A Multi-Site, Single-Blinded, Prospective Pilot Clinical Trial for Non-Invasive Fat Reduction of the Abdomen and Flanks Using a Monopolar 2 MHz Radiofrequency Device

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Background and Objectives: Demand for non-invasive body sculpting procedures has been steadily increasing, spurring the development of new energy-based technologies. This study assessed the safety and efficacy of a new monopolar 2 MHz radiofrequency (RF) device for fat reduction of the flanks and abdomen.
Study Design/Materials and Methods: Nineteen subjects from two clinical sites were enrolled in this study and received a single 15-minute treatment with the 2 MHz RF device. Up to six applicators were placed on the abdomen and/or flanks during the treatment. Follow-up assessments were scheduled 12 weeks after treatment. Efficacy evaluations included live ratings and Global Aesthetic Improvement Scale (GAIS) ratings by blinded investigators, ultrasound measurements of fat thickness, and patient-reported outcomes before and after treatment.
Results: Investigator assessments showed more than one-point change in the GAIS scale at the 12-week follow-up visit. Ultrasound measurements revealed a significant reduction in fat thickness in both the abdomen (average 24%) and the flanks (22%). The majority of the patients were satisfied with the treatment and mild self-resolving side effects were observed. No serious adverse events were reported.
Conclusions: Treatment of local adiposities with a new monopolar 2 MHz radiofrequency device leads to improvement of body contour with no downtime or side effects. Lasers Surg. Med. © 2020 Wiley Periodicals LLC

Key words: adipocytes; body contouring; fat reduction; monopolar; radiofrequency

INTRODUCTION

Body contouring procedures are one of the most sought-after cosmetic interventions in this day and age. Several factors contribute to this reality such as increased socioeconomic status across ethnicities, widespread accessibility to treatments, and media perpetuating messaging that emphasizes the importance of physical appearance [1]. While diet and exercise can ameliorate the body contour, some body areas such as the abdomen and flanks can present stubborn localized fat deposits that do not respond to lifestyle changes. In the past, invasive surgical procedures such as liposuction and abdominoplasty were the mainstay solution to this problem, and while these techniques have evolved to be safer than ever, they not only require significant downtime but commonly result in side effects such as scarring, swelling, skin necrosis, burns, and contour irregularities [2-4]. The factors, combined with technological innovation and fueled by ever increasing patient demand, has led to an explosion of non-invasive body contouring devices dominating the market. Testament to this are the latest statistics from the American Society of Dermatologic Surgery (ASDS) that show that the number of consumers seeking non-invasive body contouring procedures increased by a staggering 43% in 2018, compared with the previous year [5].

One of the leading technologies in this space are devices that, by emitting radiofrequency (RF) energy waves, provide preferential volumetric heating of the mid-to-deep dermis or subcutaneous fat layer leading to collagen stimulation and adipocyte damage, respectively [6]. These devices have a variety of applications in the field of aesthetic dermatology as they can improve laxity, reduce cellulite, rhytides, and mitigate body contouring [7]. Depending on their electrode configuration they can be classified as either monopolar or bi/multi-polar, which influences the way they affect the tissue [8]. In monopolar devices, RF waves are passed from a single electrode to subcutaneous tissues through the skin and to a return pad, whereas in devices with two or more electrodes within the same handpiece the energy passes between the electrodes. Thus, energy from monopolar devices can penetrate deeper in the tissues [9,10]. The mechanism via which RF energy leads to fat reduction is by volumetrically heating the subcutaneous layer, causing adipocyte

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instability and cell-mediated death. This was demonstrated by *ex vivo* experiments performed by Franco and colleagues that showed that heating cultured adipocytes to 45°C for 3 minutes, decreased their viability by more than 60% within 72 hours leading to gradual phagocytosis. This process was not associated with hyperlipidemia [11].

One of the early prototypes developed for fat reduction was a monopolar RF device (truSculpt™, Cutera®, Brisbane, CA) that featured an applicator consisting of a series of tightly spaced concentric rings, designed to couple energy into tissue across its entire surface. The distribution of surface electric potential could be controlled by adjusting the frequency to create uniform heating at specified volumes. Placing the applicator in a perpendicular manner to the dermal–subcutaneous junction resulted in significant, targeted heating of the fat. Importantly, thermal damage to the adipose tissue could be achieved without causing adverse side effects to the epidermis and dermis [12]. The first-generation model of this device operated at a frequency of 1 MHz and had a handpiece that could be used to treat localized fat pockets via a stamp method [13]. A later generation model operated at a higher frequency (2 MHz), had two handpieces (16 and 40 cm^2) and was improved to provide real-time temperature feedback. Two small-scale clinical trials using this device demonstrated its efficacy and safety in fat reduction in the face and submental area after two 1-hour treatments [14,15].

In this study a next generation model of this monopolar RF device (TruSculpt iD™, Cutera, Inc., Brisbane, CA) has been evaluated for its safety and efficacy in reducing localized fat from the flanks and abdomen. The device has recently been cleared by the Food and Drug Administration for non-surgical fat reduction, deep tissue heating, and lipolysis [16]. This RF device consists of six handpieces optimized to deliver treatment in glide or stamp mode while maintaining uniform energy distribution (Fig. 1A). Each handpiece incorporates a temperature sensor measuring skin temperature to assure appropriate energy delivery and thus safety. The system adjusts energy output based on this measurement. At 2 MHz, an inverted temperature gradient is created such that the fat heats up more than the skin, so it efficiently induces adipocyte apoptosis without damaging the cutaneous layers. This was shown by inserting a thermal probe into the fat at 1.5 cm and taking measurements while ramping up the temperature (Fig. 1B). However, the efficacy is increased, enabling treatment times to be shortened to 15 minutes.

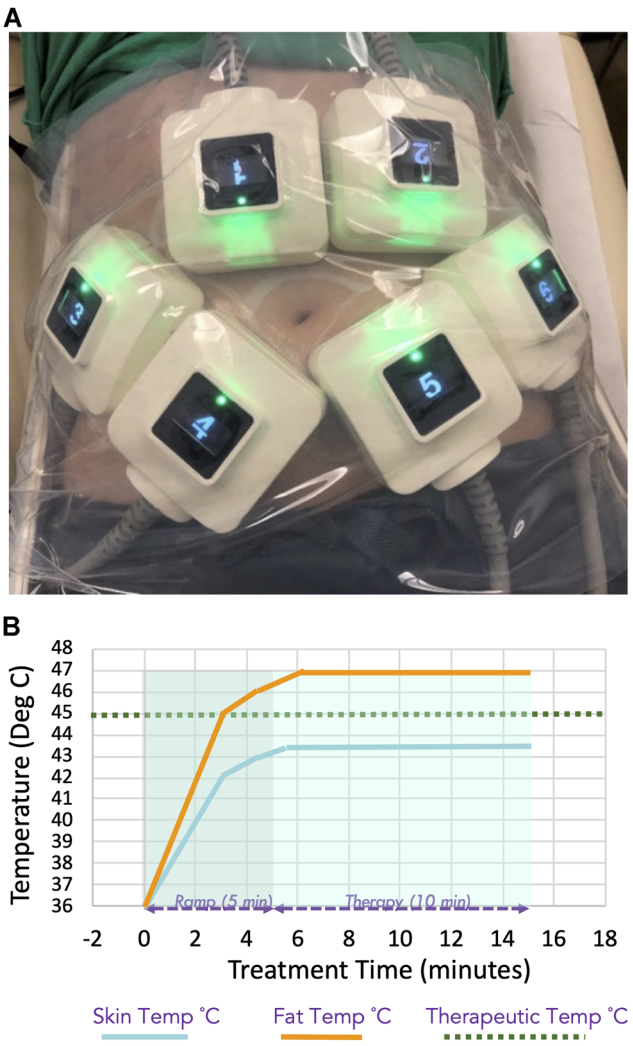

Figure 1 (**A**) Example of a six handpiece 2 MHz radiofrequency device configuration applied to the abdominal region of a patient; (**B**) graph depicting the inversion curve unique to this device (i.e., skin temperature is continuously monitored and energy delivery is automatically adjusted to reach and hold a therapeutic temperature of ~43°C in the skin, while maintaining a fat temperature of >3–4°C higher). A thermal probe was inserted at 1.5 cm in the fat layer of a subject and temperature measurements were taken while ramping up the temperature. This evaluation was done in the clinic under the direction of our Medical Director Dr. Ronan.

MATERIALS AND METHODS

Study Participants

Nineteen participants from two clinical sites were enrolled in the study after meeting the inclusion/exclusion criteria and signing informed consent forms. Eligible participants were 18–65 years old, non-smokers for at least 6 months before the study start, and with visible fat bulges in the treatment area (flanks/abdomen). Participants also had to refrain from undergoing other procedures in the treatment area and had to maintain the same weight, diet, and lifestyle during the study. Exclusion criteria included pregnancy, breastfeeding, any medical condition contraindicating the application of an electromagnetic field, heart disorders, unhealed wound in abdominal area, presence of metal implants, skin abnormality in the treatment area, allergy/sensitivity to adhesive pads, prior non-invasive cosmetic procedures within 3 months of the study start in the treatment area, and any prior invasive cosmetic surgery to the target area, such as liposuction. The mean age of the participants was 40.3 (26–59) and mean body mass index (BMI) prior to treatment was 24.5. See Table 1 for the baseline demographic profile.

TABLE 1. Demographic and Baseline Characteristics of Subjects Enrolled in the Study

Age (years; mean)	40.3 (26–59)
Gender	
Female	15
Male	4
Ethnicity	
Hispanic	2
Non-Hispanic	17
BMI (mean)	24.5 (18–31.5)
Treatment area	
Flanks	17
Abdomen	19

BMI, body mass index.

Study Design

This was a prospective, multi-center, single-blinded pilot clinical trial conducted in accordance with the principles of the Declaration of Helsinki, current GCP guidelines, and IRB approval. Subjects received a treatment in the flanks and/or abdomen with a follow-up at 12 weeks post-treatment.

Treatment

Subjects received a 15-minute treatment with the monopolar RF 2 MHz device (TrusculptiD, Cutera, Brisbane, CA) to the abdomen and/or flanks. The device features six 40 cm^2 hands-free RF handpieces with 300 W output at 2 MHz that can be placed simultaneously over multiple localized fat pockets. These handpieces can cover an area up to 300 cm^2 on the abdomen and flanks, and the treatment can be completed in 15 minutes. In this study, up to six RF handpieces were applied using an adhesive return pad, which served as the grounding point to return the electric current to the console during operation. The gap between handpieces was up to 0.75 cm to consistently induce apoptosis of the subcutaneous fat across and between handpieces. The temperature setting started at 43°C, was increased gradually to >45°C within 5 minutes and maintained there for 10 minutes for deep volumetric heating of the fat tissue. Skin surface temperature was continuously monitored.

Study Efficacy Assessments

Efficacy assessments comprised of a combination of blinded investigator evaluations, change in ultrasound measurements, and subject satisfaction ratings. The primary endpoint was change of one point on the Global Aesthetic Improvement Scale (GAIS) scale during live ratings by three blinded reviewers; GAIS scale: 0 = no improvement, 1 = mild improvement, 2 = moderate improvement, 3 = significant improvement. Additional investigator evaluations were correct identification of the baseline and final treatment digital photographs by at least two of the three blinded reviewers in 75% of the subjects. Biophysical assessments included changes in ultrasound measurements of the subcutaneous fat from the baseline visit to the 12-week follow-up visit. Subject ratings were conducted using five-grade patient satisfaction scale: 1 = extremely satisfied, 2 = satisfied, 3 = neutral, 4 = dissatisfied, and 5 = extremely dissatisfied. The likelihood of repeating the treatment and recommending it to others were also addressed in subject questionnaires.

Safety and Tolerability Assessments

For the assessment of pain intensity, a visual analog pain scale (VAS) was used during and after treatment. Skin responses occurring up to 30 minutes following treatment were evaluated by the study physician and documented. Expected responses included erythema, edema, purpura, and hematoma. The severity of the response was rated, with "0" indicating none and "4" indicating severe. The occurrence of adverse events was monitored throughout the study.

Ultrasound Analysis

Fat thickness was measured by a single technician by ultrasound (Philips HD 11 XE; Philips, Amsterdam, Netherlands) using a linear transducer with a frequency of 6 to 18 MHz before the treatment and at the 12-week follow-up visit. To minimize variability, the probe was positioned on the previously demarcated points in the treatment area with coupling gel and without tissue compression. Images were analyzed through quantitative measurements of the subcutaneous tissue between the anatomic planes (dermis and muscular fascia), and the thickness of the fat layer at the treatment area was measured in millimeters.

Photography

The 3D LifeViz (QuantifiCare, Paris, France; Keller) medical imaging system was used to photograph subjects before treatment and at the 12-week follow-up visit. All patients were photographed in standing positions in three views: the back view, right view, and left view; the image was taken at a distance of 1 m. Finally, before and after photographs were calculated using the three-dimensional (3D) image analysis of LifeViz App (QuantifiCare).

Statistical Analyses

Statistical analysis was performed with GraphPad Prism 6 (La Jolla, CA). The normal-distribution assumption was assessed with a Shapiro–Wilk test. Comparisons before and after treatments were performed using a paired t test or Wilcoxon's signed-rank test. Pairwise comparisons were also undertaken using the Bonferroni adjustment for multiple comparisons. A $P < 0.05$ was considered statistically significant.

RESULTS

All 19 subjects completed the study visits. Five subjects were excluded from the analysis as they had a weight gain in excess of 5% at the 12-week follow-up.

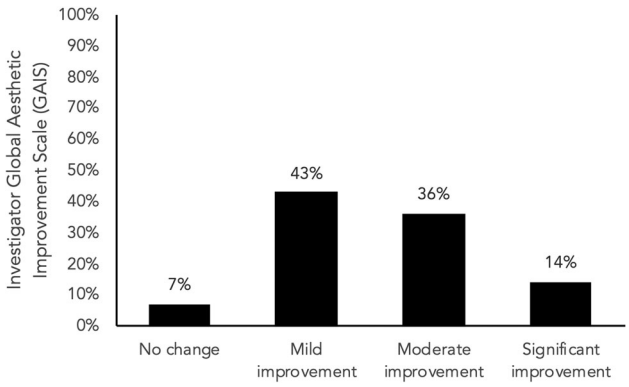

Figure 2 Physicians' Global Aesthetic Improvement Scale assessments at baseline and 12-week follow-up.

Efficacy Assessments

The primary endpoint for efficacy was met as results showed an increase of more than one point in the GAIS scale. The average improvement at the 12-week follow-up compared with baseline was 1.6 ± 0.85 ($n = 14$), according to the blinded investigator GAIS ratings; 50% of the subjects had moderate/significant improvement while 43% had mild improvement (Fig. 2). Photographic review performed by three blinded investigators of the 3D digital photos of the subjects showed that they were accurately able to differentiate between the pre- and post-treatment photographs in 82% of the cases. Digital photos of two representative subjects are shown in Figure 3.

Ultrasound Assessments

Results from the ultrasound measurements of each subject's target zone comparing subcutaneous fat layer thickness (mm) at baseline prior to treatment and at the 12-week follow-up indicate a mean reduction in fat thickness in the abdomen of 4.24 ± 2.3 mm ($P < 0.01$), representing an average of 23.8% FTR, and a mean reduction in fat thickness in the flanks of 2.57 ± 0.8 mm ($P < 0.01$), average 22.3% FTR (Fig. 4). An echography example illustrating clinical improvement at the 12-week follow-up from baseline is shown in Figure 5.

Subject Assessments

The 12-week satisfaction questionnaire ($n = 14$) revealed that 64% of subjects were extremely satisfied with their results, 29% were satisfied with their results, and 7% were neutral. When asked about having the treatment again, 86% of subjects responded they were very likely to repeat the treatment (79% very likely, 7% likely, and 14% neutral). Furthermore, 53% of subjects were very likely and 40% likely to recommend this treatment to others.

Safety and Tolerability

No serious immediate or delayed adverse effects were reported during the treatment and throughout the follow-up period. The most common immediate skin response to the treatment was mild erythema/edema (Fig. 6). Skin reactions persisting for up to 30 minutes following treatment included erythema, edema, and purpura. One pa-

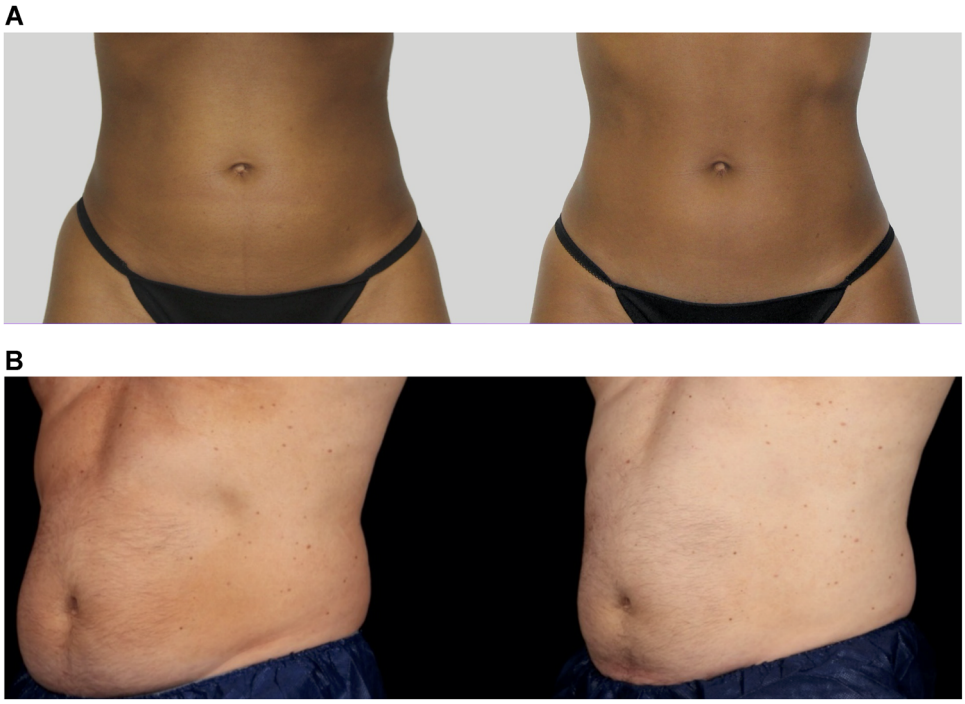

Figure 3 Digital photographs and ultrasound images of two subjects before and after treatment. (**A**) Thirty-five-year-old female before and at 12-week following treatment in the flank area. (**B**) Fifty-nine-year-old male before and at 12-week following treatment in the abdominal area.

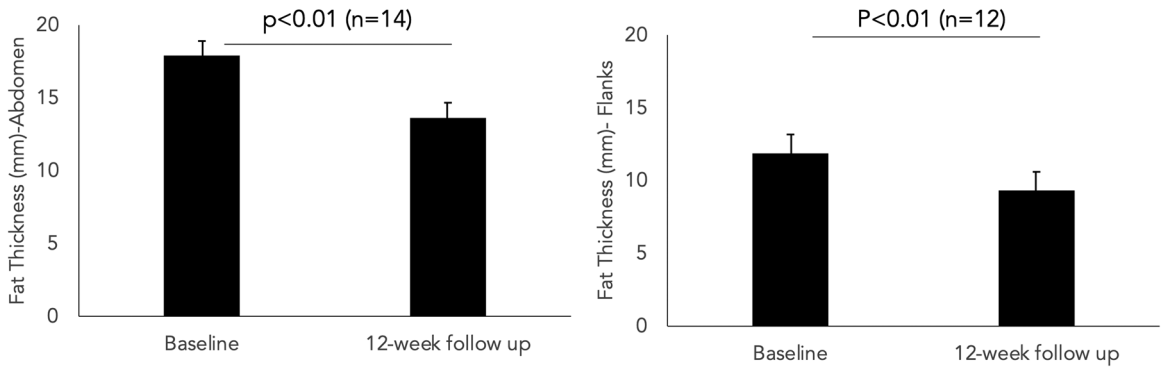

Figure 4 Changes in fat thickness measured by ultrasound (mm) in the abdomen and flanks from baseline to 12-week follow-up.

tient experienced palpable nodules a week post-treatment that were resolved with hand massage. No signs of these skin responses were noted at the 12-week follow-up visit. Patients reported the treatment as being tolerable with an average pain rating of 4.5 ± 0.7. The average temperature at the skin surface was maintained at 43.5°C.

DISCUSSION

Noninvasive fat reduction is a continually growing field in aesthetic medicine with a number of new and improved devices entering the market each year. By incorporating heating, cooling, ultrasound, mechanical, or a combination of these energies, these modalities are continuously finely tuned to improve body contour and laxity in a quick, safe, efficient, no-downtime manner. Since technology is constantly evolving in the body-contouring arena, "the best treatment" is a moving target. Nevertheless, when patients seek the "best" fat reducing treatment they consider its safety, efficacy, side effects, duration, and number of treatments required to achieve their goals. Companies developing new technologies need to take all these parameters under consideration to be competitive, with an emphasis of course on safety, clinical efficacy, and patient satisfaction.

In this study, a third-generation monopolar hands-free 2 MHz RF device with real-time temperature feedback was evaluated for its safety and efficacy in reducing localized fat pockets in the flanks and abdomen after a single 15-min treatment. The clinical study included subjects of various ages, genders, BMI, and skin types. Due to the surplus of devices claiming to reduce fat, and since there is no single measure of subcutaneous fat change that supersedes all others in reliability and utility, it has been proposed that investigators conducting efficacy studies need to apply multiple methodologies to assess the efficacy of their body contouring approach [17]. To this end, ultrasound measurements, blinded investigator live ratings, ratings of digital photographs, as well as patient-reported outcomes were utilized to comprehensively assess the clinical results. Results from the GAIS assessment and digital photograph ratings by three blinded investigators showed that the treatment promoted fat reduction in the target areas in the majority of patients. Ultrasound measurements demonstrated that thickness of body fat was significantly reduced from baseline, at the 12-week follow-up in both the abdomen and the flanks (23.8% and 22.3%, respectively). These improvements were independent of weight, since any patients with more than 5% fluctuation in their weight from baseline during the follow-up were excluded from the analysis. Patient satisfaction was also high: the majority of patients were satisfied with the results (93%), indicated they would have the treatment again and would recommend it to others. Treatments were well-tolerated, and no serious adverse events were reported. Minor side effects after treatment such as erythema and edema resolved on their own without requiring any intervention.

There are currently various energy-based devices in the market offering body contouring but a paucity of head-to-head comparative studies of their relative efficacy and safety for abdominal/flank fat reduction [6,10]. From the radiofrequency type devices, the non-contact focused field RF device (Vanquish, BTL) can temporarily reduce circumference and shrink fat cell size by heating the dermis and upper quarter layer of fat. By using a large applicator, the focus field RF device leads to bulk heating (temperatures between 40 and 45°C) at a depth of less than 10 mm [18]. An average of four 45 minutes treatments are required to achieve the desired results, taking a total of 2.5 hours to complete [18,19]. Other RF devices, such as the bipolar (Velashape; Syneron) or multi-polar (Venus Legacy, Venus Concept) generation of devices, often combined with mechanical suction are also promoted for body contouring. These devices however primarily address laxity issues, as they can induce neocollagenesis by superficially heating the dermis and upper quarter layer of fat that is exposed to the suction to approximately 42–43°C for more than 5 minutes [20,21]. Moreover, results are temporary, requiring more than six to eight treatments, 1 week apart to achieve results. Other types of energy-based devices such as cryolipolysis and ultrasound-based have also been shown to induce adipocyte apoptosis leading to a 15–25% reduction fat. In contrast to the monopolar 2 MHz RF device, however, they require multiple sessions, and take at least twice the time

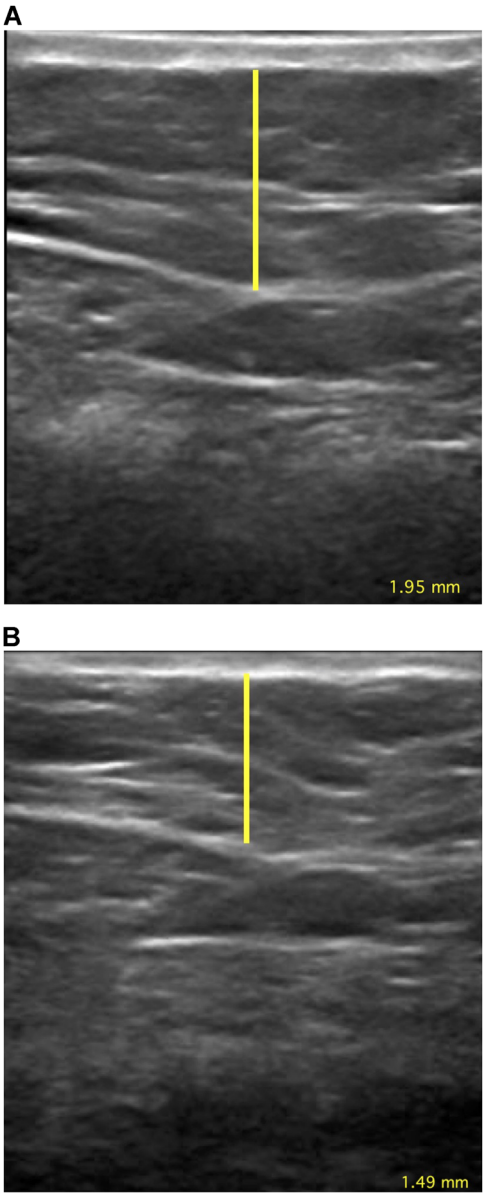

Figure 5 Ultrasonography of representative fat thickness assessment. Fat thickness of baseline (**A**) and 12 weeks after treatment (**B**) shows a 0.46 mm reduction of the fat layer and increased fibrous septa.

per session (around 30 minutes) [22,23]. Moreover, in the case of cryolipolysis, unfavorable side effects have been reported, such as paradoxical adipose hyperplasia and reversible nerve damage [24]. Thus, compared with treatments with other non-invasive body contouring devices that require multiple sessions, our results showed significant reduction in body fat after a single 15-minute treatment, highlighting a competitive advantage of this device. Moreover, the six-piece arrangement of the applicators allows for their customized placement regardless of the patients' body type.

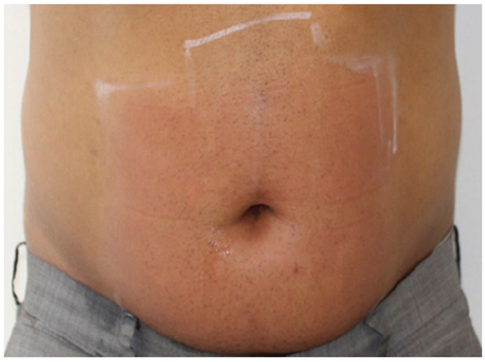

Figure 6 Example of mild erythema immediately post-treatment of the abdomen.

There are, of course, limitations to this study. First, the study examined only 19 subjects, which may limit the power of the results; however, the results were statistically significant with the number of subjects enrolled. Second, while the study demonstrated significant improvement 12 weeks after a single treatment, it remains unknown whether this clinical improvement will be maintained over years. Finally, we did not address the ability of this RF device to improve skin laxity. Heating of the dermal/subcutaneous fat junction could lead to synchronous dermal remodeling/skin tightening as well as non-invasive fat reduction. This would leverage the benefit of the device in its ability to reduce fat and simultaneously improve laxity in one single treatment. Future studies using more subjects, longer follow-up times, and with skin laxity assessments using this device are merited.

CONCLUSION

Multiple non-invasive energy-based devices for body contouring have been investigated and developed to overcome the risk, financial costs, and recovery time associated with surgical treatments. The results obtained by the clinical study presented here show that a 15 minutes treatment with a monopolar 2 MHz radiofrequency device led to significant fat reduction in the abdominal and flank regions, requiring no downtime. Patient satisfaction was high and no serious side effects were reported.

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