



# OPEN Individualized HIFU in women over 60: ultrasound assessment of layer-specific facial soft-tissue thickness changes

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High-intensity focused ultrasound (HIFU) is widely used for facial rejuvenation, but standardized depth settings may not adequately account for age-related variation in facial soft tissue architecture in women aged 60 years and older. In this exploratory pilot study, 20 women underwent three HIFU sessions at 4-week intervals (Weeks 0, 4, and 8) and were evaluated at Week 16 (8 weeks after the final session). Participants received either a conventional protocol or an anatomy-guided protocol individualized using high-frequency ultrasound (HFUS) measurements. HFUS assessed superficial fat thickness, deep fat thickness, and skin-to-SMAS distance at baseline and Week 16. Both protocols produced reductions in lower-face and submental tissue thicknesses. Across all HFUS endpoints, the anatomy-guided protocol showed larger mean reductions than the conventional protocol. In this exploratory analysis, nominal, unadjusted between-group differences were observed for lower-face skin-to-SMAS distance (difference in change,  $-0.19$  mm; 95% CI,  $-0.38$  to  $-0.02$ ;  $p=0.035$ ), submental superficial fat thickness ( $-0.20$  mm; 95% CI,  $-0.39$  to  $-0.02$ ;  $p=0.032$ ), and submental skin-to-SMAS distance ( $-0.19$  mm; 95% CI,  $-0.38$  to  $-0.02$ ;  $p=0.035$ ). These differences were small in absolute magnitude and should be interpreted cautiously in relation to ultrasound measurement precision. Investigator-rated improvement of “much improved” or better occurred in 40% of the conventional group and 60% of the anatomy-guided group. These preliminary findings suggest that anatomy-informed HIFU may be associated with small, layer-specific ultrasound-measured soft-tissue thickness changes in older women; however, the submillimeter magnitude of the differences, small sample size, parallel-group design, and short follow-up warrant cautious interpretation.

**Keywords** High-intensity focused ultrasound, Facial aging, High-frequency ultrasound, Soft-tissue thickness, Anatomy-guided treatment, Lower face

High-intensity focused ultrasound (HIFU) has become a widely used noninvasive modality for facial and neck rejuvenation, based on its ability to deliver focused thermal energy to predetermined tissue depths and induce tissue tightening through thermal coagulation and subsequent remodeling<sup>1</sup>. By selectively targeting the deep dermis, subcutaneous tissue, and superficial musculoaponeurotic system (SMAS), HIFU has demonstrated favorable safety profiles and modest clinical improvement in skin laxity and contour in various facial regions<sup>2</sup>.

Most clinical studies to date have relied on conventional HIFU protocols, in which standardized focal depths, fixed energy settings, and uniform line distributions are applied according to manufacturer guidelines or generalized anatomical assumptions<sup>3–5,22</sup>. This anatomy-agnostic approach has shown acceptable outcomes in younger patients or those with relatively preserved facial architecture, and has therefore served as the foundation for routine clinical practice<sup>6</sup>.

However, facial aging is not a uniform or linear process. Contemporary anatomical and clinical studies have demonstrated that aging-related changes occur in a layer-specific and region-dependent manner, involving differential alterations in superficial and deep fat compartments, progressive attenuation of the SMAS, and variable loss of mechanical coupling between facial tissue layers<sup>7–9,19,20</sup>. These changes become particularly

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pronounced in older individuals, especially in the lower face and submental region, where gravitational forces, deep fat compartment behavior, and ligamentous weakening converge to produce contour blunting and cervicomentalar angle deterioration<sup>10,11</sup>.

In women aged 60 years and older, such structural heterogeneity results in substantial inter-individual variability in tissue thickness and anatomical relationships<sup>10,12</sup>. Under these conditions, the application of uniform focal depths and fixed energy settings may not optimally correspond to the measured depth of relevant soft-tissue layers in all individuals, potentially leading to less consistent energy delivery across the intended treatment planes<sup>13,14</sup>.

Therefore, this exploratory pilot study was designed to compare ultrasound-measured structural and clinical outcomes after conventional HIFU and an individualized HIFU approach in women aged 60 years and older. Participants underwent three sessions at 4-week intervals, and the primary assessment for this report was performed at Week 16 (8 weeks after the final session) to capture early-to-intermediate changes rather than long-term durability. In the individualized approach, treatment parameters were modified according to region-specific facial anatomy, as assessed by HFUS measurements of superficial and deep fat thickness and the distance between the skin surface and the SMAS. We hypothesized that tailoring HIFU treatment to patient-specific anatomy would be associated with more consistent, layer-specific ultrasound-measured soft-tissue thickness changes than a standardized protocol in this older cohort.

Results

Participant characteristics

Twenty female participants were included in the final analysis (conventional HIFU, *n* = 10; anatomy-guided HIFU, *n* = 10). All participants completed the Week 16 follow-up without protocol deviations.

Participant age ranged from 60 to 72 years (conventional: 64.28 ± 3.14 years; anatomy-guided: 65.12 ± 3.38 years), with Fitzpatrick skin types III-V represented in both groups. Baseline HFUS measurements of the lower face and submental region were comparable between groups (all baseline *p* > 0.58; Table 1).

High-frequency ultrasound outcomes

The intra-observer reliability analysis for HFUS measurements showed an overall intraclass correlation coefficient (ICC) of 0.94 (95% CI, 0.90 to 0.97), indicating high relative reproducibility of layer-specific thickness rankings across repeated measurements. However, ICC does not directly quantify absolute measurement error in millimeters, and the submillimeter magnitude of the observed changes should therefore be interpreted cautiously. Both treatment protocols produced ultrasound-measured changes between baseline and Week 16 (Table 2; absolute baseline and Week 16 values are shown in Supplementary Table S1). In the conventional group, nominal within-group reductions were observed for superficial and deep fat thickness in both the lower face and the submental region, with within-group *p*-values ranging from 0.012 to 0.015. Changes in skin-to-SMAS distance were small and did not reach nominal significance in either region (lower face, *p* = 0.142; submental area, *p* = 0.151). In the anatomy-guided group, all six HFUS endpoints showed nominal within-group reductions, with *p*-values ranging from < 0.001 to 0.002.

Between-group comparisons of change from baseline numerically favored the anatomy-guided protocol across all HFUS endpoints. Nominal between-group differences were observed for lower-face skin-to-SMAS distance (− 0.19 mm; 95% CI, − 0.38 to − 0.02; *p* = 0.035), submental superficial fat thickness (− 0.20 mm; 95% CI, − 0.39 to − 0.02; *p* = 0.032), and submental skin-to-SMAS distance (− 0.19 mm; 95% CI, − 0.38 to − 0.02; *p* = 0.035). Differences in deep fat thickness also favored the anatomy-guided protocol numerically in both regions (− 0.20 mm for the lower face and − 0.20 mm for the submental area), but these did not reach nominal statistical significance in this pilot sample (*p* = 0.148). Because the statistically observed between-group differences were small in absolute magnitude, generally 0.19–0.20 mm, these findings should be interpreted as exploratory ultrasound-based observations rather than definitive evidence of clinically meaningful tissue remodeling. Relative changes were greatest in the submental region, where the anatomy-guided protocol achieved a 17.1% reduction in superficial fat thickness and a 12.6% reduction in deep fat thickness, compared with 8.0% and 7.7%, respectively, in the conventional group.

| Variable                                         | Conventional HIFU<br>( <i>n</i> = 10) | Anatomy-guided HIFU<br>( <i>n</i> = 10) | Baseline<br><i>p</i> -value |
|--------------------------------------------------|---------------------------------------|-----------------------------------------|-----------------------------|
| Age, years                                       | 64.28 ± 3.14                          | 65.12 ± 3.38                            | 0.589                       |
| Lower face: superficial subcutaneous fat, mm     | 2.18 ± 0.38                           | 2.12 ± 0.42                             | 0.583                       |
| Lower face: deep fat, mm                         | 3.42 ± 0.46                           | 3.48 ± 0.56                             | 0.690                       |
| Lower face: skin-to-SMAS distance, mm            | 3.98 ± 0.44                           | 4.08 ± 0.48                             | 0.628                       |
| Submental area: superficial subcutaneous fat, mm | 2.38 ± 0.47                           | 2.28 ± 0.51                             | 0.660                       |
| Submental area: deep fat, mm                     | 3.76 ± 0.58                           | 3.88 ± 0.68                             | 0.736                       |
| Submental area: skin-to-SMAS distance, mm        | 4.32 ± 0.62                           | 4.42 ± 0.57                             | 0.714                       |

**Table 1.** Baseline participant and HFUS characteristics. Values are presented as mean ± standard deviation. Baseline *p*-values were calculated using Welch’s *t*-tests.

| Variable                                     | Conventional HIFU:<br>change from baseline     | Anatomy-guided HIFU:<br>change from baseline    | Between-group difference<br>in change (AG - conventional) |
|----------------------------------------------|------------------------------------------------|-------------------------------------------------|-----------------------------------------------------------|
| Lower face: superficial subcutaneous fat     | $-0.20 \pm 0.22$ mm<br>( $-9.2\%$ ); $p=0.015$ | $-0.31 \pm 0.24$ mm<br>( $-14.6\%$ ); $p=0.002$ | $-0.11$ (95% CI, $-0.28$ to $0.08$ ) $p=0.278$            |
| Lower face: deep fat                         | $-0.30 \pm 0.28$ mm<br>( $-8.8\%$ ); $p=0.014$ | $-0.50 \pm 0.31$ mm<br>( $-14.4\%$ ); $p<0.001$ | $-0.20$ (95% CI, $-0.47$ to $0.07$ ) $p=0.148$            |
| Lower face: skin-to-SMAS distance            | $-0.10 \pm 0.18$ mm<br>( $-2.5\%$ ); $p=0.142$ | $-0.29 \pm 0.21$ mm<br>( $-7.1\%$ ); $p=0.001$  | $-0.19$ (95% CI, $-0.38$ to $-0.02$ ) $p=0.035$           |
| Submental area: superficial subcutaneous fat | $-0.19 \pm 0.23$ mm<br>( $-8.0\%$ ); $p=0.012$ | $-0.39 \pm 0.19$ mm<br>( $-17.1\%$ ); $p<0.001$ | $-0.20$ (95% CI, $-0.39$ to $-0.02$ ) $p=0.032$           |
| Submental area: deep fat                     | $-0.29 \pm 0.27$ mm<br>( $-7.7\%$ ); $p=0.014$ | $-0.49 \pm 0.28$ mm<br>( $-12.6\%$ ); $p<0.001$ | $-0.20$ (95% CI, $-0.49$ to $0.07$ ) $p=0.148$            |
| Submental area: skin-to-SMAS distance        | $-0.09 \pm 0.17$ mm<br>( $-2.1\%$ ); $p=0.151$ | $-0.28 \pm 0.22$ mm<br>( $-6.3\%$ ); $p=0.002$  | $-0.19$ (95% CI, $-0.38$ to $-0.02$ ) $p=0.035$           |

**Table 2.** Change in HFUS measurements from baseline to Week 16. Values are mean change  $\pm$  standard deviation unless otherwise indicated. Relative change (%) was calculated descriptively as the group mean change divided by the group mean baseline value. Within-group  $p$ -values were derived from paired  $t$ -tests. Between-group  $p$ -values and 95% confidence intervals were derived from Welch's  $t$ -tests comparing change from baseline. Because this was an exploratory pilot study,  $p$ -values are nominal and were not adjusted for multiple comparisons. The absolute magnitude of the observed between-group differences should be interpreted cautiously in relation to the potential limits of ultrasound measurement precision.

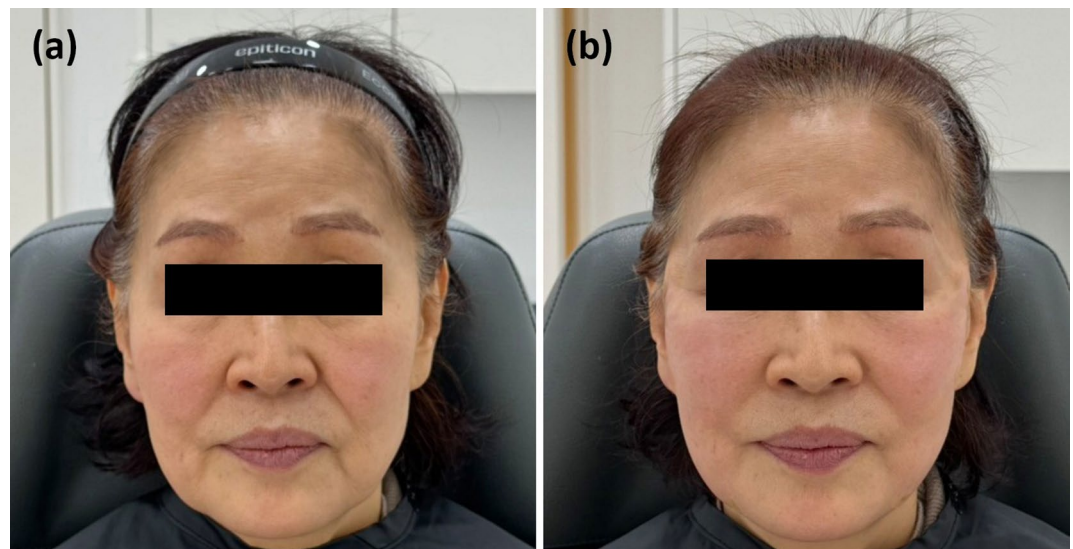


**Fig. 1.** Representative clinical photographs of a 72-year-old female treated with the anatomy-guided HIFU protocol. (a) Baseline and (b) Week 16, after three treatment sessions at Weeks 0, 4, and 8.

### Investigator-rated aesthetic outcomes (GAIS)

At Week 16, investigator-rated Global Aesthetic Improvement Scale (GAIS) scores demonstrated mild to moderate visible improvement in both treatment groups. Because of the small sample size and the ordinal structure of the scale, GAIS results were summarized descriptively.

In the conventional HIFU group, 5 participants (50%) were rated as “improved,” 4 participants (40%) as “much improved,” and 1 participant (10%) as showing no appreciable change. In the anatomy-guided HIFU group, 4 participants (40%) were rated as “improved,” 5 participants (50%) as “much improved,” and 1 participant (10%) as “very much improved.” Representative clinical photographs are shown in Figs. 1 and 2.

### Patient satisfaction

Patient-reported satisfaction was favorable in both groups. The mean satisfaction score was  $3.6 \pm 0.7$  in the conventional group and  $3.9 \pm 0.6$  in the anatomy-guided group on a 5-point Likert scale. Although numerically higher in the anatomy-guided group, the between-group difference was small ( $p=0.317$ ), and most participants in both groups reported improvement in lower facial contour and submental appearance rather than dramatic visible change.



**Fig. 2.** Representative clinical photographs of a 68-year-old female treated with the anatomy-guided HIFU protocol. (a) Baseline and (b) Week 16, after three treatment sessions at Weeks 0, 4, and 8.

### Safety and tolerability

No serious adverse events were observed in either group. Transient post-treatment discomfort and mild localized edema were reported in both groups and resolved spontaneously within 48–72 h. No cases of persistent pain, nodularity, or unexpected tissue changes were identified during the follow-up period.

### Discussion

Facial aging is a complex, multilayered process involving progressive changes in the skin, subcutaneous fat compartments, the superficial musculoaponeurotic system (SMAS), and underlying skeletal support. Contemporary aging models emphasize that these changes occur in a layer-specific and region-dependent manner rather than as a uniform process of volumetric deflation or tissue descent<sup>15,16</sup>. In women over 60 years of age, these alterations are particularly pronounced in the lower face and submental region, where gravitational dependency, deep fat compartment behavior, and attenuation of ligamentous and fascial support converge to produce contour blunting and deterioration of the cervicomental angle.

A key strength of the present study is its quantitative, layer-specific ultrasound assessment, which enabled comparison of tissue responses to different HIFU strategies based on measured changes in superficial fat, deep fat, and skin-to-SMAS distance rather than subjective grading alone. In this pilot sample, the anatomy-guided protocol showed numerically larger reductions across all HFUS endpoints, with nominal between-group differences for lower-face skin-to-SMAS distance, submental superficial fat thickness, and submental skin-to-SMAS distance. It is important to acknowledge that these absolute between-group differences were small, generally 0.19–0.20 mm, and did not translate into clearly superior visible improvement, as reflected by the mild-to-moderate GAIS outcomes in both groups.

The observed submillimeter reductions in ultrasound-measured thickness should therefore be interpreted cautiously. Because this study measured HFUS-derived tissue thickness only, it cannot directly demonstrate thermal coagulation point formation, collagen contraction, fascial compaction, or histological remodeling. Prior histological and preclinical studies have shown that HIFU can generate focal thermal injury zones and subsequent tissue responses in targeted facial or subcutaneous layers<sup>1,13,14,17</sup>. Within this context, the present findings may be consistent with small layer-specific soft-tissue responses after HIFU, particularly within the skin-to-SMAS unit, but they should not be interpreted as direct mechanistic evidence of target engagement. Similarly, reductions in measured superficial or deep fat thickness should not be interpreted as simple fat loss or definitive fat remodeling. Rather, these ultrasound findings are best regarded as exploratory indicators of layer-specific soft-tissue thickness change that require confirmation in larger studies with more rigorous measurement-error analysis and longer follow-up.

The 4-week inter-session interval deserves careful interpretation. This schedule was selected as an exploratory retreatment strategy to examine whether repeated, depth-specific energy delivery during the early post-treatment phase could produce cumulative ultrasound-measured changes while remaining practical in an outpatient setting. We do not interpret the 4-week interval as evidence that collagen or fascial tissue response is complete by that time. On the contrary, prior histologic and mechanistic studies suggest that tissue responses after thermal coagulation may continue for weeks to months<sup>1,13,18</sup>. For this reason, the Week 16 assessment, which occurred 8 weeks after the final session, should be viewed as an early-to-intermediate endpoint rather than a definitive measure of maximal or durable response, especially in women over 60 years of age.

This study has several limitations. First, the sample size was small and feasibility-based, and although randomization and outcome assessor blinding were employed, the parallel-group design leaves the results

susceptible to inter-individual variability; a split-face design would further strengthen internal validity by controlling for inter-individual variation. Second, multiple regional endpoints were analyzed in an exploratory manner, and p-values were not adjusted for multiplicity; accordingly, the reported between-group significance should be interpreted as nominal. Third, HFUS measurements, although objective, remain operator-dependent. The intra-observer ICC was high (0.94; 95% CI, 0.90 to 0.97), but ICC is a relative reliability index and does not directly express absolute measurement error in millimeters. In addition, the repeated-measurement assessment was performed in a limited subset of participants, which restricts the precision of the reproducibility estimate. The observed between-group differences were small, generally 0.19–0.20 mm, and may approach the practical limits of ultrasound measurement precision. Therefore, these findings should be interpreted as exploratory and hypothesis-generating rather than definitive evidence of a clinically meaningful structural effect. Fourth, this study measured ultrasound-derived tissue thickness only and did not directly assess thermal coagulation point formation, collagen remodeling, fascial compaction, or histological change. Fifth, follow-up ended at Week 16 and therefore does not address long-term durability or the possibility of later tissue responses in older patients. Larger studies with longer follow-up, more rigorous internal controls, and formal quantification of absolute measurement error are needed before the protocol can be considered broadly generalizable.

## Methods

### Study design and participants

This exploratory comparative pilot study enrolled 20 female participants aged 60 years or older. The study was reviewed and approved by a Public Institutional Review Board in the Republic of Korea (IRB Approval Number: 2025-2354-001). The study was conducted in accordance with the principles of the Declaration of Helsinki, and written informed consent was obtained from all participants prior to enrollment.

Eligible participants underwent three sessions of high-intensity focused ultrasound (HIFU) treatment to the lower face and submental region at 4-week intervals (Weeks 0, 4, and 8). Participants were randomly assigned in a 1:1 ratio to either the conventional HIFU group ( $n=10$ ) or the anatomy-guided HIFU group ( $n=10$ ) using a computer-generated randomization sequence with permuted blocks of four. The allocation sequence was generated by an independent researcher prior to enrollment and concealed using sequentially numbered, opaque, sealed envelopes that were opened only after each participant completed baseline assessment. The primary assessment for this report was performed at Week 16, corresponding to 8 weeks after the third treatment session. No additional energy-based or injectable procedures were performed during the study period. The study timeline is shown in Supplementary Fig. S1.

### Technical characteristics

All treatments were performed using a high-intensity focused ultrasound system designed for depth-specific energy delivery (ULTRAFORMER MPT; Classys Inc., Seoul, Korea). The system allows energy delivery within an output range of 0.1–1.0 J with 0.1 J increments.

For facial treatment, linear-type cartridges with nominal focal depths of 3.0 mm and 4.5 mm were used. The 3.0 mm cartridge operates at a center frequency of 7 MHz and targets the dermal-to-subcutaneous layer, whereas the 4.5 mm cartridge operates at 4 MHz and targets the deep fat layer and the SMAS. Energy was delivered in a linear pattern with a fixed intraline shot spacing of 1.5 mm. All energy settings applied in this study remained within the predefined output range of 0.1–1.0 J, with parameter adjustments made according to the conventional or anatomy-guided treatment protocol.

### Blinding

Because of the nature of the interventions, treating physicians could not be blinded to group assignment; the anatomy-guided protocol required reference to HFUS measurements, whereas the conventional protocol did not. However, outcome assessors were blinded to treatment allocation. HFUS measurements at baseline and Week 16 were performed by a single trained operator who was not involved in treatment delivery and remained blinded to group assignment throughout the study. GAIS assessments were conducted by an independent investigator who reviewed standardized photographs presented in randomized order without identifying information or treatment labels.

### Pre-treatment assessment

At baseline, all participants underwent standardized clinical photography and HFUS imaging. HFUS assessment was used to quantitatively evaluate facial soft tissue architecture across the layered anatomy of the lower face and submental region, with the following comparative endpoints: superficial fat thickness, deep fat thickness, and the distance from the skin surface to the SMAS. The layered anatomy used for treatment planning is illustrated in Fig. 3, and the measurement axes are summarized in Supplementary Fig. S3.

HFUS measurements were obtained at predefined, standardized points for each treatment region. In the lower face, measurements were performed lateral to the oral commissure and superior to the mandibular border, corresponding to the typical jowl region. In the submental area, measurements were obtained at the midline immediately inferior to the menton, representing the area of maximal submental soft tissue fullness. The same anatomical landmarks and probe orientation were used at baseline and Week 16.

At each site, the ultrasound probe was positioned perpendicular to the skin surface with minimal compression (using a generous layer of acoustic gel to prevent tissue deformation) to ensure consistent visualization of the dermis, superficial and deep fat layers, and the SMAS. To assess intra-observer reproducibility, a subset of baseline measurements ( $n=5$ ) was repeated twice by the same operator. This repeated-measurement assessment was used to estimate relative reproducibility by ICC. Because the repeated-measurement subset was limited, the resulting reliability estimate was interpreted cautiously and was not considered sufficient on its own to establish

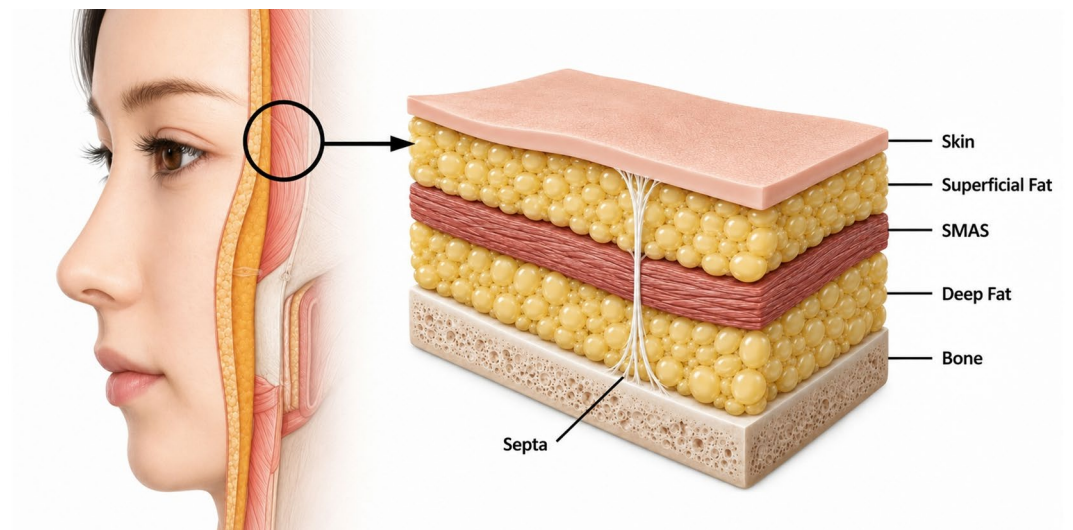


**Fig. 3.** Schematic representation of the layered facial soft tissue anatomy relevant to HIFU treatment planning and layer-specific HFUS assessment, including the skin, superficial fat, superficial musculoaponeurotic system (SMAS), deep fat, septa, and bone.

the absolute measurement error for submillimeter between-group differences. Baseline HFUS measurements were used for outcome evaluation in both groups and to inform treatment depth selection and parameter adjustment in the anatomy-guided group.

### Treatment protocols

Participants were treated using one of two HIFU protocols: a conventional protocol based on clinical practice patterns or an anatomy-guided protocol incorporating HFUS assessment.

#### Conventional HIFU protocol

In the conventional treatment group, HIFU was delivered using a standardized treatment protocol without reference to individual HFUS measurements. Treatment consisted of one pass with a 4.5 mm cartridge followed by one pass with a 3.0 mm cartridge, with fixed energy settings of 0.7 J and 0.4 J, respectively.

Intraline shot spacing was fixed at 1.5 mm, and line spacing was set at 3.0 mm. The approximate distribution of treatment lines was as follows: lower face, 120 lines (4.5 mm) and 160 lines (3.0 mm); submental area, 60 lines (4.5 mm) and 60 lines (3.0 mm). This resulted in approximately 400 total shots per treatment session.

#### Anatomy-guided HIFU protocol

In the anatomy-guided group, treatment parameters were individualized prior to treatment based on HFUS findings, including cartridge selection, energy adjustment, and line distribution for each treatment area. HFUS measurements obtained from each anatomical region were applied independently to the corresponding treatment area, allowing treatment parameters to be adjusted on a region-specific basis within each participant.

Quantitative ultrasound-based criteria were applied as follows: a skin-to-SMAS distance  $\geq 4.2$  mm favored predominant use of the 4.5 mm cartridge; a skin-to-SMAS distance  $< 4.0$  mm favored predominant use of the 3.0 mm cartridge; superficial fat thickness  $< 2.0$  mm prompted reduction of energy when using the 3.0 mm cartridge; deep fat thickness  $\geq 3.5$  mm increased the proportion of 4.5 mm treatment lines; and submental fat thickness  $\geq 6.0$  mm increased the number of 4.5 mm lines in the submental region.

Energy settings were adjusted according to tissue thickness, with values ranging from 0.6 to 0.8 J for the 4.5 mm cartridge and from 0.3 to 0.5 J for the 3.0 mm cartridge. Intraline shot spacing was fixed at 1.5 mm. Line spacing was adjusted based on tissue characteristics, with 3.0 mm used as standard spacing, 2.5 mm in thicker regions, and 3.5 mm in thinner regions. The total number of treatment lines was individualized, resulting in approximately 380–450 total shots per session.

HFUS findings were translated into region-specific treatment plans rather than line-by-line image guidance. The lower-face treatment field was referenced to the jowl region lateral to the oral commissure and superior to the mandibular border, whereas the submental field was centered on the midline inferior to the menton. The same standardized regions were reassessed and treated at each session. A practical comparison of the conventional and anatomy-guided workflows is provided in Supplementary Fig. S2.

### Statistical analysis

This pilot study was feasibility-driven, and no formal a priori sample size calculation was performed. Continuous variables are presented as mean  $\pm$  standard deviation. All HFUS summary statistics are reported to two decimal places. Baseline between-group comparisons were performed using Welch's t-tests. Within-group changes from baseline to Week 16 were assessed using paired t-tests, and between-group differences in change from baseline

were examined using Welch's t-tests. For continuous outcomes, mean differences, 95% confidence intervals, and two-sided nominal p-values are reported.

Because multiple regional HFUS endpoints were analyzed in this exploratory pilot study, no formal correction for multiple comparisons was applied and the p-values should be interpreted descriptively. Relative change (%) was calculated descriptively as the group mean change divided by the group mean baseline value. GAIS category distributions and safety outcomes were summarized descriptively. Intra-observer reproducibility of HFUS measurements was summarized using the intraclass correlation coefficient (ICC). Because ICC is a relative reliability measure and does not directly quantify absolute measurement error in millimeters, the magnitude of submillimeter between-group differences was interpreted cautiously in relation to the potential limits of ultrasound measurement precision. Statistical analyses for the revised tables were performed in Python using SciPy version 1.17.0.

## Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

## Code availability

No custom algorithm, bespoke computational tool, or new analysis pipeline was developed for this study. Statistical analyses were performed using standard Python packages, including SciPy version 1.17.0. The analysis code is available from the corresponding author upon reasonable request.

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All authors have reviewed and approved the final manuscript. Conceptualization: Kyu-Ho Yi. Methodology: Kyu-Ho Yi, Yerin Park. Investigation: Yerin Park, Jong-Keun Song, Chang-Il Yoon, Kyu-Eun Lee. Formal Analysis: Yerin Park, Jin-Hyun Kim. Writing – Original Draft Preparation: Yerin Park. Writing – Review & Editing: Kyu-Ho Yi, Hugues Cartier, Sebastien Garson. Visualization: Yerin Park. Supervision: Kyu-Ho Yi.

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### Declarations

### Competing interests

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### Ethical approval and informed consent

This study was conducted in accordance with the Declaration of Helsinki. Written informed consent for participation and publication of clinical data and images was obtained from all participants. All data were handled in a de-identified manner to ensure patient confidentiality.

### Additional information

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