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● *Original Contribution*

ULTRASONOGRAPHIC ANALYSES OF THE FOREHEAD REGION FOR INJECTABLE TREATMENTS

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Abstract—Botulinum toxin type A (BoNT-A) injections in the forehead region should only target the frontalis. This study applied ultrasonography with the aim of providing guidelines for predicting the layered structure and soft-tissue thickness of the forehead. We performed ultrasound scanning at 7 facial landmarks in 40 Korean adults. Allowing for the error range, the minimum depth from the skin to exclude the muscle layer was 2.3 mm, and the maximum depth from the skin to include the muscle layer was 2.8 mm. Of the total 7 points from the skin to muscle surface, significant differences between the males and females were found in 6 points ($p < 0.05$). Clinicians can use ultrasonography to identify the structural layers of the scalp. Even if ultrasound-guided injections are not performed, it is possible to target only muscle layers in BoNT-A injections by maintaining a needle depth of around 2.5 mm. (E-mail: hjk776@yuhs.ac) © 2019 The Author(s). Published by Elsevier Inc. on behalf of World Federation for Ultrasound in Medicine & Biology. This is an open access article under the CC BY-NC-ND license. (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Key Words: **Ultrasonography, Botulinum toxin type A, Forehead, Frontalis, Soft tissue thickness.**

INTRODUCTION

Wrinkles on the forehead contribute to the aesthetic function of the face. These wrinkles are caused by the contraction and relaxation of facial expression muscles, and they are concentrated in areas related to emotional expressions such as the forehead, eyes, nose and mouth. These wrinkles are not clearly evident on an expressionless face, and can be used to create an exaggerated appearance in emotional expressions (Arnaoutakis et al. 2018; Wieder et al. 1998).

The forehead is a cosmetically important area, but it is also the region where headaches occur internally. Headaches are pains that anyone can experience in everyday life. Among them, the tension-type headache, which occurs in the forehead, causes a dull, non-pulsatile pain similar to wearing a tight headband on both sides of the forehead and temporal region (Amirlak et al. 2018; Fernández-de-Las-Peñas et al. 2006).

Botulinum toxin type A (BoNT-A) injections are widely used to treat both facial wrinkles and tension-type headaches (Blumenfeld et al. 2010; Carruthers et al. 2003, 2008). The most important point in BoNT-A injectable procedure is to identify the target layer. Injections in the forehead region should target only the frontalis (Ascher et al. 2010; Choi et al. 2016). Making injections more accurate and effective requires a sound knowledge of the anatomic structures of the forehead. This study therefore applied ultrasonography with the aim of providing guidelines for predicting the layered structure and soft tissue thickness of the forehead.

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METHODS

Patients

From June to August 2017, 40 Korean adults participated in this study (23 males and 17 female, mean age: 24.3 y). Because the consumers in the aesthetics market are predominantly young, patients in their twenties were preferentially recruited for this study. The volunteers were allowed to participate in the study once only, and their participation took about 2 h. Each volunteer was placed in a semisupine position, and landmarks were marked on the face. The examiner sat adjacent to the volunteer's head to record ultrasound images. A real-time

ultrasound scanner (E-CUBE 15 EX, ALPINION, Seoul, Korea) with a 30-mm-wide linear-array transducer (8.0−17.0 MHz; IO8-17 High-Frequency Hockey Stick, Seoul, Korea) was used in this study. The ultrasound gel (SONO JELLY, MEDITOP Corporation, Youngin, Korea) used for this study caused no irritation to the skin because its components are harmless to the human body, and facial cleansers and moisturizers were prepared for the convenience of the volunteers.

All of the study procedures were approved by the institutional review board of the Yonsei University College of Dentistry (IRB No. 2-2017-0023), and they were fully explained to the volunteers, who then provided written consent forms.

Measurement protocol

We performed ultrasound scanning at seven facial landmarks (only on the left side, including the midline). We first defined the midsagittal line as VL1. On this line, the point meeting the hair line was defined as point 1, the midpoint between the two frontal eminences (point 4) as point 2 and the midpoint between point 2 and the glabella as point 3. In addition, the intersection points between the horizontal line passing through point 3 (HL1) and the vertical lines passing through the medial canthus (VL2), middle of the pupil (VL3) and lateral canthus (VL4) were defined as points 5, 6 and 7, respectively (Fig. 1). The soft tissue thickness was measured at each point using an image analysis program (ImageJ, National Institutes of Health, Bethesda, MD, USA). The statistical calculations and analysis were performed using standard software (SPSS Version 23.0 for Windows, IBM, Armonk, NY, USA). A p value <0.05 was considered to indicate statistical significance. Differences in measurement values between males and females were analyzed using Student's t test. The soft tissue thickness was measured using an image analysis program (ImageJ) at each point.

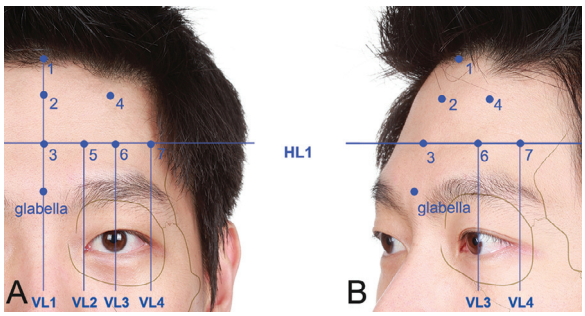

Fig. 1. The seven facial landmarks used in this study: (a) frontal aspect. (b) oblique aspect. (1) trichion; (2) metopion; (3) halfway point between point 2 and the glabella; (4) frontal eminence; (5) meeting point between VL2 and HL1; (6) meeting point between VL3 and HL1; (7) meeting point between VL4 and HL1. HL1 = horizontal line passing through point 3; VL1 = midsagittal line; VL2 = vertical line passing through the medial canthus; VL3 = vertical line passing through the middle of the pupil; VL4 = vertical line passing through the lateral canthus.

RESULTS

Anatomy at the seven points

Points 1−3. Point 1 is the meeting point between VL1 and the hairline, and so part of the hair can be observed above the skin in ultrasound images. The frontalis is not present in the muscular third layer of the scalp, and so we considered it to be the galea aponeurotica in ultrasound images (Fig. 2a).

Point 2 is the midpoint between the two frontal eminences. This part is similar to the medial border of the frontalis that divides into the left and right sides. It is therefore not possible to clearly identify whether the third layer in an ultrasound image is the frontalis or the galea aponeurotica. However, other structures such as the skin, subcutaneous layer and loose connective tissue layer could be clearly distinguished (Fig. 2b).

Point 3 is the midpoint between point 2 and the glabella, and only the frontalis exists in this area. We therefore observed the frontalis to be thicker than at points 1 and 2 in ultrasound images. There was no significant difference in the other layers (Fig. 2c).

Point 4

Point 4 refers to the left frontal eminence. This is the area where only the frontalis exists (Fig. 3a). In some cases (16/40, 40%), a frontal branch of the superficial temporal artery that travels over the frontalis muscle may be observed in ultrasound images (Fig. 3b).

Points 5−7

Point 5 is the meeting point between the HL1 and the VL2, and its layered structure is also clearly distinguishable in ultrasound images. Because the muscle layer appears so thick, in a manner similar to that at point 3, we can consider this point a merging area with the corrugator supercilii muscle. However, this point also belongs only to the frontalis area (Fig. 4a).

Point 6 is the meeting point between HL1 and VL3. Compared with point 5, the muscle layer is thinner and the loose connective tissue layer is thicker. In addition, the retro-orbicularis oculi fat (ROOF) exists in this region. ROOF is the one of the types of deep fat of the face. Fibrous connective tissues pass through facial fat tissues and play a role in connecting the fat tissue, facial muscles, dermis and bone. Therefore, we can identify that the morphology of the loose connective tissue layer is slightly different from that for points 1−3 in ultrasound images (Fig. 4b).

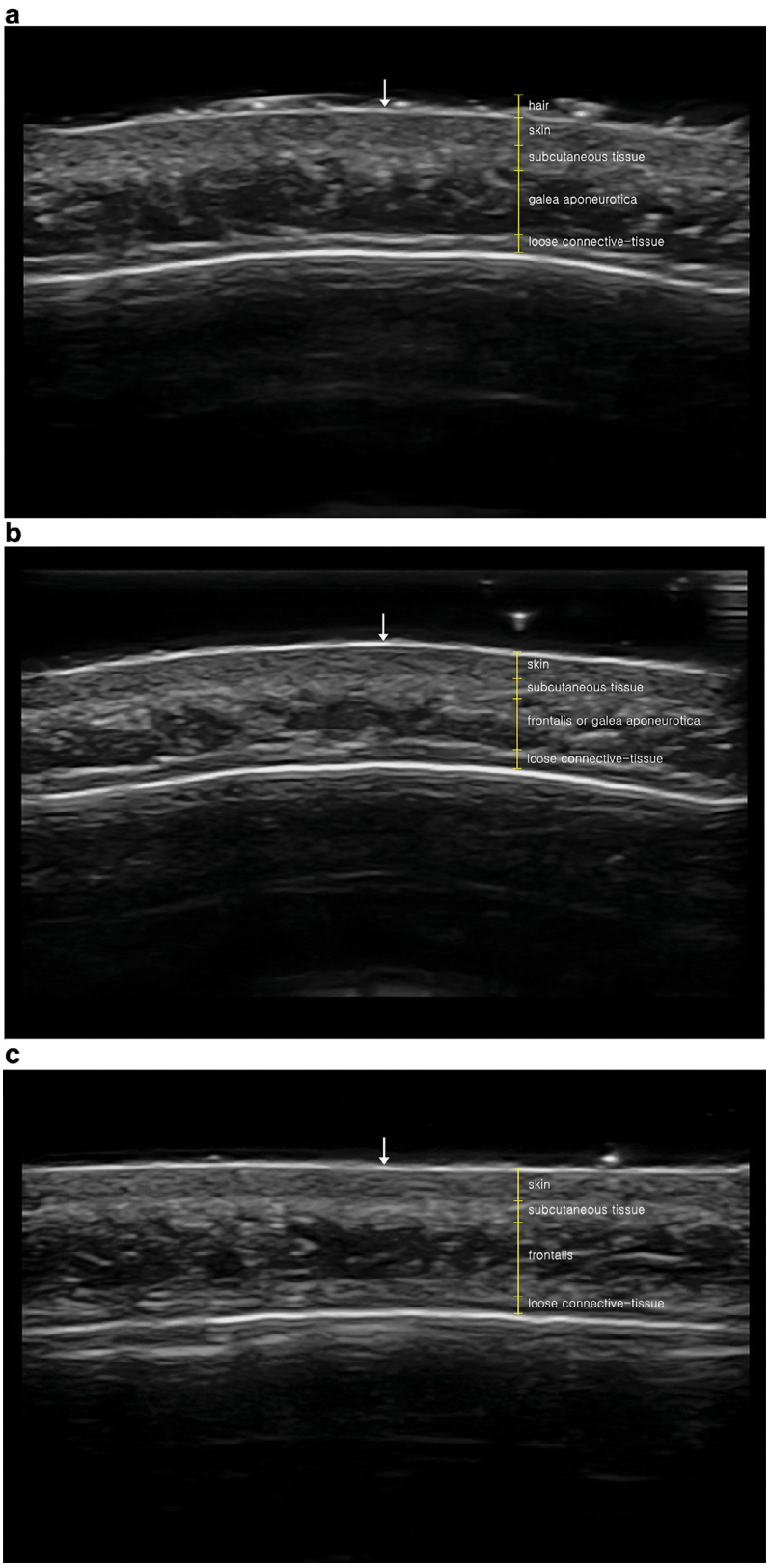

Fig. 2. Ultrasound transverse views at point 1 (a), point 2 (b) and point 3 (c). The *arrows* indicate the location of each point. All images were obtained using a highly linear 15-MHz probe with the maximum depth set to 1.5 cm.

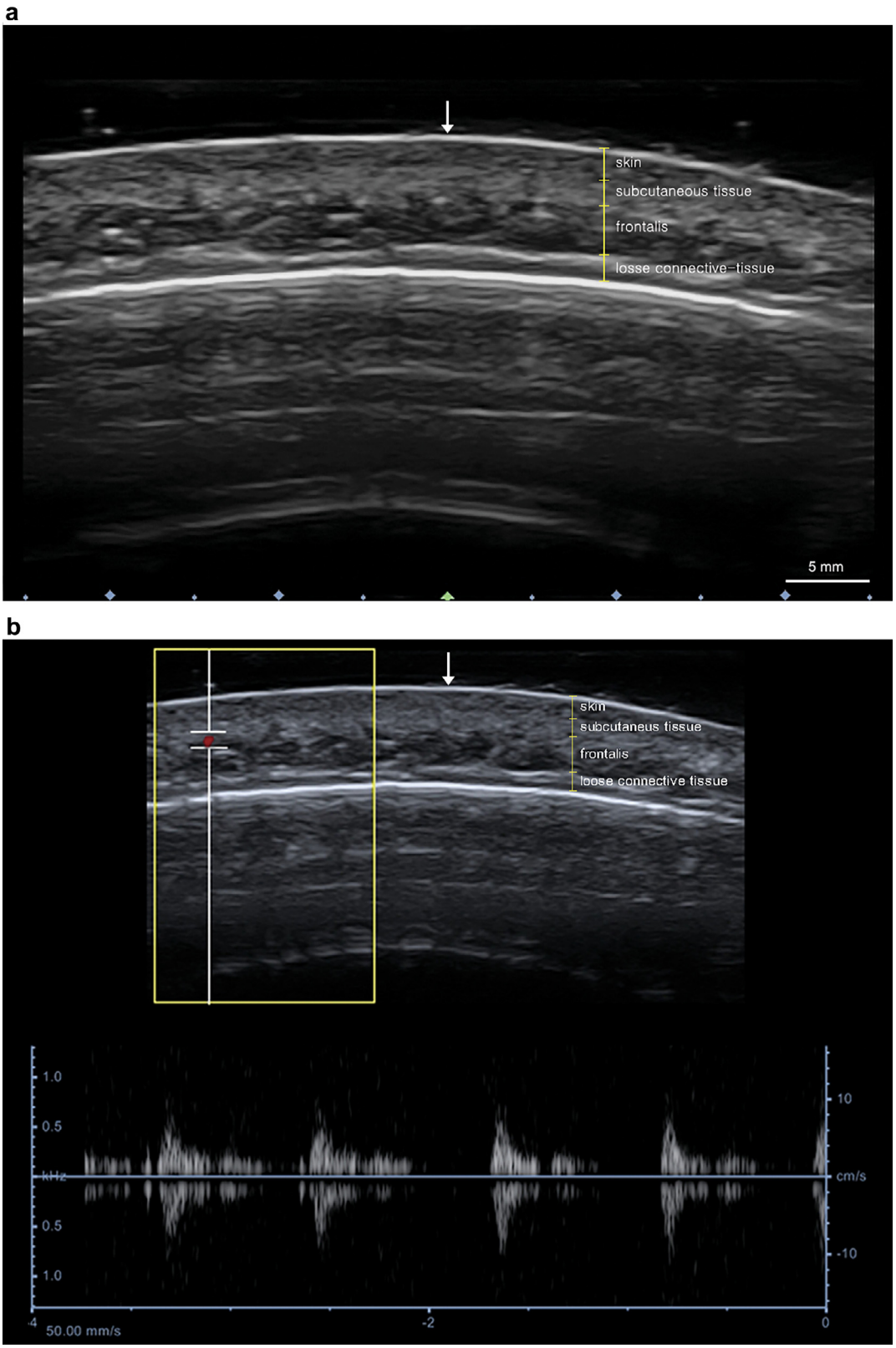

Fig. 3. Ultrasound transverse view at point 4 (a). The color Doppler imaging mode makes it easy to identify the frontal branch of the superficial temporal artery (b). The *arrow* indicates the location of the point. The image was obtained using a highly linear 15-MHz probe with the maximum depth set to 1.5 cm.

Fig. 4. Ultrasound transverse views at point 5 (a), point 6 (b) and point 7 (c). The arrows indicate the location of each point. All images were obtained using a highly linear 15 MHz probe with the maximum depth set to 1.5 cm. An *arrowhead* indicates the location of the temporal line. ROOF, retro-orbicularis oculi fat.

Point 7 is the meeting point between HL1 and VL4, and is observed as a layered structure similar to point 6. The temporal line can be observed in the lateral part of point 7, which is the boundary between the forehead and the temporal fossa (Fig. 4c).

Soft tissue thicknesses at the seven points

The soft tissue thicknesses in the various scalp layers (skin, subcutaneous tissue, muscle and loose connective tissue) are outlined in Table 1. In all cases, the muscle layer (the third layer of the scalp) is thicker than the other layers, which makes it easy to identify. In particular, the thickness exceeded 2 mm at points 3 and 5. The thickness of skin, subcutaneous tissue and loose connective tissue tended to differ significantly between males and females, whereas muscle thickness exhibited no sex-related differences.

The overall soft tissue thickness of the forehead region ranged from 4.3−5.3 mm, with an average of 4.7 ± 0.3 mm (mean ± standard deviation). The soft tissue was significantly thicker in males than in females at every point, except the muscle layer ($p < 0.05$; Table 1).

DISCUSSION

The use of ultrasound guidance to perform diagnostic and therapeutic injections is increasing rapidly. There is a considerable amount of ultrasound-related information available in the literature; however, there is very little information related to ultrasound imaging of the face. The reason for this discrepancy is very simple: anatomical differences between skeletal and facial expression muscles (Sauer et al. 2016; Volk et al. 2013, 2014).

Facial expression muscles differ from skeletal muscles in several ways. First, in contrast to typical skeletal muscles, facial muscles are not surrounded by a fascia. This means that if facial muscles are arranged in multiple layers, it becomes very difficult to identify the boundaries between muscles in ultrasound images. Second, in contrast to typical skeletal muscle mass, the facial expression muscles are thin and flat, which also makes it very difficult to identify overlapping facial muscle groups. Third, in contrast to typical skeletal muscle insertions, facial muscles merge together, which makes it impossible to separate the muscles in ultrasound images. All of these characteristics make it difficult to establish ultrasound guidelines for facial muscles. However, an awareness of various morphologic factors and variations in facial muscles may be more helpful in developing an ultrasound-guided injection technique.

Ultrasound is one of the most commonly used devices in image-guided injection techniques. Injections were traditionally performed without visual guidance, requiring the clinician to have a certain degree of experience, delicacy and anatomic know-how. But even experienced clinicians cannot guarantee success in the traditional hit-or-miss approach, and so today clinicians largely avoid this by utilizing guiding technologies such as ultrasound. Once the clinician has identified anatomic landmarks on the

Table 1. Soft tissue thicknesses at the various points

	Point 1	Point 2	Point 3	Point 4	Point 5	Point 6	Point 7
Skin							
All	1.0 ± 0.2	1.1 ± 0.1	1.3 ± 0.2	1.1 ± 0.2	1.1 ± 0.2	1.0 ± 0.2	1.1 ± 0.2
Male	1.1 ± 0.2	1.1 ± 0.2	1.3 ± 0.2	1.1 ± .0.2	1.1 ± 0.2	1.1 ± 0.1	1.1 ± 0.1
Female	0.9 ± 0.2	1.0 ± 0.1	1.2 ± 0.2	1.0 ± 0.2	1.0 ± 0.2	0.9 ± 0.1	1.0 ± 0.2
p Value	0.032*	0.103	0.022*	0.064	0.267	0.008*	0.072
Subcutaneous tissue							
All	1.0 ± 0.3	0.7 ± 0.3	0.8 ± 0.3	0.8 ± 0.2	0.9 ± 0.3	0.8 ± 0.2	0.7 ± 0.2
Male	1.1 ± 0.3	0.8 ± 0.3	0.9 ± 0.3	0.8 ± 0.3	1.0 ± 0.3	0.9 ± 0.2	0.8 ± 0.2
Female	0.9 ± 0.2	0.7 ± 0.2	0.7 ± 0.2	0.8 ± 0.2	0.8 ± 0.2	0.8 ± 0.3	0.6 ± 0.2
p Value	0.013*	0.047*	0.018*	0.391	0.103	0.119	0.002*
Muscle							
All	1.9 ± 0.5	1.8 ± 0.4	2.2 ± 0.5	1.6 ± 0.5	2.2 ± 0.5	1.8 ± 0.4	1.6 ± 0.4
Male	1.9 ± 0.5	1.8 ± 0.4	2.2 ± 0.5	1.5 ± 0.4	2.2 ± 0.4	1.8 ± 0.4	1.7 ± 0.3
Female	1.8 ± 0.5	1.7 ± 0.4	2.1 ± 0.5	1.8 ± 0.5	2.2 ± 0.5	1.8 ± 0.5	1.4 ± 0.3
p Value	0.231	0.451	0.621	0.103	0.687	0.674	0.016*
Loose connective tissue							
All	0.6 ± 0.2	0.8 ± 0.2	0.8 ± 0.2	0.9 ± 0.2	1.1 ± 0.2	1.2 ± 0.3	1.4 ± 0.3
Male	0.6 ± 0.2	0.8 ± 0.2	0.8 ± 0.2	1.0 ± 0.2	1.2 ± 0.2	1.3 ± 0.2	1.5 ± 0.3
Female	0.6 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	1.0 ± 0.1	1.2 ± 0.4	1.4 ± 0.3
p Value	0.118	0.168	0.046*	0.000*	0.047*	0.867	0.317
Total							
All	4.5 ± 0.8	4.3 ± 0.7	5.0 ± 0.7	4.4 ± 0.7	5.3 ± 0.7	4.9 ± 0.8	4.7 ± 0.7
Male	4.8 ± 0.8	4.5 ± 0.7	5.2 ± 0.7	4.5 ± 0.6	5.4 ± 0.6	5.0 ± 0.6	5.0 ± 0.6
Female	4.1 ± 0.7	4.1 ± 0.6	4.6 ± 0.6	4.3 ± 0.7	5.1 ± 0.7	4.7 ± 0.9	4.4 ± 0.7
p Value	0.006*	0.043*	0.006*	0.507	0.191	0.090	0.001*

Results expressed as the mean ± standard deviation in millimeters.
* p value < 0.05.

ultrasound monitor, she or he can deliver the injection using a standard needle and syringe.

The most important aspect differentiating the present study from other ultrasonographic studies is that the transducer was used without applying any pressure on the skin. Most previous ultrasound images were obtained while applying pressure with direct contact between the skin and the transducer to observe deep structures such as muscles, blood vessels and the intrauterine fetus. However, we attempted to observe the entire layered structure without such deformation and to measure the soft tissue thicknesses of all layers from the skin to the periosteum. The application of a sufficient amount of gel allowed ultrasound images to be obtained without any direct contact or pressure between the transducer and the skin.

Clinicians need to be able to clearly distinguish the layered structure of the facial muscles through ultrasound imaging. The results of this study indicate that the five-layer structure of the forehead (skin, subcutaneous layer, muscle layer, loose connective tissue layer and periosteum) can be distinguished using ultrasound with comparative ease at all of the points analyzed. Though it is slightly difficult to distinguish between the skin and the subcutaneous layer, the muscle and the loose connective -tissue layer—which are the main injection targets—can be clearly distinguished.

We found that the thicknesses of the skin and muscle layers decreased from medial to lateral positions, whereas the thickness of the loose connective tissue layer increased. Along reference line HL1, point 3 and points 5−7, the skin thickness gradually decreased to 1.26, 1.07, 1.07 and 1.01 mm. The muscle layers exhibited a similar tendency. In contrast, the thickness of the loose connective tissue layer gradually increased to 0.75, 1.11, 1.25 and 1.43 mm. This can be explained by the existence of ROOF, located at the lateral forehead, especially at points 6 and 7.

Both the skin and subcutaneous tissue thicknesses indicate the distance from the skin to the surface of the frontalis. The maximum value was 2.0 mm at point 3. In a similar manner, the thicknesses of the skin, the subcutaneous tissue and the muscle layer define the distance from the skin to the muscle border, which includes the frontalis. The minimum value was 3.3 mm at point 7. Allowing for the error range, the maximum value was 2.3 mm (2.0 mm + 0.3 mm), and the minimum value was 2.8 mm (3.3mm − 0.5 mm). There were significant differences in both the skin and subcutaneous tissues between males and females. Among the seven points, the maximum gap between the two layers was 0.4 mm at point 1, but this small difference is not widely applicable to injectable treatments in clinical applications ($p < 0.05$; Table 2).

These values mean that an injection at a depth of about 2.5 mm (and within depths ranging from 2.3−2.8 mm) will target only the frontalis at all points on the forehead, with the exception of point 1, where the frontalis does not exist (Fig. 5).

This study was subject to some limitations. First, as only 40 Korean patients were analyzed, the results might only be representative of the Korean population. Further research is therefore needed to identify if similar tendencies are observed in other populations. Second, this study focused on the layered structure and thickness of the forehead and not the nerve and artery distributions. The results obtained therefore cannot be used to provide an injection guide for targeting nerve twigs or avoiding blood vessels in the forehead region. Because the supratrochlear and supraorbital nerve branches are so thin, it is impossible to detect them using ultrasound. It is theoretically possible to avoid blood vessels when inserting a needle under ultrasound guidance, but this method is rarely used because of its inconvenience in clinical applications. Third, this study focused on healthy patients aged 20−30 y to confirm the normal structures observed by ultrasound. This limits the ability to apply the results to older people and those with soft tissue diseases of the forehead.

CONCLUSIONS

Clinicians can use an ultrasound device to identify the layers of the scalp. If they do not perform injections

Table 2. Soft tissue thicknesses of the various layers from skin to muscle

	Point 1	Point 2	Point 3	Point 4	Point 5	Point 6	Point 7
Skin + subcutaneous tissue							
All	2.0 ± 0.2	1.8 ± 0.3	2.0 ± 0.3†	1.9 ± 0.3	2.0 ± 0.3	1.8 ± 0.3	1.8 ± 0.3
Male	2.2 ± 0.4	1.9 ± 0.3	2.2 ± 0.3	1.9 ± 0.3	2.0 ± 0.3	2.0 ± 0.3	1.9 ± 0.2
Female	1.8 ± 0.3	1.7 ± 0.3	1.8 ± 0.2	1.8 ± 0.3	1.8 ± 0.3	1.7 ± 0.3	1.6 ± 0.3
p Value	0.001*	0.012*	0.000*	0.097*	0.045*	0.012*	0.001*
Skin + Subcutaneous tissue + muscle							
All	3.9 ± 0.7	3.6 ± 0.6	4.2 ± 0.7	3.5 ± 0.6	4.1 ± 0.6	3.6 ± 0.7	3.3 ± 0.5‡
Male	4.1 ± 0.7	3.7 ± 0.6	4.4 ± 0.7	3.5 ± 0.5	4.2 ± 0.6	3.8 ± 0.6	3.6 ± 0.5
Female	3.6 ± 0.7	3.4 ± 0.6	3.9 ± 0.6	3.5 ± 0.6	4.1 ± 0.7	3.5 ± 0.7	3.0 ± 0.5
p Value	0.015*	0.087	0.033*	0.678	0.466	0.138	0.001*

Results expressed as the mean ± standard deviation in millimeters.
* p value < 0.05.
† The minimum depth from the skin to exclude the muscle layer was 2.3 mm (2.0 mm + 0.3 mm).
‡ The maximum depth from the skin to include the muscle layer was 2.8 mm (3.3 mm − 0.5 mm).

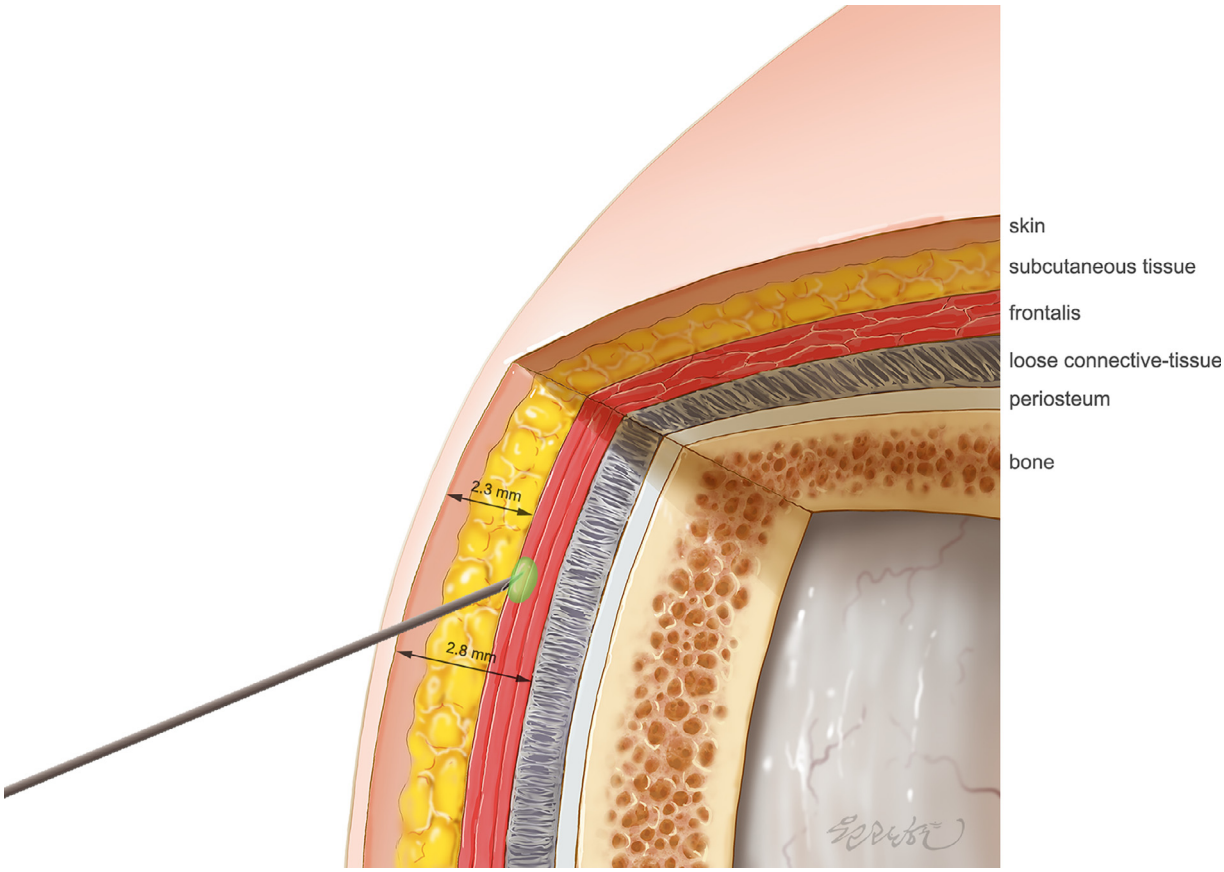

Fig. 5. Botulinum toxin type A should be injected in the forehead region at a depth ranging from 2.3−2.8 mm. For an injection at a depth of exactly 2.5 mm, the needle can approach *via* only the intramuscle layer of the frontalis.

with ultrasound guidance, it is possible to target only muscle layers using BoNT-A by injecting with the needle at a depth of around 2.5 mm. For the filler injections that target the loose connective tissue layer, it is relatively easy for clinicians to detect when the needle has contacted the bone. If the injection is performed after touching the bone, clinicians can specifically target only the loose connective tissue layer.

Clinicians can utilize the present results to easily perform various injectable treatments in the forehead region.

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