Comparative Study of Monopolar Radiofrequency and High-Intensity Focused Ultrasound for Facial Rejuvenation: A Split-Face Approach

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BACKGROUND The increasing demand for nonsurgical antiaging treatments has popularized monopolar radiofrequency and high-intensity focused ultrasound. Although both skin laxity and wrinkles improve, the optimal treatment sequence is unclear.

OBJECTIVE To evaluate the efficacy and safety of sequential monopolar radiofrequency and high-intensity focused ultrasound treatments for facial rejuvenation by specifically examining the impact of the treatment sequence on clinical outcomes.

MATERIALS AND METHODS A split-face study of 24 Korean adults compared monopolar radiofrequency followed by high-intensity focused ultrasound and high-intensity focused ultrasound followed by monopolar radiofrequency. Clinical assessments were conducted on days 30 and 90, and a three-dimensional camera was used to evaluate changes in wrinkles and pores.

RESULTS Both treatment sequences resulted in clinical improvements with minimal side effects; however, the three-dimensional camera analysis indicated that monopolar radiofrequency followed by high-intensity focused ultrasound demonstrated slightly better wrinkle reduction. The histological results indicated increases in collagen I, III, and IV and laminin; however, marked differences between sequences were not observed.

CONCLUSION Monopolar radiofrequency and high-intensity focused ultrasound are safe and effective for facial rejuvenation. However, wrinkle reduction with monopolar radiofrequency followed by high-intensity focused ultrasound was better than that with high-intensity focused ultrasound followed by monopolar radiofrequency.

Monopolar radiofrequency (MRF) generates heat through a high-frequency current that flows from a transducer to a grounding pad on the patient's body, thus influencing collagen production based on the duration and intensity of heating of the connective tissue.[1] MRF provides broad volumetric heating that affects multiple dermal layers. Conversely, high-intensity focused ultrasound (HIFU) enhances skin elasticity and regeneration by directing high-intensity ultrasound waves to create small microthermal lesions at intended depths from the reticular dermis to the fibromuscular layer. MRF raises tissue temperatures to 40°C to 45°C, thus promoting collagen remodeling without coagulative necrosis, whereas HIFU reaches temperatures of 60°C to 70°C, leading to immediate tissue contraction and long-term neocollagenesis.[2,3] Treatments comprising both HIFU and MRF have resulted in synergistic effects on skin lifting and tightening.[4]

The aim of this study was to determine whether HIFU followed by MRF or MRF followed by HIFU performed on the same day yields better clinical outcomes and safety. The authors used a MRF device (Volnewmer; Classys Inc., Seoul, Korea) and a HIFU device (Shurink Universe; Classys Inc., Seoul, Korea) for this study. In addition, they used a three-dimensional (3D) camera and histological analysis to compare improvements in wrinkles and pores obtained with these treatment sequences.

Materials and Methods

Twenty-four Korean adults (mean age, 48.7 years; range 31–72 years) with facial wrinkles participated in this study. Of these patients, 17 were women (mean age, 51.5 years) and 7 were men (mean age, 41.8 years). All participants were informed of the potential risks and benefits of treatment. The study protocol followed the 1975 Declaration of Helsinki and was approved by the Institutional Review Board of Hallym University Sacred Heart Hospital.

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Treatment included 150 pulses of MRF immediately followed by 150 lines of HIFU (MRF-HIFU) on one side of the face and 150 lines of HIFU immediately followed by 150 pulses of MRF (HIFU-MRF) on the other side. To decide which side of the face would receive MRF-HIFU, a dermatologist who was not involved in the treatment of the patients used a computer to generate random sequences for all patients. The sequences remained unknown to the evaluator of the clinical photographs until the evaluation was completed on day 90.

MRF treatment was performed with a 4-cm^2 V Tip set at energy levels of 2.5 to 4.5 that delivered total energy of 19 to 33 kJ/cm^2 (mean, 27 kJ/cm^2) and average energy of 16.2 to 28.1 J/cm^2 (mean, 23.2 J/cm^2). HIFU treatment was performed with a 4.5-mm cartridge with energy levels of 0.6 to 0.9 J (mean, 0.81 J) and a 3.0-mm cartridge with energy levels of 0.3 to 0.4 J (mean, 0.38 J).

Clinical photographs were obtained using a facial skin analyzer (Mark-Vu; PSI Plus, Gyeonggi-do, Korea) before treatment and on days 30 and 90 after treatment. During each examination, an experienced dermatologist who did not participate in the treatment of the patients assessed both sides of the face using the Physician Global Aesthetic Improvement Scale (PGAIS) (score range, 1–5). Similarly, the participants performed self-evaluations using the Subject Global Aesthetic Improvement Scale (SGAIS) (score range, 1–5). The same dermatologist evaluated erythema, edema, contour irregularity, and bruising on both sides of the face on days 30 and 90. Pain during the procedure was assessed using a Visual Analog Scale (VAS) immediately after completion.

The 3D photographs were captured with a LifeViz Mini Pro camera (Quantificare S.A., Valbonne, France) before treatment and on day 90. Changes in wrinkles and pores between baseline and day 90 were analyzed. Wrinkle scores were calculated based on their length, width, and depth, and pore scores were based on the pore count (scale, −10 to +10) using the QuantifiCare database for similar skin types, sexes, and ages.

Biopsy specimens were obtained from three participants using a 3-mm punch on both treated areas before treatment and on day 90. All specimens were stained with hematoxylin and eosin as well as collagen I, III, and IV and laminin subunit alpha 1 (LAMA1) antibodies (TmBio Inc., Gyeonggi-do, Korea). Staining was performed simultaneously and under identical conditions to minimize variability. Intensities were assessed using ImageJ software (https://ij.imjoy.io/). The assessment excluded the epidermis and focused on signs of dermis rejuvenation. The tissue size was analyzed, thresholds were adjusted to isolate the stained particles, and proportions of these particles in the total tissue were calculated.

Nonparametric analyses (the Shapiro-Wilk test confirmed non-normal distributions) included the Friedman test for the PGAIS, SGAIS, and safety scores across time points. Wilcoxon signed rank tests with the Bonferroni correction were performed to assess VAS scores, wrinkle and pore scores, and changes in collagen I, III, and IV and LAMA1 levels in biopsy specimens. All statistical analyses were performed using SPSS version 30.0 for Windows (SPSS Inc., Chicago, IL).

The initial draft of this article was prepared with the assistance of an artificial intelligence (AI)-based language model (ChatGPT) to ensure clarity of the English expressions. The authors independently reviewed and finalized all content before publication.

Results

PGAIS and SGAIS Scores

The median PGAIS and SGAIS scores for both treatment sequences were evaluated on days 30 and 90. The median PGAIS scores of both groups decreased from 3.0 (interquartile range [IQR]: 2.0 to 3.0) on day 30 to 2.0 (IQR: 2.0–3.0) on day 90. The SGAIS scores showed a similar trend. The median SGAIS scores of both groups decreased from 3.0 (IQR: 2.0–3.0) on day 30 to 2.0 (IQR: 2.0–3.0) on day 90. The PGAIS scores decreased from day 30 to day 90 with both treatment sequences; however, the differences were not significant after Bonferroni correction (HIFU-MRF: $Z = -2.236$, $p = .025$; MRF-HIFU: $Z = -2.236$, $p = .025$). By contrast, the SGAIS scores significantly decreased with both treatment sequences and remained significant after Bonferroni correction (HIFU-MRF: $Z = -2.646$, $p = .008$; MRF-HIFU: $Z = -2.646$, $p = .008$). However, on day 30, statistically significant differences in the PGAIS and SGAIS scores based on the treatment sequence were not observed. Similarly, significant differences in the SGAIS and PGAIS scores were not observed on day 90 when the two treatment sequences were compared. These findings suggest that the treatment sequence did not significantly affect the PGAIS and SGAIS scores at any specific time point.

Safety Scores

Erythema scores of both treatment sequences were significantly reduced on day 30 compared with those on day 0 ($Z = -3.771$ and $p < .001$ for both HIFU-MRF and MRF-HIFU). Similarly, edema was significantly reduced on day 30 compared with that on day 0 with both treatment sequences ($Z = -3.742$ and $p < .001$ for both HIFU-MRF and MRF-HIFU). Similar to the PGAIS and SGAIS scores, no differences in the safety scores were observed across all assessed items based on the treatment sequence at each specific time point. The contour irregularity and bruising scores were zero across all conditions, indicating no variation between groups.

VAS Scores

The VAS scores were not significantly different between treatment sequences. Although the VAS scores with HIFU-MRF were lower than those with MRF-HIFU ($Z = -1.127$; $p = .260$), the difference was not statistically significant.

3D Camera Analysis: Wrinkle and Pore Scores

Wrinkle and pore scores of both sides of the face were determined using a LifeViz Mini Pro camera at baseline (day

0) and on day 90. The results indicated no significant differences in wrinkle scores with both treatment sequences; however, wrinkle scores tended to increase from day 0 to day 90. For the MRF-HIFU group, wrinkle scores on day 90 were higher than those on day 0 ($Z = -2.264$; $p = .024$); however, this difference was not statistically significant after Bonferroni correction. Similarly, pore scores of both treatment sequences were not significantly different.

Table 1 summarizes the Z-values and *p*-values for the PGAIS, SGAIS, erythema, edema, VAS, wrinkle, and pore scores across sequences and time points. Photographs of one participant before treatment and on day 90 are presented in Figure 1.

Antibody Staining

Biopsy specimens from three participants were stained with collagen I, III, and IV and LAMA1 antibodies before and after treatment to evaluate their expressions. Significant differences in the staining proportions of all markers were not observed. Although a general trend of an increased staining proportion after treatment was observed, a few samples exhibited a reduced staining proportion after treatment. Compared with that at baseline, collagen I antibody staining was increased in biopsy specimens after treatment, regardless of the treatment sequence. In addition, collagen III antibody staining was increased in all biopsy specimens, except for that from the side of patient 2 who was treated with HIFU-MRF, after treatment. Collagen IV antibody staining of all biopsy specimens, except for that from the side of patient 1 who was treated with HIFU-MRF and that from the side of patient 2 who was treated with MRF-HIFU, increased after treatment. LAMA1 antibody staining increased in all biopsy specimens, except for that from the side of patient 2 who was treated with HIFU-MRF and that from the side of patient 3 who was treated with MRF-HIFU, after treatment (Figure 1, **Supplemental Digital Content** 1, http://links.lww.com/DSS/B694).

Discussion

Although the use of both MRF and HIFU on the same day is common, no studies have investigated the optimal treatment sequence for achieving the best clinical outcomes and safety. During this split-face comparison, HIFU-MRF was applied to one side of the face and MRF-HIFU was applied to the other side. This approach was designed to minimize confounding variables.

The median PGAIS and SGAIS scores decreased from day 30 to day 90 with both treatment sequences, indicating improvement over time. Significant reductions in SGAIS scores between day 30 and day 90 with both treatment sequences suggested that participants perceived more post-treatment decline over time compared with that perceived by the clinicians. This trend indicates that treatment efficacy is subjective and, compared with clinicians, participants may perceive it as more rapidly diminishing, thus highlighting the potential discrepancy between patient-perceived and clinician-observed outcomes. However, significant differences in PGAIS and SGAIS scores were not observed with the treatment sequences on days 30 and 90. This suggests that the treatment sequence does not significantly affect the objective or subjective clinical effectiveness.

Safety outcomes (erythema, edema, contour irregularity, and bruising) were evaluated across both treatment sequences. Significant reductions in erythema and edema

TABLE 1. PGAIS, SGAIS, Erythema, Edema, VAS, wrinkle, and Pore Scores Across treatment Sequences and Time Points

Outcome	Procedure Sequence	Time Comparison	Z-value	*p*	Bonferroni-Corrected Significance
PGAIS score	HIFU-MRF MRF-HIFU	Day 30 vs 90 Day 30 vs 90	−2.236 −2.236	.025 .025	n.s. n.s.
SGAIS score	HIFU-MRF MRF-HIFU	Day 30 vs 90 Day 30 vs 90	−2.646 −2.646	.008 .008	Significant Significant
Erythema score	HIFU-MRF MRF-HIFU	Day 0 vs 30 Day 0 vs 30	−3.742 −3.742	<.001 <.001	Significant Significant
Edema score	HIFU-MRF MRF-HIFU	Day 0 vs 30 Day 0 vs 30	−3.771 −3.771	<.001 <.001	Significant Significant
VAS score	HIFU-MRF	Compared with MRF-HIFU	−1.127	.260	n.s.
Wrinkle score	HIFU-MRF	Compared with MRF-HIFU	−2.264	.024	n.s.
Wrinkle score	HIFU-MRF MRF-HIFU	Day 0 vs 90 Day 0 vs 90	−0.184 −2.489	.854 .013	n.s. n.s.
Pore score	HIFU-MRF	Compared with MRF-HIFU	0.663	.507	n.s.
Pore score	HIFU-MRF MRF-HIFU	Day 0 vs 90 Day 0 vs 90	−0.570 −1.527	.569 .127	n.s. n.s.

Z-values and *p*-values are presented for PGAIS and SGAIS scores (day 30 vs 90), erythema and edema (day 0 vs 30), and wrinkle/pore scores (day 0 vs 90). VAS scores represent pain during HIFU-MRF versus MRF-HIFU treatments.
n.s., not significant.

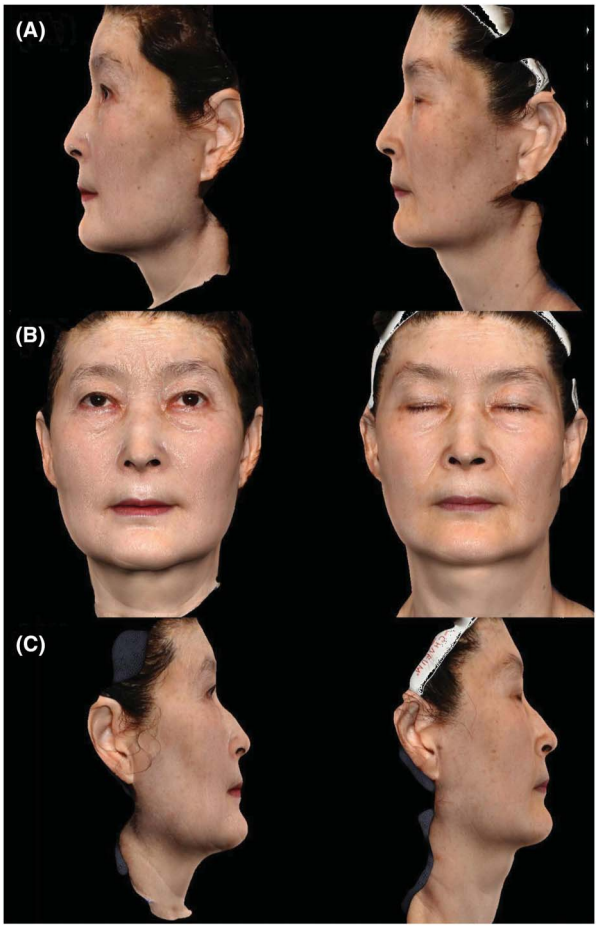

Figure 1. Photographs of a 61-year-old woman (participant 2) obtained with a 3D camera before and after treatment. (A) Left side of the face treated with MRF-HIFU. (B) Center of the face (reference image for symmetry). (C) Right side of the face treated with HIFU-MRF.

were observed between day 0 and day 30 with both treatment sequences. No significant differences were observed, indicating that both treatment sequences were safe and well tolerated without notable bruising or contour irregularities.

The VAS scores with MRF-HIFU were slightly higher than those with HIFU-MFR; however, the difference between scores was not significant. Because HIFU targets deeper layers and MRF affects both the superficial and deep layers, MRF-HIFU may affect blood circulation, potentially leading to faster anesthetic resolution.[5] A study of EMLA anesthetic cream showed that when heat was applied, the treated areas demonstrated a continuous slow increase in blood perfusion, whereas the untreated areas did not.[6] According to previous studies that evaluated VAS scores for HIFU and MRF treatments, HIFU is more painful than MRF.[7,8] Because the effects of topical anesthesia gradually decrease and the pain intensity of HIFU is more than that of MRF, patients may experience more pain with MRF-HIFU than with HIFU-MRF.

The 3D camera analysis revealed no significant differences in wrinkle and pore scores with both treatment sequences between day 0 and day 90. Although wrinkle improvement with MRF-HIFU and that with HIFU-MRF were not statistically significant, a noticeable trend was observed. A similar trend of improvement in the wrinkle scores between day 0 and day 90 was observed with MRF-HIFU; however, a statistically significant difference was not observed. Byun and colleagues[9] reported improvements in the pore volume and number as well as in facial wrinkles after HIFU treatment. Combining HIFU with MRF may result in a tightening effect on the deep and superficial dermis around the hair follicles. In actual practice, HIFU-MRF is considered safer than MRF-HIFU. Furthermore, when MRF is performed first, it may cause dermal edema, leading to the formation of dots associated with HIFU at depths shallower than those intended. One study documented the occurrence of edema in the facial region after MRF therapy.[10] In this study, the improved wrinkle scores with MRF-HIFU according to the 3D camera analysis may have been attributable to dermal edema resulting from MRF treatment, which caused dot formation with HIFU at a more superficial layer and led to neocollagenesis. Further research should compare the extent of neocollagenesis in each skin layer to confirm whether combining HIFU with MRF results in a tightening effect on the deep and superficial dermis around the hair follicles.

Reduced synthesis of type I collagen occurs in aged skin. One study reported that dermal fibroblasts isolated from the skin of older individuals exhibited less in vitro production of type I procollagen compared with that in skin of younger individuals.[11] This reduction in collagen synthesis was attributed to both fibroblast cell aging and decreased mechanical stimulation in aged tissue. The proportion of type III collagen may decrease with age.[12] One study found that collagen IV decreased with age, but that the epithelial basement membrane thickness increased.[13] A significant reduction in laminin-332 and reductions in various collagen types have been observed in aged skin.[14] These alterations may play a role in the deterioration of structural integrity and increased fragility of aged skin. During aging, collagens undergo modifications such as the accumulation of advanced glycation end products, depletion of glycosaminoglycans, and mineralization, which affect their stability and degradation.[15]

One study reported a notable increase in the average levels of collagen types I and III and found that their expressions consistently increased over 3 months after radiofrequency treatment.[16] A study by Kwon and colleagues[4] found an increase in collagen fibers across the whole dermis after sequential treatment comprising 600 pulses of MRF followed by 300 lines of HIFU. Suh and colleagues[5] compared the effects of HIFU and MRF on neocollagenesis and neoelastogenesis at various depths of the dermis and found that HIFU produced the highest levels of neocollagen and neoelastin in the deep reticular dermis when targeting focal areas; additionally, they found that MRF affects deep tissue but tends to have a more diffuse impact and demonstrates lower efficacy in the deep reticular dermis compared with those associated with HIFU. One

study demonstrated that collagen I and III levels significantly increased in the dermis after MRF treatment, thus confirming that radiofrequency induces collagen synthesis independent of stem cell count changes in the skin.[16] Another study found that HIFU increased collagen and elastin expressions as well as collagen fiber accumulation and elastin fiber density in aging skin.[17] This study showed a nonsignificant increase in collagen I levels across all participants and increases in collagen III and IV and LAMA1 levels in most biopsy specimens after treatment. Increases in collagen I and III levels after HIFU and MRF treatments were consistent with the results of previous studies. However, this study was limited by its small sample size, short follow-up period, and the inherent limitation of skin biopsy, which only assesses the reticular dermis and does not capture changes in deeper structures such as the subcutaneous fat and SMAS. Future studies including advanced imaging techniques could provide a more comprehensive evaluation of tissue remodeling beyond the dermis. In addition, future research should incorporate specific patient characteristics, such as baseline skin laxity severity, photoaging degree, and skin thickness, using validated assessment tools. Stratifying patients based on these factors may help refine treatment selection and optimize outcomes of MRF, HIFU, and their combination.

Conclusion

MRF and HIFU treatments are safe and effective. However, their sequences may introduce carryover effects, with the first treatment affecting the outcomes of the second treatment. Both treatments improved PGAIS and SGAIS scores and resulted in minimal side effects. Wrinkle reduction with MRF-HIFU was slightly better than that with HIFU-MRF, as indicated by the 3D camera analysis. A histological analysis showed increased collagen I, III, and IV and LAMA1 levels after treatment, suggesting reversal of age-related effects. Further studies with larger sample sizes are required to confirm these results. Despite the use of fewer MRF pulses than those used during stand-alone studies, significant improvements were achieved with the authors' approach, thus suggesting the potential efficacy of combined MRF and HIFU treatment, even with reduced pulses. Most existing studies of MRF have included 600 pulses; however, in clinical practice, one session generally includes either 600 or 900 pulses. During the next study, the authors plan to compare MRF with 600 pulses alone, MRF with 300 pulses and HIFU, and MRF with 600 pulses and HIFU; additionally, the follow-up period will be extended to at least 6 months to assess the long-term effects and identify the most cost-effective skin rejuvenation method. Treatment comprising both MRF and HIFU is a promising nonsurgical option that can reduce the signs of aging.

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