

### Review Article

# Use of LetibotulinumtoxinA for Aesthetic Treatment of Asians: A Consensus

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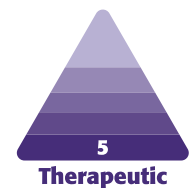
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### Abstract

Treatment of wrinkles and dynamic lines with botulinum toxin has been a routine practice for years in aesthetic clinical settings. The effective treatment of wrinkles requires a comprehensive understanding of facial expression muscles and their interactions, the mechanism of action of botulinum toxin, and individual patient preferences. The dose adjustment practice and injection technique of physicians are affected by cultural differences; most Asian patients prefer natural-looking results. This article aims to present an expert consensus on the injection sites, doses, and levels of botulinum toxin for various indications in Asians, with the hope of providing guidance to some clinicians. This consensus paper reviews LetibotulinumtoxinA for patient evaluation, dosage, and delivery techniques in Asians from the time LetibotulinumtoxinA was approved up to December 2022. Panelists proposed individualized treatment plans for botulinum toxin type A (BTxA) treatments in 3 areas—wrinkle removal, contour adjustment, and face lifting—for Asians based on their extensive experience and knowledge of facial anatomy. When using a different BTxA, clinicians should start with a conservative dose and carefully individualize the treatment for each patient, and adjust it according to feedback to obtain a higher satisfaction level.

### Level of Evidence: 5

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Botulinum toxin type A (BTxA) injection is one of the most commonly performed nonsurgical aesthetic procedures. In 2019, more than 1.7 million botulinum toxin–related procedures were performed in the United States.<sup>1</sup> Patients are familiar with the mechanism of BTxA; it reduces wrinkles by diminishing muscle action. However, BTxA is utilized for purposes other than reducing muscle activity. BTxA reduces muscle action by blocking neurotransmitters, which causes a decrease in mimetic muscle action, thereby reducing facial wrinkles.<sup>2,3</sup> BTxA injections are also employed to reduce the volume of masseter muscles and reduce the activity of salivary glands.<sup>4,5</sup> Subcutaneous or intramuscular injections of botulinum toxin are used for wrinkle smoothing and lifting.<sup>6</sup> BTxA injections are utilized for many additional treatments; however, further studies are needed to reveal its unknown mechanisms, both clinically and scientifically.<sup>7</sup>

There are multiple guidelines for BTxA injections. Global consensus panels suggest injecting different dosages of BTxA intramuscularly or subcutaneously.<sup>8</sup> Additionally, there are consensus recommendations for BTxA injections in Asians.<sup>9</sup> The dosages proposed should consider the muscle activity of each patient; therefore, understanding the dynamic anatomy before injecting the recommended botulinum toxin dosages is essential.

Recently, various botulinum toxin products have become commercially available. LetibotulinumtoxinA (Letybo, Hugel Pharma Inc., Seoul, South Korea), the first Korean BTxA approved in China, demonstrated non-inferiority to onabotulinum toxin A in phase 3 clinical trials conducted on 500 Chinese patients (Trial.gov registration no. NCT05380154). In this review article, an expert panel composed of professional medical aesthetic and dermatologic specialists in Asia recommends proper BTxA injection dosages depending on the range of the patient's muscle action, techniques for effective aesthetic results, and prevention of possible complications in Asians. LetibotulinumtoxinA has been approved for the indication of frown-line injections in many Asian countries, such as China, Thailand, India, Mongolia, the Philippines, and Indonesia, and it has also been approved for the indication of crow's feet in Indonesia. In this consensus article, in addition to glabellar lines and crow's feet, we have included a number of off-label indications that have not yet been approved by regulatory authorities. As with any injectable treatment, adverse events related to the injection itself can occur, including local pain, infection, abnormal sensations, hypesthesia, swelling, erythema, local infections, bleeding, and abrasions. Physicians should sufficiently understand the recommended dosages, proper procedures, and administration frequencies required for BTxA.

## PATIENT ASSESSMENT AND TREATMENT PLANNING

### Pretreatment

BTxA injections are recommended for patients wishing to resolve issues related to excessive muscular contractions. Therefore, it is important to fully assess the static and dynamic status of the target muscles and comprehensively understand the relationship between the muscle and overlying skin tissue.<sup>10</sup> Muscle volume can be effectively assessed by palpation, and the injection dose can be adjusted accordingly.<sup>11</sup> The injection sites and doses should be based on individual requirements, objective anatomic characteristics, and the relationship between local improvements and overall facial structure.<sup>8</sup> It is also recommended to mark the injection points for identification. Communication and photography before aesthetic treatment are mandatory. Moreover, the static and dynamic states of the treatment area should be considered for future comparisons. An informed consent document must be signed by the patient before possible adverse events occur.

In this review, the consensus panel will focus on LetibotulinumtoxinA for injections. LetibotulinumtoxinA is added to a vial containing a freeze-dried neurotoxin complex, and the powder in each vial is reconstituted with 0.9% nonpreserved saline to a final concentration according to its prescribing information. The members of the consensus panel agreed that a range of dilutions and injection volumes (a dilution of 2.0 to 4.0 mL per vial) is acceptable and depends primarily on the number of units to be injected and the preference of the practitioner.<sup>12</sup> Physicians should choose a dilution that minimizes the likelihood of diffusion to neighboring muscle groups. The recommendations for reconstitution and handling are summarized in [Table 1](#).

To alleviate pain during injection, the application of lidocaine cream at least 30 minutes before treatment is recommended by some panel members. The cream is more effective when an occlusion dressing (plastic wrap) is employed to cover the treatment area. Many authors have demonstrated that the use of surface anesthetic cream before BTxA injections can provide significant pain relief during needle insertion.<sup>13,14</sup> To prevent cross-contamination, patients are required to remove their makeup, and facial disinfection is required.

### Tailored Approach

Most studies and published consensus on the use of BTxA have focused on Western populations, targeting

**Table 1.** Recommendations for Reconstitution and Handling of LetibotulinumtoxinA

Parameter		Recommendation
Diluent		Nonpreserved 0.9% saline
Concentration		4 U/0.1 mL or any convenient concentration to deliver required units per injection site 1.25 mL of diluent for a 50U vial and 2.5 mL for a 100U vial
Storage	Before reconstitution	2°C to 8°C up to 36 months
	After reconstitution	24 hours at 2°C to 8°C and up to 6 weeks at 4°C
	Handling	Special precautions are not required

Caucasians. However, Asians have different morphotypes, anatomy, and cultural expectations than Caucasians. Compared with Caucasians, Asians tend to have a wider face with shorter vertical height and a flat or concave medial cheek, and they lack anterior projection of the brow, medial cheek, nose, and chin.<sup>10</sup> Recently, the desire for aesthetic improvement has significantly increased and presented a trend toward a more youthful appearance, which may be the result of economic growth and awakening of self-consciousness. Younger patients seek to improve their facial appearance and optimize intrinsic weakness, whereas older patients wish to reduce their wrinkles and signs of aging. Nevertheless, regardless of the age group, most Asians seek natural-looking results that preserve unique features with BTxA treatment.<sup>15</sup> The key to successful treatment is individualized patient assessment. Although there is a previous consensus on BTxA injections for Asians, in these consensus guidelines, we have divided the recommendations on facial botulinum toxin into 3 sections, including wrinkle removal, contour adjustment, and lifting. We provide a detailed description of the anatomy and doses for LetibotulinumtoxinA injection in Asians.<sup>9,16</sup>

## Posttreatment Recommendations

Posttreatment information should be emphasized by practitioners, and posttreatment instructions should be provided to patients in writing. Regular follow-up appointments and repeat treatments are recommended for maintaining satisfactory results.<sup>17</sup> The treatment interval, which is approximately 6 to 12 months, depends on the area treated, the dose utilized, and the patient's satisfaction. Ice or cooling after treatment for 10 to 15 minutes helps decrease pain and prevent swelling and bruising. Patients may resume normal activities after 4 to 6 hours. Documents and photographs should be saved for follow-up.

## CONSENSUS RECOMMENDATIONS

### Anti-wrinkle

Facial wrinkles are manifestations of the underlying muscles of facial expressions. Anti-wrinkle treatment aims to evenly weaken the muscles responsible for wrinkles instead of completely paralyzing them. The keystone of anti-wrinkle treatment is the uniform neuromodulation of 1 or multiple groups of target muscles. The injection sites and doses are summarized in [Table 2](#) and [Figure 1](#).

### Horizontal Forehead Lines

The frontalis is responsible for forehead wrinkles and brow elevation.<sup>9,18</sup> To evenly efface the wrinkles while preserving the eyebrow position and some movement of the frontalis, the dose of BTxA should be controlled, and the lower frontalis, a once “forbidden” area because of the risk of brow ptosis, should be carefully addressed.<sup>9,19-21</sup> Uneven weakening of the frontalis can potentially result in an exaggeration of previously unidentifiable wrinkles due to overcompensation by the untreated part of the frontalis.<sup>22</sup>

**Anatomy:** In the view of the upper face, the frontalis muscle is rectangular, originates from the galea aponeurosis, and runs in an inferior direction to insert with the fibers of the orbicularis oculi, procerus, depressor supercillii, and corrugator supercillii near the superciliary arch before finally inserting into the frontal skin above the eyebrow.<sup>23-27</sup> Transverse forehead lines are formed. The width of the frontalis muscle varies between individuals. In cases in which the lateral border of the frontalis muscle is located lateral to the temporal crest, the elevation of the eyebrow tail may occur due to only medial injection.<sup>28-30</sup>

**Injection Technique:** The injection site and depth should be tailored according to the distribution and severity of the horizontal forehead lines. For wrinkles in the lower frontalis or mild forehead wrinkles, intradermal injection with a lower dose per site facilitates superficial delivery of the toxin, thereby reducing rhytids without brow ptosis.<sup>21</sup>

### Glabellar Lines

The muscles responsible for glabellar lines include the procerus, corrugator supercillii, depressor supercillii, orbicularis oculi, and frontalis muscles.

**Anatomy:** The superficial procerus, depressor supercillii, and deep corrugator supercillii muscles are connected to the frontalis and orbicularis oculi muscles. The latter consist of transverse and oblique bellies, which are more lateral and deeper than the oblique belly.<sup>29-34</sup> The contraction of these 3 muscles may drag the brow inferomedially as a

**Table 2.** Consensus Recommendations for Anti-wrinkle Treatment With LetibotulinumtoxinA in Asian Patients

Indication	Target muscle	Injection points (n)	Dose per injection point (units)	Typical total dose range (units)	Preferred injection level
Horizontal forehead lines	Frontalis	6-12 (nmd)/ 10-40 (md)	0.5-1 (nmd)/ 0.2-0.25 (md)	4-12 (nmd)/ 2-10 (md)	ID, IM, SC
Glabellar lines	Procerus, corrugator supercilia, depressor supercilia, orbicularis oculi, (and/or frontalis)	5-9 (nmd)	0.5-4 (nmd)	10-40 (nmd)	ID, IM, SC
Crow's feet	Orbicularis oculi	10-25 (nmd)	0.25-2 (nmd)	5-25/side (nmd)	ID, SC
Nasal oblique lines (bunny lines)	Nasalis, LLSAN	2-6 (nmd)	2-4 (nmd)	4-20 (nmd)	ID, SC
Perioral wrinkles	Orbicularis oris	4-10 (nmd)/ 40-80 (md)	0.25-0.5 (md)	2-8 (nmd)/2-8 (md)	ID, SC
Dynamic nasolabial fold	LLSAN, LLS, LAO, ZM, Zmi	8-14 (nmd)	0.25-1 (nmd)	2-20 (nmd)	ID, SC
Parentheses lines	LLSAN, LLS, LAO, ZM, Zmi, Orbicularis Oris, Risorius, DAO	10-12 (md)	0.25-0.5 (md)	2.5-6 (md)	ID, SC

The dose shown in this table is for females, and the dose for males is 20% to 30% higher than that for females. DAO, depressor anguli oris; ID, intradermal; IM, intramuscular; LAO, levator anguli oris; LLS, levator labii superior muscle; LLSAN, levator labii superioris alaeque nasi; md, microdroplet; nmd, nonmicrodroplet; SC, subcutaneous; ZM, zygomaticus major muscles; Zmi, zygomaticus minor muscles.

brow depression and cause frown lines. These muscles function as glabellar complexes.<sup>35,36</sup>

**Injection Technique:** Several classifications of the shapes of frown lines have been proposed.<sup>37,38</sup> However, a detailed classification cannot cover all patterns. It is critical to determine the muscles involved in the manifestation of glabellar lines to determine the injection sites. Muscle strength determines the dose at the corresponding sites. The corrugator is interdigitated with the orbicularis oculi and frontalis. Intradermal injections can evenly weaken these muscles and reduce the risk of eyelid ptosis. The orbicularis oculi and frontalis should also be targeted if involved.

### **Crow's Feet**

The orbicularis oculi is a large, thin sphincter whose contraction produces periocular wrinkles. The glabellar complex and nasal dorsalis sometimes contribute to wrinkles by acting as synergistic muscles.<sup>18</sup> At the superior lateral canthal level, the orbicularis oculi is antagonistic to the frontalis. The goal is to evenly weaken the orbicularis oculi and its synergistic muscles while maintaining the dynamic balance between the orbicularis oculi and its antagonistic muscles.

**Anatomy:** The orbicularis oculi muscle is an elliptical muscle consisting of orbital and palpebral parts. The orbital part concentrically encircles the orbit, including the depressor supercillii, whereas the palpebral portion, with finer muscle fibers than the orbital part, sweeps across the eyelid

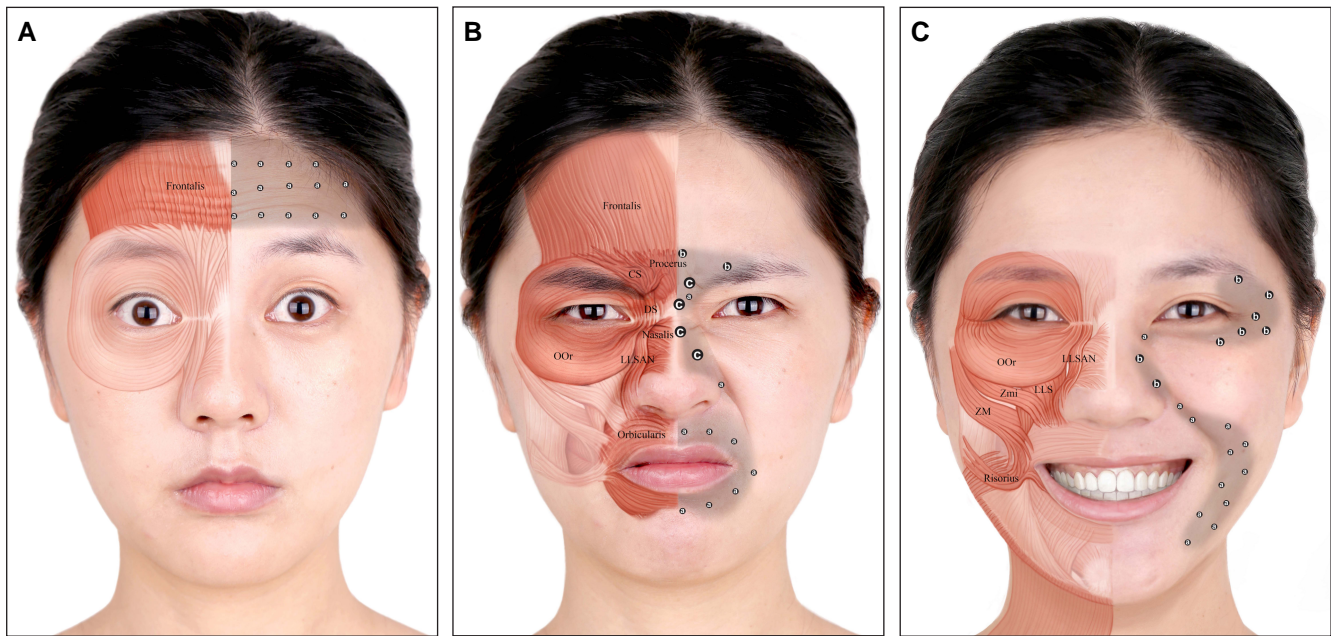
anterior to the orbital septum (preseptal part of the palpebral portion) and arises from the medial palpebral ligament (pretarsal part of the palpebral portion).<sup>32,33,36</sup> Its contraction causes the pretarsal roll and crow's feet.

**Injection Technique:** Multipoint intradermal injections provide a more precise and uniform toxin action to the orbicularis oculi.<sup>39,40</sup> Pretreatment evaluation and delicately controlled dosage in the orbital orbicularis muscle and around the insertion of the zygomaticus major are critical for infraorbital rhytids.<sup>41</sup> The frontalis should be balanced if an eyebrow elevation is unwanted. It should be noted that the injection only focuses on the lateral portion of the orbital part, which may lead to an increase in wrinkles at the medial orbit and nasal dorsum portions.<sup>42</sup>

### **Nasal Oblique Lines (Bunny Lines)**

The nasalis muscle is the main muscle responsible for bunny lines. However, the levator labii superioris alaeque nasi, procerus, and depressor supercilli muscles are also sometimes involved. Asians usually have a stronger nasalis than Caucasians; therefore the total injection dose for Asians is higher than that described in previous studies focusing on Caucasians.<sup>43,44</sup>

**Anatomy:** The nasalis muscle is a wide paired muscle on the nasal dorsum and ala. The transverse part is C-shaped, originating from the maxilla, thin and flat with a triangular shape, and covers and compresses the nasal dorsum. It



**Figure 1.** Anatomy and injection for anti-wrinkle treatment with LetibotulinumtoxinA in Asian patients. (A) Anatomy and injection for treatment of horizontal forehead lines; (B) anatomy and injection for treatment of glabellar lines and bunny lines; and (C) anatomy and injection for treatment of crow's feet, dynamic nasolabial fold, and perioral wrinkles. a, 0.25 to 0.5 U/Point; b, 0.5 to 1 U/Point; c, 2 to 4 U/Point; CS, corrugator supercilia; DS, depressor supercilia; LAO, levator anguli oris; LLS, levator labii superioris muscle; LLSAN, levator labii superioris alaeque nasi; OOr, orbicularis oris muscle; ZM, zygomaticus major muscles; Zmi, zygomaticus minor muscles.

is located deep in the alar region, ascends to the dorsum of the nose, and contracts to form bunny lines.<sup>42,45</sup>

**Injection Technique:** The total recommended dose for the nasalis in Asians is approximately 2 to 4 units per side. Synergistic muscles (levator labii superioris alaeque nasi, or LLSAN) should be treated simultaneously if needed.

### Perioral Wrinkles

Movements of the orbicularis oris contribute to radial perioral rhytids. The minimum dose is recommended because the perioral area is highly delicate, and unwanted diffusion of the toxin can lead to functional impairment of the lips.<sup>46,47</sup> Deeper rhytids should be treated in combination with injectable fillers or laser resurfacing.

**Anatomy:** The orbicularis oris, a constrictor of the mouth, is a layered sphincter muscle that encircles the mouth and is located in the upper and lower lips. Most muscle fibers originate from other facial muscles that converge in the mouth. Anatomically, the orbicularis oris is divided into 4 quadrants, which are further divided into the pars peripheralis and pars marginalis. When contracted, the orbicularis oris muscle closes the mouth and puckers the lips in the manner of a sphincter.

**Injection Technique:** Nonmicrodroplet injection involves 4 to 12 intradermal injection sites within 5 mm of the vermilion border.<sup>48</sup> It is important to ensure symmetry and avoid philtral ridges and oral commissures. Fine lines can be treated with microdroplet injections, which involve evenly distributed intradermal injection sites around the mouth with a total dose of no more than 6 units.

### Dynamic Nasolabial Fold

The dynamic nasolabial fold (NLF) is related to increased tone of muscles such as the LLSAN, the LLS (levator labii superioris muscle), the LAO (levator anguli oris), and/or the ZM (zygomaticus major muscles).<sup>49</sup> Patients with dynamic NLFs may exhibit gummy smiles as well. Treatment with BTxA weakens the corresponding muscle tone. However, if a dynamic NLF is accompanied by other formations, such as midface sagging, fillers or other facial rejuvenation treatments should be performed together with BTxA.<sup>50</sup>

**Anatomy:** The origin of the ZM is found at the anterior zygomatic arch immediately posterior to the zygomaticotemporal suture. Although the ZM arises medially, the muscle attaches to the upper lip area, and most of these muscle fibers originate from the superficial part of the orbicularis oculi muscle and the bone. The LLS originates from the orbital

**Table 3.** Consensus Recommendations for Contour Adjustment With LetibotulinumtoxinA in Asian Patients

Indication	Target muscle	Injection points (n)	Dose per injection point (units)	Typical total dose range (units)	Preferred injection level
Masseter hypertrophy	Masseter	3-5/side	5-10	12-50	IM
Parotid gland hypertrophy	Parotid gland	3-8/side	2-4	12-32	IG
Temporalis hypertrophy	Temporalis	3-8/side	5-10	12-32	IG
Nasal tip ptosis	Depressor septi nasalis	1	2-4	2-4	IM
Dilator naris flaring	Dilator nasalis, levator labii superioris alaeque nasi	1-2/side	0.25-1	2-4	IM, SC
Mentalis tension	Mentalis	3-5	2-4	4-10	IM, SC

This section does not involve microdroplet injections. The dose shown in this table is for females, and the dose for males is 20% to 30% higher than that for females. IG, intragastric; IM, intramuscular; SC, subcutaneous.

rim of the maxilla and zygomatic bone above the infraorbital foramen and inserts into the upper lip. The most medial location is the LLSAN, which elevates the upper lip. When muscles contract together, they pull the lip and mouth corners superolaterally, lifting soft tissues of the middle face.<sup>51-53</sup> Injection into these 3 muscles can correct asymmetric smiles and release the NLF.

**Injection Technique:** The key to achieving satisfactory correction when treating dynamic NLFs is the proper diagnosis of the corresponding muscles. Evenly weakening the muscles involved is important; otherwise, compensation of untreated muscles will lead to a change in the lip shape when smiling, especially in patients without a gummy smile before treatment.<sup>49,54</sup>

### Parentheses Lines

In some cases, the NLF curves downward around the mouth. The lines formed due to this are called parentheses lines because they resemble parentheses around the mouth. The parentheses lines result from both muscle movements and soft tissue loss around the mouth corners and the cheeks. BTxA combined with dermal fillers is usually applied to prevent or alleviate the formation of parentheses lines.

**Anatomy:** Aside from the NLF, targets of the treatment for parentheses lines include the orbicularis oris, the risorius muscles, and/or the depressor anguli oris (DAO). The risorius muscle originates in the superficial fascia above the masseter muscle and attaches to the modiolus. The anatomy of the orbicularis oris has been described in the section on perioral wrinkles. The anatomy of the DAO will be described in the section on mouth corner lifting.

**Injection Technique:** Although dermal fillers are the most common treatment for parentheses lines, BTxA prevents or

slows the development of deeper lines, especially in patients with hyperactive muscle forces. These muscles are highly individualized and important for facial expression, the oral sphincter, and articulation. Therefore, physicians applying this treatment must first have a complete understanding of facial anatomy and conduct a thorough evaluation.

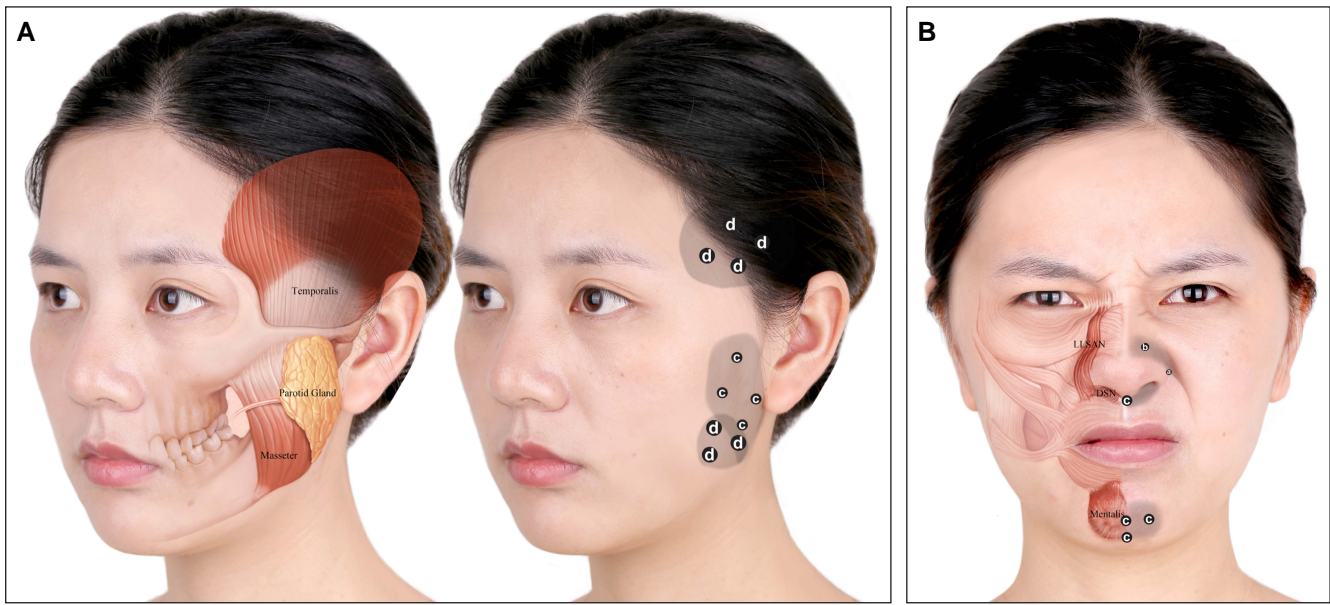
## Contour Adjustment

Neurotoxins have been utilized to treat hyperfunctional rhytids of the face at an early stage and have been expanded to improve facial reshaping of the front view and adjust the profile of the facial contour. Neurotoxins can help with masseter hypertrophy, parotid gland hypertrophy, temporalis hypertrophy, nasal tip ptosis, dilator naris flaring, and mentalis tension.<sup>55</sup> Injection sites and doses are shown in Table 3 and Figure 2.

### Masseter

The masseter muscle elevates the mandible and plays an important role during chewing; it may become enlarged from repeated clenching of the jaw, resulting in masseteric hypertrophy that can lead to a wide contour of the lower face.<sup>56</sup> In 1994, Moore and Wood first used neurotoxins for functional reasons.<sup>57</sup> Rijdsdijk et al later employed the toxin for aesthetic improvement, resulting in a decrease in masseter thickness and improved contour of the lower face.<sup>58</sup>

**Anatomy:** The masseter muscle consists of the superficial, middle, and deep layers. Myofibers within these layers are arranged in different directions. The superficial layer arises from the anterior zygomatic arch, passes posteriorly and inferiorly, and inserts into the masseter tuberosity. The thinner middle layer arises from the posterior arch, travels down to the front, and inserts into the masseter tuberosity.



**Figure 2.** Anatomy and injection for contour adjustment with LetibotulinumtoxinA in Asian patients. (A) Anatomy and injection for masseter hypertrophy, temporalis hypertrophy, and parotid gland hypertrophy treatment; and (B) anatomy and injection for dilator naris flaring, nasal tip ptosis, and mentalis tension treatment. a, 0.25 to 0.5 U/Point; b, 0.5 to 1 U/Point; c, 2 to 4 U/Point; d, 5 to 10 U/Point; DSN, depressor septi nasalis; LLSAN, levator labii superioris alaeque nasi.

The deep layer also arises from the posterior arch and passes back and downward to insert into the masseter tuberosity. These 3 layers fuse in the lower third of the muscle.<sup>59</sup>

**Injection Technique:** It is advised to inject BTxA into the safety zone located below an imaginary line from the ear lobe to the oral commissure and between the palpable posterior border of the masseter and 1 cm posterior to the palpable anterior border of the muscle.<sup>4</sup> Before the injection, the patient should be asked to clench and the injection points should be marked on the prominent bulge. BTxA is injected at 3 to 5 sites on each side of the face. A dose of 5 to 10 units of BTxA should be delivered at each site with the needle inserted perpendicular to the skin to its full depth. Superficial and higher injections may cause asymmetry during animation.<sup>60</sup>

### **Parotid Gland**

Neurotoxins are frequently employed in the masseter muscles to reduce the width of the lower face. The parotid glands are located at the mandibular angle. Therefore, reducing the volume of the parotid glands by neurotoxin injection also helps make the lower face appear slimmer.<sup>61,62</sup>

**Anatomy:** The parotid gland, in front of and beneath the ears, is located deep in the lateral superficial musculoaponeurotic system and covers the posterior portion of the masseter muscle. When a patient clenches, the posterior border

of the masseter muscle can be palpated, making it easier to isolate the parotid gland.<sup>63</sup>

**Injection Technique:** BTxA injection sites are located within the parotid glands. A 31-gauge insulin syringe with an 8-mm needle insert is inserted perpendicularly to place 3 units per site. Treatment is performed at 8 points on each side of the face. The injection depth depends on the volume of the parotid gland.<sup>64</sup>

### **Temporalis**

Neurotoxin injection into the temporalis muscles is usually performed to treat headaches and bruxism. However, there are limited reports on neurotoxin injections into the temporalis muscles for cosmetic purposes.<sup>65</sup>

**Anatomy:** The fan-shaped temporalis originates from the bony surface of the temporal fossa and inserts into the tip of the coronoid process and the anteromedial side of the mandibular ramus. The temporalis and masseter muscles are a pair of collaborative masticatory muscles that contribute to the mandibular chewing movement.<sup>66</sup> The 2 muscles work synergistically to achieve chewing and maintain mandibular stability in the sagittal direction. Masseter atrophy following injection of neurotoxins sometimes causes compensatory hypertrophy of the temporalis.

**Injection Technique:** The injection sites are within the area of the temporalis. A 31-gauge insulin syringe with an 8-mm

**Table 4.** Consensus Recommendations for Lifting With LetibotulinumtoxinA in Asian Patients

Indication	Target muscle	Injection points (n)	Dose per injection point (units)	Typical total dose range (units)	Preferred injection level
Eyebrow lifting	Depressor supercilli, orbicularis oculi	1/side (medial eyebrow), 1-3/side (lateral eyebrow)	0.25-0.5 (md)	1-4	ID, SC
Mouth corner lifting	Depressor anguli oris	1/side	0.5-1	1-2	ID, SC
Mandibular margin lifting	Platysma	40-60/side (md)	0.25-0.5 (md)	60-100 (md)	ID, SC

ID, intradermal; md, microdroplet (only for mandibular margin lifting); SC, subcutaneous.

needle insert is inserted perpendicularly to place 5 units per injection point. Treatment is performed on 3 to 8 points on each side of the temple. The injection depth depends on the volume of the temporalis.<sup>64</sup>

### **Depressor Septi Nasi**

The depressor septi nasi creates ptosis of the nasal tip with smiling (animation ptosis) as well as shortening of the upper lip.<sup>67</sup>

**Anatomy:** The depressor septi nasi arises from the incisive fossa and inserts into the lower part of the membranous septum as a paired muscle, which drags the tip of the nose.<sup>68</sup>

**Injection Technique:** The injection is placed at the base of the anterior nasal spine, at the columellar-labial junction at the midline. A dose of 2 to 4 units of BTxA can be injected intramuscularly.<sup>69</sup>

### **Dilator Naris**

The neurotoxin can be utilized in the nose to address nasal flaring.<sup>10</sup>

**Anatomy:** Nasal flaring is promoted by the dilator nasalis (an alar portion of the nasalis) and occurs in individuals who unconsciously flare their nostrils. This is caused by the alar nasalis and the medial alar portion of the levator labii superioris alaeque nasi.<sup>23,45</sup> The alar part of the nasalis originates from the transverse part of the nasalis muscle at the maxilla and inserts into the alar facial crease and adjacent deep surface of the external skin of the lobule. The LLSAN lies in the sulcus between the nose and cheek, arises from the upper part of the frontal process of the maxilla, and descends to partly insert into the ala of the nose and the skin of the lateral half of the upper lip. The LLSAN raises the lateral half of the upper lip and wing of the nose.<sup>68</sup>

**Injection Technique:** BTxA (0.25 to 1 unit) is injected intramuscularly at the center of each alar rim.<sup>55</sup>

### **Mentalis**

The mentalis muscle is a cone-shaped paired muscle inserted into the skin of the chin around the midline. The mentalis muscle supports the lower lip. Hypercontraction of the mentalis muscle can result in a cobblestone appearance in the chin area. BTxA injection into this muscle can release the tension of the mentum to correct Ricketts' aesthetic line.<sup>70</sup>

**Anatomy:** The mentalis is a paired muscle that originates from the mandible, courses downward, and is inserted into the skin of the chin. When contracted, it raises the chin and protrudes the lower lip.<sup>71</sup>

**Injection Technique:** Because the muscle originates cephalad to its insertion site, the needle should be angled superiorly and inserted at its full depth. A single injection in the midline of 4 to 10 units of BTxA can be performed approximately 0.5 to 1 cm above the inferior-most point of the chin and no closer than 1.5 cm from the lower lip.<sup>71</sup> If one chooses to inject bilaterally, on each side of the midline, 2 BTxA injections can be performed with 2 to 4 units per injection site lateral to the midpoint.<sup>46,55,72</sup>

### **Lifting**

In addition to facial wrinkles, the appearance of sagging is a characteristic of aging.<sup>69</sup> Additionally, sagging of the corner of the mouth can give an appearance of sadness, tiredness, or angeriness. BTxA can be employed for facial lifting by weakening relevant mimetic muscles. The recommended injection sites and doses are shown in Table 4 and Figure 3.

### **Eyebrow Lifting: Corrugators, Depressor Supercilli, Procerus, and Orbicularis Oculi**

The brow depressors include the corrugators (medial eyebrow), depressor supercilli (medial eyebrow), procerus (medial eyebrow), and orbicularis oculi (lateral and mid-eyebrow).<sup>69</sup> Previous studies have reported that BTxA can be applied for eyebrow lifting by targeting the brow depressors.<sup>46,70,71</sup> BTxA injection is a minimally invasive and less complicated method for eyebrow elevation; however, its effect is temporary, lasting for 3 to 6 months.<sup>73,74</sup>





**Figure 3.** Anatomy and injection for lifting (eyebrow, mouth corner, and mandibular margin) with LetibotulinumtoxinA (Letybo, Hugel Pharma Inc., Seoul, South Korea) in Asian patients. a, 0.25 to 0.5 U/Point; b, 0.5 to 1 U/Point; DAO, depressor anguli oris; DLI, depressor labial; DS, depressor supercilia; OOR, orbicularis oris muscle.

**Anatomy:** The anatomy of these muscles has been described in the Anti-wrinkle subsection described above.<sup>2,23-27,30-36</sup>

**Injection Technique:** BTxA injection into the glabella (corrugators, depressor supercilia, procerus) can elevate the medial eyebrows. The orbicularis oculi is another target muscle for lateral eyebrow lifting.<sup>5</sup>

### **Mouth Corner Lifting: Depressor Anguli Oris**

The DAO is the main depressor of the mouth corners. The excessive contraction of the DAO draws the mouth corners downward.<sup>75,76</sup> Injection of BTxA into the DAO inhibits its contractile force for oral corner lifting clinically.<sup>75</sup> However, if BTxA is inappropriately injected in an uncorrected location or by overdosage, other perioral muscles may be affected, which may lead to dysfunction of the perioral musculature and unsatisfactory facial expression.<sup>77</sup> Therefore, physicians should understand the facial anatomy in detail and individual muscle variations before performing BTxA injections.<sup>77</sup>

**Anatomy:** To maximize the effects and minimize complications, a detailed understanding of the DAO and determination of the exact injection points are necessary. The DAO is triangular in shape, starting from the oblique line of the mandible, and its fibers converge with the fibers of the depressor labii inferioris (DLI).<sup>23</sup> The DAO converges with the risorius and the orbicularis oris in the mouth corner and inserts into the modiolus. The modiolus can be touched by fingers at the lateral border of the mouth corner, which is a common insertion point for the DAO, orbicularis oris,

risorius, LAO, zygomaticus major, and buccinator. The DAO is primarily located less than 30 degrees medial and less than 45 degrees lateral to a sagittal line passing through the modiolus and the margin of the mandible.<sup>77</sup>

**Injection Technique:** BTxA injection into the DAO can lift a droopy appearance of the mouth corner. To minimize the unsatisfactory effects of BTxA, it should be injected into the lower lateral depressor anguli oris muscle.<sup>78</sup>

### **Jawline Lifting: Platysma**

The contraction of the platysma muscle pulls down the cheek and jawline, which contributes to an undefined jawline and cervicomental contouring. Microdroplet injection of BTxA releases the downward tension of the superficial muscle fibers of the platysma muscle and alleviates the depressor effect of the muscle, while the deeper muscle fibers continue to function normally and render the platysma muscle more tightly attached, creating a more defined cervicomental angle and an elevated jawline.<sup>39,79</sup>

**Anatomy:** The platysma muscle ascends to the lower facial areas after crossing the mandibular border and ramus. In the lower facial area, the platysma fibers usually terminate behind the DAO and at the lower margin of the risorius muscle. However, in the cheek area, just anterior to the auricle, some muscle fibers terminate in the zygomatic arch area. These fibers are called the facial portion of the platysma. The platysma muscle draws the mouth angle downward together with the DAO muscle and draws the lip downward together with the DLI muscle. Injection into the platysma muscle can achieve face lifting.<sup>80,81</sup>

**Injection Technique:** BTxA is injected into the dermis or the junction of the dermis and subcutaneous tissue to lift the jaw and jawline.<sup>39</sup> To avoid undesired consequences, it is recommended that LetibotulinumtoxinA be administered where it is bounded by areas of 1 finger-width above the mandibular margin, behind the marionette line, behind the anterior border of the platysma muscle, and above the clavicle. The needle should be carefully injected as superficially as possible into the skin. To evaluate this, resistance should be felt when pressing the plunger, and a small, raised, blanched bleb in the skin should be observed, indicating a good injection depth. This injection results in an improved cervicomental angle, and elevation and flattening of jowls.

## **DISCUSSION**

The panel believes that the injection levels for anti-wrinkle treatment and lifting are primarily in the dermis or subcutaneous tissue, and that the injection dose is more conservative than that recommended for Caucasians. The specific

injection sites and doses are shown in the figures and tables of this article. The representation of the injection sites, doses, and levels will provide a guide for clinicians. The existing evaluation criteria for BTxA aesthetic treatments are relatively crude, and there are differences in drug formulations and injection methods in each clinical trial. Furthermore, the subjective perception of the patient is an important indicator of the success of the treatment. The units and the potency of BTxA provided here are specific to the method used for its preparation and content testing and are not interchangeable with other BTxA preparations. When utilizing different BTxA preparations, clinicians should start with a conservative dose and carefully individualize the treatment for each patient, adjusting it according to feedback to obtain a higher satisfaction level. BTxA has been widely utilized clinically; however, patients of different races have different features and aesthetic requests. Therefore, an appropriate clinical treatment regimen and dosage should be developed for each race or culture.

## CONCLUSIONS

In this consensus, panelists proposed individualized treatment plans for BTxA in the 3 areas of wrinkle removal, contour adjustment, and face lifting in Asians, based on their extensive experience and knowledge of facial anatomy. The limitation of this article is that no clinical examples are provided to illustrate the results of these recommendations.

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