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Efficacy and safety of a novel monopolar radiofrequency device with a continuous water-cooling system in patients with age-related facial volume loss

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ABSTRACT

Background: Esthetic radiofrequency (RF) technology has much attracted public attention with the increasing demand for skin rejuvenation. A continuous water cooling-based monopolar RF (MRF) device was designed for the first time to protect the epidermis and maximize clinical outcomes.
Objective: Assess the efficacy and safety of the proposed MRF device in patients with mild-to-moderate sunken cheeks and jawline laxity.
Methods: Twenty-one patients underwent a single session of MRF treatment. Quantitative analysis was performed using a 3D imaging technique. Postprocedural clinical improvements were assessed with the Merz Scale. Regarding safety, adverse events (AEs), thermal sensation (TS) and pain intensity were explored. Patient satisfaction was surveyed with the Self-Assessment Questionnaire (SAQ).
Results: The follow-up investigation demonstrated that facial volume increased across the cheek and jawline, with lifting effects throughout the treatment area. The Merz Scale assessment revealed that sunken cheeks, sagging jawlines and wrinkles were markedly improved. In addition, there were transient AEs, mild TS and moderate pain. In SAQ, 81% patients were satisfied with the procedure.
Conclusions: This study provided quantitative evidence for postprocedural volumetric increases along with enhanced lifting effects, strongly implying that the proposed MRF device can be an attractive option for improving facial skin volume loss and laxity.

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KEYWORDS
Continuous water-cooling system; monopolar radiofrequency; laxity; facial volume loss; facial rejuvenation

Introduction

Skin senescence is characterized by reduced skin volume and elasticity, wrinkle formation, flattened dermo-epidermal junction (DEJ) and uneven skin texture, which are mainly associated with the structural and functional alterations in connective tissue (1–3). In addition, an age-driven decrease in the number of fibroblasts and their reduced functional activity lead to the decline of collagen and elastin levels in the deeper layer of the skin (4) and to the attenuated activity of other extracellular matrix (ECM) components much involved in skin aging (5), having a detrimental effect on the integrity of the tissue (6,7). Consequently, it results in skin volume loss and laxity (8). In this context, a great deal of effort has been made to ameliorate ECM microenvironment for skin rejuvenation (5,9,10).

Growing evidence indicates that monopolar radiofrequency (MRF) augments skin thickness and improves skin laxity (11,12). Basically, MRF devices use a high-frequency electric current to generate heat. This heat penetrates the deep part of the skin and stimulates the synthesis of a variety of ECM components with an effect on supporting tissue volume and elasticity such as collagen, elastin, glycosaminoglycans (GAGs), proteoglycans (PGs) and growth factors (5,10), then it contributes to the restoration of sunken and sagging skin. Based on this mode of action, MRF devices have been utilized in a diversity of face and body areas mainly for improving wrinkles, double chin, skin texture and excessive submental fat (13,14). However, the heat energy may damage the epidermis, thereby cooling system has been designed to regulate skin temperature and protect the epidermis (15–17). The existing cooling system uses a pulsed or intermittent gas-cooling method in which cryogen gas is released multiple times according to its own protocol during RF treatment (18,19). However, a number of studies revealed that the gas cooling-based RF devices produced high pain scores of more than 6 (0–10 range) even after (local) anesthesia, showing severe or intense pain (20,21). Accordingly, a new modality of cooling technology that can reduce pain and enhance clinical efficacy is currently required.

It is well established that reduced skin volume and elasticity is crucial phenotypes of aged skin, and their restoration is therefore an important parameter to assess the extent of skin rejuvenation (22,23). Three-dimensional (3D) imaging analysis has been introduced to investigate age-dependent skin volume changes in esthetic clinical settings, and it offers quantitative data for the changes, helping us to objectively figure out postprocedural

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outcomes after RF treatment (24,25). In addition, this imaging analysis allows us to investigate the degree of skin lifting effects for each region of the face, which is also very useful to figure out changes in the effects before and after treatment. Accumulating data reveal that this 3D methodology can track and evaluate quantitatively post-treatment alterations in skin rejuvenation beyond the existing methods that have remained largely in a subjective observation of dermatologists (26,27).

Accordingly, in the present study, we introduced a novel MRF device equipped with a continuous water-cooling system and explored facial volume changes and skin lifting effects in patients with mild-to-moderate sunken cheeks and jawline laxity before and after MRF treatment using a 3D imaging technique. In addition, diverse assessment tools were used for other postprocedural esthetic improvements, safety and patient satisfaction.

Methods

Study participants

A total of 21 Asian patients were enrolled in this study in accordance with the inclusion and exclusion criteria. They were all health and of Korean ethnicity between 26 and 72 years old (47.38 ± 2.74) and showed mild-to-moderate sunken cheeks and jawline laxity with a type II or type III Fitzpatrick skin phenotype.

Inclusion and exclusion criteria

Adult Asian patients who have mild-to-moderate sunken cheeks and skin laxity of the mid and lower face but have no other health problems were included in the study. In addition, patients with collagen or cutaneous disorders, metal or electrical implants in the body, scars in the treatment area, active infections, prior cosmetic surgery experience (derma fillers not applicable) and pregnant or breastfeeding women were excluded from the study.

MRF treatment

This MRF device consists of a generator, two handpieces, four interchangeable tips, and a water-cooling unit (VOLNEWMER, CLASSYS Inc., South Korea). All patients underwent a single session of MRF treatment without anesthetics. In this procedure, F (size: 3.0 cm^2) and V (4.0 cm^2) tips were used for the face with energy levels of 1.5–3.5 (corresponding to the energy of 11.7–21.7 J/cm^2 for F tip or 11.3–21.3 J/cm^2 for V tip), and approximately 260–650 shots per patient (5–6 passes for the cheek, 4–5 passes for the chin, and 2–3 passes for other areas including wrinkles) were applied over the mid and lower face. Specifically, F tip was used for upper and lower cheeks and wrinkles, V tip for jawline areas. Prior to treatment, a return pad was attached to one side of the upper back. In addition, coupling gel containing glycinamide, which is a potent anti-melanogenic agent and increases type I and III collagen levels (28), was applied to the treatment area to facilitate the penetration of RF waves into the skin and prevent the risk of skin burning. The treatment area of the mid-face extends laterally from the nasolabial folds to the mandibular angle and the preauricular area. For the lower face, the area extends inferomedially from the marionette lines to the mandible. During treatment, the epidermis temperature was measured using an infrared camera (FLIR E-5, FLIR Systems, OR, USA) and ranged 38–41 °C under the continuous water-cooling system in which chilled water circulates around the contact surface of tips (Supplementary Figure S1).

Efficacy assessment: 3D imaging analysis, Merz Scale, and GAIS

The Vectra XT 3D imaging system and Vectra 3D Analysis Module (VAM) software (VECTRA, CANFIELD Inc., NJ, USA) was used to quantitatively analyze facial volumetric changes and investigate the regions where the lifting effect occurred and the strength of this effect. This setup has a total of six cameras in three pods and shows high resolution and accuracy (3.6 mega pixel color resolution, 1.2 mm geometry resolution, 0.1 mm accuracy), which can cover 180° field of view. The VAM solution provides 3D images and multiple analytical tools for them, thus automatically measuring volume differences in the defined area and identifying lifting effects (29,30). In the VAM, the pretreatment volume value is assumed to be 'zero', and the VAM calculates the post-treatment volume value by measuring the amount of volume gain or loss after treatment compared to before treatment (zero) (see also Figure 2). In addition, the proportion (%) of each volume gain (or loss) area in the entire volume gain (or loss) area was calculated by dividing the area of each volume gain (or loss) area by that of entire volume gain (or loss) area (if a region is designated on the 3D image, the area of that region can be determined) (see also Figure 3). The 3D imaging data were obtained from patients before treatment (baseline) and at 4 and 12 weeks after treatment (follow-up visits).

The Merz Scale, which is a standardized and globally accepted tool for measuring the process of skin aging, was used by two independent dermatologists to assess the degree of improvements in sunken cheeks, jawline sagging, nasolabial folds (NF), and marionette lines (ML) at both follow-up visits after treatment. This rating system is based on a scale of 0–4. In general, each score indicates 0 = normal (no issue), 1 = mild, 2 = moderate, 3 = severe, and 4 = very severe. For instance, in case of rating cheek fullness, each score indicates as follows: 0 = full cheek, 1 = mildly sunken cheek, 2 = moderately sunken cheek, 3 = severely sunken cheek, and 4= very severely sunken cheek (31).

Investigator Global Aesthetic Improvement Scale (IGAIS) and Subject GAIS (SGAIS) were also used to rate the overall esthetic improvements of patients at both follow-up visits. This rating system is based on a scale of 0–4, and each score indicates as follows: 0 = no change, 1 = minimal improvement, 2 = mild improvement, 3 = moderate improvement, and 4 = marked improvement (32).

Safety and satisfaction survey

Two independent dermatologists performed safety assessment immediately, 4 weeks, and 12 weeks after treatment. Initially, adverse events (AEs) were identified by the dermatologists immediately after treatment. At 4 and 12 weeks after treatment (follow-up visits), they investigated how long the AEs lasted, whether the AEs were still present and there were any new AEs. Next, thermal sensation (TS) and pain levels were investigated using the TS Scale (TSS) (revised suitable for our study) (33) and the Numeric Rating Scale (NRS) (34), respectively, immediately after treatment and at the two follow-up visits. Patients were asked to rate their TS on a scale of 1–5. Each score indicates as follows: 1 = comfortable, 2 = slightly warm, 3 = warm, 4 = hot, and 5 = very hot. Similarly, patients were asked to rate their pain on a scale of 0–10. Each score indicates as follows: 0 = no pain, 1–3 = mild pain, 4–6 = moderate pain, and 7–10 = severe pain.

In addition, at the final visit, patient satisfaction was surveyed using the Self-Assessment Questionnaire (SAQ), which is composed of the following questions based on a five-point Likert scale: (1) Are you overall satisfied with the procedure for facial rejuvenation? (2) How much has your facial skin improved? (3) Did you feel comfortable throughout the procedure? (4) Would you recommend the procedure to your friends? (35).

Statistical analysis

Statistical analysis was performed using SPSS software ver. 26 (IBM, Armonk, NY, USA). All the values produced during the study were represented as mean ± standard errors of mean (SEM). In the 3D volumetric analysis, changes in facial volume over time were analyzed using a one-way repeated measures (RM) analysis of variance (ANOVA), followed by a *post hoc* Tukey test or Holm-Sidak for multiple comparisons. Regarding the Merz Scale, IGAIS, and SGAIS assessments, comparison between groups was also carried out using a one-way RM ANOVA, followed by a *post hoc* Tukey test or Holm-Sidak for multiple comparisons. Notably, data, which did not pass the normality test, were analyzed using the Friedman's test with a *post hoc* Tukey test for multiple comparisons. *p* Values of less than .05 were considered statistically significant.

Results

Patient demographics and study timeline

Twenty-one patients, who met the inclusion criteria, were enrolled in this study. They were 18 female (85.7%) and 3 male (14.3%) patients and were of Korean ethnicity with a type II ($n = 9$, 42.9%) or type III ($n = 12$, 57.1%) Fitzpatrick skin phenotype. The mean age of the patients was 47.38 ± 2.74 (mean ± SEM) (Table 1).

After completing the enrollment process, a single session of MRF treatment was performed according to the study timeline (0 W) and subsequently multiple parameters were assessed at each time point (4 W, 12 W) (Figure 1).

Visual assessment and 3D photos

Following treatment, changes in facial volume and appearance were identified at 4 weeks and 12 weeks. Visual observation found that the sunken cheek was improved (blue arrow) and the sagging jawline was tightened and lifted (red dotted line) 12 weeks after treatment compared to baseline (Figure 2(A)). Consistent with this result, 3D imaging analysis revealed that facial volume was augmented mainly across the cheek and the jawline (blue dotted line) while decreasing predominantly around the ML (red dotted lines) 12 weeks after treatment (Figure 2(B), left panel). Skin lifting effects were found over the entire face, but they were most evident around the cheek and the jawline (blue dotted line), and the perioral areas (red dotted line) (Figure 2(B), right panel).

Table 1. Patient demographics.

Demographic	Value
Total no.	21
Gender, n (%)	
Female	18 (85.7%)
Male	3 (14.3%)
Age, mean ± SEM (range)	47.38 ± 2.74 (33–72)
Skin phototype, n (%)	
II	9 (42.9%)
III	12 (57.1%)
Ethnicity	Korean (all)

Measurement of volumetric alterations

Next, quantitative analysis was conducted to investigate how much volume was increased or decreased in the mid-lower face, the cheek, and the jawline after treatment. It was shown that compare to baseline (assumed to be zero on the VAM), face volume rose by 3.42 ± 0.54 cc and 7.98 ± 1.27 cc around the cheek, jawline, and others at 4 and 12 weeks after treatment, respectively (Figure 2(C), left bars). Conversely, there was a slight volume loss by 0.67 ± 0.26 cc and 1.03 ± 0.31 cc around the nose, perioral area, and others at 4 and 12 weeks after treatment, respectively (Figure 2(C), right bars). Notably, after comparing volume changes between 4-week and 12-week follow-ups, there was a significant difference in terms of volume gain ($p < .001$) but a slight difference in terms of volume loss (statistically not significant) (Figure 2(C)). Specifically, the volume of upper cheeks increased by 2.12 ± 0.34 cc and that of lower cheeks by 3.49 ± 0.55 cc at 12 weeks post-treatment. The overall cheek volume rose by 5.66 ± 0.90 cc at 12 weeks post-treatment. And the cheek volume gain at 12 weeks was markedly greater than that at 4 weeks in both upper and lower cheeks ($p < .001$) (Figure 2(D)). The jawline volume was also significantly increased at 12 weeks (1.33 ± 0.21 cc) compared to 4 weeks (0.57 ± 0.09 cc) (Figure 2(E)) ($p < .001$). Overall results were summarized in Table 2.

Volume gain or loss areas

The main areas where volume gain or volume loss was observed were identified using 3D imaging analysis. At 12-week follow-up

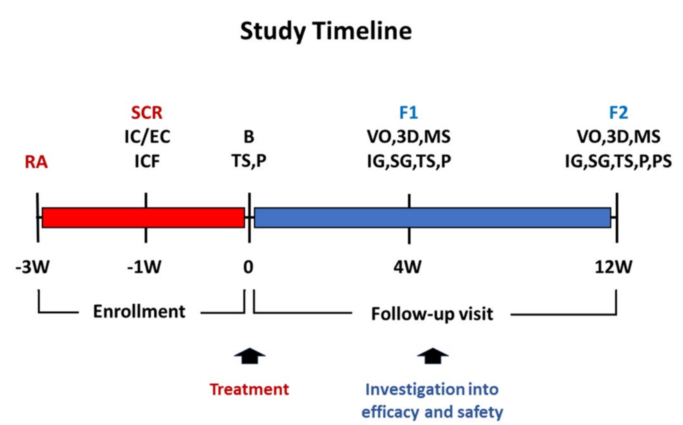

Figure 1. This procedure was conducted according to the schedule, which was composed of the enrollment period, the treatment time point, and the follow-up visit period. In addition, after MRF treatment (0W), a variety of parameters related to the efficacy and safety of this procedure were investigated at each time point (4W, 12W). RA: recruitment announcement; SCR: screening; IC: inclusion criteria; EC: exclusion criteria; ICF: informed consent form; B: baseline; TS: thermal sensation; P: pain; F1: first follow-up visit; F2: second follow-up visit; VO: visual observation; 3D: three-dimensional imaging analysis; MS: Merz Scale; IG: Investigator Global Aesthetic Improvement Scale; SG: Subject Global Aesthetic Improvement Scale; PS: patient satisfaction; W: week.

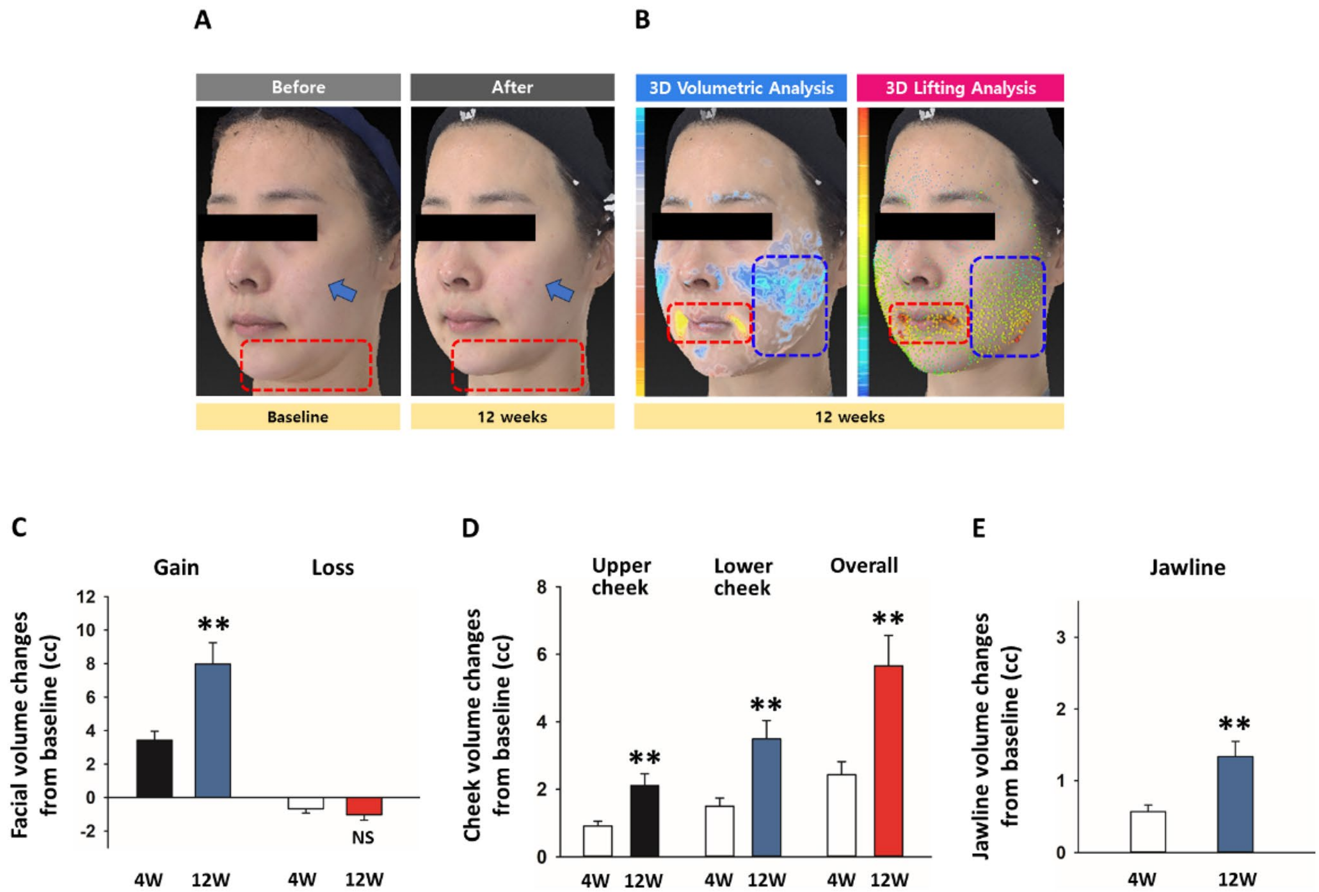

Figure 2. In a representative case for a 37-year-old female patient (A, B), visual esthetic improvements were found mainly around the cheek (bule arrow) and the jawline (red dotted line) before and after treatment (A). In the color scale bar (B, left panel), going toward the bright blue color (upper part) indicates more volumetric increases, conversely, going closely to the bright yellow (lower part) indicates more volumetric decreases. A volumetric increase was found predominantly around the cheek (blue dotted line) and a volumetric decrease was found mainly around the ML (red dotted line) (B, left panel). In another color scale bar (B, right panel), going toward the red color (upper part) indicates stronger lifting effects, conversely, going closely to the blue color indicates weaker lifting effects. Similarly, lifting effects were also found most strongly in the cheek (blue dotted line) and the ML (red dotted line) (B, right panel). Overall volumetric changes were significantly enhanced at 12 weeks, compared to 4 weeks, after treatment ($p < .001$) (C). More specifically, the volume in upper and lower cheeks was markedly augmented at 12 weeks compared to 4 weeks ($p < .001$) (D), the jawline volume also significantly rose at 12 weeks compared to 4 weeks ($p < .001$) (E). The symbol, *, indicate statistical significance between 4W and 12W (**, $p < .001$). NS: not significant; W: week.

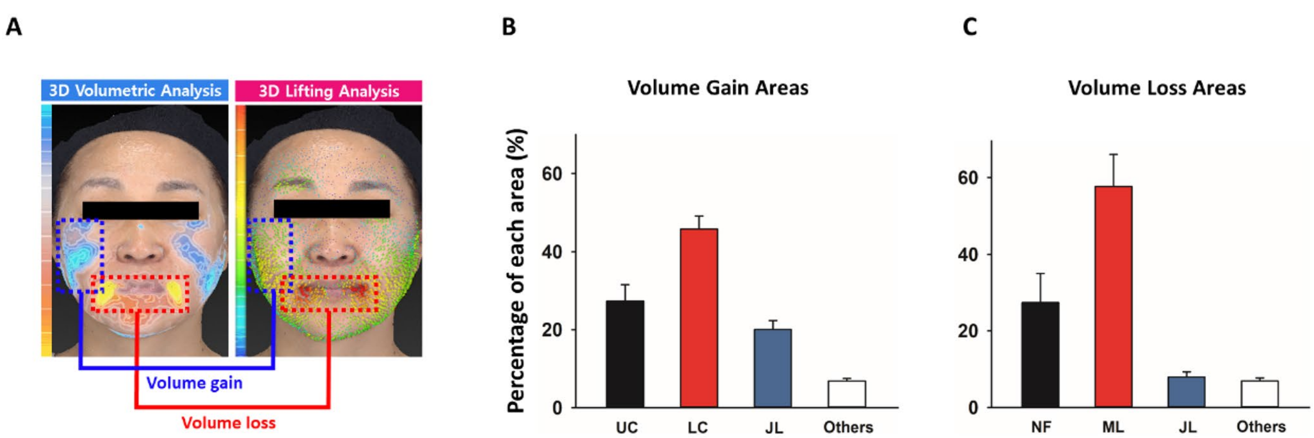

Figure 3. Volumetric increases were most evident in the cheek (blue dotted line) (A, left panel) and this area was found to be where the lifting effects were strong (A, right panel). In addition, volumetric decreases were most evident in the ML (red dotted line) (A, left panel) and in this area, the lifting effects were also evident (A, right panel). Collectively, in all patients, most of the volume gain area was observed in upper (26.56 ± 4.04%) and lower (43.75 ± 3.20%) cheeks, followed by the jawline (19.62 ± 2.20%) (B). And most of the volume loss area was found around NF (27.37 ± 7.62%) and ML (57.69 ± 8.32%) (C). UC: upper cheek; LC: lower cheek; JL: jawline; NF: nasolabial fold; ML: marionette line.

visit, volume gain was clearly shown over the cheek (blue dotted line) (Figure 3(A), left panel), and this region was found to be coincided with the region where lifting effects were evident (blue dotted line) (Figure 3(A), right panel). In detail, it was found that main volume gain areas included upper cheek, lower cheek, and jawline, which account for 26.56 ± 4.04%, 43.75 ± 3.20%, and 19.62 ± 2.20% of the entire mid-lower face, respectively (Figure 3(B)).

Meanwhile, volume loss was shown predominantly around ML (red dotted line) (Figure 3(A), left panel), and importantly, this region was be coincided with the region where lifting effects were most evident (red dotted line) (Figure 3(A), right panel). In all patients, approximately 85% of the volume loss area was found around wrinkles near to the cheek and the mouth such as NF (27.37 ± 7.62%) and ML (57.69 ± 8.32%) (Figure 3(C)).

Table 2. Changes in facial volume around cheek and jawline areas.

	Volume change (cc)		Increase/decrease rate (%)
Area	4W	12W	4W vs 12W
Mid-lower face			
Gain	3.42 ± 0.54	7.98 ± 1.27	133.33 (**)
Loss	0.67 ± 0.26	1.03 ± 0.31	53.73 (decrease) (NS)
Cheek			
Upper cheek	0.91 ± 0.14	2.12 ± 0.34	132.97 (**)
Lower cheek	1.49 ± 0.24	3.49 ± 0.55	134.23 (**)
Overall	2.43 ± 0.38	5.66 ± 0.90	132.92 (**)
Jawline	0.57 ± 0.09	1.33 ± 0.21	133.33 (**)

Note: W: week; NS: not significant.
** indicates a statistical significance ($p < .001$).

Merz Scale and GAIS assessment

Two independent dermatologists graded comprehensively the degree of improvements in the upper and lower cheek, the jawline, and wrinkles (NF, ML) using the Merz Scale. It was shown that upper (1.65 ± 0.10 at 4W, 0.65 ± 0.09 at 12W) (Figure 4(A)) and lower (1.59 ± 0.11 at 4W, 0.72 ± 0.10 at 12W) (Figure 4(B)) cheeks were significantly improved 4 and 12 weeks or 12 weeks after treatment compared to baseline (2.31 ± 0.13 for upper cheek, 2.06 ± 0.17 for lower cheek) (all, $p < .05$). In addition, the jawline was also improved 4 (1.72 ± 0.18) and 12 (0.72 ± 0.22) weeks after treatment compared to baseline (2.19 ± 0.20, $p < .05$) (Figure 4(C)). Lastly, for the wrinkles, there was a slight improvement at 4 weeks (1.50 ± 0.18 for NF, 1.47 ± 0.17 for ML) and subsequently a significant improvement at 12 weeks (0.65 ± 0.09 for NF, 0.81 ± 0.12 for ML) compared to baseline (1.78 ± 0.22 for NF, 1.84 ± 0.22 for ML, $p < .05$) (Figure 4(D,E)). Overall results were summarized in Table 3.

In addition, the I/SGAIS assessments revealed that there were minimal-to-mild improvements at 4 weeks after treatment. And these improvements were markedly enhanced at 12 weeks after treatment, notably, the SGAIS score (3.19 ± 0.13, $p < .001$) was slightly higher than the IGAIS score (3.05 ± 0.16, $p < .05$)

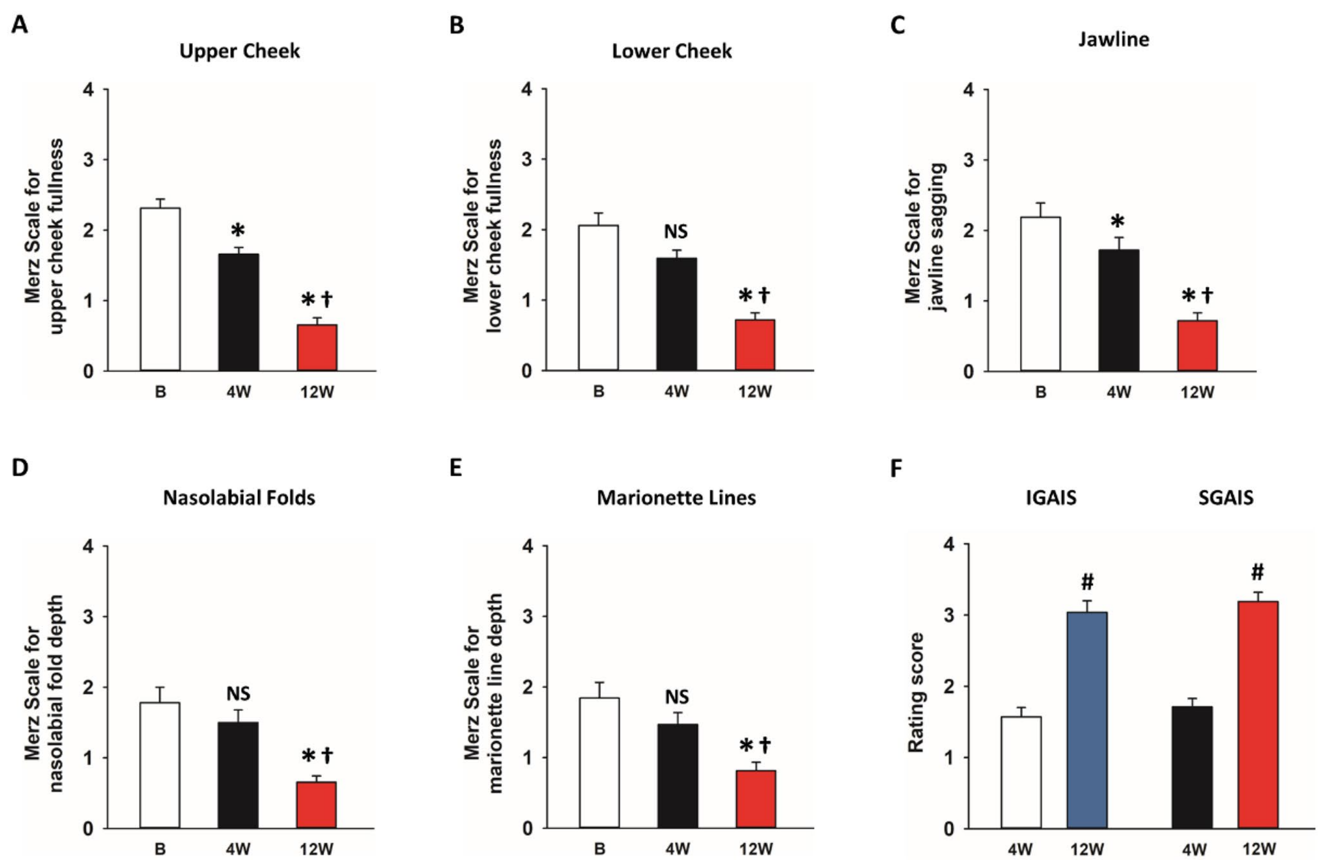

Figure 4. The Merz Scale assessment showed that compared to baseline, there were marked improvements in the upper cheek (A), the lower cheek (B), and the jawline (C) at 4 weeks or 4 and 12 weeks after treatment (all, $p < .05$). NF (D) and ML (E) were also significantly improved at 12 weeks after treatment (all, $p < .05$). In addition, the IGAIS and SGAIS assessments showed that overall esthetic improvements were significantly enhanced at 12 weeks, compared to 4 weeks, after treatment (both, $p < .05$) (F). The symbols, *, †, and #, indicate statistical significance between baseline and 4W or 12W, 4W and 12W (Merz Scale), and 4W and 12W (IGAIS, SGAIS), respectively (*, †, and #, $p < .05$). B: baseline; W: week; NS: not significant.

Table 3. Merz Scale: assessment of cheek fullness, jawline sagging, and wrinkle depth.

	Score			Decrease rate (%)		
Area	B	4W	12W	B vs 4W	B vs 12W	4W vs 12W
Cheek						
Upper cheek	2.31 ± 0.13	1.65 ± 0.10	0.65 ± 0.09	28.57 (*)	71.86 (*)	60.60 (*)
Lower cheek	2.06 ± 0.17	1.59 ± 0.11	0.72 ± 0.10	22.81 (NS)	65.04 (*)	54.71 (*)
Jawline	2.19 ± 0.20	1.72 ± 0.18	0.72 ± 0.22	21.46 (*)	67.12 (*)	58.14 (*)
Wrinkle						
NF	1.78 ± 0.22	1.50 ± 0.18	0.65 ± 0.09	15.73 (NS)	63.48 (*)	56.67 (*)
ML	1.84 ± 0.22	1.47 ± 0.17	0.81 ± 0.12	20.11 (NS)	55.98 (*)	44.90 (*)

Note: W: week; NF: nasolabial fold; ML: marionette line; NS: not significant.
* indicates a statistical significance ($p < .05$).

Table 4. Global Aesthetic Improvement Scale.

	Rating score					
Scale	0	1	2	3	4	Mean
IGAIS, n (%)						
4 weeks	1 (4.8%)	7 (33.3%)	13 (61.9%)	0	0	1.57 ± 0.13
12 weeks	0	1 (4.8%)	2 (9.5%)	13 (61.9%)	5 (23.8%)	3.05 ± 0.16
SGAIS, n (%)						
4 weeks	1 (4.8%)	4 (19.0%)	16 (76.2%)	0	0	1.71 ± 0.12
12 weeks	0	0	2 (9.5%)	13 (61.9%)	6 (28.6%)	3.19 ± 0.13

Notes: Numbers in cells indicate the number of patients. GAIS score: 0 = no change, 1 = minimal improvement, 2 = mild improvement, 3 = moderate improvement, and 4 = marked improvement.

(Figure 4(F)), showing more-than-moderate improvements (both). In effect, at the 12-week follow-up visit, number of patients with a GAIS score of 3 or 4 increased in both IGAIS and SGAIS (Table 4). Accordingly, consistent with the Merz Scale results, the I/SGAIS results also showed esthetic improvements at both 4-week and 12-week follow-up visits. Overall results were summarized in Table 4.

Safety assessment

AEs were reported immediately, 4 and 12 weeks after treatment, including erythema (76.2%, 16 out of 21 patients), edema (42.8%, 9 out of 21), skin numbness (14.3%, 3 out of 21), tingling sensation (19%, 4 out of 21), and soreness (4.8%, 1 out of 21) (Figure 5(A)). However, they were trivial and transient, and were restored within 24 h (erythema, edema, soreness) or a week (skin numbness, tingling sensation). Notably, other possible AEs such as tissue irregularities, scarring, burning, and blistering were not reported and new AEs that were not detected immediately after treatment did not occur at both follow-up visits.

TS and pain intensity were rated immediately, 4 and 12 weeks after treatment. The mean TSS score was 3.31 ± 0.12 immediately after treatment and showed a 'warm' level (Figure 5(B), left bar), which was fully relieved within an hour. The mean NRS score was 4.28 ± 0.25 immediately after treatment and showed moderate pain, which was fully relieved within an hour (Figure 5(B), right bar).

Patient satisfaction survey

The survey of patient satisfaction with the procedure was performed using the SAQ at the 12-week follow-up visit. Each patient filled out the questionnaire, showing that 17 out of 21 patients (80.9%) were found to be satisfied with the procedure, and further, 7 out of 21 patients (33.3%) reported being 'very satisfied' (Table 5, upper column).

More than 85% of patients reported being 'very improved' or 'improved'. Notably, 6 out of 21 patients (28.6%) reported being 'very improved'. In addition, more than 85% of patients reported that they felt 'comfortable' or 'very comfortable' throughout the procedure (Table 5, middle column).

Lastly, it was found that more than 76% of patients were willing to recommend the procedure to their friends. And 23.8% of patients reported that they would 'very likely' recommend it to their friends (Table 5, lower column).

Discussion

Sunken cheeks and sagging jawlines are representative phenotypes of aged skin and restoring them is therefore a crucial goal for facial skin rejuvenation (9). In the present study, we attempted a quantitative analysis for facial volume changes in patients with mild-to-moderate sunken cheeks and jawline laxity using the 3D imaging system, finding that facial volumetric increases and skin lifting effects were markedly enhanced mainly around the cheek (Figure 2(B,D)) and the jawline (Figure 2(B,E)) at 12 weeks after treatment. These results indicate that MRF treatment restored sunken cheeks and sagging jawlines by increasing their volume and lifting them up.

A variety of modalities have been used for stimulating the production of ECM components for skin rejuvenation because ECM contains multiple proteins and molecules that can improve overall facial skin conditions as well as sunken and sagging skin, such as mainly collagen, elastin, GAGs, PGs, and growth factors (5,36,37). Importantly, growing evidence demonstrates that RF devices are effective in encouraging the production of ECM components and have a great impact on ECM microenvironment (9,10,38). In a molecular level, these events are facilitated *via* transforming growth factor-beta (TGF-β)/Smad signaling post-RF treatment. Initially, RF treatment upregulates TGF-β, a major regulator of ECM, which in turn binds to TGF-β type II receptors, followed by phosphorylation of TGF-β type I receptors. This phosphorylation activates Smad2 and Smad3, then leading to the combination with Smad4 to form Smad complexes. And these complexes translocate into the nucleus to positively modulate ECM components. In this way, MRF or RF treatment is deeply engaged in their expression

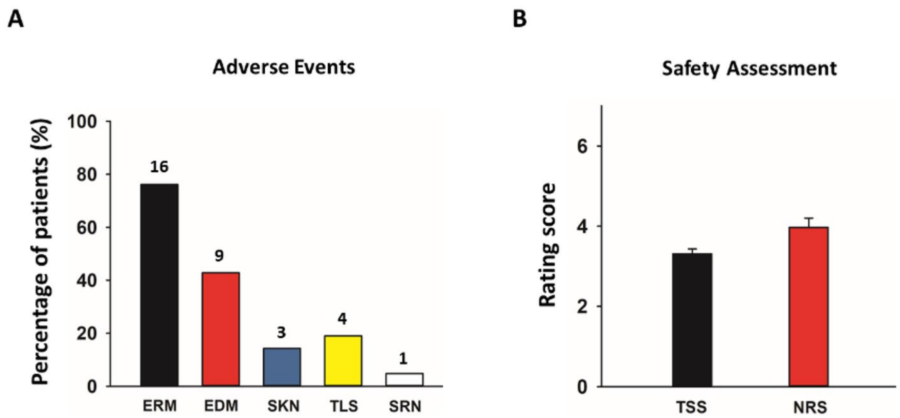

Figure 5. AEs were identified immediately after treatment, and erythema (76.2%) and edema (42.8%) were most frequently reported in the patients. At the two follow-up visits, these AEs were no longer found and there were no new AEs (data not shown) (A). In addition, thermal sensation and pain intensity were investigated immediately after treatment, and TSS and NRS showed mild or moderate levels of thermal sensation (B, left bar) or pain (B, right bar), respectively, which were fully relieved within an hour. In the graph, numbers above each bar represent the number of patients corresponding to each AE. ERM: erythema; EDM: edema; SKN: skin numbness; TLS: tingling sensation; SRN: soreness; TSS: Thermal Sensation Scale; NRS: Numeric Rating Scale.

Table 5. Self-assessment questionnaire for patient satisfaction.

No.	Questions and answers				
Q1	Are you overall satisfied with the procedure for face rejuvenation?				
A1	Very dissatisfied	Dissatisfied	Neutral	Satisfied	Very satisfied
P1	0	0	19% (4)	47.7% (10)	33.3% (7)
Q2	How much has your facial skin improved?				
A2	Much worse	Worse	No change	Improved	Much improved
P2	0	0	14.3% (3)	57.1% (12)	28.6% (6)
Q3	Did you feel comfortable throughout the procedure?				
A3	Very uncomfortable	Uncomfortable	Neutral	Comfortable	Very comfortable
P3	0	4.8% (1)	9.5% (2)	14.3% (3)	71.4% (15)
Q4	Would you recommend the procedure to your friends?				
A4	Very unlikely	Unlikely	Neutral	Likely	Very likely
P4	0	4.8% (1)	19% (4)	52.4% (11)	23.8% (5)

Notes: Numbers in parentheses indicate the number of patients. Q: question; A: answer; P: percentage.

and activation (9,38–40). Previous studies showed that collagen and elastin levels significantly increased in the epidermal and dermal layers of the skin post-MRF or RF treatment, thereby leading to the augmentation of skin thickness and elasticity (41–44). In addition, GAGs, PGs, and growth factors, also participated in improving skin conditions. It is well known that GAGs, especially hyaluronic acid, are greatly involved in increasing or maintaining tissue volume and hydration (37). PGs have a critical role in maintaining hydration, supporting tissue structure, regulating cell-cell interaction for tissue repair, and acting as molecular reservoirs of growth factors, potentially contributing to the improvement of skin volume and elasticity (36). The current study showed actual volumetric increases along with enhanced lifting effects mainly around the cheek and the jawline using a quantitative analysis. In detail, the cheek volume rose by 5.66 ± 0.90 cc and the jawline volume by 1.34 ± 0.21 at 12 weeks post-treatment (Figure 2(D,E)). Thus, it can be speculated that the volume increases and lifting effects observed in our study might be due to augmented collagen and elastin levels, as well as to activated and upregulated other ECM components (GAGs, PGs, etc.) after MRF treatment. Further studies are warranted to demonstrate actual changes in the expression level of ECM components in human subjects, parallel with facial volume change.

By contrast, the current study also reported volume loss in the face of the patients (Figure 3). Most of the volume loss area was detected in NF and ML (approximately 85%) (Figure 3(C)), and intriguingly, lifting effects were most evident around those regions (Figure 3(A,C)), indicating that this volume loss is closely associated with the lifting effects. Accordingly, it could be interpreted that MRF-induced lifting effects around NF and ML pull the areas upward, resulting that postprocedural volume in the areas was measured to be relatively reduced than preprocedural one. In effect, volume restoration can improve wrinkles and then give it contour, consequently leading to a morphological alteration (45). Collectively, our results suggest that this volume loss is attributed to a morphological change by the lifting effects around NL and ML, rather than actual volume loss.

In addition, two independent dermatologists assessed comprehensively postprocedural esthetic improvements using the Merz Scale. It was shown that sunken cheeks and sagging jawlines were significantly improved 4 weeks or 4 and 12 weeks after treatment compared to baseline (all, $p < .05$) (Figure 4(A–C)). Notably, the Merz assessment scores on the wrinkle depth of NF and ML were also significantly improved 12 weeks after treatment compared to baseline (both, $p < .05$) (Figure 4(D,E)). It is believed that these achievements are attributed to the actual volume increases and lifting effects observed in the 3D images. Consequently, mild-to-moderate sunken cheeks, jawlines, and wrinkles were restored to mild or less-than-mild level. Furthermore, the I/SGAIS assessments supported these outcomes (Figure 4(F)). Collectively, it was demonstrated that this MRF device has sufficient efficacy to ameliorate sunken cheeks, sagging jawlines, and wrinkles.

With regard to safety, our study showed that TSS and NRS scores were 3.15 ± 0.15 (1–5 range) and 4.28 ± 0.25 (0–10 range), respectively, showing a 'warm' level and moderate pain (Figure 5(B)). In addition, there were minor and temporary AEs (Figure 5(A)). We used 3.0-cm^2 and 4.0-cm^2 tips at energy levels of 1.5–3.5 (approximately, 11.7–21.7 J/cm^2 for the former and 11.3–21.3 J/cm^2 for the latter), applying a total of 260–650 shots per patient with 20–50% overlapped without anesthetics. Meanwhile, Suh et al. reported the latest update of a MRF device based on an intermittent gas-cooling system. This questionnaire-based study showed that the latest version of a gas cooling-based MRF device is more effective (57.4% of dermatologist users), more convenient (19.1%), faster (66%), but more painful (25.5%) than its prior version. And 23.5% of dermatologists who experienced post-treatment complications reported severe pain, suggesting that there is a safety issue in the device (18). In effect, a high level of pain was reported on the same device in another study. Angra et al. reported that even under pain control with ketorolac 60 mg, the mean pain score was 6.9 (0–10 range) during and after treatment. They delivered a total of 900 pulses at energy levels of 0.5–5 (approximately, 6.3–28.5 J/cm^2) (20). However, compared to the studies above, our study showed less pain and better safety profile while achieving significant improvements even with no anesthesia. It suggests that the water-cooling system is effective in controlling pain and further contributes to promoting clinical outcomes. In contrast to the existing intermittent gas-cooling system, the water-cooling system uses circulating chilled water (12–20 °C) to continuously cool the epidermis. Under this system, 1000-ms single RF pulse can be irradiated at a time, and therefore even and sufficient RF energy can be delivered to the skin (Supplementary Figure 1S). Notably, heat capacity of water is higher than gas and is constant throughout the temperature range, putatively more helpful in preventing excessive bulk heating, especially in sparing the skin surface (46,47). It is believed that these functional differences may allow this device to show sufficient efficacy and less pain in treating the patients. For an accurate comparison, studies should be warranted to directly compare efficacy and safety between water cooling-based and gas cooling-based devices in the future.

The present study also reveals a number of limitations. In particular, the ethnicity of study participants limited to East Asians (Koreans). Skin conditions differ depending on ethnicity, and even within East Asia populations. Therefore, further studies should be conducted with participants of various ethnicities to report more reliable clinical outcomes for this device and procedure, thus providing better insights into generalizability. Second, this study did not investigate the expression patterns of ECM proteins and molecules with crucial roles in improving and delaying skin aging before and after treatment. If such effects are reported together with those of MRF-induced volume increase and skin lifting, it could serve as strong evidence for the efficacy of water-cooling based MRF devices. Lastly, this study did not directly compare our device with a gas-cooling based MRF device. To elucidate more accurately the advantages and disadvantages of water-cooling system, further studies are warranted, possibly designed to compare the efficacy and safety of the two cooling modalities in a well-established randomized controlled trial.

Conclusions

The present study reported the efficacy and safety of a novel MRF device equipped with a continuous water-cooling system. Importantly, we offered quantitative evidence for post-treatment volumetric changes in the major regions of the face and showed reliable clinical outcomes using various assessment tools. Interestingly, this water cooling-based device showed moderate pain even without anesthetics while delivering high energy. Therefore, these results show that our novel MRF device is effective and safe in treating mild-to-moderate sunken cheeks and jawline laxity in Asian patients, strongly implying that the continuous water-cooling system can be a new alternative that makes up for the weak point of the conventional cooling modality.

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Ethics statement

This study was conducted complying with the ethical guidelines of the 1975 Declaration of Helsinki (revised in 2000) and with the local guidelines. Ethical approval was granted from the Institutional Review Board of the Clinical Trial Center of COREDERM Inc. (Approval no.: CDIRB-QR-24-002).

Consent form

All patients were given information about the overall details of this study and signed an informed consent form.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The data that support the findings of this study are available from the corresponding author, BL Goo, upon request.

References

1. Franco AC, Aveleira C, Cavadas C. Skin senescence: mechanisms and impact on whole-body aging. Trends Mol Med. 2022;28(2):1–10. doi: 10.1016/j.molmed.2021.12.003.
2. Ho CY, Dreesen O. Faces of cellular senescence in skin aging. Mech Ageing Dev. 2021;198:111525. doi: 10.1016/j.mad.2021.111525.
3. Wlaschek M, Maity P, Makrantonaki E, et al. Connective tissue and fibroblast senescence in skin aging. J Invest Dermatol. 2021;141(4S):985–992. doi: 10.1016/j.jid.2020.11.010.
4. Gruber F, Kremslehner C, Eckhart L, et al. Cell aging and cellular senescence in skin aging - recent advances in fibroblast

and keratinocyte biology. Exp Gerontol. 2020;130:110780. doi: 10.1016/j.exger.2019.110780.

5. Adele S. Role of the extracellular matrix in skin aging and dedicated treatment - state of the art. Plast Aesthet Res. 2020;7:14.
6. Kümper M, Steinkamp J, Zigrino P. Metalloproteinases in dermal homeostasis. Am J Physiol Cell Physiol. 2022;323(4):C1290–C1303. doi: 10.1152/ajpcell.00450.2021.
7. Baumann L, Bernstein EF, Weiss AS, et al. Clinical relevance of elastin in the structure and function of skin. Aesthet Surg J Open Forum. 2021;3(3):ojab019. doi: 10.1093/asjof/ojab019.
8. Zargaran D, Zoller F, Zargaran A, et al. Facial skin ageing: key concepts and overview of processes. Int J Cosmet Sci. 2022;44(4):414–420. doi: 10.1111/ics.12779.
9. Lyu J-J, Liu S-X. Radiofrequency in facial rejuvenation. Int J Dermatol Venereol. 2022;5(2):94–100. doi: 10.1097/JD9.0000000000000193.
10. Louis F, Fujii N, Katsuyama M, et al. Effects of radiofrequency and ultrasound on the turnover rate of skin aging components (skin extracellular matrix and epidermis) via HSP47-induced stimulation. Biochem Biophys Res Commun. 2020;525(1):73–79. doi: 10.1016/j.bbrc.2020.02.020.
11. Suh DH, Ahn HJ, Seo JK, et al. Monopolar radiofrequency treatment for facial laxity: histometric analysis. J Cosmet Dermatol. 2020;19(9):2317–2324. doi: 10.1111/jocd.13449.
12. Wanitphakdeedecha R, Yogya Y, Yan C, et al. Efficacy and safety of monopolar radiofrequency for treatment of lower facial laxity in Asians. Dermatol Ther. 2022;12(11):2563–2573. doi: 10.1007/s13555-022-00817-8.
13. Hwang Y, Arayaskul S, Vachiramon V, et al. Subjective evaluation of monopolar radiofrequency treatment by patients in aesthetic rejuvenation. Skin Res Technol. 2024;30(2):e13593. doi: 10.1111/srt.13593.
14. Park J-H, Kim J-I, Park HJ, et al. Evaluation of safety and efficacy of noninvasive radiofrequency technology for submental rejuvenation. Lasers Med Sci. 2016;31(8):1599–1605. doi: 10.1007/s10103-016-2023-7.
15. Foster KR, Ziskin MC, Balzano Q. Time-temperature thresholds and safety factors for thermal hazards from radiofrequency energy above 6GHz. Health Phys. 2021;121(3):234–247. doi: 10.1097/HP.0000000000001447.
16. Levy AS, Grant RT, Rothaus KO. Radiofrequency physics for minimally invasive aesthetic surgery. Clin Plast Surg. 2016;43(3):551–556. doi: 10.1016/j.cps.2016.03.013.
17. Delgado AR, Chapas A. Introduction and overview of radiofrequency treatments in aesthetic dermatology. J Cosmet Dermatol. 2022;21(S1):S1–S10. doi: 10.1111/jocd.15026.
18. Suh DH, Hong ES, Kim HJ, et al. A survey on monopolar radiofrequency treatment: the latest update. Dermatol Ther. 2020;33(6):e14284. doi: 10.1111/dth.14284.
19. Carruthers J, Fabi S, Weiss R. Monopolar radiofrequency for skin tightening: our experience and a review of the literature. Dermatol Surg. 2014;40(Supplement 12):S168–S173. doi: 10.1097/DSS.0000000000000232.
20. Angra K, Alhaddad M, Boen M, et al. Prospective clinical trial of the latest generation of noninvasive monopolar radiofrequency for the treatment of facial and upper neck skin laxity. Dermatol Surg. 2021;47(6):762–766. doi: 10.1097/DSS.0000000000003005.
21. Gökalp HJ. Efficacy of monopolar radiofrequency in middle and lower face laxity. J Turgut Ozal Med Cent. 2017;24:274–278.
22. Russell-Goldman E, Murphy GF. The pathobiology of skin aging: new insights into an old dilemma. Am J Pathol. 2020;190(7):1356–1369. doi: 10.1016/j.ajpath.2020.03.007.
23. Zhang S, Duan E. Fighting against skin aging: the way from bench to bedside. Cell Transplant. 2018;27(5):729–738. doi: 10.1177/0963689717725755.
24. Adatto M. Clinical evaluation of the efficacy of fractional radiofrequency for the treatment and reduction of stretch marks: a prospective study. J Cosmet Dermatol. 2023;22(1):214–221. doi: 10.1111/jocd.15463.
25. Kim BR, Kim M, Kim JW, et al. Efficacy and safety of the micro-insulated needle radiofrequency device for reduction of submental fat. Dermatol Surg. 2023;49(4):389–394. doi: 10.1097/DSS.0000000000003723.
26. Machado BHB, De Melo E, Silva ID, et al. Scientific validation of three-dimensional stereophotogrammetry compared to the IGAIS clinical scale for assessing wrinkles and scars after laser treatment. Sci Rep. 2021;11(1):12385. doi: 10.1038/s41598-021-91922-9.
27. De Stefani A, Barone M, Hatami Alamdari S, et al. Validation of Vectra 3D imaging systems: a review. Int J Environ Res Public Health. 2022;19(14):8820. doi: 10.3390/ijerph19148820.
28. Lee JE, Boo YC. Combination of glycinamide and ascorbic acid synergistically promotes collagen production and wound healing in human dermal fibroblasts. Biomedicines. 2022;10(5). doi: 10.3390/biomedicines10051029.
29. Sawh-Martinez R, Steinbacher DM. Commentary on: three-dimensional imaging of the face: a comparison between three different imaging modalities. Aesthet Surg J. 2018;38(6):586–589. doi: 10.1093/asj/sjy025.
30. Sharma S. Implementation of 3D technologies for quantification and improvement of clinical diagnostics [master's thesis]. Enschede (Netherlands): University of Twente; 2020.
31. Stella E, Di Petrillo A. Standard evaluation of the patient: the Merz scale. In: Goisis M, editor. Injections in aesthetic medicine: atlas of full-face and full-body treatment. Milano: Springer; 2014. p. 33–50.
32. Yalici-Armagan B, Elcin G. Evaluation of microfocused ultrasound for improving skin laxity in the lower face: a retrospective study. Dermatol Ther. 2020;33(6):e14132.
33. Liu W, Tian X, Yang D, et al. Evaluation of individual thermal sensation at raised indoor temperatures based on skin temperature. Build Environ. 2021;188:107486. doi: 10.1016/j.buildenv.2020.107486.
34. Nguyen L, Blessmann M, Schneider SW, et al. Radiofrequency microneedling for skin tightening of the lower face, jawline, and neck region. Dermatol Surg. 2022;48(12):1299–1305. doi: 10.1097/DSS.0000000000003607.
35. Shome D, Vadera S, Ram MS, et al. Use of micro-focused ultrasound for skin tightening of mid and lower face. Plast Reconstr Surg Glob Open. 2019;7(12):e2498. doi: 10.1097/GOX.0000000000002498.
36. Ruiz Martínez MA, Peralta Galisteo S, Castán H, et al. Role of proteoglycans on skin ageing: a review. Int J Cosmet Sci. 2020;42(6):529–535. doi: 10.1111/ics.12660.
37. Wang ST, Neo BH, Betts RJ. Glycosaminoglycans: sweet as sugar targets for topical skin anti-aging. Clin Cosmet Investig Dermatol. 2021;14:1227–1246. doi: 10.2147/CCID.S328671.
38. El-Domyati M, El-Ammawi TS, Medhat W, et al. Expression of transforming growth factor-β after different non-invasive facial rejuvenation modalities. Int J Dermatol. 2015;54(4):396–404. doi: 10.1111/ijd.12435.

39. Hu H-H, Chen D-Q, Wang Y-N, et al. New insights into TGF-β/ Smad signaling in tissue fibrosis. Chem Biol Interact. 2018;292:76–83. doi: 10.1016/j.cbi.2018.07.008.
40. Shin JW, Kwon SH, Choi JY, et al. Molecular mechanisms of dermal aging and antiaging approaches. Int J Mol Sci. 2019;20(9):2126. doi: 10.3390/ijms20092126.
41. el-Domyati M, el-Ammawi TS, Medhat W, et al. Radiofrequency facial rejuvenation: evidence-based effect. J Am Acad Dermatol. 2011;64(3):524–535. doi: 10.1016/j.jaad.2010.06.045.
42. Kaplan H, Gat A. Clinical and histopathological results following TriPollar radiofrequency skin treatments. J Cosmet Laser Ther. 2009;11(2):78–84. doi: 10.1080/14764170902846227.
43. Kinney BM, Kanakov D, Yonkova P. Histological examination of skin tissue in the porcine animal model after simultaneous and consecutive application of monopolar radiofrequency and targeted pressure energy. J Cosmet Dermatol. 2020;19(1):93–101. doi: 10.1111/jocd.13235.
44. Baek EJ, Oh DY, Suh SB, et al. Treatment for aging skin with multifrequency radiofrequency. Dermatol Ther. 2023;2023:1–6. doi: 10.1155/2023/7551039.
45. El-Mesidy MS, Alaklouk WT, Azzam OA. Nasolabial fold correction through cheek volume loss restoration versus thread lifting: a comparative study. Arch Dermatol Res. 2020;312(7):473–480. doi: 10.1007/s00403-019-02031-7.
46. Kim J-K, Smith R. Cooling water system design. Chem Eng Sci. 2001;56(12):3641–3658. doi: 10.1016/S0009-2509(01)00091-4.
47. ToolBox E. Specific heat of common substances. The Engineering ToolBox; 2003. Available at: https://www.engineeringtoolbox.com/specific-heat-capacity-d_391.html