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ORIGINAL ARTICLE

Evaluation of safety and efficacy of noninvasive radiofrequency technology for submental rejuvenation

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Abstract Recently, a number of modalities have been used for noninvasive fat reduction. Radiofrequency (RF) technology is a promising tool for noninvasive body and face contouring. The aim of this study is to evaluate the efficacy and safety of novel noninvasive RF technology for the reduction of submental fat with 6 months of follow-up. Twenty-one subjects with submental fat accumulation were treated twice at 1-month intervals with monopolar RF, which could also be used to monitor real-time temperature. The submental fat thickness and the circumference were evaluated with ultrasonography and a tape measure, respectively, at baseline followed by 1 and 6 months after the last treatment (0, 2, and 7 months). Pain and adverse effects were documented through a questionnaire. The submental circumference and thickness showed a statistically significant reduction after treatments. There was no subject who was not satisfied with the treatment and a physician's assessment showed that 82.3 and 52.9 % of patients showed above mild improvement at 2 and 7 months. The mean pain score corresponded with discomfort or moderate pain. There were no significant adverse effects such as scars or hyper/hypopigmentation. A novel noninvasive RF technology is shown to be effective and safe for submental fat reduction. The effectiveness of fat reduction was maintained for 6 months after the last treatment.

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Introduction

Submental fat accumulation causes skin sagging and a double chin. Skin sagging under the chin is a sign of aging in mature and elderly people while a double chin gives the impression of one being an endomorphic figure in young or middle-aged people. Diet and exercise alone cannot remove fat from specific parts and may induce fat loss in unwanted areas. For this reason, concepts of body contouring and facial remodeling have emerged. Conventional methods of body and facial contouring are surgical lipectomy and suction-assisted liposuction. These invasive procedures have several limitations including bleeding, ecchymoses, long downtime, postoperative discomfort, and a risk of pulmonary emboli and seroma. Efforts to overcome these weaknesses include various minimally invasive fat reduction techniques, such as cryolipolysis, laser-assisted lipolysis, radiofrequency (RF) device, high-frequency focused ultrasound (HIFU) energy devices, and mesotherapy with phosphatidylcholine or deoxycholic acid. Among these, RF energy devices have received much attention in the noninvasive body-contouring device market [1]. Since the first RF device was approved by the FDA for cellulite in 2005, various RF devices have been developed. RF devices generate heat energy through the high tissue resistance of adipocytes. Adipocytes have relatively low heat transfer coefficients and therefore transmit little heat to surrounding structures. This action mechanism results in localized adipocyte thermolysis. In addition, RF heating is known to improve dermal collagen, elastin, and ground substances, contributing to skin tightening. In this study, we evaluated the efficacy and safety of a novel RF device (TruSculpt, Cutera Inc., Brisbane, CA, USA). This device is designed based on the theory that a properly induced electric field results in greater heating of fat, rather than skin and muscle. According to the results of in vivo human skin experiments, ex vivo animal tissue experiments, and mathematical modeling, this device can control the size of the RF-heated subcutaneous tissue and the depth of heating with the adjustment of the operational frequency [2]. Viability assays performed on adipocytes exposed to hyperthermic conditions showed that viable cells decreased to 20 % during 1 min of exposure at 50 °C and to 40 % during 3 min of exposure at 45 °C. The lowest temperature threshold for epidermal blister formation is above 55.6 °C [3]. The heat-pain threshold, which is the lowest thermal stimulation that causes pain, is known to be about 43 °C, as shown in previous studies [4–6]. While heating up fat tissue to 50 °C is safe for the skin, it can be painful for patients, and so it depends on the body part, starting temperature, pressure, and so on. In an in vivo preliminary study with this device (1 MHz), the pain was tolerable and the temperature of the fat tissue at 7−12-mm depth increased to 50 °C, while that of the epidermis was <30 °C during the RF exposure [3]. Based on previous experimental studies, we conducted a clinical trial to evaluate the efficacy and safety of a novel RF device targeting submental fat. The device (TruSculpt, Cutera Inc., Brisbane, CA, USA) is a high powered monopolar radiofrequency with a real-time temperature feedback system.

Materials and methods

Ethical oversight and registration

The study was conducted in accordance with the Declaration of Helsinki for the ethical conduct of research involving human subjects, and the protocol was approved by the Institutional Review Board at the Kangbuk Samsung Hospital (KBC13251D). This clinical trial was registered at ClinicalTrials.gov (NCT02512822).

Design and study population

This was a prospective, single-center, clinical trial at the outpatient dermatologic facility of the Kangbuk Samsung Hospital, Sungkyunkwan University, Seoul, Korea. A monopolar RF device was used in this study. The device has a unique coating electrode to eliminate hot spots or edges and provides real-time monitoring of treatment temperature. The device does not require suction, pressure, or an additional pinch. Eligible patients had skin sagging or a double chin, were aged 18–75 years, and could give signed informed consent. And, when the submental skin in the center was held with the thumb and index finger, the width had to be more than 1 cm. The exclusion criteria were specified as: age < 20 years, mental impairment, infectious disease, keloid in the face and neck, connective tissue disease, pregnancy, pacemaker, and undergoing a facelift procedure within the previous 6 months.

Experimental procedure

The procedure was carried out twice at a 1-month interval. We chose a 16 cm^2 handpiece applicable to the submental area. The submental area was divided into three separate parts (right, center, and left; see Fig. 1). Each part was treated in a stamped mode without an overlap for 5 min. The temperature setting started at 43 °C and was increased gradually to 45 °C within 2 min. The peak temperature was sustained for a minimum of 3 min.

Evaluation measures

The patients visited the clinic at 0, 1, 2, and 7 months. Clinical assessments were measured at 1 and 6 months after the last treatment. These visits were defined as short-term and long-term follow-ups, respectively. We ruled out patients who gained or lost 5 % or more of their initial body weight during the study since significant body weight change can affect the contour of a face. Photographs were taken at 45° incremental rotations in frontal, front-profile, and side (0°, 45°, and 90°) views in order to document the appearance of each subject. A tape measure was used to record the submental length in a standing position at 0, 2, and 7 months; the tape measure was kept in constant contact with the skin along the circumference from one earlobe to the other via the center of the chin. The submental fat thickness was measured by an external ultrasound probe (Philips HS 11 XE, Germany) prior to the treatment as well as at 2 and 7 months. Ultrasound measurements were performed by a single radiologist. Measurements were taken at three points (right median, median, left median) three consecutive times, and the average scores were recorded

Fig. 1 Area of the procedure under the chin

at each point. At 2 and 7 months, the overall improvement of the submental contouring was assessed by the patients and dermatologists. The overall improvement of clinical status was evaluated using a five-grade patient satisfaction scale: 0 = not satisfied, 1 = slightly satisfied, 2 = satisfied, 3 = very satisfied, and 4 = extremely satisfied. Physicians assessed the overall improvement using a four-point scale: 0, worse; 1, unchanged; 2, mild improvement; 3, marked improvement. The physicians' assessments were performed blindly based on the before and after photographs. For the assessment of pain intensity, a visual analog pain scale (VAS) was used at the first and second treatments. The immediate side effects and tolerability were assessed in the clinic after treatment, and the short-term side effects were evaluated by means of a telephone follow-up 1 week after the treatment.

Statistics

The means, standard deviations, and 95 % confidence interval for each characteristic were reported. Statistical analysis was performed by ANOVA with repeated measures to compare the differences between baseline data and the short- and long-term follow-up data. Pairwise comparisons were also undertaken using the Bonferroni adjustment for multiple comparisons. The level of statistical significance was set at $P < 0.05$.

Results

Twenty-one patients were enrolled, and three patients were lost by the last follow-up. One patient was ruled out because of significant weight gain. The 17 remaining patients were analyzed statistically. They were phototype III or IV, and their mean age was 50.4 ± 16.0 years (range 22–73 years). There were 2 men and 15 women. There was no subject who chose to discontinue because of an adverse effect or pain. Erythema was the most common adverse effect reported; it occurred in eight subjects at the first treatment and in five subjects at the second treatment. However, erythema mostly subsided within 6 h, but lasted for a week in one subject during the first treatment. Edema and vesicles were reported to be resolved within a week in one subject at the first treatment and in another subject at the second treatment. Furthermore, adverse effects did not result in a scar or pigmentation. The mean pain score at the first treatment was 4.9 ± 2.3 and at the second treatment, 4.8 ± 1.7.

At 1 month after the last treatment (i.e., short-term follow-up), the mean reduction in the submental circumference was 1.4 ± 0.6 cm (5.7 % of the mean submental circumference before treatment, $P < 0.001$). On ultrasonography evaluation, the mean reduction in fat thickness was 5.4 ± 5.7 mm (9.7 % of mean fat thickness before treatment, $P = 0.005$) (Fig. 2). At 6 months after the last treatment (i.e., long-term follow-up), the mean reduction in the submental circumference was 0.9 ± 0.7 cm (3.8 % of mean submental circumference before treatment, $P < 0.001$) and the mean reduction in fat thickness was 5.8 ± 6.3 mm (10.5 % of mean fat thickness before treatment, $P = 0.006$) (Fig. 2). Table 1 summarizes the pairwise comparisons between baseline and short-term and long-term follow-ups.

The physicians' evaluation revealed that 82.3 % of patients showed improvement at the short-term follow-up, whereas 52.9 % of patients showed improvement at the long-term follow-up (Figs. 3 and 4). There was no subject considered to be worse. At the short-term follow-up, all patients expressed a slightly above satisfied grade and the satisfaction was maintained at the long-term follow-up (Fig. 5).

Discussion

The primary results of this study indicate that the RF device significantly reduces submental fat and improves facial contouring, as compared with the baseline. The submental circumference and fat thickness decreased significantly after treatment. The circumference measurement might not be exact, so we employed various methods for assessment including ultrasound measurement and assessment by physicians using pictures. Using repeated measures ANOVA for repeatedly measured parametric data of 17 subjects, the means of submental circumference and fat thickness for submental fat at short- and long-term follow-ups were statistically significantly different compared with the baseline (Table 1). At the short-term follow-up, all subjects showed a decrease in submental circumference and this effect was maintained, with the exception of one subject, until the long-term follow-up. The mean difference in submental circumference (0.9 cm) at the long-term follow-up was 64.3 % of that (1.4 cm) at the short-term follow-up. The difference in submental fat thickness differed slightly depending on the site (right, median, and left), but the mean fat thickness at the three sites decreased in all subjects at the short-term follow-up. The difference in fat thickness at the long-term follow-up (5.8 mm) increased more than that at the short-term follow-up (5.4 mm). However, the results of the physicians' assessment by photos indicated that more patients showed improvements at short-term follow-up than at long-term follow-up. This is because RF devices affect skin tightening as well as fat reduction and the effect of tightening does not last for a long time. The thickness of the fat layer was measured by ultrasonography, and the physicians' assessment was evaluated based on the shape of the face. Therefore, there was a difference between the thickness measurement and the physicians' assessment. We assumed that fat necrosis lasted several weeks and the effect of fat reduction was maintained longer than that of skin tightening by improving dermal collagen, elastin, and ground substance. The objective

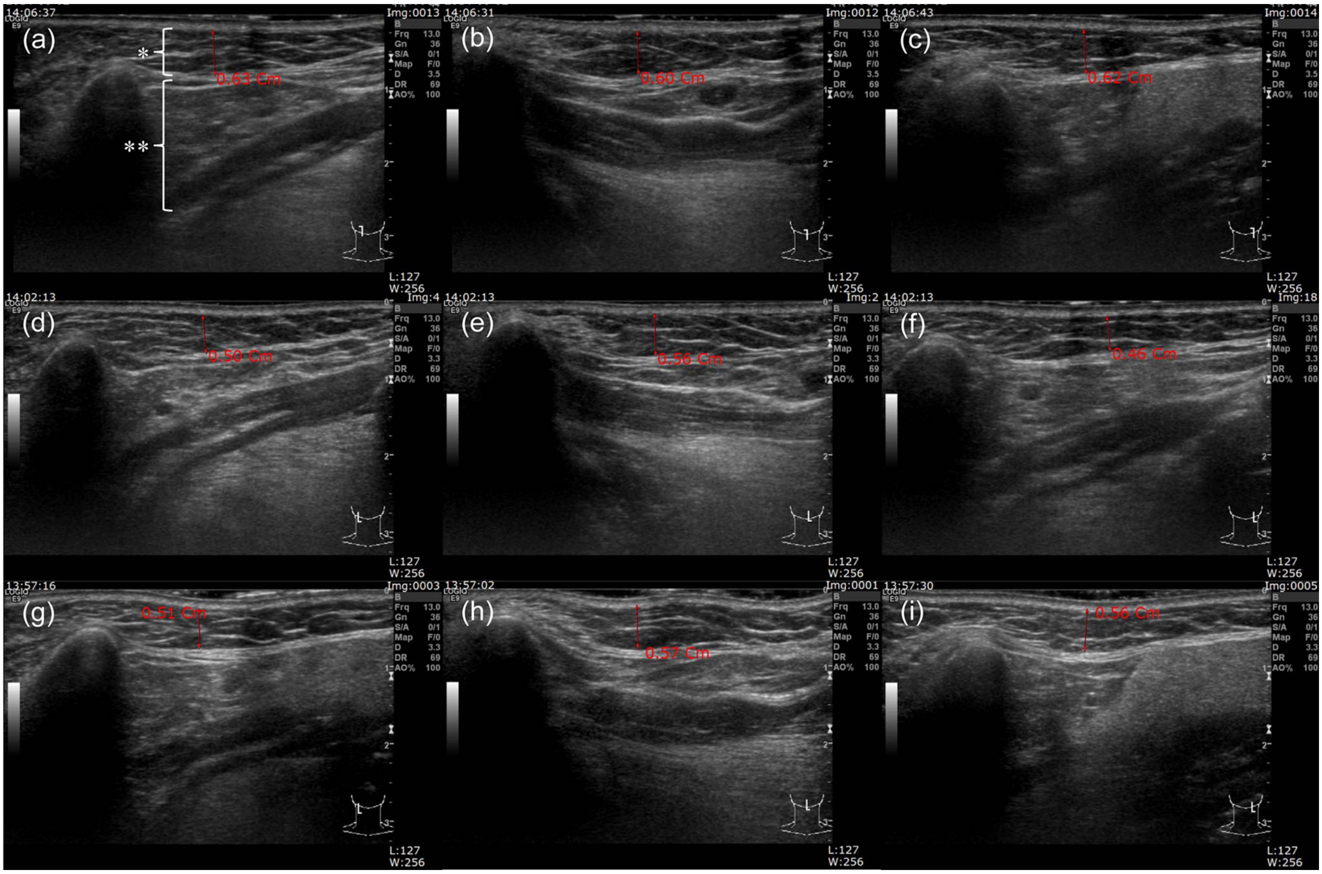

Fig. 2 Ultrasound photography of the right-median (**a**, **d**, **g**), median (**b**, **e**, **h**), and left-median (**c**, **f**, **i**) submental area in a patient. **a**, **b**, **c** At pretreatment (baseline); **d**, **e**, **f** at 1 month after the last treatment; **g**, **h**, **i** at 6 months after the last treatment (*asterisk*, subcutaneous fat; *double asterisk*, muscle)

measurements were associated with a physicians' evaluation and the patients' satisfaction. There was no subject deemed to be worse in the assessments by the physicians or the patients. The pain score was higher at the first treatment than at the second treatment. The pain scores corresponded to discomfort or moderate pain. At the first treatment, two patients complained of soreness, which lasted for a week. At the second treatment, one patient complained of soreness lasting for a

Table 1 Results with pairwise comparisons between time periods

	Before treatment	Short-term follow-up	Long-term follow-up	*P* value[a]	Between baseline and short-term follow-up		Between baseline and long-term follow-up	
					Difference in means	*P* value[b]	Difference in means	*P* value[b]
Submental circumference (mean ± SD, cm)								
	23.8 ± 2.1	22.4 ± 2.0	22.9 ± 2.2	<0.001	1.4 ± 0.7	<0.001	0.9 ± 0.7	0.001
Thickness of submental fat (mean ± SD, mm)								
Right	54.3 ± 9.3	47.7 ± 10.5	48.3 ± 10.9	0.006	6.6 ± 8.1	0.012	6.0 ± 8.8	0.038
Median	57.7 ± 14.9	51.4 ± 14.2	52.2 ± 15.3	0.082	6.3 ± 12.4	0.163	5.4 ± 13.6	0.356
Left	54.3 ± 8.4	50.8 ± 10.3	48.4 ± 8.7	0.010	3.6 ± 7.7	0.224	5.9 ± 7.5	0.015
Average	55.4 ± 8.0	50.0 ± 9.3	49.6 ± 9.7	0.001	5.4 ± 5.9	0.005	5.8 ± 6.4	0.006

Short-term follow-up, 1 month after the last treatment; long-term follow-up, 6 months after the last treatment

[a] Statistical analysis by repeated measures ANOVA

[b] Adjustment for multiple comparisons: Bonferroni method

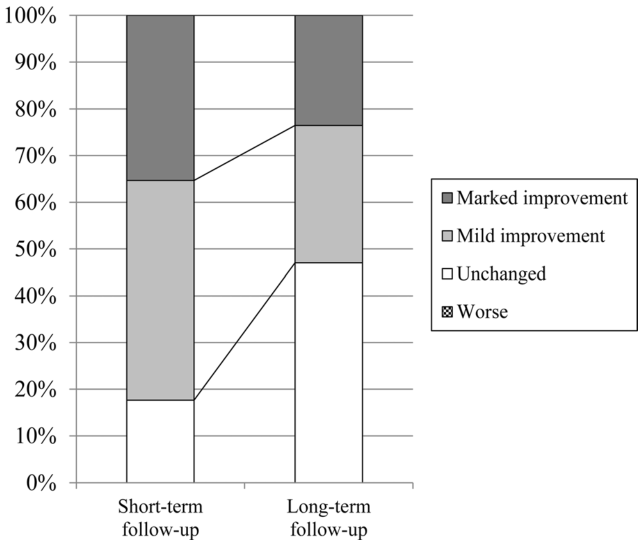

Fig. 3 Physicians' assessments at the short-term and long-term follow-ups

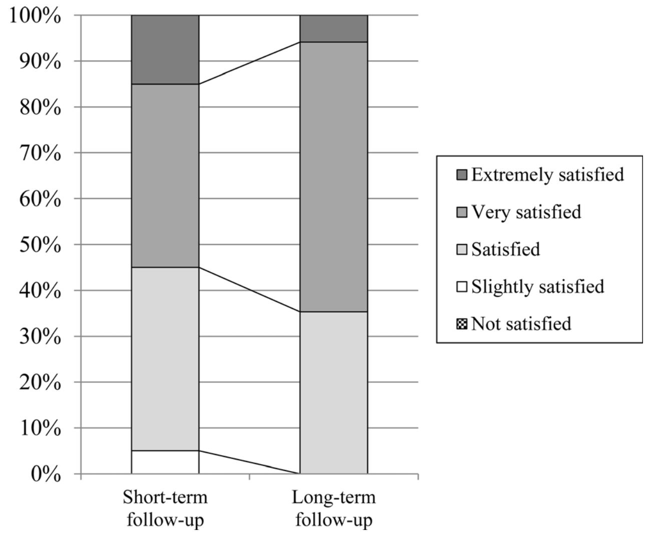

Fig. 5 Overall satisfaction for the reduction of submental fat at the short-term and long-term follow-ups

week. All subjects answered that the pain was tolerable, and they were inclined to undergo additional treatment. Furthermore, there were no serious adverse effects such as scars, hyperpigmentation, or hypopigmentation.

Noninvasive fat reduction is a continually growing field in aesthetic medicine. Suction-assisted liposuction is still regarded as the gold standard in nonexcisional body contouring, but many patients are seeking noninvasive cost-effective procedures and minimal downtime. To date, many novel methods have been introduced, such as using heating, cooling, laser, RF, and ultrasound sources for improving skin sagging and laxity. These technologies may minimize ecchymosis, edema, and pain [7, 8]. Cryolipolysis is a noninvasive technology for selective fat reduction, using controlled, localized cooling, which induces an inflammatory reaction within adipose tissue and apoptosis of adipocytes [9]. In theory, fat cells are more sensitive to cold than other tissues and may be damaged by cold stimulus at temperatures above freezing but below body temperature for a certain duration. Several clinical trials have shown fat reduction [9–11]. However, there is a risk of temporary dysesthesia and there are several disadvantages, such as a relatively long application time (30–60 min for one application), discomfort during treatment, and limitations of the contour of an applicator. External

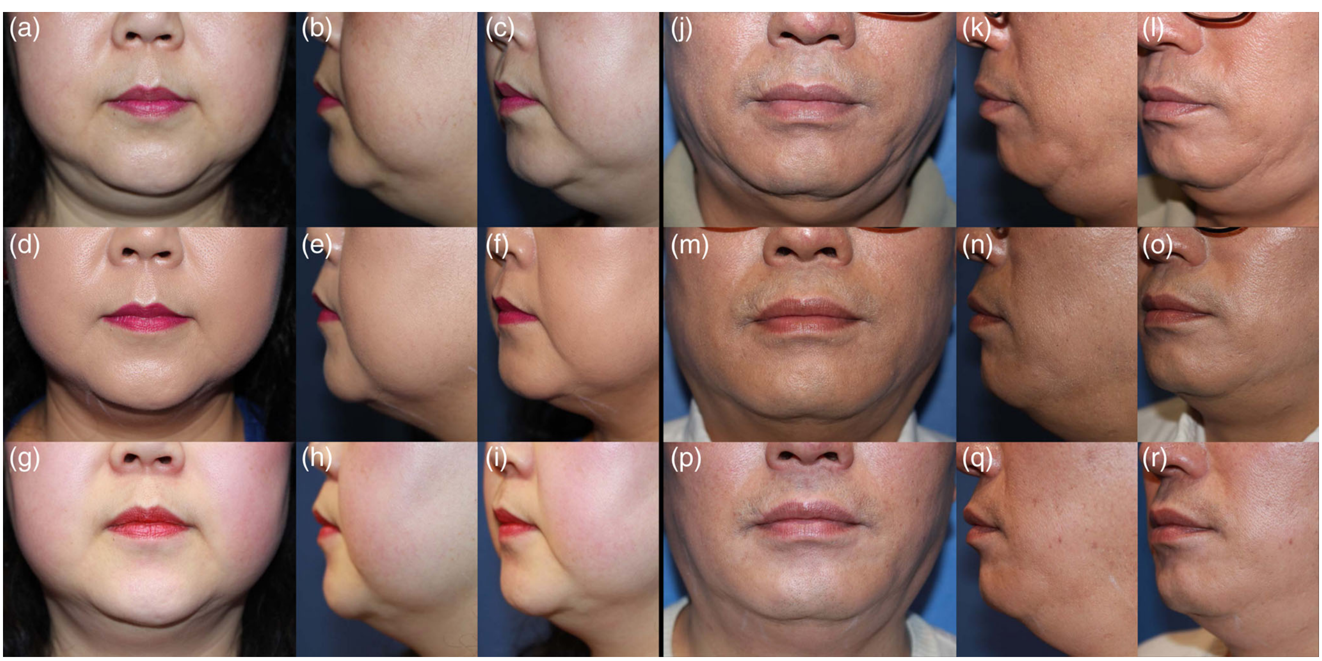

Fig. 4 Clinical photographs of two patients (F, 55 years old, and M, 60 years old). **a**–**c**, **j**–**l** At baseline; **d**–**f**, **m**–**o** at 1 month after the last treatment; **g**–**i**, **p**–**r** at 6 months after the last treatment

low-level laser is used as a noninvasive lipolysis method and is approved in the USA and Canada. This laser works by making pores in adipose cell membranes through which lipids are released [12]. There is a concern that fat released from adipocytes flows into the blood stream, affecting the lipid profile, but the issue is controversial [13]. Recently, a new 1060 diode laser with specific affinity for adipose tissue was introduced, but clinical trial data are still needed. Ultrasound can lyse adipocytes using a mechanical compression wave (>20 kHz) and by generating heat. Ultrasound techniques can be divided into two: low-intensity/low frequency nonthermal ultrasound and HIFU. Nonthermal ultrasound uses mechanical stress generated from inertial cavitation to disrupt adipose tissue. However, cavitation is less predictable and harder to control than HIFU [13]. HIFU provides focused, high-intensity ultrasonic ablation energy to deep fat tissue. The energy produces rapid heating in the focal zone to ablate adipocytes and remodel the collagen. The clinical response is obvious but there is a lack of long-term data from more than 3 months [14, 15]. Radiofrequency (RF) is used for skin tightening, as well as fat or cellulite reduction. RF can be utilized in two ways with monopolar and bi/multi-polar devices. In the former, energy is passed from a single electrode to subcutaneous tissues through the skin and to a return pad. The latter has two or more electrodes within the same hand piece and the energy passes between the electrodes to generate heat. Therefore, monopolar devices can penetrate deeper than bipolar devices [13]. Older RF devices worked through skin tightening rather than fat destruction, and there were some limitations in managing pain during the procedure and prolonging the transient effect [16, 17]. Recently, several RF devices have been developed to overcome the limitations, with reported effectiveness in fat reduction. One of the devices is the transcutaneous monopolar RF device, which was reported to be a safe and effective modality in preliminary study [18].

The novel RF device introduced in this study demonstrated fat reduction, evident through in vitro human fat tissue, in vivo human skin, and ex vivo animal tissue experiments, and managed pain without anesthesia for an in vivo human experiment. Based on the in vivo human skin experiments, the device was set up with a treatment temperature and time to achieve an adequate effect with tolerable pain. This study provides clinical data for the safety and efficacy of a novel RF device. Measurements at 6 months after the last treatment support the long-term effects of fat reduction.

In brief conclusion, there are various body and face contouring technologies available; thus, it is important to select the proper device, depending on the treatment region and therapeutic aim. A novel RF device is one that is safe, results in effective treatment, and can be used in small areas such as for submental fat. Further clinical trials of this RF, with variable-sized applicators, are expected to evaluate the viability in other parts of the human body.

Compliance with ethical standards The study was conducted in accordance with the Declaration of Helsinki for the ethical conduct of research involving human subjects, and the protocol was approved by the Institutional Review Board at the Kangbuk Samsung Hospital (KBC13251D). This clinical trial was registered at ClinicalTrials.gov (NCT02512822).

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Conflict of interest The authors declare that they have no conflict of interest.

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