

## Multiple Pass Ultrasound Tightening of Skin Laxity of the Lower Face and Neck

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**BACKGROUND** Skin laxity is a common complaint of patients who request skin rejuvenation. Radiofrequency and infrared light are widely used for nonablative treatment of skin laxity. Intense focused ultrasound (IFUS) has been investigated as a tool for the treatment of solid benign and malignant tumors for many decades but is only now beginning to emerge as a potential noninvasive alternative to conventional nonablative therapy.

**OBJECTIVES** To evaluate the efficacy of IFUS for the treatment of face and neck laxity.

**METHODS** Twelve female volunteers were enrolled in the study, and 10 were ultimately evaluated. The device under investigation was an IFUS. Areas treated included the face and neck. For treatment, the 4-MHz, 4.5-mm probe was used first, followed by the 7-MHz, 3.0-mm probe. Two blinded, experienced clinicians evaluated paired pretreatment and post-treatment (day 90) photographs. Patient self-assessments were also obtained.

**RESULTS** On the first primary outcome measure, two blinded clinicians felt that 8 of 10 subjects (80%) showed clinical improvement 90 days after treatment. Nine of 10 subjects (90%) reported subjective improvement.

**CONCLUSIONS** IFUS has many advantages for skin tightening.

*The authors have indicated no significant interest with commercial supporters.*

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Redundant facial, neck, or body laxity is a feature of aging. As such, skin laxity is a common complaint of patients requesting skin rejuvenation. Until recently, the only treatment option for skin laxity was surgery. As technology continues to evolve, minimally invasive techniques are gradually replacing procedures that once required major surgical intervention.<sup>1</sup> Recently, nonablative treatment of skin laxity has been made possible using devices that create uniform heating of the dermis and the underlying tissue;<sup>2</sup> radiofrequency and infrared light sources are widely used for nonablative treatment of skin laxity.

Intense focused ultrasound (IFUS) is an energy modality that can propagate through tissues, resulting in selective thermal coagulative changes within the focal region of the beam while leaving the remaining regions unaffected.<sup>3</sup> IFUS has been investigated as a tool for the treatment of solid benign and malignant tumors for many decades but is only now beginning to emerge as a potential noninvasive alternative to conventional therapies.<sup>4</sup> Gliklich and colleagues<sup>3</sup> first applied IFUS to human facial tissue, but the treatment was performed only on periauricular skin. Alam and colleagues<sup>5</sup> investigated IFUS for the tightening of

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facial skin, but they evaluated only the efficacy of IFUS for eyebrow-lift procedures using just one pass of IFUS treatment. The most common complaints of patients requesting skin rejuvenation involve cheek, chin, and neck laxity; no optimized protocols exist for the treatment of these areas.

The purpose of this prospective study was to evaluate the efficacy of IFUS treatment for face and neck laxity using a two-pass protocol.

## Materials and Methods

### Patients

Twelve female volunteers who provided informed consent were enrolled in the present study. Two subjects dropped out, leaving 10 subjects to be evaluated. The median age of the subjects was 59 (range 55–71), and subjects had Fitzpatrick skin types III and IV.

Exclusion criteria were active systemic or local infections, local skin disease that might alter wound healing, scarring in the test areas, diagnosed psychiatric illness, history of smoking, and insertion of soft-tissue augmentation materials or application of ablative or nonablative laser procedures within the previous 6 months.

### Equipment

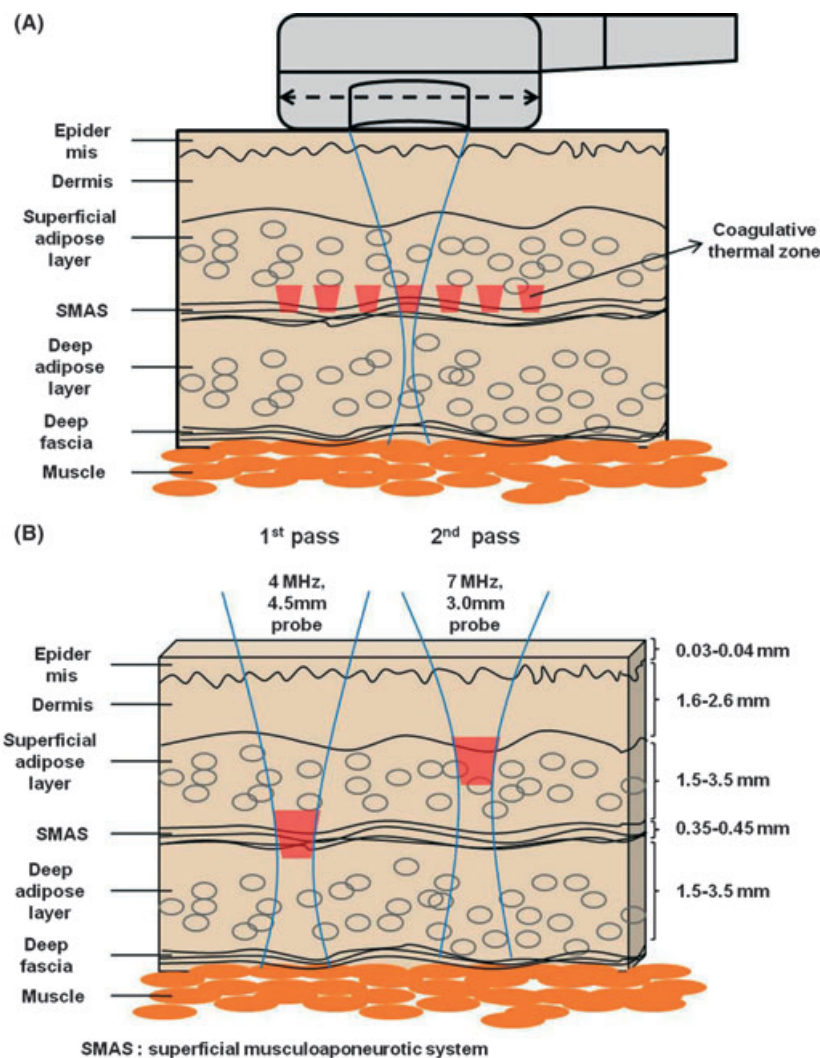
The investigational device was an IFUS device (Ulthera System; Ulthera, Inc., Mesa, AZ). With the use of ultrasound, it is possible to visualize the skin and subcutis. After adequate visualization, a therapeutic ultrasound device can create small ( $\sim 1 \text{ mm}^3$ ) geometric zones of thermal coagulation in the tissue. The source energy (0.5–1.2 J) of the probes can be adjusted, allowing the operator to determine the depth and volume or size of the thermally induced lesions. There are three types of probes, with preset focus depths and frequencies: 4 MHz, 4.5-mm focal depth (source energy 0.75–1.2 J); 7 MHz, 4.5-mm focal depth (source energy 0.75–1.05 J); and 7 MHz, 3.0-mm

focal depth (source energy 0.4–0.63 J). Higher-frequency probes have been found to have greater effects in superficial tissue compared to lower-frequency probes. On activation and firing, each probe delivers a series of ultrasound pulses along a 25-mm exposure line (Figure 1A). Each individual pulse duration in the line ranges from 25 to 40 milliseconds. The spacing between thermal coagulation points is 1.5 mm when energy is delivered at a depth of 4.5 mm (4-MHz, 4.5-mm-focal-depth and 7-MHz, 4.5-mm-focal-depth transducers) and is 1.1 mm when the energy is delivered to a depth of 3.0 mm (7-MHz, 3.0-mm-focal-depth transducers).

### Experimental Procedures

Topical anesthetic ointment (9% lidocaine; M's Well Pharmacy, Seoul, Korea) was applied to the face and neck areas receiving treatment 45 to 60 minutes before the procedure. The anesthetic was washed off immediately before energy delivery. Areas treated included the temples, cheeks, submental region, and neck. The dermis and subcutaneous tissue were targeted using the 4-MHz, 4.5-mm-focal-depth and 7 MHz, 3.0-mm-focal-depth probes. For treatment, the 4-MHz, 4.5-mm probe was used first, followed by the 7-MHz, 3.0-mm probe (Figure 1B).

Ultrasound gel was first applied to the skin. The probe was then placed firmly on the targeted skin surface to achieve uniform coupling with the skin surface. The operator moved the probe parallel to the first exposure line, placing the second row of ultrasound exposures 3 to 5 mm from the first line. A treatment planning card with a grid was used to illustrate proper placement of treatment lines to achieve a treatment density that would produce consistent, significant lifting of tissue. Ultrasound imaging confirmed that the probe was acoustically coupled to the skin tissue and that the geometric focal depth for therapy was in the target tissue. On average, 238 exposure lines were placed on the treated area of each subject using



**Figure 1.** Schematic view of the ultrasound device being applied to the skin. (A) The probe emanates a series of wedge-shaped focused ultrasound beams along a 25-mm-long exposure line and makes thermal coagulative zones. (B) The thermal coagulation zone of the first pass (using the 4-MHz, 4.5-mm probe) extended from the superficial adipose layer through the SMAS to the deep adipose layer. The thermal coagulation zone of the second pass (using the 7-MHz, 3.0-mm probe) extended from the deep dermis to the superficial adipose layer.

the 4-MHz, 4.5-mm probe and the 7-MHz, 3.0-mm probe of the focused ultrasound system, as indicated by the protocol. The total number of lines was adjusted to accommodate variations in facial size. An interval of approximately 3 mm is appropriate to achieve good treatment density. The total estimated treatment density on two different treatment planes (4.5 and 3.0 mm) was approximately 20% to 25%. Complete treatment of the face and neck required 15 to 25 minutes per patient.

The energy setting was 1.2 J for the 4-MHz, 4.5-mm-focal-depth probe and 0.63 J for the 7-MHz, 3.0-mm-focal-depth probe.

Clinical photographs of the face and neck were taken using a digital camera (Canon EOS 40D, Tokyo, Japan, 6.0 megapixels) before treatment; immediately after treatment; and at 7, 30, and 90 days after treatment. Frontal, 45°, and 90° still digital photographs of the face and neck were obtained. Baseline photographs were displayed in a

computer monitor for the photographer to match the positioning of the patient as closely as possible.

### **Assessment**

Two blinded, experienced clinicians who were not involved in patient treatment evaluated paired pretreatment and post-treatment (day 90) photographs of the 10 subjects in a randomized fashion (pretreatment and post-treatment not identified as such) to determine whether discernible clinical improvement was noted. Each reviewer was asked to identify the posttreatment image. If the correct image was identified as the post-treatment image, the assessment from the reviewer was considered to indicate improvement; if the reviewer identified the wrong image as the posttreatment image, the assessment was considered to indicate detriment. If the reviewer reported no difference between the two photographs, the assessment was considered indicative of no change. As such, if two reviewers noted improvement, the patient was said to have improved; if two reviewers noted detriment, or one reviewer noted detriment and one reviewer noted no change, the patient was said to have worsened; and if two reviewers noted no change, or one reviewer noted improvement and one reviewer noted detriment, or one reviewer noted no change and one reviewer noted improvement, then it was determined that no change had occurred. After this initial assessment of the photographs, the same clinicians reevaluated the photographs considered to represent improvements. The reviewers were asked to score the degree of skin laxity according to the following categories: mild improvement (improvement of superficial laxity), moderate improvement (focal improvement of structural laxity with or without improvement of superficial laxity), and significant improvement (overall improvement of structural laxity with or without improvement of superficial laxity).

Patient self-assessments were also obtained by comparing the subjective degree of skin tightening after treatment with that from before treatment. Patients reported improvement as worse, none, mild, moderate, and good.

After treatment, patients were asked to grade intra-procedure pain on a visual analogue scale from 0 to 10, with 0 denoting no pain and 10 the most pain possible. All subjective and objective side effects after treatment were recorded.

### **Results**

Ten of the 12 individuals enrolled in this study attended all required study visits. Two individuals were lost to follow-up.

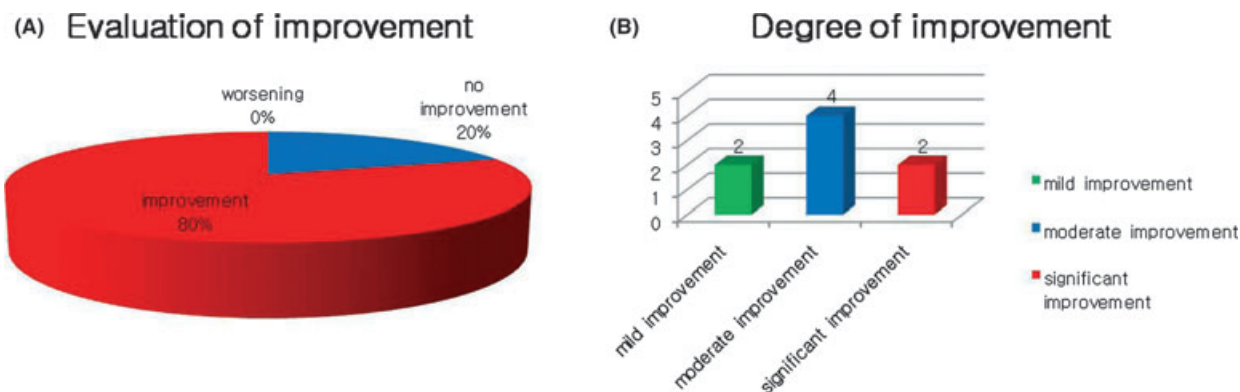
On the first primary outcome measure for efficacy of skin tightening, two blinded experienced clinicians judged 8 of 10 subjects (80%) as showing clinical improvement 90 days after treatment. Two subjects were judged to show no change (Figure 2A). The photographs of improved patients were reevaluated to score the degree of improvement; 2 of 8 subjects (25%) were assessed as significantly improved, four (50%) as moderately improved, and two (25%) as mildly improved (Figures 2B, 3, and 4).

Patient assessments of response 90 days after treatment were as follows: 1 of 10 (10%) reported no improvement, two (20%) reported mild improvement, five (50%) reported moderate improvement, and two (20%) reported significant improvement (Figure 5).

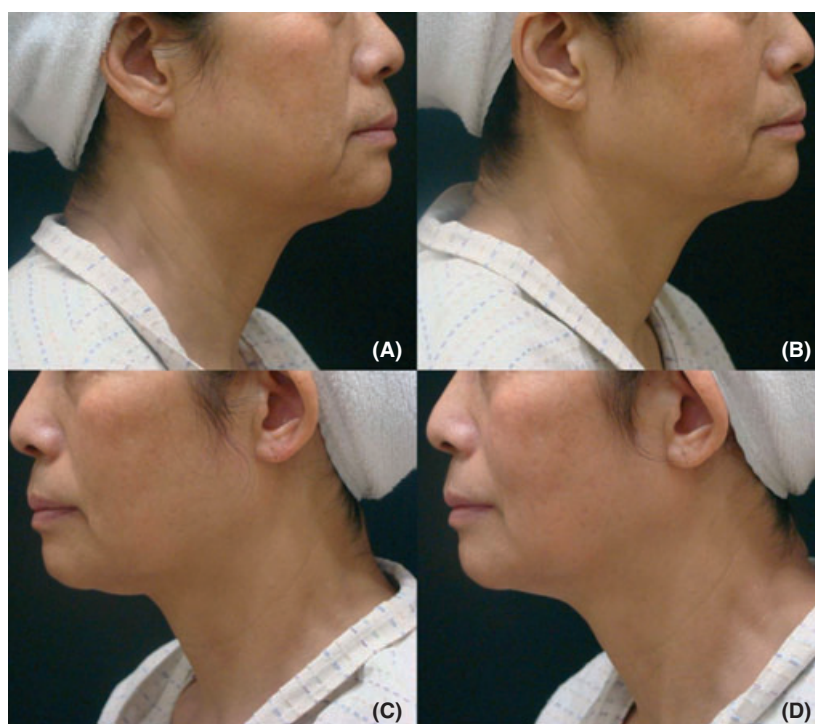
All subjects developed slight erythema and edema immediately after treatment. Mean pain score immediately after treatment was  $3.9 \pm 1.66$  (range 2–7), although no subjects reported pain at any of the follow-up visits. No other adverse events were observed.

### **Discussion**

As noninvasive, nonablative rejuvenation techniques have become more popular, nonsurgical skin tightening has opened up another frontier in aesthetic medicine. Nonablative treatment of skin tightening is performed by heating the dermis and underlying tissue. Collagen is the primary protein



**Figure 2.** Graphs displaying the efficacy of intense focused ultrasound treatment as evaluated by two clinicians. (A) Initial results of the clinicians attempting to identify the post-treatment image. (B) Results of reevaluating the post-treatment photographs.



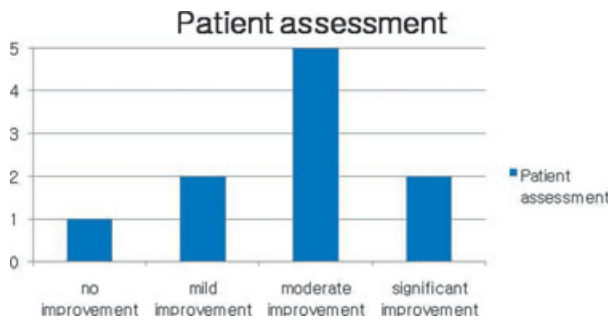
**Figure 3.** A 59-year-old woman shows moderate improvement. (A and C) Before treatment. (B and D) Ninety days after treatment.

in the dermis, along with subcutaneous fat septae and the superficial musculoaponeurotic system (SMAS). It is a family of structural proteins and is responsible for the strength and resilience of the skin and other tissues.<sup>6,7</sup> Collagen fibers are composed of triple helixes of protein chains with inter-chain bonds that create a crystalline structure.<sup>6</sup> As

collagen is heated, it becomes denatured. This process is not completely understood but is thought to involve the breakage of hydrogen bonds and conversion from a crystalline to an amorphous state.<sup>8</sup> This results in thickening and shortening of collagen fibrils, greater tissue tension due to the rubber-elastic properties of collagen, and ultimately



**Figure 4.** A 62-year-old woman shows significant improvement (A and C) Before treatment. (B and D) Ninety days after treatment.



**Figure 5.** Graph of patient assessment of response 90 days after treatment.

tissue tightening.<sup>8</sup> After the initial effects, the skin initiates a wound healing response, resulting in the formation of new collagen, which provides longer-term tightening of the skin.<sup>2</sup>

The attractive features of nonablative skin tightening are limited postprocedure healing time, ability to return to work or social engagements, and lower risk of adverse events than with ablative or surgical skin resurfacing. IFUS, like such modalities as intense light, lasers, and radiofrequency energy, is suitable technology for nonablative skin tightening

and has its own distinctive characteristics. First, it is widely believed that energy delivery to the deeper subcutaneous layers of the face, or even the SMAS, is most effective in inducing skin tightening.<sup>5</sup> Second, IFUS is able to spare the epidermis and avoid damage to the papillary dermis without simultaneous skin cooling while creating a zone of thermal coagulation deep within the reticular dermis and subcutaneous layers.<sup>4</sup> The focused field produced by IFUS vibrates tissue and creates friction between molecules. These molecules absorb the mechanical energy, leading to the secondary generation of heat. Selective coagulative changes are produced within the focal region of the beam, but other tissue proximal and distal to the focal region of the ultrasound field is preserved.<sup>5</sup> Third, absorption of IFUS energy is independent of chromophores such as melanin and hemoglobin.<sup>4</sup> Therefore, IFUS may be helpful in overcoming some of the difficulties encountered with light-based treatment of darker skin types.<sup>4</sup>

A number of studies have reported on the measurement of skin thickness at different facial locations

using different methods. Despite the specimen-to-specimen variability of skin thickness, in general, the skin is thickest on the cheeks, followed by the forehead.<sup>5</sup> On average, the epidermal thickness of facial skin is 0.03 to 0.04 mm, and the skin thickness (epidermis + dermis) of the face is 2 to 3 mm.<sup>9,10</sup> Macchi and colleagues<sup>11</sup> observed that the subcutaneous tissue of the face consists of a superficial adipose layer, SMAS, a deep adipose layer, and deep fascia. They also found that total subcutaneous tissue thickness is 3 to 7 mm, superficial adipose thickness is 1.5 to 3.5 mm, and SMAS thickness is 0.35 to 0.45 mm (Figure 1B).

We created a new treatment protocol for our study. Two treatment passes were performed using two different probes. The first pass was performed using a 4-MHz, 4.5-mm-focal-depth probe. White and colleagues<sup>12</sup> evaluated thermal coagulation zones and observed that the depth of the thermal coagulation zone was extended from 4.5 mm to 5.5 mm when the 4.4-MHz, 4.5-mm-focal-depth IFUS probe was used at 2.2 J. If the aforementioned theory is correct, the thermal coagulation zone of the first pass extended from the superficial adipose layer through the SMAS and finally to the deep adipose layer (Figure 1B). The second pass was performed using a 7-MHz, 3.0-mm-focal-depth probe. Data regarding the thermal coagulation zone produced by this probe could not be found, but if it produces similar effects to the 4-MHz, 4.5-mm-focal-depth probe; the thermal coagulation zone of the second pass extended from the deep reticular dermis to the superficial adipose layer (Figure 1B). The thermal coagulation zone is an inverted cone shape, and average estimated area of thermal coagulation zone is 1 mm<sup>3</sup>.<sup>3,4</sup> Although the location of the thermal coagulation zone may differ slightly in different regions of the face, this method can theoretically create a wider vertical zone of thermal injury while still sparing the epidermis and papillary dermis. Because IFUS affect double layers of the dermis and subcutaneous tissue, this protocol may be more effective than one-pass protocols for

skin tightening. A previous clinical study performed by Alam and colleagues<sup>5</sup> used a one-pass protocol and found that 86% of subjects showed clinical improvement. In our study, 80% of subjects were found to show clinical improvement, but Alam and colleagues<sup>5</sup> evaluated the efficacy of an eyebrow lift procedure, whereas we evaluated the efficacy of treatment of skin laxity of the face and neck. Therefore, the results of these two studies cannot be directly compared. In our study, we did not lower the fluence with multiple-pass treatment. In contrast, Bogle and colleagues<sup>13</sup> who performed a clinical study of radiofrequency tightening, lowered the fluence with multiple-pass treatment. IFUS creates a focused zone of thermal coagulation while preserving the areas proximal and distal to this zone. As such, when IFUS skin tightening is performed, the fluence does not need to be lowered, but in most multiple-pass skin tightening procedures using other energy sources, the fluence must be lowered.

What remains unclear is why some treated individuals respond well to treatment, whereas others do not. In our nonresponsive individuals, IFUS may have contracted the lax skin, but the small amount of excess skin relative to the underlying structure constrained the degree of visual effect.

IFUS has many advantages for skin tightening, but only two clinical studies (including the present study) regarding IFUS have been performed. Future studies should be performed to assist in the creation of new devices and protocols that maximize the advantages of IFUS.

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