Comparison of Effect Between Two Different High Intense Focused Ultrasound for Facial tightening: Evaluator-blinded, split-face comparative study

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Abstract

**Background** Variable devices using high intense focused ultrasound (HIFU) has been introduced to tighten the skin laxity with satisfactory results. However, there is no comparative study about the efficacy and side effect between HIFU devices.

**Objective**

To compare the efficacy and safety between Ulthera and Ultraskin and evaluate the validation of quantitative assessment in facial skin tightening.

**Methods & Materials**

We performed a split-face comparative study of 20 Korean patients (Fitzpatrick skin type III and IV) with skin laxity. Patients received one treatment sessions with each HIFU device at setting to the same number of coagulative zones. Patient assessments were recorded, and three blinded, experienced clinicians evaluated paired pretreatment and post-treatment (2 month) photographs. Quantitative assessment using fixed point additionally was analyzed for more objective evaluation.

**Results**

Qualitative assessments evaluated by clinicians and patients of both devices generally showed mild to moderate improvement similar to previous studies. Ulthera and Ultraskin reported similar efficacy in aspect of blinded clinician assessment, and quantitative assessment, although Ulthera were more preferable in patient assessments than Ultraskin.

Also, there was correlation between clinician qualitative scores and quantitative values suggesting skin tightening objectively.

**Conclusion**

To the author’s knowledge, variable HIFU devices could be used safely and effectively for facial skin tightening.

**Introduction**

Since Ulthera system (Ulthera, Inc., USA) was introduced, various high intense focused ultrasound (HIFU) devices delivering inducible energy to selected foci within reticular dermis and subcutaneous tissue leading to the heating and thermal coagulative changes has been released.

Several studies showed satisfactory results of HIFU for lifting or tightening of skin laxity on eyebrow, lower face and neck. However so far, there is no comparative clinical study on the effects and safety between the different equipments.

We prospectively conducted this study to evaluate the difference of efficacy and degree of pain between two different HIFU devices for facial tightening in 20 Korean patients.
Materials and methods

Patients

Twenty patients (Fitzpatric skin type III-V) with moderate to severe facial laxity were recruited in this study. All patients gave written informed consent for treatment and photographs. The exclusion criteria included cosmetic procedure regarding facial laxity within previous six months, local skin disease that might delay wound healing, scarring in the treatment region.

Equipment

Two different HIFU devices (Ulthera, Ulthera Inc., USA and Ultra-Skin, WON TECH Inc., KOR) was used in each side of face for comparative study. Ulthera has a transducer that was used for imaging the treatment region and contains three types of probes: superficial, 7.0MHz with a focal depth of 3.0mm (source energy 0.25-0.45J); intermediate, 7.0MHz with focal depth of 4.5mm (source energy 0.66-1.05J); and 4.0MHz with a focal depth of 4.5mm (source energy 0.75-1.2J). On the other hand, Ultra-Skin 7.0MHz with a focal depth of 3.0mm (source energy Max. 3J); intermediate, 4.0MHz with focal depth of 4.5mm(source energy Max. 3J).

Principle of both devices was not different in aspect to create small zones of thermal coagulation by microfocused ultrasound waves and be determined the depth of target tissue and volume/size of the thermally induced lesions by the preset frequency and energy of given probes.

Experimental design

The study was split-face, evaluator blinded, prospective randomized clinical trial. All patient randomized select the HIFU devices to implement at each side of face.

Treatment region within each face was defined with midface as shown at figure 1A.

Procedure was performed by one practitioner and reviewed the efficacy by three blinded reviewer with photographs obtained at baseline and 2 month post-treatment.

Treatment setting

The spacing between the pulses and energy per ultrasound of Ulthera was set to 1.5mm, 0.7J respectively. The Ultraskin was set at 1.0mm of spacing, 1.3J of energy. Ulthera and Ultraskin were utilized with the 7.0MHz/3.0mm, 4.0Mz/4.5mm transducer respectively.

Thermal coagulative zones within each exposure line of Ulthera was set at 17 in contrast to Ultraskin with 21 zones.
Experimental procedures

A topical anesthetic cream (a mixture of 2.5% lidocaine and 2.5% prilocaine; AstraZeneca AB, Södertälje, Sweden) was used with occlusion one hour before the treatment. Then ultrasound gel was applied to the skin and operator moved the probe parallel to the first exposure line, placing the second row of ultrasound exposures 3 to 5mm from the first line (Figure 1A). The total exposure line per one side of the face in each patient are shown in Table 1. The total number of lines was adjusted to accommodate variations in facial size. To make same coagulative zones on each side of face, ratio of exposure lines of each device was adjusted at five versus four (Ulthera versus Ultraskin). After treatment, the ultrasound gel was wiped off.

Outcome Analysis

Patient assessment

During treatment, the patient was asked to rate sensation of pain on a scale of 0 to 10, with 0 denoting no sensation and 10 denoting the worst possible pain. At the 2 month follow up visit, participants were asked to complete a patient satisfaction questionnaire, which entailed recording their perception of the clinical outcome about facial tightening.

Qualitative clinician assessment

Frontal and 45-degree digital photographs of face were taken before treatment, at 2 months post treatment. Treatment results subjectively was analyzed by three blinded dermatologists (two male and one female) with paired before and after photographs.

The reviewers were not aware of which side of face was applied to what kind of device. The reviews were asked to evaluate degree of improvement of the facial tightening and skin laxity. The criteria for evaluation were much improvement = 3, moderate improvement = 2, mild improvement = 1, no change = 0, worse = -1. The reviewers requested to assess twice the photographs at long intervals. Then, if the score was constant, the score was confirmed, but if the score at first was different from at second, the reviewer was additionally claimed to decide which score is more suitable.

Comparison of clinician assessment between two devices was evaluated by each score of three reviewers.
**Quantitative assessment**

For this assessment, frontal image were analyzed to measure the ratio of width of face for each patient. First, a line x was drawn horizontally between lateral canthus. A line a and b was drawn horizontally from upper margin and lower margin of philtrum to lateral borderline of face, respectively. (Figure 1B). In contrast to line x which remains same after treatment, line a and b are suggest of decrease by tightening for ultrasound treatment. To compensate for difference of length caused by the subtle change of the angle and size of photograph, we calculated the ratio of width of face such as line a/x, line b/x.

**Safety assessment**

The treatment site was visually examined, and the patients was queried about treatment-related adverse events (erythema, edema, purpura, hyperpigmentation, hypopigmentation, scarring). At follow up visit, the treatment site was re-examined, and patients were queried again about adverse events.

**Statistical analysis**

Independent t-test was used to examine differences of A/X and B/X ratio before and after treatment in the patients treated with high intensity focused ultrasonography. With that, we compared changes of A/X and B/X between each side of face treated with Ulthera or Ultraskin. Analysis of variance (ANOVA) was used to compare observer’s evaluation with changes of A/X and B/X ratio between Ulthera and Ultraskin. Continuous variables were expressed as mean ± standard deviations. Statistical analysis was performed using SPSS 18.0 (SPSS, IBM Corp, Armonk, NY, U.S.A.). Statistical significance was considered when p value was less than 0.05.

**Results**

**Demographic Characteristics**

No patients did not complete the study due to intolerable treatment or side effects (Figure 2. and 3). Two (10%) of the 20 enrollees were men and mean patient age was 59.8 years (range, 45-70 years) with Fitzpatrick skin types III (75%), and IV(25%).

**Comparison of Qualitative assessment**

Score regarding the degree of improvement analyzed by each reviewer was shown Table 1. The comparison of qualitative assessment between two devices by reviewer was not
devices (Fig. 4). In contrast with Reviewer’s assessment, assessment of improvement by patients was more preferable to 35% of Ulthera than 10% of Ultraskin (Fig. 4). However, 65% of patients felt the similar efficacy about two devices, which was same result to reviewer’s assessment.

**Comparison of Quantitative assessment**

After 2 month posttreatment, reduction of line a/x was observed in 70% of patients treated by Ulthera and 65% by Ultraskin. Also, decrease of line b/x after treatment by Ulthera and Ultraskin was observed in 65% and 60% respectively. Mean value of Line a/x and line b/x after 2 month post treatment showed decreased tendency in both devices. Especially, line b/x showed statistically significant difference in both devices after treatment (Table 2). However, Mean value of reduction of line a/x and line b/x between Ulthera and Ultraskin was not observed statistically significant difference (Table 2).

**Relevance of the Qualitative and Quantitative assessment**

For analysis of relevance of the qualitative and quantitative assessment, we evaluate statistically the difference of reduction of line a/x and line b/x according to the degree of improvement (moderate improvement = 2, mild improvement = 1, no change = 0). The degree to the reduction of line a/x and line b/x showed increasing tendency according to the increase of improvement’s score, although not statistically significant (Table 3, Figure 5).

**Comparison of Safety assessment**

There were no reports of serious or permanent adverse events in both devices. All of patients felt more severe pain and mean pain scores during treatment showed was 5.4 in Ulthera and 2.2 in Ultraskin, which was statistically significant.

**Discussion**

The goal of this prospective study was to identify that the results about two HIFU devices is similar with previous studies for facial tightening and lifting and compare the efficacy and pain between two different HIFU equipment (Ulthera and Ultraskin) at 2 month after treatment. Clinicians judged from 58.1% to 91% as showing clinical improvement in previous studies. Clinical result of Ulthera and Ultraskin evaluated by blinded reviewers was rather good showing 95%, 90.3% improvement respectively, although satisfaction of patient reported 80% of Ulthera and 75% of Ultraskin was not
First of all, there was no significant difference of efficacy between Ulthera and Ultraskin both in blinded reviewer’s evaluation and quantitative score, although 30% of patients feel better after Ulthera treatment than Ultraskin. Also, among the patients reported improvement, 56% of patient treated with Ulthera showed moderate or much improvement in contrast to 40% of Ultraskin. On the other hand, pain duration the treatment was much more severe in Ulthera than Ultraskin, which could make patient feel the difference of improvement.

Generally, superficial muscular aponeurotic system (SMAS) is a continuous fibrous network with much greater holding properties why be thought to be most effective structure in inducing skin lifting and tightening.2,8-11 The SMAS is intimately associated with specific facial muscles, including the platysma, orbicularis oculi, occipitofrontalis, zygomatici, and levator labii superioris where is not much matched in the middle of face treated mainly in this study.8,12 Therefore, we think that SMAS joined with these muscles relatively less could be influenced of tightening because of discordance of position between HIFU and SMAS and skin depth over 4.5mm of middle face. Instead of SMAS level, both HIFU is likely to affect at mid to reticular dermis and subcutaneous fat layer, which might make the similar efficacy between two devices.

Based on these hypothesis, efficacy among HIFU devices can be suggested to be not much different under the conditions of sufficient energy output at least in the middle of face.

In this study, we used the quantitative score to analyze the facial tightening more objectively. The primary physical mechanism of HIFU is tissue necrosis with heating due to acoustic energy, which expect dermal neocollagenesis and tissue contraction afterward.13-15 Therefore, method using ratio of variable point and fixed point not changed after treatment could be practical.

Actually, there was partly correlation between mean score of reduction of line a/x, line b/x and degree of clinical improvement in this study.

There are some limitation of this study. The patients could know which device was utilized to their face because of difference of pain, which can make bias against degree of improvement.

And, compared to other HIFU studies, the period of follow up could be short to evaluate final outcome exactly.

First of all, comparative analysis for histological change such as size and depth of thermal coagulation zone produced by each device setting, which might estimate degree and consistence of efficacy was not proven. Therefore, further experimental studies with newly emerging HIFU equipment and clinical comparative study in area matched SMAS such as eyebrow, forehead, and submentum should preferentially performed to understand exactly about the principle of effect and safety.
References

### Table 1. Summary of treatment effects in 20 patients

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<th>Patients number</th>
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### Table 1. Demographic data of the study population (n=20)

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<th>Characteristics</th>
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<td>Sex, female:male</td>
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<td>Total treatment shots</td>
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<td>Ulthera</td>
<td>104.8 (8.4)</td>
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<td>Ultraskin</td>
<td>85.1 (7.1)</td>
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Table 2. Comparison of A/X and B/X ratio before and after treatment in the patients treated with high intensity focused ultrasonography

<table>
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<th>Characteristics</th>
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<td><strong>Ultraskin</strong></td>
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<td>0.7064 (0.0537)</td>
<td>0.6868 (0.0459)</td>
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Table 3. Comparison of changes of A/X and B/X between each side of face treated with Ulthera or Ultraskin

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* Changes between initial and follow up ratio

Figure 1. (A) Outline of treatment area by high intensity focused ultrasonography for the treatment of facial laxity (B) Measuring the ratio of width of face

*A: Upper margin of philtrum to lateral facial margin B: Lower margin of philtrum to
lateral facial margin X: Between lateral canthus of both eyes

Figure 2. Representative subject with acne showing improvement between baseline (A, C) and 60 weeks after treatment completion (B, D) (A, B) Ulthera-treated side (C, D) Ultraskin-treated side

Figure 3. Comparison of clinical efficacy between Ulthera and Ultraskin
Figure 4. Correlation of observer's evaluation with changes of A/X (A) and B/X ratio (B) between Ulthera and Ultraskin

* Changes between initial and follow up ratio