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Efficacy and Safety of Microfocused Ultrasound With Visualization in Abdominal Skin Laxity: A Randomized, Comparative Study

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Background and Objectives: Microfocused ultrasound with visualization (MFU-V) has been approved for the treatment of skin laxity on several areas including the eyebrows, neck, and submental area. This study aims to determine the efficacy of MFU-V for the treatment of abdominal skin laxity using two different treatment protocols.
Study Design/Materials and Methods: Thirty female patients with abdominal skin laxity were enrolled. Each side of the abdomen was randomly assigned to receive a single session of single-plane MFU-V treatment (4.5 mm) or dual-plane MFU-V treatment (4.5 and 3.0 mm). Improvement scores (0–10) were assigned by a blinded physician and patients at 1, 3, and 6 months after treatment.
Results: Twenty-eight female patients completed the study. The physician-evaluated mean improvement scores in single-plane treatment were 3.03 (±1.26), 3.43 (±1.35), and 2.18 (±0.86) at 1-, 3-, and 6-month follow-up, respectively. For dual-plane treatment, the scores were 3.11 (±1.23), 3.39 (±1.34), and 2.02 (±0.79). There was no statistically significant difference between single- and dual-plane treatment at each time point. A similar pattern of improvement was observed in patient-rated mean improvement scores. Patients who had undergone childbirth had significantly higher physician and patient-rated mean improvement scores than those who had not in both single- and dual-plane treatments. In addition, a significant reduction of mean waist circumference was observed in patients who had undergone childbirth. The median pain scores were 5.25 for single-plane treatment and 4.29 for dual-plane treatment ($P = 0.20$).
Conclusion: Both single- and dual-plane MFU-V treatments showed comparable efficacies in treating abdominal skin laxity. The effect is more pronounced in patients who had undergone childbirth. Lasers Surg. Med. © 2020 Wiley Periodicals, Inc.

Key words: body contouring; HIFU; laser; pregnancy; skin tightening

INTRODUCTION

Increasingly microfocused ultrasound with visualization (MFU-V) has been widely used for skin tightening. It works by delivering focused energy pulses to the deep reticular dermis and superficial musculoaponeurotic system, inducing collagen denaturation and tissue thermal coagulation [1]. This, in turn, stimulates the synthesis and remodeling of a new tissue [2]. The United States Food and Drug Administration (USFDA) has approved the use of MFU-V in eyebrow lifting, submental lifting, neck tissue lifting, and improving lines and wrinkles of décolletage. Various studies have demonstrated its efficacy in improving skin laxity of other body areas such as the arms, thighs, knees, elbows, and buttock [3,4]. However, data regarding the efficacy of MFU-V for the treatment of abdominal laxity is limited. The aim of this study was to determine the efficacy and safety of MFU-V and compare two different treatment protocols in treating abdominal skin laxity.

MATERIALS AND METHODS

Patients

Female patients with abdominal skin laxity were recruited in this prospective, single-blinded, randomized controlled study. The inclusion criteria were ages of 18–70 years and the presence of abdominal skin laxity. Exclusion criteria included inflammation or infection, scar, metal implants, prior surgery, or aesthetic procedure at the treatment site, history of lidocaine allergy, any known bleeding disorder, concomitant use of anticoagulants, history of connective tissue disease, smoking, pregnancy, and lactation. The study received institutional review board approval from the Committee of Human Rights Related to Research Involving Human Subjects, Ramathibodi Hospital, Mahidol University (Protocol number MURA2018/255) and Thai Clinical Trial Registration number TCTR20190417007. Informed consent was obtained from the patients after having

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thoroughly reviewed the research protocol, possible outcomes, and adverse events. Upon enrollment, the patients' demographic data such as sex, age, Fitzpatrick's skin type, and height were recorded.

Treatment Procedure

The abdomen of each patient was divided into left and right sides at the midline using the umbilicus as a landmark. Block randomization was used to assign single-plane treatment to one side and dual-plane treatment to the contralateral side. Each side was measured as 5×5 inches lateral and inferior to the umbilicus. Local anesthesia was obtained using 1% lidocaine with adrenaline injection in a field block manner throughout the assigned treatment area. MFU-V (Ulthera System; Ulthera, Inc., Mesa, AZ) was used on both sides of the abdomen. For single-plane treatment, a transducer with a frequency of 4 MHz, focal depths of 4.5 mm, energy of 1.2 J, and treatment length of 25 mm was used for a total of 200 lines (100 lines for 2 passes). For dual-plane treatment, the 4.5 mm transducer with the same settings was used for the first 100 lines. Then, the second pass was performed using a 7 MHz, 3.0 mm transducer with energy of 0.45 J, and 25 mm of treatment length for an additional 100 lines. All treatments were performed in one session and the patients were followed up at 1, 3, and 6 months post-treatment.

Outcome Evaluation

Standardized two-dimensional digital photographs were taken at baseline, immediately after treatment, and 1, 3, and 6 months after the treatment. Fixed camera and lighting conditions were used in all photographic sessions. Waist circumferences were also measured at the narrowest section of the torso at every visit with a single measuring tape. Body mass index (BMI) was calculated by subtracting the weight (kg) by height^2 (m^2). Each patient was asked to rate the improvement score at every follow-up visit using a continuous visual analog scale with scores ranging from 0 (no improvement) to 10 (significant improvement). A blinded dermatologist also rated digital photographs of each follow-up visit for improvement of skin laxity from baseline using the same continuous visual analog scale.

Adverse Effects

Possible adverse effects including pain during the procedure, skin tenderness, edema, and bruising were recorded at each visit. Pain scores were evaluated using a visual analog scale (0 = no pain; 10 = extremely pain).

Statistical Analysis

Numerical data were expressed as mean ± standard deviation for data with normal distribution and median (range) for data with nonnormal distribution. Categorical data were expressed as frequency (percentage). STATA/SE version 14.2 (STATA Corp., College Station, TX) was used for data analysis. Repeated one-way analysis of variance was used for repeated measurement data (i.e., waist circumference, BMI). A linear mixed-effects model was used to determine statistical relevance of the outcomes. Mann–Whitney test was used for pain scores. A $P < 0.05$ was considered statistically significant.

RESULTS

Patients' Characteristics

A total of 30 female subjects were enrolled in the study. Two subjects were lost to follow-up and 28 were retrieved and analyzed. Nine of the 28 patients had undergone childbirth in the past. The mean age of the subjects was 43.3 (±8.79). Most of the subjects (90%) had Fitzpatrick's skin type III. Demographic data are summarized in Table 1.

Physician Evaluation

The overall mean improvement scores in single-plane treatment were 3.03 (±1.26), 3.43 (±1.35), 2.18 (±0.86) at 1-, 3-, and 6-month follow-ups, respectively. For dual-plane treatment, the mean improvement score at 1-, 3-, and 6-month follow-ups were 3.11 (±1.23), 3.39 (±1.34), and 2.02 (±0.79). There was no statistically significant difference between single-plane and dual-plane treatment at each time point.

On the basis of the subgroup analysis, the physician-rated improvement scores at 1-month follow-up in subjects who had undergone childbirth were 3.89 (±1.45) and 4.11 (±1.27) for single-plane treatment and dual-plane treatment, respectively. In patients who never gave birth, the scores were 2.63 (±0.96) for single-plane treatment and 2.63 (±0.96) for dual-plane treatment. Both scores were increased at 3-month follow-ups but trended downwards at 6-month follow-ups in single-plane and dual-plane treatments. Subjects who had undergone childbirth

TABLE 1. Demographic Data

Data	Undergone childbirth ($N = 9$)	Never gave birth ($N = 19$)	P value
Mean age, years (SD)	40.78 (±6.51)	44.53 (±9.8)	0.309
Skin type; N (%)			0.234
3	7 (77.8%)	18 (94.7%)	
4	2 (22.2%)	1 (5.3%)	
Baseline mean waist circumference (cm)	82.89 (±6.25)	86.74 (±9.13)	0.235
Baseline mean BMI (SD)	22.70 (±2.57)	24.59 (±0.89)	0.196

BMI, body mass index.

TABLE 2. Physician- and Patient-Rated Improvement Scores for Single-Plane Treatment

Evaluation	Undergone childbirth, mean improvement score (SD)	Never gave birth, mean improvement score (SD)	*P* value
Physician evaluation			
Visit 2 (1 month)	3.89 (±1.45)	2.63 (±0.96)	<0.01
Visit 3 (3 month)	4.22 (±1.56)	3.05 (±1.08)	<0.01
Visit 4 (6 month)	2.61 (±1.05)	1.97 (±0.70)	0.13
Patient evaluation			
Visit 2 (1 month)	5.71 (±2.42)	4.20 (±2.13)	0.12
Visit 3 (3 month)	6.48 (±1.46)	4.68 (±2.45)	0.06
Visit 4 (6 month)	5.21 (±2.14)	2.63 (±3.29)	<0.01

showed statistically significant higher improvement scores in comparison with those who never gave birth in both single-plane treatment at 1- and 3-month follow-up periods ($P < 0.01$) and dual-plane treatment at 1- and 3-month follow-up periods ($P < 0.01$). There was no statistically significant difference in improvement scores between the two groups at the 6-month follow-up period in both treatment protocols (Tables 2 and 3). Digital photographs of the subjects who had undergone childbirth (before treatment and at each follow-up visits) are shown in Figures 1 and 2.

TABLE 3. Physician-Rated and Patient-Rated Improvement Scores for Dual-Plane Treatment

Evaluation	Undergone childbirth, mean improvement score (SD)	Never gave birth, mean improvement score (SD)	*P* value
Physician evaluation			
Visit 2 (1 month)	4.11 (±1.27)	2.63 (±0.90)	<0.01
Visit 3 (3 month)	4.33 (±1.58)	2.95 (±0.97)	<0.01
Visit 4 (6 month)	2.44 (±0.81)	1.82 (±0.71)	0.11
Patients evaluation			
Visit 2 (1 month)	5.80 (±2.10)	4.05 (±2.20)	0.07
Visit 3 (3 month)	6.54 (±1.46)	4.48 (±2.50)	<0.05
Visit 4 (6 month)	5.32 (±2.33)	2.55 (±3.28)	<0.01

Patients Evaluation

The overall patient-rated mean improvement scores in single-plane treatment were 4.69 (±2.30), 5.26 (±2.32), and 3.46 (±3.18) at 1-, 3- and 6-month follow-ups, respectively. For dual-plane treatment, the mean improvement scores at 1-, 3-, and 6-month follow-ups were 4.61 (±2.29), 5.14 (±2.40), and 3.44 (±3.24). There was no statistically significant difference between single and dual-plane treatment at each time point.

When taking into consideration the history of childbirth, similar patterns were observed in patient-rated improvement scores. At 1-month follow-up, improvement scores in subjects who had undergone childbirth were 5.71 (±2.42) and 5.8 (±2.10) for single-plane treatment and dual-plane treatment, respectively. In patients who never gave birth, the improvement scores were 4.20 (±2.13) for single-plane treatment and 4.05 (±2.20) for dual-plane treatment. The improvement scores were further increased at 3-month follow-up, but trended downwards at 6-month follow-up visits in both single-plane treatment protocols. Subjects who had undergone childbirth had statistically significant higher improvement scores than those who never gave birth in both single- and dual-plane treatment protocols at 6-month follow-ups ($P < 0.01$) (Tables 2 and 3).

Waist Circumference and BMI

The mean waist circumference in subjects who had undergone childbirth was reduced from 82.89 (±6.25) cm at baseline to 80.30 (±7.68) cm at 6-month follow-up ($P < 0.01$) while in those who never gave birth, it was reduced from 86.74 (±9.13) to 86.41 (±8.97), $P = 0.40$ (Fig. 3). On the contrary, the mean BMIs were slightly increased in both groups (22.70 ± 2.57 to 22.96 ± 3.45, $P = 0.20$ in subjects who had undergone childbirth vs. 24.59 ± 0.89 to 24.82 ± 3.71, $P = 0.11$ in those who had not) (Fig. 4).

Adverse Effects

The median pain scores were 5.25 (2–10) for single-plane treatment and 4.29 (0–8) for dual-plane treatment ($P = 0.20$). Erythema and edema were noted in all treated sites, which resolved spontaneously within 1–2 weeks. Bruising was observed along local anesthesia injection sites, which also resolved spontaneously within 10 days. Skin tenderness was observed by all patients on both treatment sides, which spontaneously subsided in 2 weeks without any treatment. No other adverse events were found.

DISCUSSION

Focused ultrasound technology is becoming increasingly and widely used in various aesthetic procedures including skin rejuvenation, improving skin laxity, body contouring, and cellulite reduction [5]. Specifically, MFU-V is known for its common use as a noninvasive skin tightening device. Compared with radiofrequency (RF), MFU-V shows higher neocollagenesis and neoelastogenesis in the deep

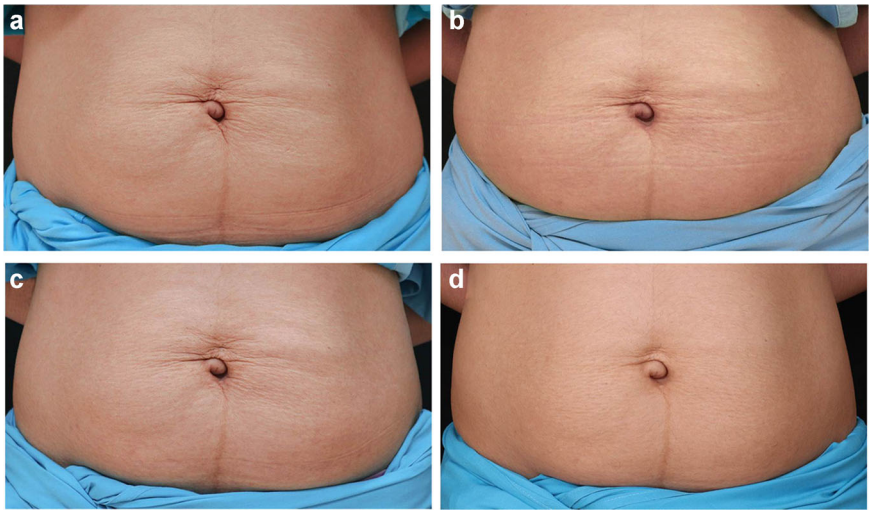

Fig. 1. Digital photographs before treatment and at each follow-up visits. The left side of the abdomen was treated with a single-plane protocol while the right side of the abdomen was treated with dual-plane protocol. (**a**) Before treatment, (**b**) 1-month follow-up, (**c**) 3-month follow-up, and (**d**) 6-month follow-up.

reticular dermis [6]. This suggests that MFU-V may be superior to RF in noninvasive skin tightening, making it a more favorable choice in this indication. In addition, MFU-V is approved by the USFDA for noninvasive browlifts, submental, and neck tissue tightening.

Over the years, an increasing number of newer indications and their appropriate settings for MFU-V had been published with promising results. This includes the treatment of perioral wrinkles, infraorbital laxity, enlarged facial pores, and skin tightening (arm, elbow, thigh, and knee) [3,4,7-11]. In our study, we evaluated the efficacy and safety of two treatment protocols of MFU-V in treating abdominal skin laxity. Although we did not compare the efficacy of MFU-V vs. placebo, we still observed improvement in both treatment arms when compared with baseline.

Our results showed no statistically significant difference in the improvement of skin laxity between single- and dual-plane treatment at 1 and 3 months after treatment. This insignificant difference between single- and dual-plane may arise from the fact that the average thickness of the skin plus subcutaneous tissue in the abdominal area in females ranges from 5.15 to 27.40 mm depending on individual BMI [12,13]. Both single- and dual-plane protocols reach a maximum depth of 4.5 mm and therefore can only target the dermis resulting in degrees of improvement that were not statistically different.

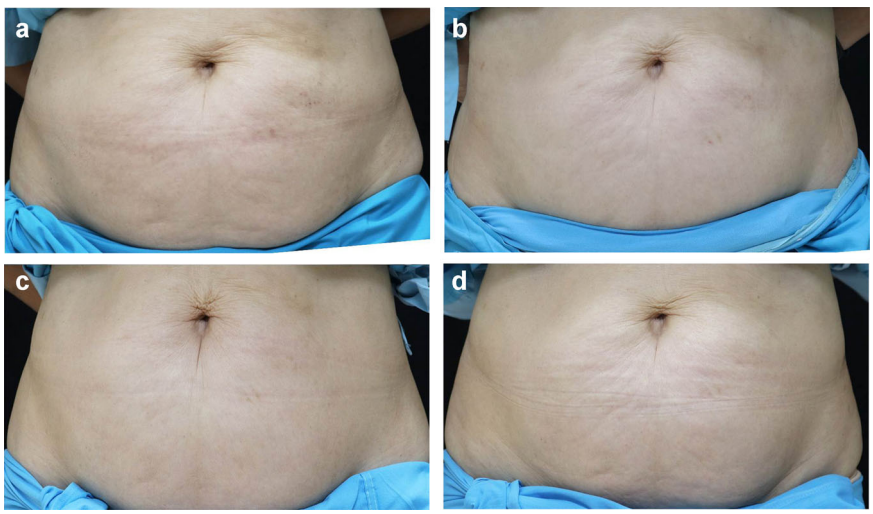

Fig. 2. Digital photographs before treatment and at each follow-up visits. The left side of the abdomen was treated with a single-plane protocol while the right side of the abdomen was treated with dual-plane protocol. (**a**) Before treatment, (**b**) 1-month follow-up, (**c**) 3-month follow-up, (**d**) 6-month follow-up.

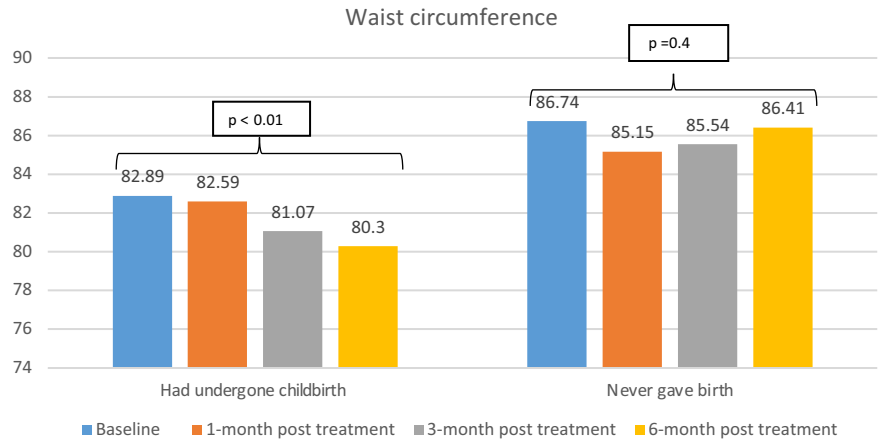

Fig. 3. Waist circumferences in subjects who had undergone childbirth versus those who had not.

Similar findings were observed in a study by Baumann et al. [14] where dual-plane MFU-V treatment for neck laxity received a higher improvement and satisfaction scores than single-plane treatment, however, the difference did not reach statistical significance. Given that there was a slightly higher overall pain score for single-plane treatment and the pain was mostly noted during the second pass with the 4.5 mm transducer and results showed an insignificant difference in improvement, we proposed that dual-plane treatment protocol should be considered over single-plane.

Another interesting observation is that the improvement scores at 6 months trended downwards in comparison with prior follow-up visits. We suspect that the diminishing treatment effect at 6 months may be a result of an inadequate number of treatment lines. A study by Alster et al conducted on the arms, thighs, and knees delivered approximately 150 lines to the three areas that showed improvement of up to 6 months [3]. Goldberg et al. [4] delivered over 900 lines of treatment on one side of the buttock and also found an improvement of up to 6 months. On the contrary, Gold et al. [11] found that patient improvement scores started to decline at 6 months after MFU-V treatment of approximately 320 lines to the knees. Notably, one study found the treatment effect to last up to 1 year after dual-plane MFU-V treatment [9]. In this study, the treatment lines varied in each individual depending on the size and location of the area treated. On the basis of these observations, we believe that changing the number of treatment lines as well as treatment sessions to appropriately address skin laxity problems on the abdomen in each individual may improve the treatment outcome at the 6-month follow-up period.

From our study, we found that subjects who had undergone childbirth had statistically higher improvement scores than those who had not. This may be due to a higher degree of skin laxity in the postpartum period and beyond. A study by Wang et al. [15] found that the skin of pregnant women had disruption in elastic fibers at the level mid to deep dermis, which is the level that MFU-V targets. These findings may explain why subjects who had undergone childbirth had higher improvement scores.

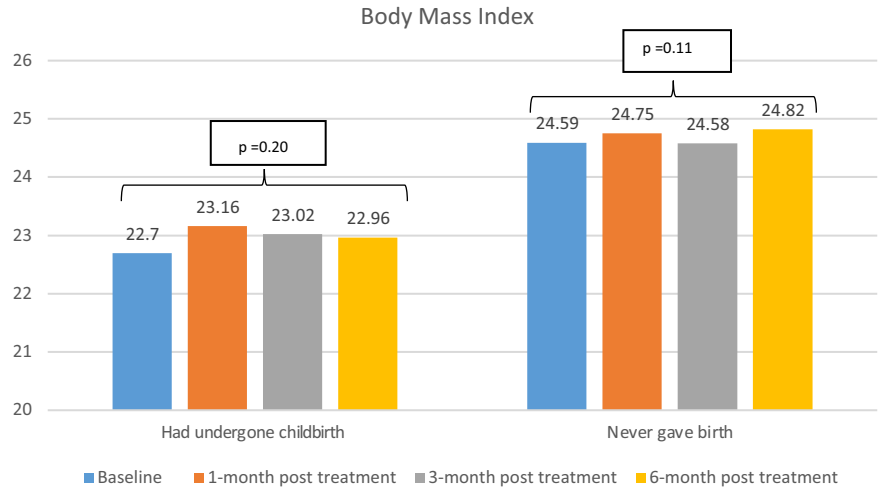

Fig. 4. Body mass index in subjects who had undergone childbirth versus those who had not.

Apart from the overall improvement scores, the mean waist circumference also followed the same trend with gradual reduction seen at 1 and 3 months. However, the mean waist circumference had a tendency to rebound at 6-month follow-up in subjects who had never undergone childbirth. Surprisingly, the mean waist circumference of subjects who had undergone childbirth continued to decrease at the 6-month follow-up visit. Again, this difference may be explained by the improvement of elastic fibers in the group that had undergone childbirth causing the overall improvement in skin laxity, which, in turn, further causes a reduction in waist circumference without a significant drop in BMI.

In terms of fat reduction, MFU-V with parameter settings used in our study was not intended to alter subcutaneous fat as the focal depth is aimed at the dermis. Therefore, the addition of a transducer that reaches a deeper level or other procedures such as cryolipolysis, radiofrequency, or low-level laser therapy that specifically target the fat may help to further improve the overall outcome in body contouring [16].

The most common side effects of MFU-V treatment in this study were transient erythema and edema that were not different between single- and dual-plane treatment. This was similar to previous studies conducted on facial and neck skin [17]. Concerning alteration of energy absorption with injectable lidocaine, lidocaine was used in a field block manner, in which lidocaine was administered in a circumferential pattern around and not under the treatment site. Therefore, we did not observe any serious side effects of MFU-V treatment as a result of injectable lidocaine. MFU-V also has no effect on epidermal barrier function or physiology of skin, making it relatively safe [18]. Another advantage of MFU-V is that skin color and chromophores have no influence on MFU-V treatment as the absorption of ultrasound energy is independent of the melanin content of the skin [19,20]. Unfortunately, bruising from MFU-V in our study could not be assessed as bruising occurred in all patients following local anesthesia injection.

The major limitations of this study were the small number of patients, the lack of histopathological evaluation, and the lack of placebo control. In addition, having a standardized method to evaluate the severity of abdominal laxity may improve the quality of results and therefore produce a more accurate assessment of the outcome.

CONCLUSION

MFU-V treatment with a 4.5 mm transducer or combined 4.5 and 3 mm transducers showed comparable results in treating abdominal skin laxity, particularly in subjects who had undergone childbirth. Pain is less in dual-plane treatment. Further studies to determine the appropriate treatment settings including the number of treatment lines and frequency of treatment sessions are required in order to produce a more pronounced and sustainable outcome.

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