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Research Article

Treatment for Aging Skin with Multifrequency Radiofrequency

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Background. Radiofrequency treatment improves skin aging-related concerns by promoting collagen production. However, studies of the efficacy of multifrequency radiofrequency (MFRF) are lacking. *Objectives*. This study aimed to analyze the efficacy of MFRF for patients with aging skin. *Methods*. Three MFRF treatment sessions were performed for patients with concerns about skin aging. During these sessions, MFRF was applied to the face (but not the forehead). Pores, wrinkles, subjective satisfaction, and side effects were evaluated at the first visit and 4 weeks after the last treatment. Additionally, histological and immunohistochemical evaluations of collagen, elastic fibers, and STRO-1 were performed. *Results*. Wrinkles and the subjective satisfaction of patients were significantly improved ($p = 0.034$ and $p = 0.001$, respectively). However, there was no significant effect on the number of pores ($p = 0.429$). All side effects that occurred after treatment were tolerable and transient. Histological findings revealed thickening of collagen bundles and elastic fibers. Additionally, increases in collagen I, collagen III, and STRO-1 levels were observed using immunohistochemistry. *Conclusions*. MFRF treatment uses less energy than the existing radiofrequency equipment and can be an effective clinicopathologic modality for facial rejuvenation.

1. Introduction

Aging of the skin is associated with various cosmetic concerns [1]. Skin laxity occurs as collagen fibrils become rigid and elastic fibers decrease [2]. In particular, facial skin wrinkles can cause significant psychosocial distress and affect the quality of life [3]. The treatment of skin laxity is relatively new, and many studies are currently underway. Although treatment modalities have been investigated, there is no consensus regarding which is the most effective.

Nonablative radiotherapy increases the tissue temperature and causes contraction of the deep layers of skin and subcutaneous fat layer through heat damage [4, 5]; furthermore, it stimulates collagen production through collagen denaturation [6, 7]. Compared to the ablative laser, nonablative radiotherapy is advantageous because it can rejuvenate the dermis layer without damaging the epidermis [5, 8, 9].

Previously, radiofrequency treatment used only a single wavelength. This study is intended to clinically and histologically evaluate whether multifrequency radiofrequency (MFRF) can improve cell metabolism, collagen production, and skin regeneration.

2. Materials and Methods

2.1. Patients and Ethical Approval. This study was approved by the Institutional Review Board of Hallym University Sacred Hospital in Korea (institutional review board number: HALLYM 2021-07-002). The study protocol was approved by the Ethics Committee of the Hallym University Medical Center. Patients were eligible for enrollment if they visited the dermatology clinic at Hallym University Sacred Heart Hospital between July 2021 and February 2022, were 20 years of age or older, and consented to participate in the clinical trial. All procedures were performed by a single dermatologist. Patients who had been treated with other cosmetic procedures within the past 6 months, pregnant women, and those with treatment site infections, facial dermatitis, or a history of keloids were excluded. The

Table 1: Wrinkle Severity Rating Scale (WSRS).

Grade	Severity	Description
1	Absent	No visible nasolabial fold, continuous skin line
2	Mild	Shallow but visible nasolabial fold with a slight indentation, minor facial feature, implant is expected to produce a slight improvement in appearance
3	Moderate	Moderately deep nasolabial fold, clear facial feature visible at normal appearance but not when stretched, excellent correction is expected from injectable implant
4	Severe	Very long and deep nasolabial fold, prominent facial feature, <2 mm visible fold when stretched, significant improvement is expected from injectable implant
5	Extreme	Extremely deep and long nasolabial fold, detrimental to facial appearance, 2–4 mm visible *V*-shaped fold when stretched, unlikely to have satisfactory correction with injectable implant alone

study protocol followed the ethical guidelines of the Declaration of Helsinki, and informed consent was obtained from all patients.

2.2. Treatment Device and Protocol. The MFRF device (Corage 2.0®; Quanteq, Hanam City, Korea) induces a tissue response by producing resonance at various frequencies (multiples of 4 between 4 and 64 MHz). The operator performed approximately four passes at a level of 35 to 45 (44.18–52.53 W) for 6 minutes on each side of the face, excluding the forehead (total treatment time of 12 minutes). To increase the surface temperature at the start of treatment, the procedure was performed with 50% overlap. When the temperature increased from 40°C to 42°C, it was performed with 20% overlap. If the skin temperature exceeded 42°C or if the patient experienced pain, then the procedure was temporarily stopped. After improvement, the procedure was repeated. Patients were treated three times, with an interval of 2 weeks between treatments. Before the first procedure and 4 weeks after the third treatment, the patients were evaluated and compared using photographs. No other skin laxity treatments were administered during this period.

2.3. Clinical Assessment. Two experienced dermatologists who did not administer the treatment evaluated the photographs before and 4 weeks after treatment. They evaluated the face using the Wrinkle Severity Rating Scale (WSRS) (1 = absent; 5 = extreme) (Table 1) [10, 11]. Facial lesions were photographed to assess the therapeutic effects and side effects using a microscope (D40; Nikon, Tokyo, Japan). The pores and wrinkles were quantified and evaluated using an A-one Lite imaging system (Bomtec, Seoul, Korea). Transepidermal water loss (TEWL) was measured using a vapometer (Delfin, Helsinki, Finland). Patient satisfaction was assessed using a 5-point scale (0 = no improvement; 1 = 1%–25% improvement; 2 = 26%–50% improvement; 3 = 51%–75% improvement; 4 = 76%–100% improvement).

2.4. Histological Assessment. To histologically evaluate the efficacy of MFRF, a 2-mm skin biopsy of the postauricular area of the volunteers who provided consent was performed before and 4 weeks after the third treatment. MFRF was applied to the face, and the tissue samples were stained with hematoxylin and eosin, Masson's trichrome, and elastin fiber. To confirm the characteristics of collagen in the dermis, immunohistochemical staining to detect collagen I, collagen III, and STRO-1 was performed. We also aimed to quantify the area fraction of the stained slide by analyzing it with the image J software (NIH, Bethesda, MD, USA).

2.5. Statistical Analysis. A paired *t*-test was performed to determine differences before and after treatment. Statistical analyses were performed using SPSS version 26.0 for Windows (Statistical Package for the Social Science; SPSS, Chicago, IL, USA). Statistical significance was defined as $p < 0.05$.

3. Results

3.1. Clinical Assessment. A total of 19 volunteers who provided consent were enrolled in this study. All volunteers were female, and their mean age was 44.7 years (standard deviation, ±5.3 years). Facial pores and wrinkles were evaluated using A-one (Bomtec) before and after the procedure and photographically evaluated 4 weeks after three treatments (Figure 1, Table 2). Although there was a statistically significant improvement in wrinkles (3.11 vs 2.79; $p = 0.034$), there was no significant difference in the change before and after treatment for pores (4.32 vs 4.11; $p = 0.429$). Using the WSRS, the two blind investigators indicated a significant improvement before and after treatment (2.11 vs 1.53; $p = 0.001$). The median patient satisfaction score was 3 points. There was no significant difference in TEWL before and after treatment (10.95 vs 8.26; $p = 0.084$). The average subjective satisfaction scores for skin elasticity and fine wrinkles were 2.47 points and 2.32 points, respectively.

3.2. Histological Findings. To observe tissue changes after MFRF treatment, a skin biopsy was performed on one patient before and after treatment. The tissues were stained with hematoxylin and eosin, Masson's trichrome, and elastin fibers. Hematoxylin and eosin staining revealed an increase in collagen bundles in the dermal layer (Figure 2). Using Masson's trichrome and elastin fiber staining, the thickness and density of collagen bundles and thickened elastin fibers were observed (Figure 3). Immunohistochemical staining was performed to detect collagen I, collagen III, and STRO-1 (Figure 4). Increased expressions of collagen I and collagen III in the upper dermis and an increased number of STRO-1-

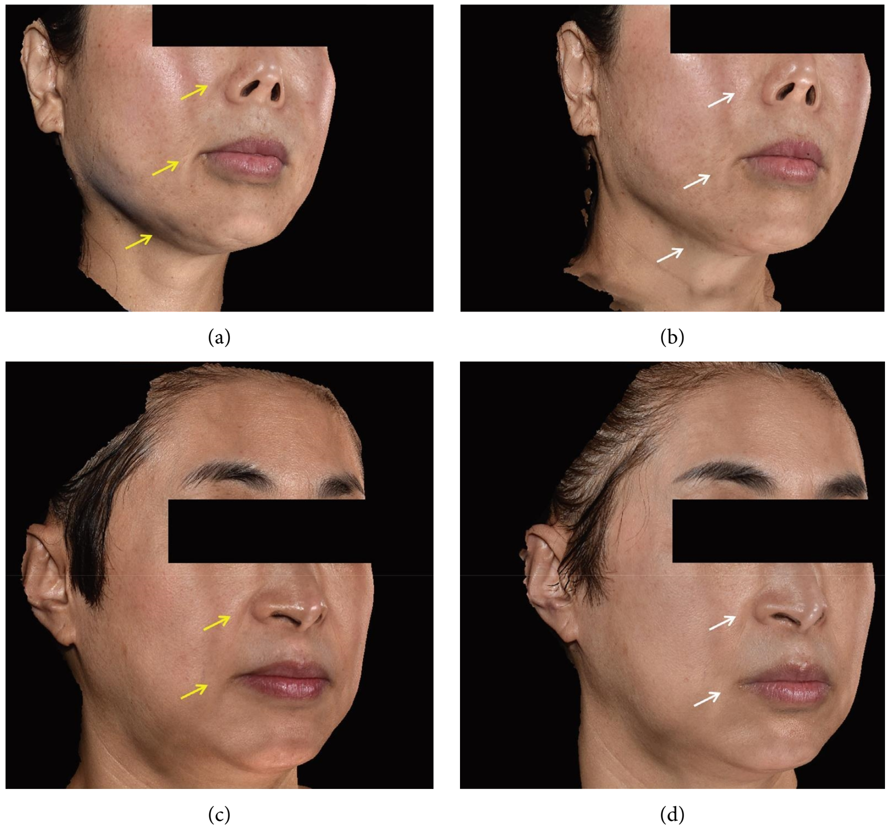


Figure 1: Clinical photographs before (a, c) and after treatment (b, d). (a, c) Fine wrinkles and decreased elasticity were observed (yellow arrows). (b, d) Improvement of wrinkles and elasticity was seen after treatment (white arrows).

Table 2: Clinical assessment of improvements in pore, wrinkle, WRSR, and TEWL before and 4 weeks after the third treatment session.

	Pretreatment	Posttreatment	p value
Pore	4.32 ± 1.00	4.11 ± 0.57	0.429
Wrinkle	3.11 ± 0.57	2.79 ± 0.42	**0.034***
WRSR	2.11 ± 0.66	1.53 ± 0.84	**0.001****
TEWL	10.95 ± 4.02	8.26 ± 3.31	0.084

Values are presented as number or mean ± standard deviation. Statistical analysis of the difference between two groups is expressed as $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$. Bold values represent statistically significant results.

positive cells were observed. We used the Image J to determine the proportion of collagen, including each type of collagen I and collagen III, elastic fibers, and STRO-1 staining in the dermis. The ratios of all these items increased after treatment (Table 3).

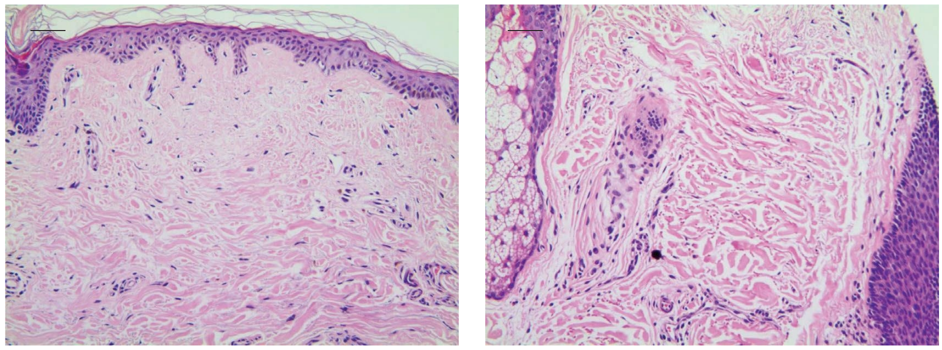
3.3. Patient's Safety. The side effects of treatment were tolerable for all patients. Some patients reported erythema, pain, and/or edema at the site of the procedure; however, the skin lesions resolved without specific findings within 3 days. There were no reports of hematoma, paresthesia, burning sensation, itching sensation, oozing, or postinflammatory hyperpigmentation. Transient aggravation was not observed.

4. Discussion

When collagen fibers are subjected to thermal damage by radiofrequency energy, collagen denaturation occurs. As a result, the intramolecular cross-link is broken, and the triple-helix structure is released. If the intramolecular cross-link is partially maintained, then shrinkage and thickening occur through collagen remodeling over time [12]. Additionally, radiofrequency induces short-term local micro-inflammatory stimulation of fibroblasts, which promotes the long-term production of new collagen and elastin [13].

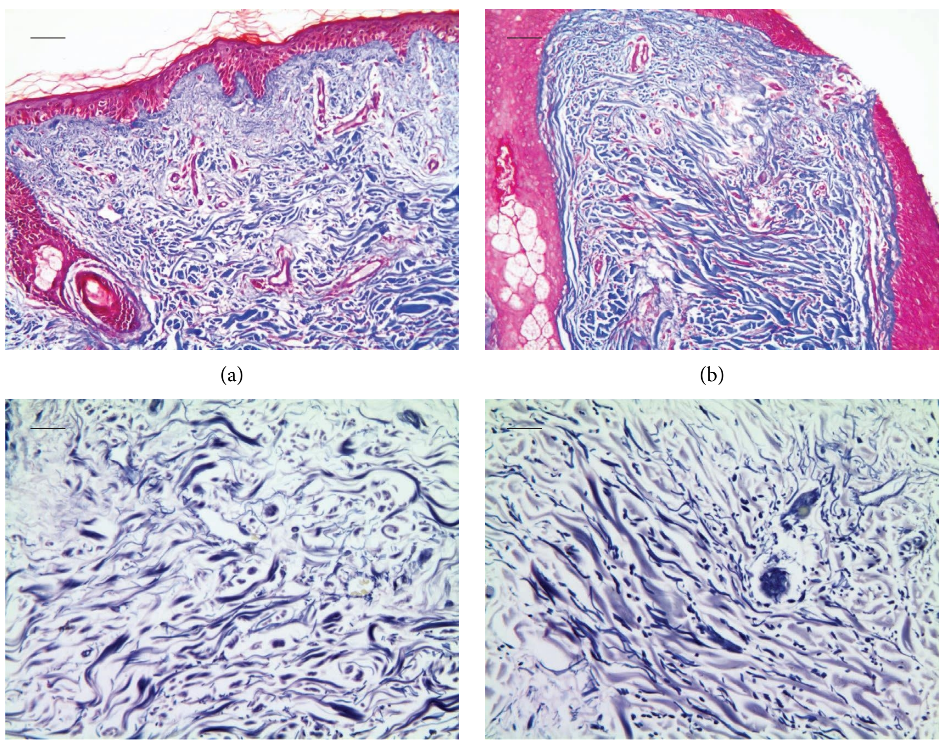
The histological findings of this study showed results consistent with these observations (Figures 2–4). Figures 2 and 3 show the increased density and thickness of the collagen bundles and elastic fibers. It was confirmed that collagen I and collagen III both increased after treatment (Figure 4). The density of collagen III was more prominent during this study because newly synthesized collagen is mainly composed of collagen III; matured collagen is mainly composed of collagen I [14].

Additionally, STRO-1 expression increased during this study (Figure 4). STRO-1 is a well-known marker of mesenchymal stem cells, and it is known to aid in odontogenesis and regeneration of dental tissues [15]. Although studies of the role of STRO-1 in the skin are lacking, it has been observed in multipotent dermal fibroblasts [16]. We believe that increased STRO-1



(a) (b)

Figure 2: Hematoxylin and eosin staining. (X200, scale bar = 0.05 mm) (a) Pretreatment and (b) posttreatment.



(a) (b)

(c) (d)

Figure 3: Staining for Masson's trichrome stain (a, b) and Verhoeff's Van Gieson stain (c, d). (X200, scale bar = 0.05 mm) (a, c) pretreatment and (b, d) posttreatment.

expression may be involved in dermal regeneration; however, further studies are necessary.

Many studies of wrinkle improvement using radiofrequency equipment have been conducted. Kassim and Goldberg reported an improvement in the laxity of thigh skin after bipolar MFRF treatment [17]. However, the effect of monopolar nonablative MFRF on the improvement of facial wrinkles has not yet been determined.

Radiofrequency devices convert the kinetic energy of charged particles into thermal energy by using electromagnetic radiation [18]. During this study, the resonance effect was induced using MFRF rather than general radiofrequency. Quantum molecular resonance generates high-frequency (multiples of 4 between 4 and 64 MHz) and low-intensity waves in the electric field. Quantum molecular resonance is widely used for medical purposes because it can break molecular bonds without tissue damage or ambient temperature increases [19]. It has been reported that tissue repair, rather than a regeneration mechanism, after quantum molecular resonance treatment is superior because of the reduced inflammatory cell infiltration and lower expression levels of metalloproteinases (e.g., metalloproteinase-9) [20]. Furthermore, quantum molecular resonance treatment is thought to contribute to tissue regeneration through remodeling of the extracellular matrix [21].

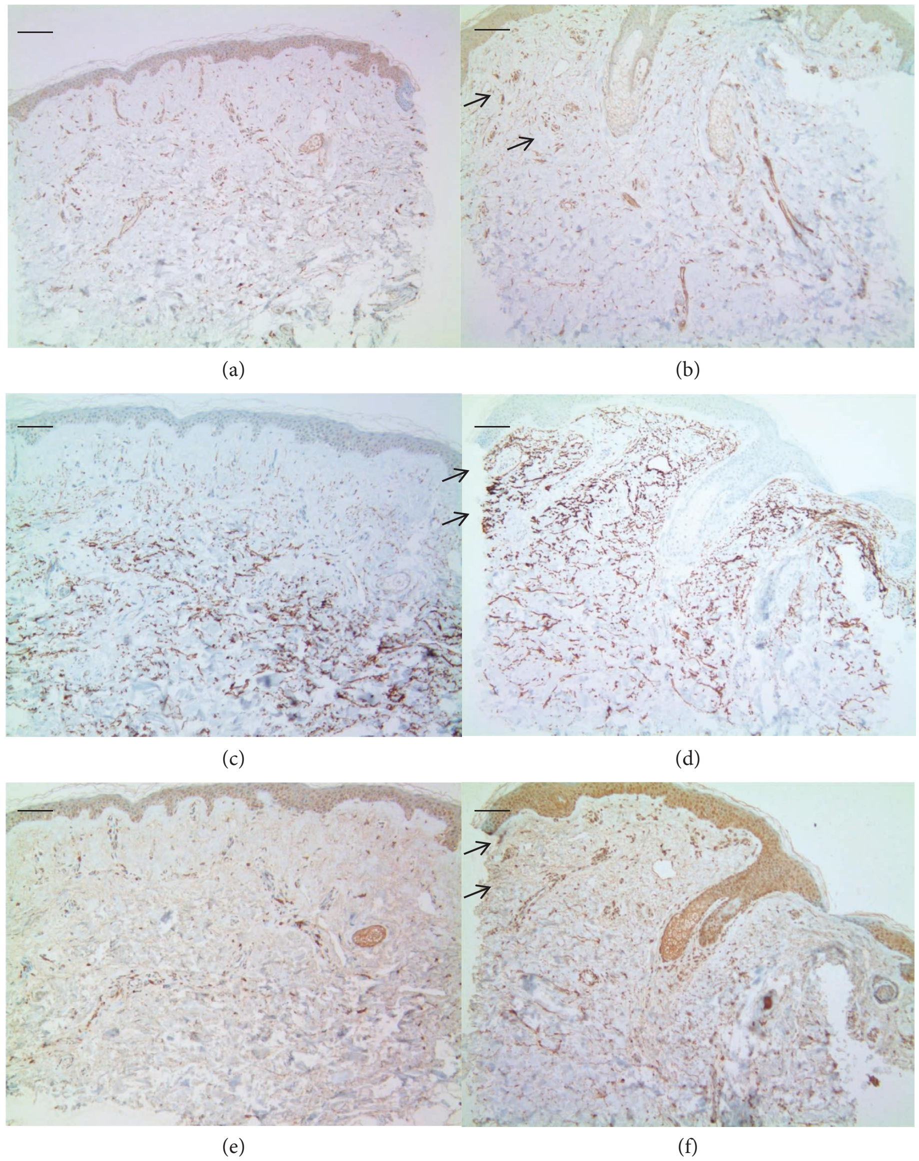


Figure 4: Immunochemical staining for collagen I (a, b), collagen III (c, d), and STRO-1 (e, f). (X100, scale bar = 0.1 mm). (a, c, e) Pretreatment and (b, d, f) posttreatment (increased areas were indicated by black arrows).

Table 3: Area fraction (%) of collagen, elastic fiber, and stro-1 in the dermis before treatment and 4 weeks after the fifth treatment session.

	Pretreatment (%)	Posttreatment (%)	Ratio
Collagen	50.73	58.70	1.16
Collagen 1	38.34	40.34	1.28
Collagen 3	34.49	48.01	1.05
Elastic fiber	37.45	47.90	1.39
Stro-1	13.00	30.83	2.37

Most radiofrequency studies to date have used a maximum power of 330 W [22]. Although lower energy was used in this experiment than in previous radiofrequency studies, a sufficiently significant wrinkle improvement effect was observed. It is also thought that this effect contributed to the resonance effect induced by MFRF.

Additionally, a vacuum-assisted device was used during this study. Radiofrequency, which is commonly used, is disadvantageous because it is difficult to apply because the scope of the procedure is limited. However, when the treatment was performed while pulling only the necessary area with the vacuum, radiofrequency could be efficiently delivered to only the necessary area using a small amount of energy. Furthermore, monopolar radiofrequency has a higher power density and deeper power penetration than bipolar radiofrequency; therefore, pain is often experienced by the patient. However, during this study, the procedure was tolerable and could be completed without using a local anesthetic cream for pain relief before treatment. Therefore, MFRF is capable of multiple low-fluence passes. Kist et al. demonstrated that multiple passes using a lower fluence resulted in collagen changes that were not inferior compared to a high-energy single pass [23].

In conclusion, MFRF treatment uses less energy than the existing RF equipment and can be an effective modality for the treatment of facial laxity.

Data Availability

The data that support the findings of this study are available upon reasonable request to the corresponding author.

Ethical Approval

This experiment was approved by the Institutional Review Board of Hallym University Sacred Hospital, Korea. All procedures in this study were conducted in accordance with the Institutional Review Board of Hallym University Sacred Hospital approved protocols.

Consent

Written informed consent was obtained from the patients for their anonymized information to be published in this article.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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