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Ultrasonographic study and anatomical guidelines for botulinum neurotoxin injection into the parotid gland

Kyu-Ho Yi[1,2,*], Soo-Bin Kim[3,*], Hyewon Hu[1], Hee-Jin Kim[1]
[1]Division in Anatomy and Developmental Biology, Department of Oral Biology, Human Identification Research Institute, BK21 FOUR Project, Yonsei University College of Dentistry, Seoul, [2]Maylin Clinic (Apgujeong), Seoul, [3]Department of Oral Anatomy, Institute of Biomaterial Implant, College of Dentistry, Wonkwang University, Iksan, Korea

Abstract: Benign enlargement of the parotid gland hypertrophy results in a bulky lateral facial contour and esthetic appearance. This study aimed to determine the depth from the skin surface to the parotid fascia, which encompasses the parotid gland. The anatomical properties of the parotid glands were evaluated in 40 patients using ultrasonography. An up-to-date understanding of the localization of botulinum neurotoxin (BoNT) injection based on anatomy could lead to better localization of the injection into the parotid gland through morphological measurements using data previously published from cadaveric studies. Measurement using the otobasion inferius as a landmark revealed parotideomasseteric fascia thickness averaging 4–6 mm from the skin surface, with the parotid gland extending approximately 15 mm anteriorly. Analysis showed a 3–7 mm thickness range, indicating an optimal injection depth for safety and efficacy in BoNT procedures. Utilizing the otobasion inferius as an anatomical landmark offers a practical approach for measuring parotideomasseteric fascia thickness, addressing cadaveric study limitations. These guidelines aim to maximize the effects of BoNT therapy, which can be useful in clinical settings, by minimizing its deleterious effects.

Key words: Botulinum neurotoxin, Parotid gland, Injections, Ultrasonography, Hypertrophy

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Introduction

Botulinum neurotoxin (BoNT), a product of *Clostridium botulinum*, inhibits the release of acetylcholine at neuromuscular junctions, thereby impeding muscular contraction [1, 2]. The parotid gland is one of the three major salivary glands, alongside the submandibular, and sublingual glands, and is the largest among these glands. However, when the salivary glands are triggered, the parotid gland plays a primary role in saliva production [3].

BoNT is usually injected into the parotid and submandibular glands to treat excessive salivation [4, 5].

BoNT is frequently administered into the parotid gland to enhance both the esthetic and functional aspects of treating conditions characterized by excessive salivation [6]. However, when BoNT injections are administered into the parotid gland, complications may arise, including parotitis and bruising, owing to the proximity of the transverse facial vessels and the parotid duct to the gland. These complications often result from inadequate awareness of the anatomical considerations inherent to the procedure [7, 8]. The objectives of this study were to measure the depth from the

Corresponding author:
Hee-Jin Kim
Division in Anatomy and Developmental Biology, Department of Oral Biology, Human Identification Research Institute, BK21 FOUR Project, Yonsei University College of Dentistry, Seoul 03722, Korea
E-mail: hjk776@yuhs.ac

*These authors contributed equally to this work.

skin surface to the parotid fascia and develop a procedure that ensures precise injections into the fascia rather than the parotid gland, to avoid potential complications, such as facial nerve damage and pain.

Materials and Methods

A total of 40 participants (21 females and 19 males) with average age of 34.4 years (range: 18–54 years) were enrolled in this study. Cadaveric dissections were performed in two individuals (74-year-old male and 83-year-old female) to explore the anatomy above the mandible. Individuals with a history of facial or neck procedures, neurodegenerative conditions, or use of anticholinergic medications were excluded. Written consent was obtained from the families of deceased patients prior to dissection, and written consent was also obtained from all participants in the ultrasonography study. This study adhered to the principles of the Declaration of Helsinki and received approval from the Institutional Review Board (IRB) of Yonsei University Dental Hospital (IRB no. 2-2017-0023, granted on June 22, 2017).

The parotid gland was assessed using ultrasonography with the participants seated upright. Cadaveric specimens were also examined in the prone position and dissected after removal of the platysma muscle. The glandular tissue was observed at the posterior margin of the mandibular border in relation to the gonion and zygomatic process of the temporal bone. In 40 patients, after palpating the gonion and the zygomatic process of the temporal bone, ultrasonography images were taken vertically and horizontally at the midpoint where the otobasion inferius crosses (Fig. 1). The thicknesses of the glands and subcutaneous tissue were measured. Specific measurements included the distance from the skin to the thickest part of the parotid gland and the distance from the skin to the parotid gland along the posterior border of the mandible.

Ultrasonographic images of the parotid glands were captured using a real-time two-dimensional B-mode Doppler ultrasound device equipped with a high-frequency (18 MHz) linear transducer (Sonimage HS1; Konica Minolta).

Results

In the ultrasonographic images of all subjects, the parotid gland is observed as a homogenous mid-gray structure on the surface of the masseter muscle. The parotideomasseteric fascia, covering the masseter muscle and the parotid gland, appears as a hyperechoic line (Figs. 2, 3). When vertical observations were performed, the distance from the skin to the

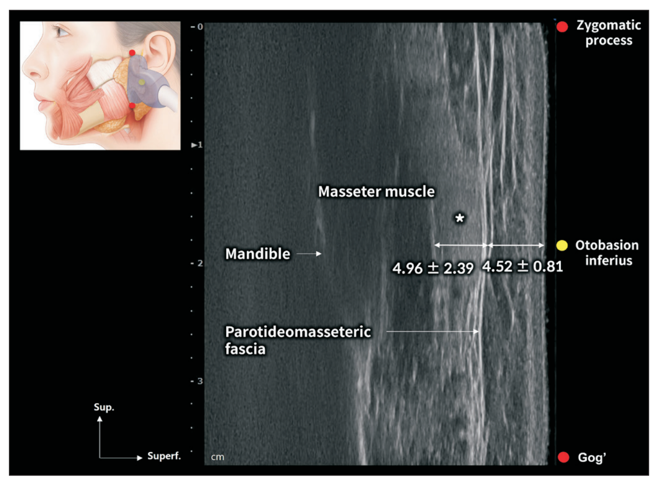

Fig. 2. When observed vertically, the distance from the skin to the parotid gland and the thickness of the gland at at otobasion inferius point were 4.52±0.81 mm and 4.96±2.39 mm, respectively. The asterisk denotes the parotid gland. Superf., superficial; Sup., superior; Gog', gonion.

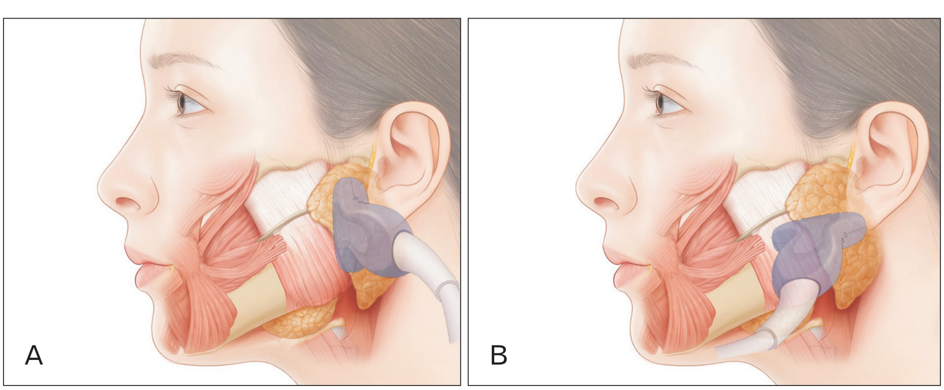

Fig. 1. The probe was positioned vertically along the gonion and the zygomatic process of the temporal bone (A), and horizontally at the midpoint where it crosses the otobasion inferius (B).

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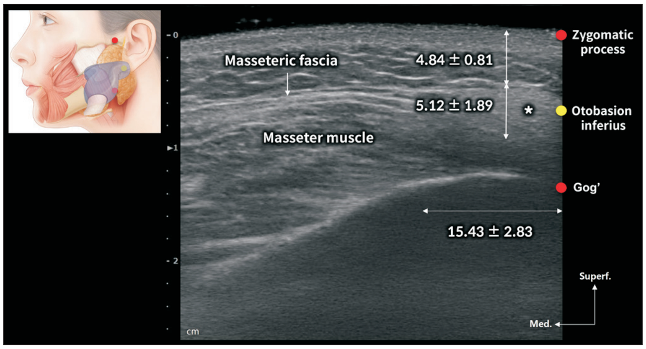

Fig. 3. When measured horizontally, the distance from the skin to the parotid gland and the thickness of the parotid gland at its thickest part were 4.84±0.81 mm and 5.12±1.89 mm, respectively. Additionally, the parotid gland extended 15.43±2.83 mm anterior to the otobasion inferius. The asterisk denotes the parotid gland. Superf., superficial; Med., medial; Gog', gonion.

Table 1. Thickness of parotid gland by sex

Sex	Parotid gland thickness	*P*-value
Male	6.79±2.88	0.029*
Female	3.94±1.18	0.029*

Values are presented as mean±SD. *P*-value was obtained from Mann–Whitney test. **P*<0.05.

parotid gland and the thickness of the gland at otobasion inferius point were 4.52±0.81 mm and 4.96±2.39 mm, respectively (Fig. 2). Conversely, when horizontal measurements were recorded, the distance from the skin to the parotid gland and the thickness of the parotid gland at its thickest part were 4.84±0.81 mm and 5.12±1.89 mm, respectively. Additionally, the parotid gland extended 15.43±2.83 mm anteriorly from the otobasion inferius (Fig. 3). Comparisons between the ultrasonographic observations and cadaveric specimens revealed no significant differences. Furthermore, no notable differences were found between the left and right sides or among the different age groups. However, a significant discrepancy was observed with respect to sex, with males tending to exhibit thicker parotid glands compared to females (*P*<0.05), as shown in Table 1.

Discussion

Benign enlargement of the parotid gland leads to a swollen appearance in the earlobe region and weakens the lateral facial contour, thereby affecting esthetics. Hypersalivation, which can cause this enlargement, is treated with BoNT injections that have been approved in both the United States and Europe. To guarantee the secure delivery of BoNT to the salivary glands, the recommendations provided by the Association of Scientific Medical Societies in Germany advocate the use of sonographically guided injections of BoNT into the larger salivary glands. This approach has been deemed effective and safe, offering a sustained reduction in salivary flow in individuals of varying ages and medical conditions [9].

In addition, Chen et al. [10] investigated the use of BoNT type A as a potential remedy for benign parotid hypertrophy, a condition characterized by swelling of the earlobe and disruption of facial aesthetics. In a cohort of 36 participants, treatment resulted in a notable reduction in the thickness of the superficial parotid gland, albeit without a significant impact on its length. Subgroup analyses revealed that the degree of parotid gland hypertrophy played a crucial role in determining treatment effectiveness and improvement, whereas age and sex had no substantial influence. Image analyses validated the enhancements in the facial contour. Notably, no instances of severe adverse reactions or complications were documented. These findings suggest that BoNT type A may serve as a secure and efficacious therapeutic avenue for addressing benign parotid hypertrophy, resulting in a reduction in parotid gland volume and enhancement of facial aesthetics [10].

To date, there are no clear criteria for the injection points applied to the parotid gland, and various methods are being employed based on the clinical experience of physicians. The direct puncture of the gland during clinical procedures poses the risk of facial nerve damage and substantial pain from inadvertently piercing the nerve itself. Insufficient comprehension of the morphological configuration of the submandibular gland and its adjacent anatomical structures may result in unforeseen side effects during injection, as evidenced by patients encountering unexpected outcomes.

The parotid gland is enveloped by the parotideomasseteric fascia, which continues from the superficial layer of the deep temporal fascia. This fascia partially crosses the zygomatic arch and extends down towards the gland. Several anatomical structures situated deeper than the parotid gland pass through it from lateral to medial border. These structures include the facial nerve (cranial nerve [CN] VII), retromandibular vein, external carotid artery, superficial temporal artery, branches of the great auricular nerve, and the maxillary artery. The parotid gland receives its arterial blood supply from the external carotid artery and its terminal branches within the gland, namely the superficial temporal artery, maxillary

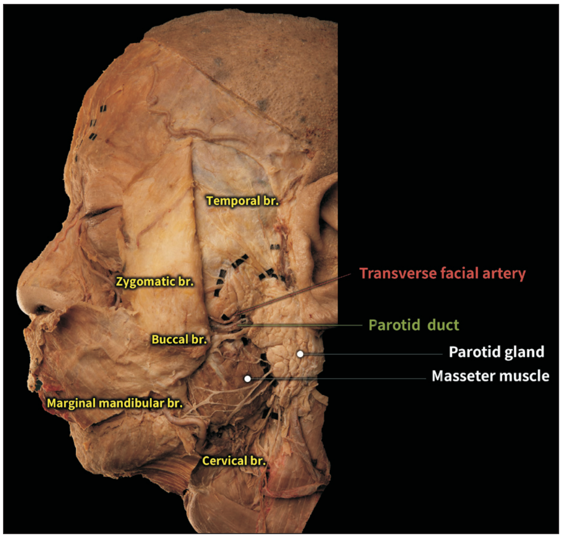

Fig. 4. Numerous anatomical structures, including branches of the facial nerve, external carotid artery, superficial temporal artery, and the parotid duct, traverse the parotid gland from its deepest part, passing through its border to reach more superficial regions. br., branch.

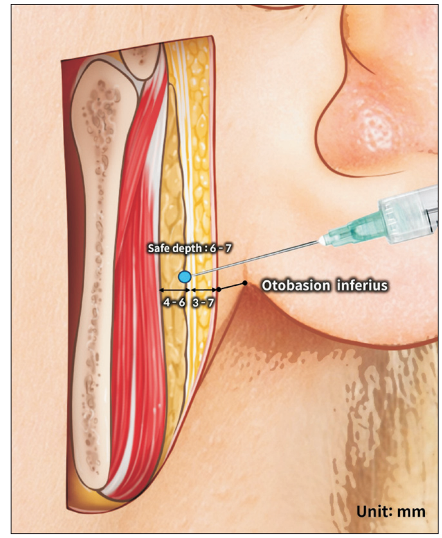

Fig. 5. The recommended points and depth for botulinum toxin injection into the parotid gland. Injection at a depth of 6–7 mm ensures safety and effectiveness, given the parotideomasseteric fascia is 4–6 mm from the skin at the otobasion inferius, and the parotid gland thickness is 3–7 mm.

artery, and posterior auricular artery. Venous drainage occurs through the retromandibular veins. Lymphatic fluid primarily flows from the gland to the preauricular or parotid lymph nodes and subsequently drains into the deep cervical chain [3-5, 11]. Within the parotid gland, the facial nerve (CN VII) divides into various branches, forming a parotid plexus. These nerves traverse the parotid gland without innervating the gland itself. Therefore, targeting the fascia for injection is considered a safe and optimal approach (Fig. 4).

Furthermore, the parotid gland typically adopts a pistol-like shape (Fig. 4). It has four distinct surfaces: superficial or lateral, superior, anteromedial, and posteromedial; and three borders: anterior, medial, and posterior. The structure of the parotid gland includes a superior end characterized by a small superior surface and an inferior end culminating at its apex. When visualized using ultrasound, this gland appears as a homogeneous grey form (Figs. 2, 3). Park et al. [12] examined the superficial lobe of the parotid gland by dissecting 30 hemisected heads and established reference lines along the lateral aspect of the face. These reference lines extended from the mandibular angle to the upper edge of the zygomatic arch, tracing the posterior border of the ramus and dividing it into four sections. Using these reference lines and sections, the researchers measured the superior, inferior, anterior, and posterior boundaries of the parotid gland. Based on their measurements, the superficial lobe of the parotid gland was divided into three distinctive types: pistol-shaped, pistol-shaped with an additional lobe, and oval-shaped [12]. The upper limit of the parotid gland begins immediately beneath the lower edge of the zygomatic arch. As the reference line was followed from the upper to the middle section, the parotid gland was identified to extend over the rear aspect of the masseter muscle. At the second reference point established by the research team, it was confirmed that the parotid duct, arising from the anterior border of the parotid gland, was also identified. Transitioning from the middle to the lower portion, the tail of the parotid gland was behind the ramus, covering the front of the sternocleidomastoid muscle.

In this study, to overcome the limitations of previous research conducted on cadavers and to provide guidelines that can be more easily applied in clinical practice, the thickness of the parotideomasseteric fascia was measured using the otobasion inferius as a surface anatomical landmark. According to the study by Park et al. [12], the second reference point, which is above the otobasion inferius, is where the parotid duct arises, suggesting that the injection point proposed in this study is relatively safe. Additionally, it was confirmed that the parotid gland extends approximately 15 mm anterior to the otobasion inferius. Therefore, it is suggested that injecting up to 15 mm anterior to the patient's otobasion inferius can ensure a safe procedure. The depth from the skin surface to the parotideomasseteric fascia was approxi-

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mately 4–6 mm, and the thickness of the parotid gland averaged 3–7 mm. These findings suggest that injecting BoNT at a depth of 6–7 mm would, in most cases, prevent nerve and vascular damage while achieving optimal results (Fig. 5).

ORCID

Kyu-Ho Yi: https://orcid.org/0000-0001-5572-1364
Soo-Bin Kim: https://orcid.org/0000-0003-2576-5723
Hyewon Hu: https://orcid.org/0000-0001-5460-6428
Hee-Jin Kim: https://orcid.org/0000-0002-1139-6261

Author Contributions

Conceptualization: KHY. Data acquisition: SBK. Data analysis or interpretation: SBK. Drafting of the manuscript: KHY, SBK. Critical revision of the manuscript: HJK. Approval of the final version of the manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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