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The efficacy of macro-focused ultrasound in the treatment of upper facial laxity: A pilot study

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ABSTRACT

Background: Recently, macro-focused ultrasound (MFU) has become a popular non-invasive aesthetic treatment for facial laxity. However, there are no studies done that evaluated the use of MFU with a 2.0 mm transducer for upper facial lifting.

Objectives: To evaluate the efficacy and safety of MFU with a 2.0 mm transducer in the treatment of upper facial laxity in Thai patients

Methods: This was a prospective, evaluator-blinded pilot study with 34 Thai patients diagnosed with mild to moderate facial laxity. Patients were treated with a single session of MFU with 2.0 mm transducer at the forehead, lateral and just below the eye area. Primary outcome was the clinical improvement of upper facial laxity graded by 2 blinded dermatologists at baseline, 1-week, 1-, 3- and 6-month follow-up. Objective measurements including eyebrow height, upper facial volume and textural irregularities were evaluated. Patients' self-assessment scores and adverse effects were also recorded.

Results: Out of 34 patients, 27 (79.4%) attended all follow-ups. Clinical improvement of upper facial laxity was observed as early as 1-week follow-up. Eyebrow height elevation was significantly increased at every follow-up (p=0.000) with an average of 1.22 mm at 6-month follow-up. Wrinkles improved significantly at 1-week and 6-month follow-up (p=0.002 and p=0.010, respectively). Skin roughness showed significant improvement at 6-month follow-up (p=0.004). Majority of the patients (53.6%) reported marked improvement at 3-month follow-up. No serious adverse event was noted.

Conclusion: MFU is a safe and effective treatment for upper facial laxity and skin textural irregularities in patients with mild to moderate degree of laxity.

INTRODUCTION

Aging is an inevitable process that manifests differently depending on a patient's skin type, exposures, and genetics.[1] Most common dermatological signs of aging includes skin thinning, xerosis, wrinkles, hyperpigmentation and skin laxity.[1,2] It was found that Asians have denser dermal tissue compared to Caucasians, which likely contributes to a lower incidence of wrinkling and skin laxity.[2]

Facial laxity and wrinkles in the aging skin are common cosmetic concerns.[3] Rhytidectomy or facelift surgery remains to be the gold standard procedure but most would prefer less invasive modalities to avoid surgical complications, prolonged downtime and to achieve a subtler and natural appearance.[4] Minimally invasive procedures for facial laxity includes lasers, soft dermal fillers, neurotoxins, energy based devices (radiofrequency, ultrasound), fat grafting and thread lifts.[5-8] High intensity focused ultrasound (HIFU) technology has been used as a noninvasive surgical tool to treat a variety of solid malignant tumors since it offers less complications compared to conventional treatment modalities such as surgery.[9] In contrast, HIFU uses a much lower ultrasound energy to treat the superficial layers of the skin.[10] In 2009, micro-focused ultrasound with visualization (MFU-V) was approved by the US Food and Drug Administration (US FDA) for non-invasive brow elevation.[11] This ultrasound device is capable of heating the tissues at approximately 65°C, by producing discrete thermal injury zones(<1mm^3) at consistent depths depending on the transducer used.[12] The ultrasound energy delivered causes contraction of the denatured collagen fibers, neocollagenesis and collagen remodeling, which leads to lifting and tightening of the skin.[13] Available MFU-V are launched with various attached transducers that emit frequencies of 10.0 MHz, 7.0 MHz and 3.0 MHz with variable depths of 1.5 mm (dermis), 3.0 mm (deep dermis) and 4.5 mm (subdermal and superficial muscular aponeurotic system).[10] Currently, the new macro-focused ultrasound (MFU) with 2.0 mm transducer has been promoted to use for upper facial skin.

In a previous study, MFU-V with a 3.0 mm transducer was reported to lift the eyebrow height by 1.7 mm at 90

days after treatment when compared to baseline.[14] At present, there are no studies done using MFU with a 2.0 mm transducer for the treatment of upper facial laxity. The result might be different among different ethnicities because of variations in the aging characteristics and dermal thickness. The objective of this study was to evaluate the efficacy and safety of HIFU with a 2.0 mm transducer in the treatment of upper facial laxity in Thai patients.

MATERIALS AND METHODS

This was a prospective, single-center, evaluator-blinded pilot study. A total of 34 Thai patients, male or female, age range between 30-50 years old, Fitzpatrick skin types III-V and diagnosed with mild to moderate facial laxity were included in the study. Exclusion criteria included patients who are pregnant or lactating, have pacemaker or metal implantation, facial surgical scar, history of keloid or hypertrophic scar formation, history of botulinum toxin or filler injection in the last 2 weeks before the study, history of thread lift, have ptotic fat, history of herpes simplex infection, history of active or systemic infection, who received non-steroidal anti-inflammatory drug (NSAID), aspirin, steroid, heparin, vitamin K or E in the last 72 hours before the study.

All patients underwent a single treatment session using the MFU device (Ultraformer III, Classys Inc., Seoul, Korea) for upper facial laxity. Preoperatively, topical anesthetic cream (EMLA®, AstraZeneca, Wilmington, DE, USA) was applied for 40 minutes prior to the treatment with occlusion. Ultrasound gel was applied to the target site and the device was gently pressed perpendicularly to the skin surface. The forehead, under and lateral eye area were treated with a 2.0 mm transducer (5.5 MHz). The application involved 90 horizontal lines in the forehead. In the lateral eye area, 5 horizontal and vertical lines are applied on each side. In the under eye area, 15 horizontal lines are applied on each side. Thus, a total of 140 lines were delivered in each patient. The energy for the ultrasound pulse was 0.2 - 0.4 J with a range of pitch at 1.5 mm.

Postoperatively, the patients were instructed to apply cold compress to the treated area to reduce pain and inflammation. They were also advised to use broad spectrum sunscreen and to avoid extremely hot or cold exposure, or any laser or radiofrequency therapy throughout the study.

The primary outcome of the study was the clinical improvement of upper facial laxity using the quartile grading scale: 0= no improvement, 1= minimal improvement (1–25%), 2= moderate improvement (26–50%), 3= marked improvement (51–75%) and 4= excellent improvement (76–100%). Subjective evaluation of the photographs was graded by 2 blinded dermatologists at baseline, 1 week, 1-, 3-, and 6-month follow-up. All clinical photographs were taken with identical camera settings, lighting, and positioning using a Canon PowerShot G9 stand-off camera (OMNIA imaging System, Canfield Scientific Inc., Fairfield, NJ).

In addition, eyebrow height, upper facial volume, wrinkles and skin texture were objectively evaluated at baseline, 1 week, 1-, 3- and 6-month follow-up. The average eyebrow height was measured using ImageJ software, by calculating the average vertical distance from the highest point of the eyebrow to the level of both mid pupils in 5 positions per side (a; medial canthus, b; medial limbus, c; mid pupil, d; lateral limbus, and e; lateral canthus to the highest point of the eyebrow) as shown in Figure 1. The upper facial volume was analyzed using 3 dimensional photographs captured by Vectra H1 Imaging System® (Canfield Scientific, NJ, USA). Skin textural irregularities (wrinkles, skin roughness, melanin concentration) were analyzed using Antera3D® (Miravex Limited, Dublin, Ireland). Patients' self-assessment score was evaluated using the same quartile scale on every follow-up. Pain score during the treatment was rated using a 10-point visual analogue scale (VAS). Adverse events were also evaluated.

Repeated measure ANOVA and paired T-test were used for parametric distribution data. Friedman test and Wilcoxon signed ranked test were used for non-parametric distribution data. A p-value < 0.05 was considered statistically significant. The statistical analysis was performed using a statistical software (SPSS version 18.0; SPSS Inc., Chicago, USA).

This study was approved by the ethics committee of the Siriraj Institutional Review Board. Written informed consents were obtained from all patients prior to their enrollment in the study.

RESULTS

Of all 34 patients recruited, 27 (79.4%) completed the follow-ups. Seven patients were not able to attend the 6-month follow-up. The demographic data of the patients enrolled were described in Table 1.

Subjective evaluation of the upper facial laxity by photographic evaluation by 2 blinded dermatologists using the quartile grading scale was presented in Figure 2. As early as 1-week follow-up, 64.7% had minimal improvement (0-25%) when compared to the baseline. At 1-month follow up, majority (82.4%) still had minimal improvement, which was consistent until the 3-month follow-up (67.6%). However, at 6-month follow-up, most (51.9%) showed no improvement (0%) when compared to baseline. The clinical improvement of the upper facial laxity after MFU treatment is presented in Figure 3.

The eyebrow height measurements taken using ImageJ Software were described in Table 2. The average mean difference in eyebrow height was significantly increased on all follow-ups when compared to the baseline (p=0.000). The average eyebrow height elevation was 1.51 mm at 1-month, 1.25 at 3-month and 1.22 mm at 6-month follow-up. There was an increasing in the upper facial volume from baseline compared to all follow-ups as presented in Table 3, although it was not statistically significant.

The evaluation of textural irregularities (wrinkles, skin roughness and melanin concentration) using Antera3D® were described in Table 4. There was a decreasing in the wrinkle index on all follow-ups when compared to the baseline, however it was significant only on 1-week and 6-month follow-up (p=0.002 and p=0.010 respectively). Skin roughness also showed significant improvement at 6-month follow-up (p=0.004). Melanin concentration showed no significant difference from baseline compared to all follow-up visits.

Patients' self-assessment was also recorded on all follow-ups. As early as 1-week follow-up, majority (46.4%) reported minimal improvement, which continued to increase at 1-month (46.4% moderate improvement) and 3-month follow-up (53.6% marked improvement). However, on the 6-month follow-up, there was a decline in the improvement score wherein majority (38.1%) had moderate improvement (Figure 4).

All patients developed mild erythema immediately after the treatment with spontaneously resolved at 1-week follow-up. No post-inflammatory hypo- or hyperpigmentation, bullous formation, scar, crusting, oozing and any serious adverse events were recorded in this study.

Characteristics	Value (n=34)
Age, mean ± SD*	35.41 ± 6.31* (range 20-49)
Sex, n (%)	
Male	5 (14.7)
Female	29 (85.3)
Skin type, n (%)	
III	1 (2.9)
IV	29 (85.3)
V	4 (11.8)
Number of Lines 2.0 mm transducer	32.29 ± 9.19
Mean pain score	3.03 ± 1.57

*SD, standard deviation

TABLE 1 Demographic data of patients enrolled in the study.

Follow-Up	Eyebrow Height Measurements		
	Mean ± SD(cm)	Mean Difference(cm)	p-value
Baseline	2.95 ± 0.45		
1-week follow-up	3.05 ± 0.50	0.095 ± 0.015	**0.000***
1-month follow-up	3.10 ± 0.48	0.151 ± 0.016	**0.000***
3-month follow-up	3.08 ± 0.45	0.125 ± 0.016	**0.000***
6-month follow-up	3.07 ± 0.46	0.122 ± 0.017	**0.000***

*p-value compared to baseline with statically significant difference

TABLE 2 Assessment of eyebrow height measurement using ImageJ Software.

Follow-Up	Difference of volume compared to baseline (mm^3)		
	Mean ± SD*	Median	p-value
1-week follow-up	0.15 ± 0.77	0.131	
1-month follow-up	0.57 ± 0.76	0.288	0.18
3-month follow-up	0.45 ± 0.59	0.454	0.96
6-month follow-up	0.36 ± 0.63	0.166	0.372

*SD, standard deviation

TABLE 3 Assessment of upper facial volume measurement using Vectra H1 Imaging System®

Evaluation	Baseline	1-week follow up	1-month follow up	3-month follow up	6-month follow up
Wrinkles	15.86 ± 3.72	14.83 ± 3.53 (p = 0.002)*	15.51 ± 3.85 (p= 1.000)	15.38 ± 4.15 (p= 0.702)	14.97 ± 3.79 (p= 0.010)*
Skin Roughness	16.07 ± 4.38	15.21 ± 4.35 (p=0.092)	15.77 ± 4.52 (p= 1.000)	15.57 ± 4.91 (p= 1.000)	15.63 ± 4.28 (p=0.004)*
Melanin concentration	0.673 ± 0.075	0.673 ± 0.073 (p= 1.000)	0.671 ± 0.073 (p= 1.000)	0.673 ± 0.079 (p= 1.000)	0.665 ± 0.081 (p=0.745)

*p-value compared to baseline with statistically significant difference

TABLE 4 Assessment of wrinkles, skin roughness and melanin concentration using Antera3D®

DISCUSSION

Upper facial aging involves progressive loss of volume, sagging of facial soft tissue, skeletal bone loss, decrease in skin elasticity, skin damage and wrinkles at the forehead and periocular area.[15] Currently, HIFU technology has become a popular non-invasive aesthetic treatment for lifting and tightening because of its excellent safety profile when compared to the gold standard, rhytidectomy.[16,17]

HIFU delivers highly focused energy that is deposited in the form of heat leaving the surrounding area unaffected. The lesion that it creates are targeted, predictable and reproducible in terms of depth, size, and shape based on hand-piece frequency and source conditions (power, exposure time, and energy).[18] A previous study concluded that HIFU delivers energy in a transcutaneous manner without damaging the skin surface since the biophysical properties of the skin (transepidermal water loss, temperature, hydration and erythema) did not change significantly after treatment and at long term follow up of 24 weeks.[19] Confirmation by histology shows that the skin tightening and lifting effect of HIFU is attributed to an increase in dermal collagen with thickening of the dermis and straightening of elastic fibers in the reticular dermis after treatment.[20]

In this study, we reported that there was an increase in upper facial volume, but no significant difference between each follow-up visits when compared to the baseline. The increase in upper facial volume indicated the eyebrow lifting effect of MFU (average of 1.51 mm and 1.25 mm at 1-month and 3-month follow-up, respectively). At 6-month follow-up, the average eyebrow height was 1.22 mm which highlights that the lifting effect of MFU was maintained until 6 months.

A study was conducted among 25 patients with facial laxity treated with MFU-V (3.0 mm transducer, 7 MHz) and the average eyebrow lift was 0.47 mm at 3-months follow-up and a 0.12 mm decrease from the baseline at 6-month follow-up.[21] The decline in brow lift after 3-months follow-up was also reported in our study, and according to the authors this could be due to possible volume loss caused by the thermal injury in MFU-V. Another study with 30 patients (86%) demonstrated an average of 1.7 mm eyebrow height elevation at 3-month follow-up after MFU-V (4.5 mm transducer, 7 MHz) treatment on the forehead.[14] The variability among the results could be due to the different transducers used in each study and the number of lines delivered to the area. It was demonstrated that higher frequency waves produce more shallow focal injury zones while lower frequency produces a greater depth of penetration with deeper thermal coagulation points.[13]

The difference between MFU-V and MFU used in this study was the transducers. MFU-V utilized 3.0 mm and 4.5 mm transducer at 7 MHz to deliver micro-focused beam in dermis resulting in coagulation at targeted areas. Each beam will create thermal coagulation point with 0.5 mm in diameter. [14,21] In contrast, 2.0 mm transducer with 5.5 MHz was used to deliver macro-focus beam to create coagulation in larger area to stimulate collagen remodeling effectively. Even though the depth of the transducer used in this study delivering the energy to

more superficial dermis (2.0 mm vs. 3.0 mm or 4.5 mm), the side of thermal coagulation point created by the macro-focused beam of energy was larger when comparing to micro-focused beam (1.0 mm vs. 0.5 mm in diameter, respectively).

We also evaluated the quantitative findings of wrinkles, which improved significantly at 1-week and 6-month follow-up. The immediate effect is theoretically related to the tissue-swelling effect that occurs after ultrasound treatment. This was consistent with a previous study done wherein the mean wrinkles score reduction at 3-months follow-up was statistically significant ($p = 0.0222$).[21]

The mean pain score was 3.03 ± 1.57, which shows that the treatment procedure was well tolerated by the patients. To further optimize patient comfort during treatment, it was recommended to recline the patient at 30 degrees instead of lying flat to prevent the increase in vascular stasis to the head and neck, which may cause heat sinking and increased perception of pain.[22] Different pharmacologic modalities such as inhalation of 50% oxygen/50% nitrous oxide, oral diazepam (5-10 mg) 30 minutes before procedure, ibuprofen (800 mg), intramuscular injection of meperidine (50-100 mg), promethazine (50 mg) or ketorolac (60 mg) and regional lidocaine block were also recommended.[22]

Unlike other energy devices, focused ultrasound is a "color-blind" technology as the energy is not selectively absorbed by chromophores.[16] In our study, we found no significant increase in the quantitative melanin concentration of the patients, which could translate there was no occurrence of post-inflammatory hyperpigmentation. In terms of safety, all our patients developed mild erythema immediately after the treatment, which resolved spontaneously. This is a commonly reported transient adverse event of HIFU.[23] Other than that no serious adverse event was noted. These supports the finding that MFU with 2.0 mm transducer is safe in Asian skin types.

Limitation of this study were the small number of patients and having no control group since this was a pilot study. There were also drop-outs because of lost to follow-up after 6 months of treatment. Moreover, we used the quartile scale in grading the clinical improvement and patients' self-assessment scores. The grading system commonly used to evaluate cosmetic results are the Subject Global Aesthetic Improvement Scale (SGAIS) and the Physician Global Aesthetic Improvement Scale (PGAIS) since it clearly defines the degree of improvement.[17,24]

We would recommend further studies to be conducted and to extend the duration of follow up, to assess if the results can be maintained for at least a year. Another study can be done to focus on histological data following 2.0 mm transducer ultrasound pulses.

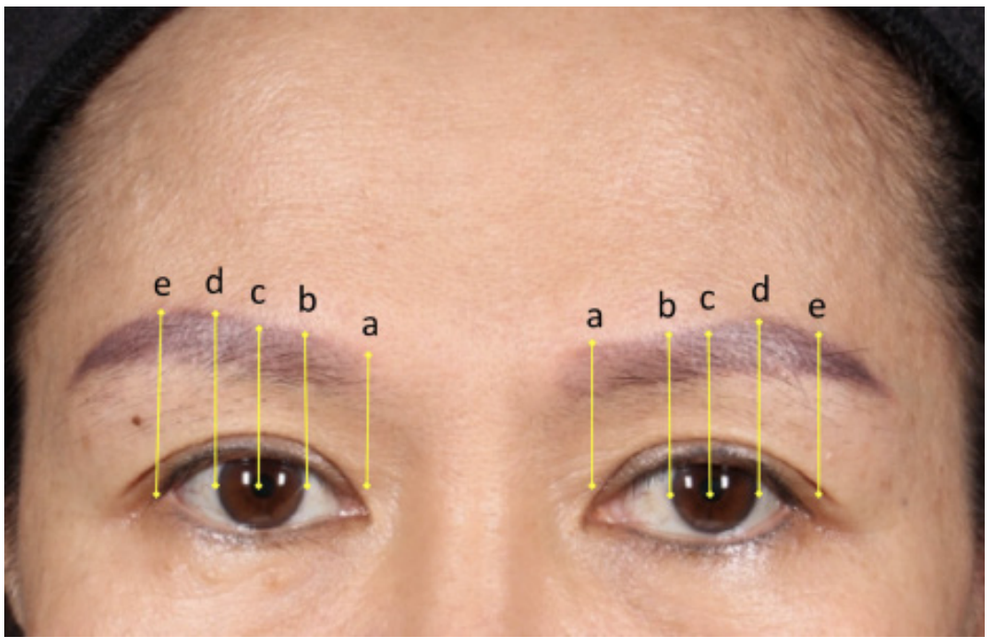
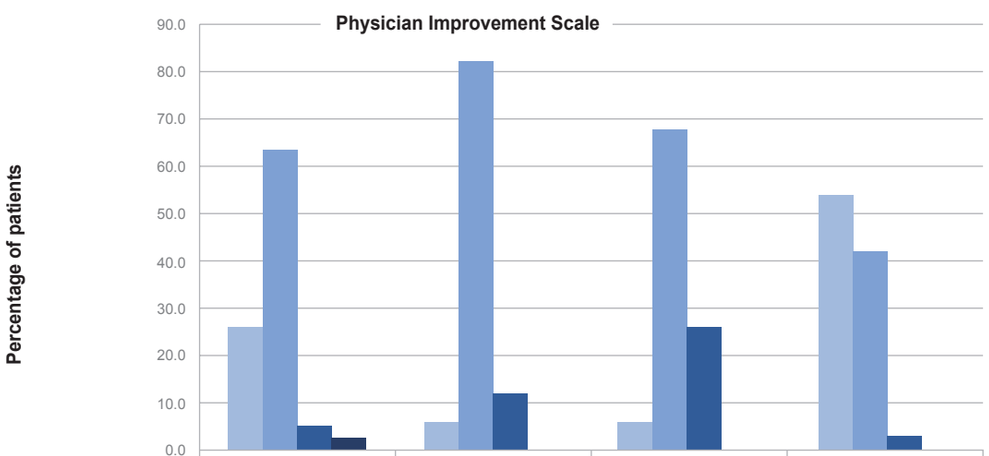


Figure 1 Eyebrow height measurement using ImageJ software.



	1-week follow up	1-month follow up3	-month follow up6	-month follow up
0 = No improvement	26.5	5.9	5.9	53.9
1 = 1%~25% improvement	64.7	82.4	67.6	42.3
2 = 26%~50% improvement	5.9	11.8	26.5	3.9
3 = 51%~75% improvement	2.9	0.0	0.0	0.0
4 = 76%~100% improvement	0.0	0.0	0.0	0.0

Figure 2 Physicians' evaluation of upper facial laxity by comparative evaluation of photographs from baseline to follow-ups.

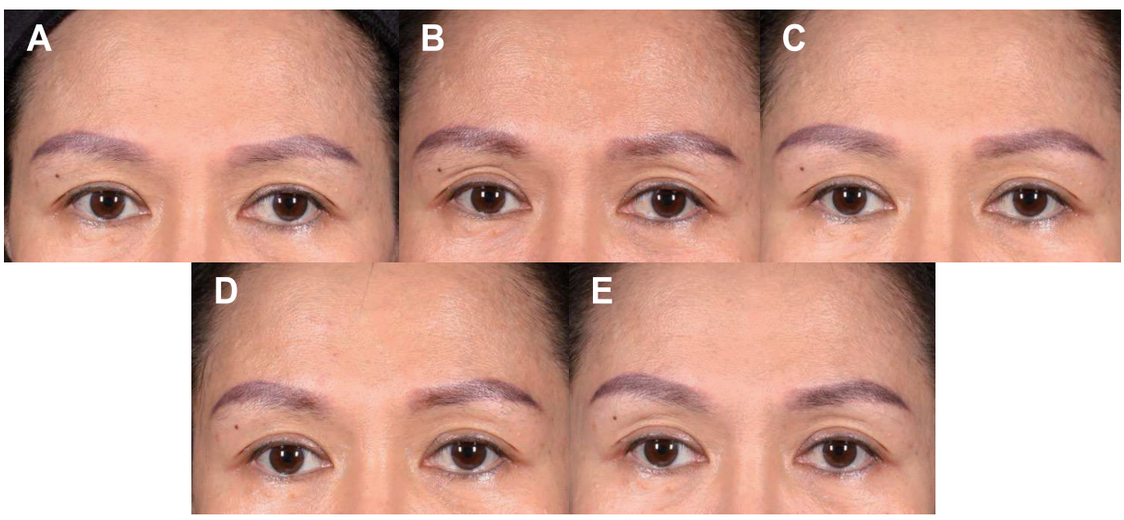
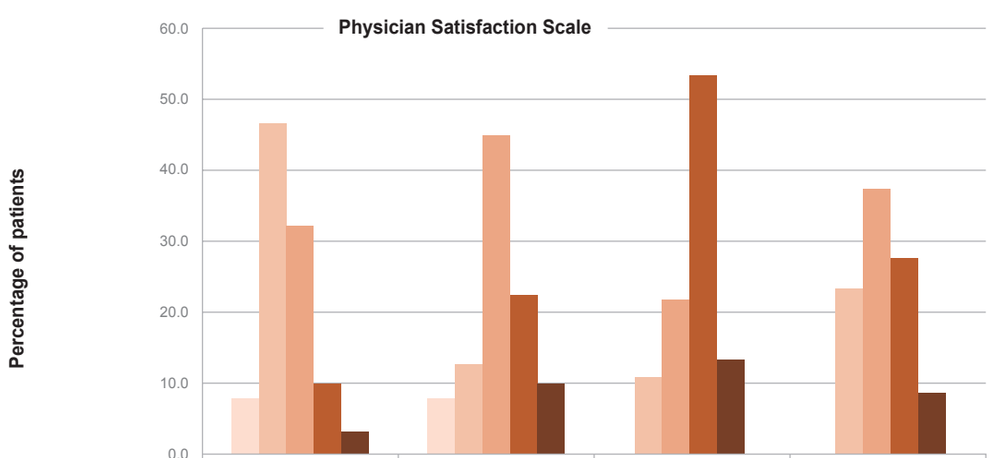


Figure 3 Clinical improvement of upper facial laxity after 1 HIFU treatment from (A) baseline, (B) 1-week follow-up, (C) 1-month follow-up, (D) 3-month follow-up and (E) 6-month follow-up.



	1-week follow up	1-month follow up	3-month follow up	6-month follow up
0 = No improvement	7.1	6.9	0.0	0.0
1 = 1%~25% improvement	46.4	13.8	10.7	23.8
2 = 26%~50% improvement	32.2	44.8	21.4	38.1
3 = 51%~75% improvement	10.7	24.1	53.6	28.6
4 = 76%~100% improvement	3.6	10.4	14.3	9.5

Figure 4 Patients' self-assessment on the improvement of upper facial laxity at baseline and follow-ups.

CONCLUSIONS

The MFU device is a safe and effective treatment for upper facial laxity and skin textural irregularities in Thai patients.

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