

ORIGINAL ARTICLE

International consensus recommendations on the aesthetic usage of botulinum toxin type A (Speywood Unit) – part II: wrinkles on the middle and lower face, neck and chest

B Ascher,^{†,*} S Talarico,[‡] D Cassuto,[§] S Escobar,[¶] D Hexsel,^{**} P Jaén,^{††} GD Monheit,^{‡‡} B Rzany,^{§§} M Viel^{¶¶}

[†]Clinique de Chirurgie Esthétique Léna, Paris, France

[‡]Universidade Federal de San Paulo, San Paulo, Brazil

[§]University of Catania, Milan, Italy

[¶]Universidad de Buenos Aires, Buenos Aires, Argentina

^{**}Pontificia Univeridade Catolica do Rio Grande do Sul, Porto Alegre, Brazil

^{††}Ramon y Cajal Public Hospital, Madrid, Spain

^{‡‡}Total Skin and Beauty Dermatology Center, Birmingham, AL, USA

^{§§}dEBM, Klinik für Dermatologie, Charite-Universitätsmedizin, Berlin, Germany

^{¶¶}London Centre for Aesthetic Surgery, London, UK

*Correspondence: B Ascher. E-mail: benjaminascher@wanadoo.fr

Abstract

Background Azzalure[®] (Galderma SA), a newly approved European botulinum neurotoxin type A (BoNT-A), is derived from Dysport[™] (Ipsen Ltd.), which has a 20-year history of product consistency and has been widely used for various aesthetic and therapeutic applications. Azzalure[®] and Dysport[™] are collectively referred to as BoNT-A (Speywood Unit) after the unit of their activity, and are distinct from other commercial BoNT-A preparations. Consensus has been developed for the treatment of upper facial wrinkles with BoNT-A (Speywood Unit).

Objective To provide consensus recommendations on the treatment with BoNT-A (Speywood Unit) for wrinkles on the middle and lower face, neck and chest region.

Methods The members of the International Board on Botulinum toxin Azzalure (IBBA) convened to develop consensus based on their extensive experience.

Results The recommended final concentration of BoNT-A (Speywood Unit) is 200 Speywood Units/ml after reconstitution. The consensus recommendations were provided for nine indications, including lower eyelid wrinkles, bunny lines, drooping nasal tip, perioral wrinkles, masseter hypertrophy, drooping mouth corners, dimpled chin, platysmal bands and décolleté wrinkles. For each indication, anatomy of the region to be treated was discussed, as were potential side-effects. The consensus recommendations included the number and location of the injection points, dose range of each point and the total injection, as well as specific injection technique.

Conclusion These recommendations provide a guideline for physicians who wish to perform safe and efficacious treatment with BoNT-A (Speywood Unit) on the less commonly treated middle and lower face, neck and chest region.

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Keywords

Botulinum toxin type A, consensus, facial wrinkles, Speywood

Conflicts of interest

B. Ascher, S. Talarico, D. Cassuto, S. Escobar, D. Hexsel, P. Jaén and M. Viel are consultants for Galderma.

G.D. Monheit is a consultant for Galderma and Ipsen. B. Rzany has served as an advisor, speaker and investigator for Galderma, Ipsen Ltd. and Merz Pharma.

Introduction

Injection with botulinum neurotoxin type A (BoNT-A) is one of the most widely performed non-invasive cosmetic procedures. BoNT-A blocks the release of the neurotransmitter acetylcholine, which is essential for neuromuscular transmission.¹ Therefore, injection of BoNT-A can help to smooth wrinkles caused by muscular activities and may improve patient's quality of life.²

Several commercial preparations of BoNT-A products are currently available for aesthetic usages. Azzalure/Dysport and Vistabel/Botox, the two most widely used products, are produced from different strains of bacteria, purified using different methods and therefore have distinct properties.^{1,3} The units of Azzalure/Dysport and Vistabel/Botox are not interchangeable, as different bioassays were employed for measuring their activities.^{4,5} Azzalure and Dysport are quantified in Speywood Units (s.U) and are therefore collectively referred to as BoNT-A (Speywood Unit).

Dysport is available in two different quantities (500 s.U and 300 s.U). Dysport (500 s.U) has a 20-year history of product consistency and safety in both therapeutic and aesthetic usages.^{6–9} Dysport (300 s.U) is approved in the U.S as abobotulinumtoxin A for the treatment of glabellar lines. Azzalure (125 s.U) is specifically designed for aesthetic usages and recently received European approvals. The efficacy and safety of glabellar line treatment with BoNT-A (Speywood Unit) were demonstrated in clinical studies involving more than 4000 patients.^{3,6,10–18}

Although treatment in the glabellar region is the only labelled aesthetic indication for BoNT-A products, it is common for physicians to treat wrinkles in other areas.^{6,19–21} A full understanding of both BoNT-A properties and related anatomy is essential to ensure optimal treatment results and should be acquired through proper trainings. As there are only a few clinical studies and regional guidelines on the off-label indications,^{21–28} international consensus recommendations should be helpful in providing a general guideline for efficacious and safe injection of BoNT-A (Speywood Unit). Consensus recommendations on the upper face treatments with BoNT-A (Speywood Unit) have already been established.²⁹ In the present article, we provide consensus recommendations on the treatment of the middle and lower face, neck and chest region with BoNT-A (Speywood Unit).

Methods of consensus development

The International Board on Botulinum toxin Azzalure (IBBA) consists of nine dermatologists/plastic surgeons who have extensive experience in the aesthetic usages of BoNT-A (Speywood Unit). Board members convened to develop consensus recommendations on common indications for the middle and lower face, neck and chest region, based on their own experience. A strong consensus was defined as approval from at least 90% of the board members (eight of nine members).

Treatment safety is ensured when the recommended reconstitution volume, injection points, dose and the correct injection tech-

nique are adopted (Table 1). Highly risky injection points or indications requiring extensive experience were not suggested. Strong consensus were achieved for all indications except décolleté wrinkles, which were not routinely treated by all members. It is important to note that the consensus provided here refers to BoNT-A (Speywood Unit), and cannot be applied to other BoNT-A products.

Consensus recommendations

General preparation

Reconstitution. The volume of reconstitution can be adapted according to the product, physician's preference and patient's needs. We recommend reconstituting the powder of BoNT-A (Speywood Unit) in preservative-free 0.9% sodium chloride solution to obtain a final concentration of 200 s.U/ml (10 s.U/0.05 ml), the concentration used in a majority of clinical studies.^{11,14–17} The recommended reconstitution volume for Azzalure (125 s.U), Dysport (500 s.U) and Dysport (300 s.U) is 0.63 ml, 2.5 ml and 1.5 ml respectively. Using the recommended volumes would result in the same concentration for all BoNT-A (Speywood Unit) and thus ensure treatment consistency.

Syringe and needle. A 1-ml insulin-type syringe bearing the graduations of 10 s.U and 0.01 ml was specially designed for reconstitution and injection of Azzalure. A 30G, 13 mm needle was most widely used for the injection of BoNT-A (Speywood Unit). The length of the needle is divided into three parts (the first, middle and last thirds), and the position of the needle is hereafter used as an indication of injection depth.

Lower eyelid wrinkles

Lower eyelid wrinkles are usually the result of hyperkinetic activities. Treatment with BoNT-A reduces the inferior wrinkles, increases the palpebral aperture and thus widens the eyes. Although it is effective in reducing the hyperkinetic lines, BoNT-A treatment is not suitable for treating the static wrinkles caused by photodamaging, or eye bags caused by muscle laxity. In those cases, combination therapy with fillers, peeling, lasers or surgery would be more appropriate.

Anatomy. The orbicularis oculi is usually divided into the lacrimal, palpebral and orbital portions. The lacrimal portion is at the medial side of the orbit, and is the smallest and the innermost part of the orbicularis oculi. The palpebral portion raises the eyelid and controls the involuntary action of blinking. The orbital portion, or pars orbicularis, surrounds the orbit with concentric fibres, blends into the frontalis and extends to the masseter. Normal functioning of all three portions is required for voluntary closing of the eyelid.

Table 1 Consensus recommendations on the injection points, dose and technique for common indications of BoNT-A (Speywood Unit) on the middle and lower face, neck and chest region

Indication	Dose per injection point (s.U)	Number of injection points	Total dose (s.U)	Injection site	Injection technique
Lower eyelid wrinkles	1–2.5	1–2 points per side, total 2–4 points	5	At the mid-pupillary line, about 2 mm below the lower eyelid border	Very superficially intradermal injections parallel to the skin, to create a white papula
Bunny lines	5–10	1 per side, total 2 points	10–20	About 1 cm above the upper lateral part of the nostril	Superficial perpendicular injections (45° angle to the nasal bone) to the first third of the needle
Drooping nasal tip	10	1	10	Just below the nasal tip, at the base of columella	Perpendicular injection to at least the middle third of the needle
Perioral wrinkles	1–2	Total 4–6 points	4–12	Inject at the vermilion border of the lips and at least 1.5 cm from the mouth corners	Very superficially intramuscular injections perpendicular to the skin with just the tip of the needle
Masseter hypertrophy	10–20	3 per side, total 6 points	60 for Caucasians and 120 for Asians	Three points per side into the masseter	Intramuscular perpendicular injection to at least the middle third of the needle
Drooping mouth corner	5–10	1 per side, total 2 points	10–20	One point per side slightly internal to the cross point of a line extending from the nasolabial fold and the jaw line	Superficially intramuscular and perpendicular injections to the middle third of the needle
Dimpled chin	5–10	2	10–20	2 points close to the centre at the bony jaw line	Superficially intramuscular and perpendicular injections to the middle 1/3 of the needle
Platysmal bands	5–10	Fewer than 10 per side	Maximum dose 50 per side	Start the first point at the jaw line and go down every 2 cm until at least the middle part of the bands.	Very superficially intramuscular injections on the bands with horizontal orientation, to the first third of the needle
Décolleté wrinkles	7.5–10	5–6 per side	75–120	V-shape technique	Perpendicular injections of at least 4 mm deep

Injection point, dose and technique. For the treatment of lower eyelid wrinkles, the board members recommend 1–2 injections at the mid-pupillary line, about 2 mm below the border of the lower eyelids (Fig. 1). A total dose of 5 s.U (2.5 s.U per side) is recommended, divided among 2–4 injection points (about 1–2.5 s.U per point). Injection should be very superficial, with the needle held tangentially to the eye, to create a white papula or a ‘bleb’ upon injection.

If applicable, lower eyelid wrinkles should be treated together with the lateral periorbital wrinkles (‘crow’s feet’) to obtain optimal results.²⁹ In this case, the same injection points should be used with a slightly lower dose per point.

Safety concerns. Patient selection is crucial for this indication. Injectors should avoid patients having dry eyes, prominent eye bags, scleral show or morning eyelid oedema. In addition, patients need to have a positive snap test and preferably good skin elasticity.

Bunny lines and drooping nasal tip

Bunny lines refer to the wrinkles on the lateral part of the nose. In some patients, the wrinkles also exist on the dorsal part of the

nose, and/or extend to the lower eyelids and cheeks. Bunny lines are usually dynamic wrinkles and appear when patients laugh or frown. They can also be the result of BoNT-A treatment on the upper face, when the nasal muscles over-contract to compensate for the paralysed muscles in the glabellar, forehead and orbital regions. If bunny lines appear in addition to glabellar lines when patients frown, they should be treated together.

Drooping nasal tip may be partially due to increased activity of the depressor septi nasi. BoNT-A treatment may improve this sign and slightly raises the nasal tip to give patients a more youthful look.

Anatomy. There are three major muscles in the nasal region: the procerus, the nasalis and the depressor septi nasi. The nasalis is the main muscle responsible for producing bunny lines, although the medial fibres of the levator labii superioris alaeque nasi, which elevate the lip and the nose, could also contribute in some patients. The nasalis has the shape of a horseshoe: the transverse fibres on the nasal dorsum form the curved part, whereas the two lower parts of the muscle are vertical and run down each side of the nose. Contraction of the nasalis moves the nose and controls the size of the nostrils.

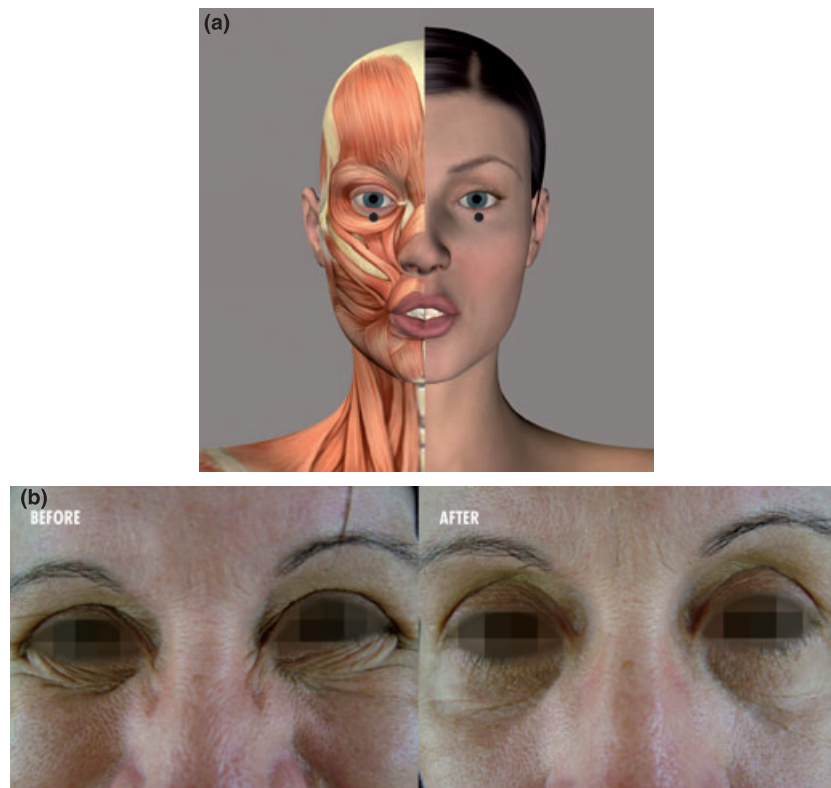


Figure 1 Treatment of lower eyelid wrinkles (a) Recommended injection points (Graph was modified from de Maio and Rzany¹⁹). (b) Photographs of a patient when smiling before and 15 days after the treatment with 6 s.U BoNT-A (Speywood Unit). *Courtesy of S. Talarico.*

The depressor septi nasi is an important muscle in determining the position of the nasal tip. Its fibres originate at the base of the nasal septum and blend with the orbicularis oris. Contraction of the depressor septi nasi leads to a shorter distance from the upper lip to the nasal tip, and thus decreases the nasal tip projection.

Injection point, dose and technique. For the treatment of bunny lines, two injection points with one on each side of the nose are recommended (Fig. 2). The injection points should be about 1 cm above the upper lateral part of the nostril. The consensus recommendation is 5–10 s.U per injection point and a total of 10–20 s.U. The injection should be very superficial to create an obvious papule, avoiding contact with blood vessels or periosteum. The orientation of the injection should be perpendicular, with an angle of about 45° to the nasal bone.

To slightly raise the nasal tip, one injection at the base of the columella is recommended. The dose should be 10 s.U, and the injection should be perpendicular and deep, to at least the middle third of the needle.

Safety concerns. For the treatment of bunny lines, it is important to inject superficially to prevent ecchymosis. Injecting into the levator labii superioris or the levator labii alaeque nasi may cause upper lip ptosis and should be avoided. For the treatment of drooping nasal tip, pain is the most commonly reported

adverse event. Upper lip ptosis is rare and occurs only when the depressor septi nasi is overly paralysed. Other indications in the nasal area such as decreasing the size of nostril aperture and treatment of ‘gummy smile’ are only recommended for experienced injectors.

Perioral wrinkles

The vertical wrinkles on the upper and lower lips can give an impression of ageing. They can be treated with BoNT-A injection alone. However, a combination therapy with filler is highly recommended to preserve the shape of the philtrum after BoNT-A treatment. Multiple muscles are adjacent to the mouth region and have important functions. Therefore, special care should be taken to avoid potential serious adverse events.

Anatomy. The orbicularis oris is a sphincter muscle of the mouth and a major muscle in the perioral region. The fibres of this muscle control the direct closure and protrusion of the lips. The lack of support in the upper lip because of ageing, combined with extensive movement of the orbicularis oris, leads to the formation of vertical perioral wrinkles.

Injection point, dose and technique. For the treatment of perioral wrinkles, 4–6 injection points are recommended, with four symmetrical points on the upper lip, and if applicable, two

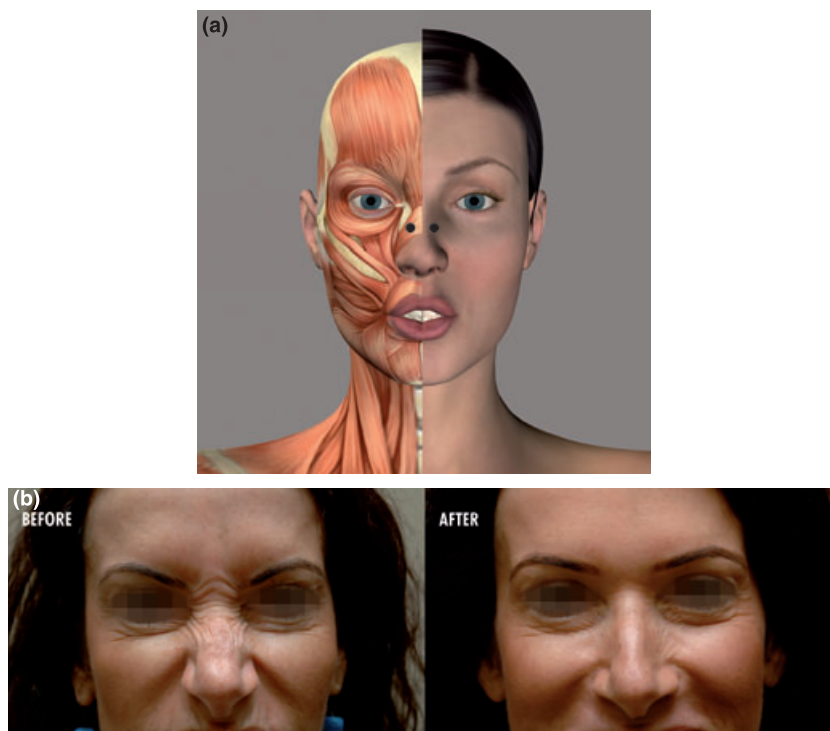


Figure 2 Treatment of bunny lines. (a) Recommended injection points (Graph was modified from de Maio and Rzyany¹⁹). (b) Photographs of a patient at maximal contraction before and 21 days after the treatment with 30 s.U BoNT-A (Speywood Unit). *Courtesy of M. Viel.*

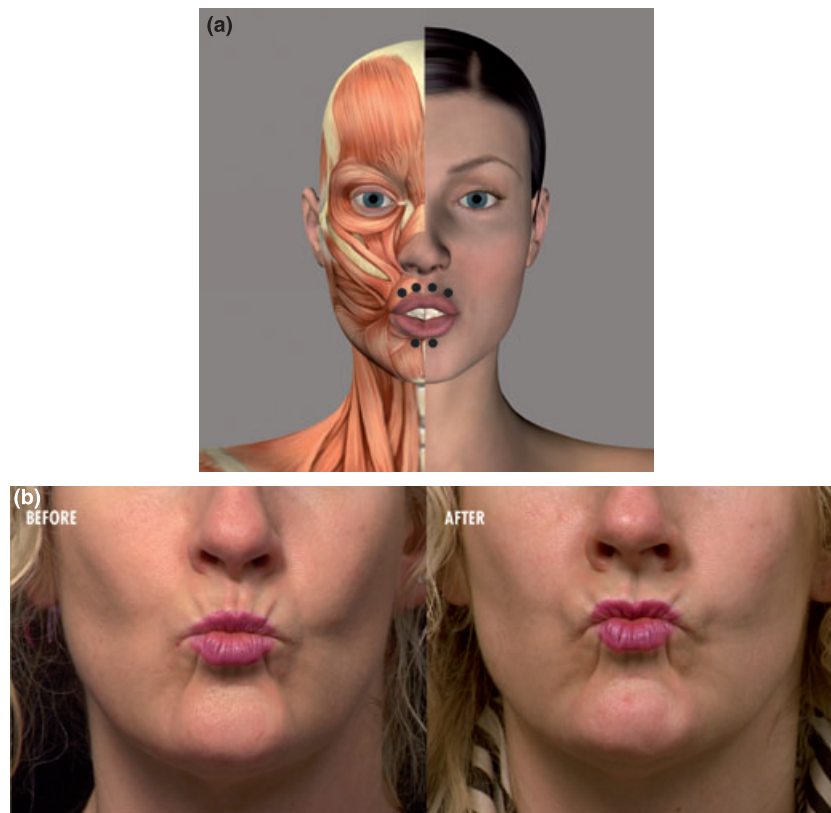


Figure 3 Treatment of perioral wrinkles. (a) Recommended injection points (Graph was modified from de Maio and Rzany¹⁹). (b) Photographs of a patient puckering before and 21 days after the treatment with 12 s.U BoNT-A (Speywood Unit). *Courtesy of B. Rzany.*

points on the lower lip (Fig. 3). Injection points should be at the vermilion border and parallel to the lips. The lateral points should be at least 1.5 cm away from the mouth corners, at the cross points of the lip vermilion border and vertical lines extended from the external ala. The medial points should be 1 mm away from the philtrum.

A total dose of 4–12 s.U is recommended, with 1 to 2 s.U per point. The dose depends on the muscle strength, severity of the hyperkinetic lines and the degree of elastosis. Injection should be perpendicular to the skin and superficially intramuscular, to the first third of the needle.

Safety concern. If high doses are administered, functional impairment of the lips may occur, and the patient's ability to drink, eat or speak can be adversely affected. Therefore, a minimal dose and superficial injection should be used, while complete wrinkle removal is not the treatment goal. To ensure safety, injectors should start with a lower dose and then gradually increase it until the desired effect is achieved. The lateral points should be sufficiently far away from the mouth corners, to avoid possible adverse events such as mouth asymmetry, drooping mouth cor-

ners and drooling. Patients whose professions rely on proper functioning of the mouth should be discouraged from this treatment. Treatment of the lower lip wrinkles is more risky and should be avoided if not necessary.

Masseter hypertrophy

Benign hypertrophy of the masseter muscle is common among Asians and contributes to an undesirable wide lower face. Injection of BoNT-A can be used to temporarily weaken the masseter, resulting in a smoother and slimmer lower face contour.^{20,30} This is a very common indication in Asia and good results can be achieved with repeated injections of BoNT-A. In Caucasians, masseter hypertrophy is uncommon and might be associated with bruxism, which can be decreased by the treatment of masseter hypertrophy with BoNT-A injection.³¹

Anatomy. The masseter is the largest and strongest muscle functioning in mastication. Its superficial portion originates from the zygomatic arch and inserts into the ramus of the mandible and the side of the mandibular angle. Its deep portion originates from the bottom or inside of the zygomatic arch and inserts

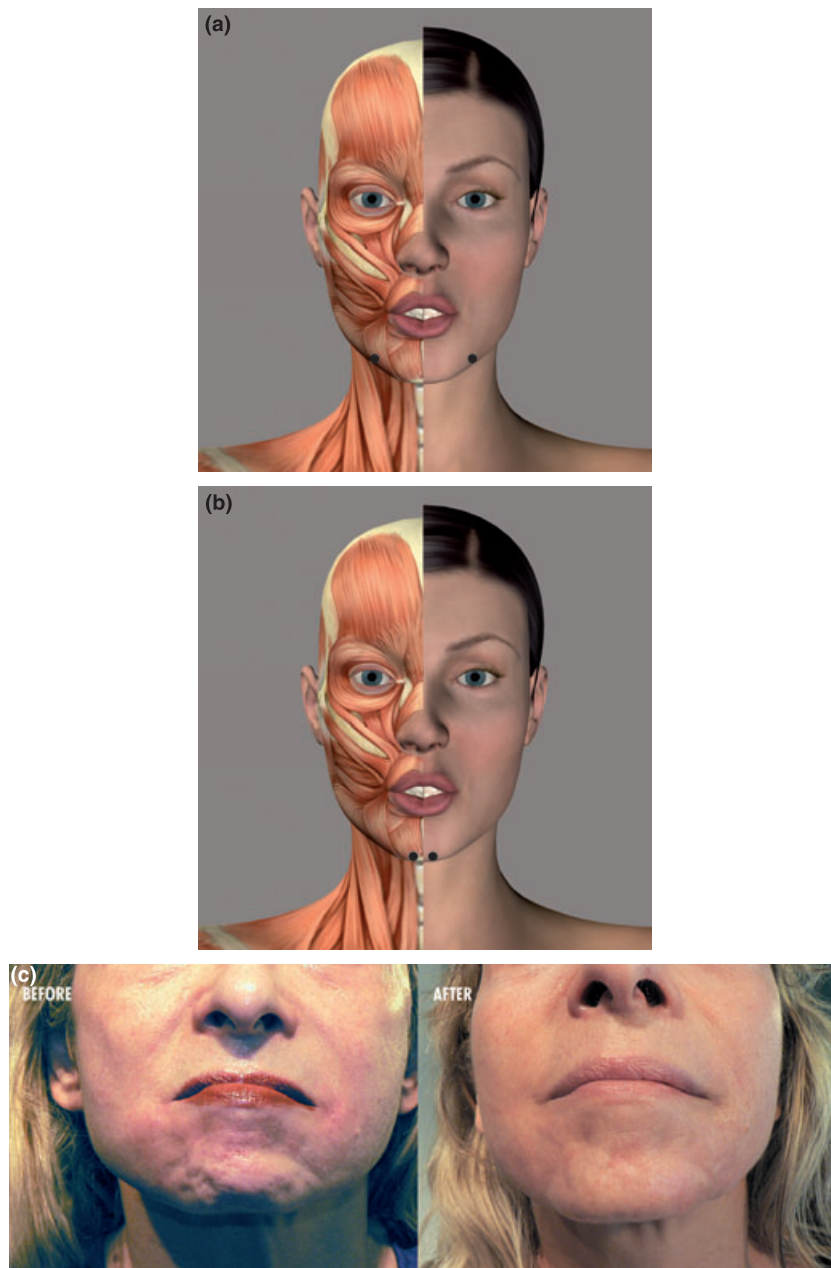


Figure 4 Treatment of the drooping mouth corner ('marionette lines') and dimpled chin. Recommended injection points for drooping mouth corners (a) and dimpled chin (b) (Graph was modified from de Maio and Rzany¹⁹). (c) Photographs of a patient at maximal contraction before and 21 days after the treatment with 20 s.U of BoNT-A (Speywood Unit) for drooping mouth corners and 14 s.U of BoNT-A (Speywood Unit) for the dimpled chin. *Courtesy of S. Escobar.*

vertically into the ramus of the mandible. It may also blend in with the temporal muscle.

Injection point, dose and technique. A 6-point injection into the masseter with three points per side is recommended by the members. The physicians can palpate the muscle by asking

the patients to clench their teeth. The injection points should be below the ear lobe–mouth corner line and about 1.5 cm above the mandibular angle border.

For Asian patients with strong masseters, treatments with a dose of 100–140 s.U per side was reported.³⁰ In Caucasians, the dosages should be lower with a total dose of 30 s.U per side, distributed

evenly into three points with about 10 s.U per point. Injection should be perpendicular to the skin and intramuscular, to the middle third of the needle.

Safety concerns. The crunching power is reported to be reduced 2–4 weeks after injection. In some cases, the masticating capability might also be reduced. Therefore, the muscle mass should be assessed before the treatment and it is recommended to start with a smaller dose. Injection just beneath the zygomatic bone should be avoided as it may impair the function of zygomatic muscles, resulting in awkward facial expression especially when smiling.

Drooping mouth corners

Drooping mouth corners give the entire face a sad and dissatisfied expression. For this indication, it is recommended to adopt a combination strategy with BoNT-A and filler, which together can correct the level of the mouth corners and reduce the ‘marionette lines’ that extend from the mouth corner to the chin.

Anatomy. The elevators of the mouth corners are the zygomatic major and the levator anguli oris muscles. The triangular-shaped depressor anguli oris intervenes with the two elevators at the mouth corners. Extensive contraction of the depressor anguli oris and some fibres of the platysma can pull the mouth corners downwards.

Injection point, dose and technique. A 2-point injection into the depressor anguli oris with one point per side is recommended by the members (Fig. 4). The injection points should be slightly internal to the cross points of the extension of the nasolabial fold and the jaw line. The muscle location can be verified by asking the patients to grind their teeth or to grimace.

A total dose of 10–20 s.U is recommended, with 5–10 s.U per point. For patients with a strong depressor anguli oris muscle, a slightly higher dose should be administered. The injector should pinch the muscle slightly to prevent its movement and inject intramuscularly and perpendicularly, to the middle third of the needle.

Safety concerns. The levator anguli oris might be affected when the injection dose is too high or when injection points are too close to the mouth corners, resulting in adverse events such as drooling, speech impairment and mouth asymmetry. It is thus crucial to start with a minimal dose/volume and inject sufficiently far away from the mouth corners.

Dimpled chin

Dimpled chin is caused by contraction of the mentalis muscle, and the BoNT-A treatment can help restore a smooth appearance of the chin. Combination therapy with fillers is more appropriate as loss of collagen and subcutaneous fat in this region contributes significantly to the formation of a dimpled chin.

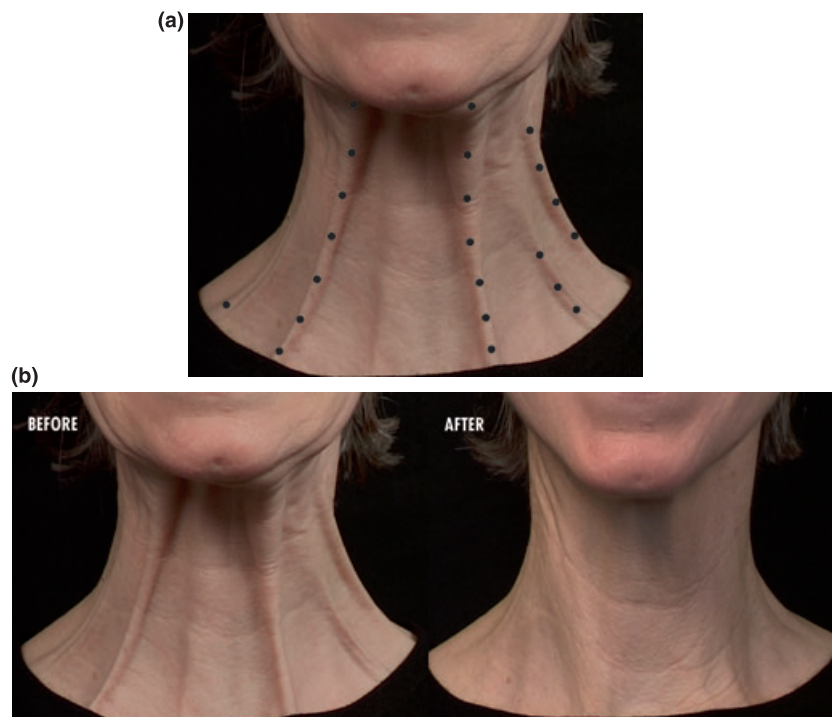


Figure 5 Treatment of platysmal bands. (a) Recommended injection points. (b) Photographs of a patient at maximal contraction before and 13 days after the treatment with 120 s.U BoNT-A (Speywood Unit). *Courtesy of B. Rzany.*

Anatomy. The mentalis is a perpendicular muscle in the perioral area. It covers the chin and inserts transversally in the dermis below the lower lip. Contraction of the mentalis raises the chin and makes the lower lip protrude.

Injection point, dose and technique. A two-point injection at the bony jaw line close to the centre is recommended (Fig. 4). The injector can identify the points by asking the patient to try to reach his/her nose with the lower lip. The total dose should be 10–20 s.U, with 5–10 s.U per injection point. The dose should be adjusted according to the mentalis muscle mass. When the dimpled chin and drooping mouth corners are treated together, the same injection points (total 4 points) should be used with a slightly lower dose per point. The needle should be perpendicular to the skin, and injection should be superficial, intramuscular to the middle third of the needle. Although the mentalis is a rather deep muscle, superficial injection usually yields satisfactory results.

Safety concerns. Injecting a higher than recommended dose or injecting close to the lower lip may affect the depressor labii inferioris and the orbicularis oris, causing drooling, speech impairment, mouth asymmetry and lower lip ptosis. Using the recom-

mended dose and injection points should prevent the occurrence of these adverse events.

Platysmal bands

The platysmal bands on the neck are apparent in some slim patients and become more prominent when they speak or smile. Treatment with BoNT-A in patients with good skin elasticity is safe and can be very effective.

Anatomy. The platysma is a thin and broad muscle, which originates from the border of the lower jaw and extends to the clavicular region. It intertwines with other muscles such as the depressor anguli oris at the mouth corners. Contraction of the platysma pulls the lower jaw, lip and mouth corners downwards.

Injection point, dose and technique. The total maximum dose recommended for this indication is 50 s.U per side, with 5–10 s.U per point. It is recommended that injectors start the first point at the jaw line, and go down every 2 cm to at least the middle of the bands (Fig. 5). The total number of injection points depends on the number and length of platysmal bands, as long as the total maximum dose is not exceeded (e.g. ≤ 20 points with 5 s.U per point). Horizontal lines or ‘necklace bands’ are usually

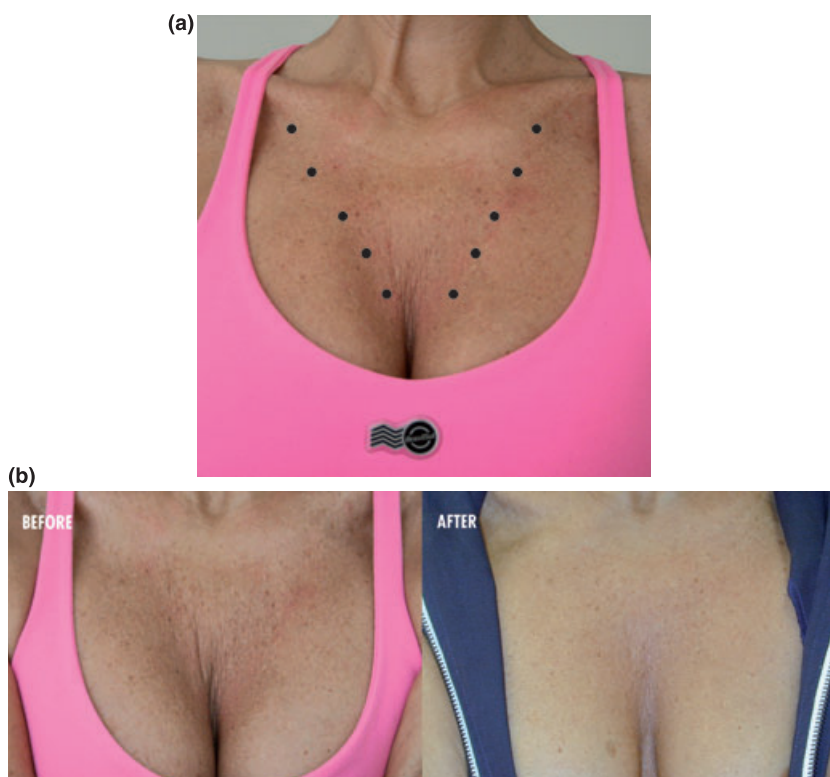


Figure 6 Treatment of décolleté wrinkles. (a) Recommended injection points (b) Photographs of a patient at maximal contraction before and 30 days after the treatment with 100 s.U BoNT-A (Speywood Unit). *Courtesy of D. Hexsel.*

related to elastosis and should be treated only if they are caused by muscular activity.

The ideal patients for this indication should have a thin neck, good skin elasticity, and little or no sagging skin, fat or muscle. The injector can examine the prominence of platysmal bands by asking the patients to pronounce the letter 'E'. Once the platysmal bands become apparent, the injector should slightly pinch it, pull it away and inject horizontally on the band with a superficially intramuscular injection.

Safety concerns. Although dysphagia, dysphonia and neck weakness were listed as potential serious adverse events, they were results of extremely high dose or very deep injection of Botox.³² When a dose lower than the maximal recommended quantity is used and horizontal injection direction is adopted, the risk of such adverse events is virtually nil.

Décolleté wrinkles

Ageing of the chest area could be due to intrinsic or extrinsic factors. As photodamage is usually involved in the ageing of this region, combination therapies with fillers, peeling and laser are often necessary. It should be noted that not all the board members have experience in this indication, and the following recommendations were provided by those who perform BoNT-A treatment in the décolleté area.

Anatomy. The major muscles in the chest area are the caudal part of the platysma and the medial fibres of the pectoralis major. The injector can palpate the muscles by asking the patient to cross their arms.

Injection point, dose and technique. A total dose of 75–120 s.U is recommended, with 7.5–10 s.U per point. The points should form a 'V' shape and the number of injection points depends on the severity and distribution of wrinkles (Fig. 6). The maximum number of injections is 12 points with 10 s.U per point, or 16 points with 7.5 s.U per point. Injection of at least 4 mm deep should be administered with a perpendicular orientation of the needle. Treatment should be avoided in patients whose wrinkles were caused by gravity or sleeping habits, because those lines would not improve after treatment. When necessary, platysmal bands should be treated together with the décolleté wrinkles.

Safety concerns. This is a very safe indication of BoNT-A, although residual wrinkles may exist. Common adverse events include haematomas, injection pain and erythema.

Summary

While upper facial wrinkles are routinely treated with BoNT-A, indications for the rest of the face, neck and chest region present more challenges for less experienced injectors. The panel members develop the consensus recommendations for commonly treated

indications in those areas and provide a simple guideline for the safe and efficacious injection with BoNT-A (Speywood Unit). For each indication, anatomy is briefly reviewed, and the recommended injection points, dose and injection technique are provided. It is also noted if combination therapy with other aesthetic techniques is more appropriate for the indication. The consensus recommendations help to ensure treatment safety and efficacy with BoNT-A (Speywood Unit), and can be further adapted in clinical practice to meet individual needs.

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