by high total strain reduction and the low percentage of patients demonstrating a less than 10 percent reduction in strain. The efficacy of bobotulinumtoxinA was similar to that of onabotulinumtoxinA at this time point. In contrast, incobotulinumtoxinA demonstrated the least strain reduction at day 4, resulting in a large percentage of patients demonstrating a less than 10 percent reduction in strain. These observations suggest that the onset of neuromodulation with incobotulinumtoxinA, at the dose and dilution used, differs from the other two formulations. This may result from either a mechanistic delay in the onset of effect, an increase in the variability of therapeutic onset, or an overall lack of equivalency in the incobotulinumtoxinA preparation applied in this study in relation to the other toxins.

At day 14, all three formulations demonstrated significant overall strain reduction, with few nonresponders in each group; however, the total strain reduction achieved by the incobotulinumtoxinA group was significantly less than that of the onabotulinumtoxinA group. These observations suggest that the maximal strain reduction achieved by incobotulinumtoxinA, at the dose and dilution used, is lower than the neuromodulatory effect achieved with onabotulinumtoxinA using the same number of units and injection technique. AbobotulinumtoxinA demonstrated an intermediary behavior and did not differ significantly from either of the other two formulations. Despite the seemingly large divergence in average strain reduction between onabotulinumtoxinA and abobotulinumtoxinA and between abobotulinumtoxinA and incobotulinumtoxinA, the differences were not statistically significant. This is most likely attributable to the large variability in individual strain reduction in each of the toxin groups in combination with the relatively small sample size. An additional limitation of the statistical analysis may be the preclusion of the vertical component of brow furrowing in this study. Although brow furrowing does result in a small amount of vertical glabellar motion, the study focused on the assessment of the more robust transverse glabellar strain. Additional work will be required to investigate the neuromodulatory effect on both vertical and horizontal glabellar strain reduction. Finally, the use of identical injection doses and technique among all patients can further contribute to the overall variability in response.

Digital image correlation, although not invasive, is time consuming and requires both facial painting and imaging. Any given patient can expect to spend up to 30 minutes for completion of a single imaging session. This time requirement likely resulted in decreased patient participation as the study progressed. Nonetheless, despite the small sample size tested at each time point, there are clear differences and remarkable trends in variability of the toxins.

Importantly, these findings confirm prior assertions that botulinum toxin type A formulations are not equivalent or interchangeable, even at classic dilution and dosing methods, as used during this work.[31] Although establishing the optimal therapeutic parameters for incobotulinumtoxinA, abobotulinumtoxinA, and onabotulinumtoxinA treatment is beyond the scope of this study, it is clear that additional data are required to minimize botulinum toxin type A therapeutic variability and optimize patient outcomes with this most commonly performed aesthetic intervention.

CONCLUSIONS

This study demonstrates that there are potential differences in glabellar strain reduction between available neurotoxins relative to each other when used at a consistent dilution and injection technique. Although all neurotoxins were efficacious at strain reduction and one formulation was not found to overwhelmingly outperform another, as applied here, there appear to be substantial differences between onabotulinumtoxinA and incobotulinumtoxinA activity at 4 and 14 days after injection. AbobotulinumtoxinA maintained an intermediate position with respect to the degree of strain reduction at any time tested. These data confirm a noninterchangeability of current neurotoxins and support the need for additional studies to better elucidate each formulation's unique neuromodulatory activity.

Ivona Percec, M.D., Ph.D.
Division of Plastic Surgery
University of Pennsylvania Perelman Center for Advanced Medicine
7th Floor South Pavilion
3400 Civic Center Boulevard
Philadelphia, Pa. 19104
ivona.percec@uphs.upenn.edu

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PATIENT CONSENT

Patients provided written consent for the use of their images.

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