



Can Microneedle Fractional Radiofrequency System Treatment Impair the Skin Barrier Function in Chinese Patients? A Prospective Clinical Trial

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ABSTRACT

Introduction: Facial cosmetic conditions can manifest as post-inflammatory erythema, scars, pigmentation, enlarged pores, skin laxity, and photoaging. The microneedle fractional radiofrequency system (MFRS) is a new device that combines radiofrequency and

microneedles and has been widely used for skin rejuvenation. Since MFRS is an invasive technique, this study aimed to evaluate whether the skin barrier functions might be impaired by this treatment, revealed by skin sensitivity and exacerbation of melasma.

Methods: Twenty patients with Fitzpatrick grades III–IV facial conditions (skin laxity with melasma, $n = 9$; post-inflammatory erythema and scars, $n = 5$; and enlarged pores, $n = 6$) and treated with MFRS were enrolled. Transepidermal water loss (TEWL, using Ultrascan UC22), skin sensitivity (ten-item Sensitive Scale, SS-10), melanin index (MI), melasma area and severity index (MASI), red areas (VISIA), and thickness

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and density of the epidermis and dermis on ultrasonography were compared between baseline and 6 months after all treatment sessions.

Results: Twenty patients completed a 6-month follow-up after two MFRS treatments. During days 1–3 post-treatment, the TEWL values gradually increased to the peak and decreased to baseline levels (BD) on day 7. There was no significant difference in TEWL compared with baseline in month (M) 1, M3, and M6. There were no significant changes in the thickness and density of the epidermis. Although the thickness and density of the dermis increased, there was no significant difference compared to baseline. There was no significant difference in the MI, MASI, and SS-10 score before and after MFRS treatment. After treatment with MFRS, the red area and scarring reduced significantly ($p < .01$), and no significant difference was observed in other patients.

Conclusions: MFRS is a safe and effective treatment for facial cosmetic conditions. The skin barrier function is not impaired by MFRS treatment, since it does not cause skin sensitivity or melasma exacerbation.

Keywords: Melasma; Microneedle; Radiofrequency; Sensitivity; Skin barrier

Key Summary Points

Why carry out this study?

Facial cosmetic conditions not only have a great impact on the appearance of patients but also seriously affect the physical and mental health of patients.

Recently, the microneedle fractional radiofrequency system (MFRS) has been widely used to improve such problems.

This study aimed to evaluate whether the skin barrier functions might be impaired by this treatment, revealed by skin sensitivity and exacerbation of melasma.

What was learned from the study?

Based on objective (transepidermal water loss, red areas, density, and thickness of the epidermis and dermis) and subjective evaluations (skin sensitivity questionnaire, melasma area, and severity index), this study found that MFRS did not cause skin irritation or melasma exacerbation in conditions of conventional treatment.

INTRODUCTION

Facial cosmetic conditions in dermatology mainly refer to pigmentation, erythema, scars, and skin laxity caused by acne, dermatitis, and photoaging. These conditions not only have a great impact on the appearance of patients but also seriously affect the physical and mental health of patients, thereby reducing their quality of life; hence, it has attracted the attention of an increasing number of clinicians and patients [1, 2].

In recent years, facial cosmetic conditions have become a major concern in dermatology, and many medical methods have been used to treat them. These methods include topical agents, chemical peeling, botulinum toxin, hyaluronic acid, laser, radiofrequency (RF), and surgery [3]. Recently, the microneedle fractional radiofrequency system (MFRS) has been widely used to improve facial cosmetic conditions [4]. The MFRS is a new minimally invasive device in aesthetics that combines both RF and microneedles and delivers RF current through a microneedle electrode assembly. The needles are inserted vertically and rapidly. The RF emission time and the depth of the needle insertion can be changed easily at the operator's discretion. Therefore, this device is suitable for superficial or deep skin therapy for various skin diseases [5]. The MFRS is commonly used in dermatology to treat sagging skin, wrinkles, acne vulgaris, scars, and axillary hyperhidrosis [6].

It has been found that ablative laser therapy is invasive and may impair skin barrier function, especially in the early post-treatment period, with an increased incidence of microbial infection and inflammatory lesions [7]. However, the MFRS is also invasive. Previous studies did not report whether MFRS could cause epidermal thinning or skin barrier function impairment. These could increase skin sensitivity and exacerbate melasma.

Therefore, this study focused on whether the clinical application of MFRS might increase skin sensitivity or induce or aggravate the risk of melasma.

METHODS

Ethics Approval

This prospective study was approved by the Ethics Committee of the Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine (SH9H-2019-T127-2). All the enrolled patients signed an informed consent form before treatment. This study complied with the ethical guidelines of the 1975 Declaration of Helsinki.

Patients

In this study, 20 patients (four men and 16 women) age 26–52 years, with Fitzpatrick skin types III or IV (skin laxity with melasma, $n = 9$; post-inflammatory erythema and scars, $n = 5$; and enlarged pores, $n = 6$), and facial cosmetic conditions were randomly selected. All patients were screened using the Sensitive Scale 10-item version (SS-10) to determine baseline (BL) skin sensitivity [8]. They were informed of the protocol and treatment risks, and they signed an informed consent form. The exclusion criteria were facial skin diseases such as eczema, psoriasis, herpes virus infection; history of keloids; pregnancy; photofacial treatments; botulinum toxin injections; any treatment that interfered with the study; or participation in other clinical trials within the past 6 months and during the follow-up.

Devices and Treatment Protocol

All patients received a full-face treatment with MFRS (INTRAcel, Jeisys, Korea). Before the treatment, superficial anesthesia with a 5% compound lidocaine cream (Tongfang Pharmaceutical Group Co., Ltd.) was applied to the patient's face for 1 h, followed by disinfection with 75% alcohol. The skin in the forehead, orbital, and periorbital areas was treated with 1.5-mm penetration depth of the microneedles, density level 3, power of 12.5 W, and duration of 80 ms. Other areas such as the cheek, jaw, and nose, used a 2-mm penetration depth of the microneedles, level 4, power of 12.5 W, and duration of 100 ms. All the patients were treated twice, with an interval of 3 months. After the procedure, no wound care was prescribed except compression of the treated areas with an ice pack for 45 min. The skin care products could be reused on the first day after treatment.

Subjective and Objective Evaluations

Twenty patients were treated with MFRS and assessed at BL and during seven follow-up sessions. Follow-up evaluations were performed on day one (D1), day three (D3), day five (D5), day seven (D7), month one (M1), month three (M3), and month six (M6) after the second treatment. At each visit, a dermatologist performed a clinical self-assessment of skin sensitivity using the SS-10 and objective testing. Images were captured by the same photographer using the VISIA Skin Analysis System (Canfield Scientific, USA) and a digital camera (Sony ILCE-7M3, Tokyo, Japan). The following equipment was used to evaluate different parameters: 7th Generation VISIA Skin Analysis System (Canfield Scientific, USA), Skintel™ Melanin Reader (Palomar Medical Technologies, Inc. Burlington, MA), and a high-frequency ultrasound imaging system (DUB SkinScanner V5.0, Germany). During the follow-up after the last treatment, all patients were evaluated using the SS-10. The Melasma Area and Severity Index (MASI) was used to evaluate the severity of nine patients with melasma before and after MFRS treatment.

Statistical Analysis

To analyze the differences before and after the MFRS treatment at different time points, a one-way analysis of variance was used to test the effect of time and organize the different parameters investigated. SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. A p value < 0.05 was considered statistically significant.

RESULTS

Demographic Characteristics of Participants

All patients completed both treatments and regular follow-up sessions for 6 months after the last treatment. The patients showed Fitzpatrick skin types III and IV and had a mean age of

35.8 ± 7.4 years (range, 26–52 years). Nine patients had skin laxity with melasma. Five patients had post-inflammatory erythema and scars, and six had enlarged pores.

Figure 1 shows a typical facial recovery process after MFRS treatment in a 38-year-old patient. On D1, erythema was seen on the face, which gradually subsided, and the face returned to normal on D5. Burning or blistering was not observed. No discomfort was reported during the follow-up evaluation. Some patients had a transient purpura-like reaction on D3 that disappeared after about 7 days without sequelae. Table 1 summarizes the demographic characteristics of the 20 participants.

Subjective Assessment

According to the self-evaluation questionnaire completed by the patients at each visit, changes

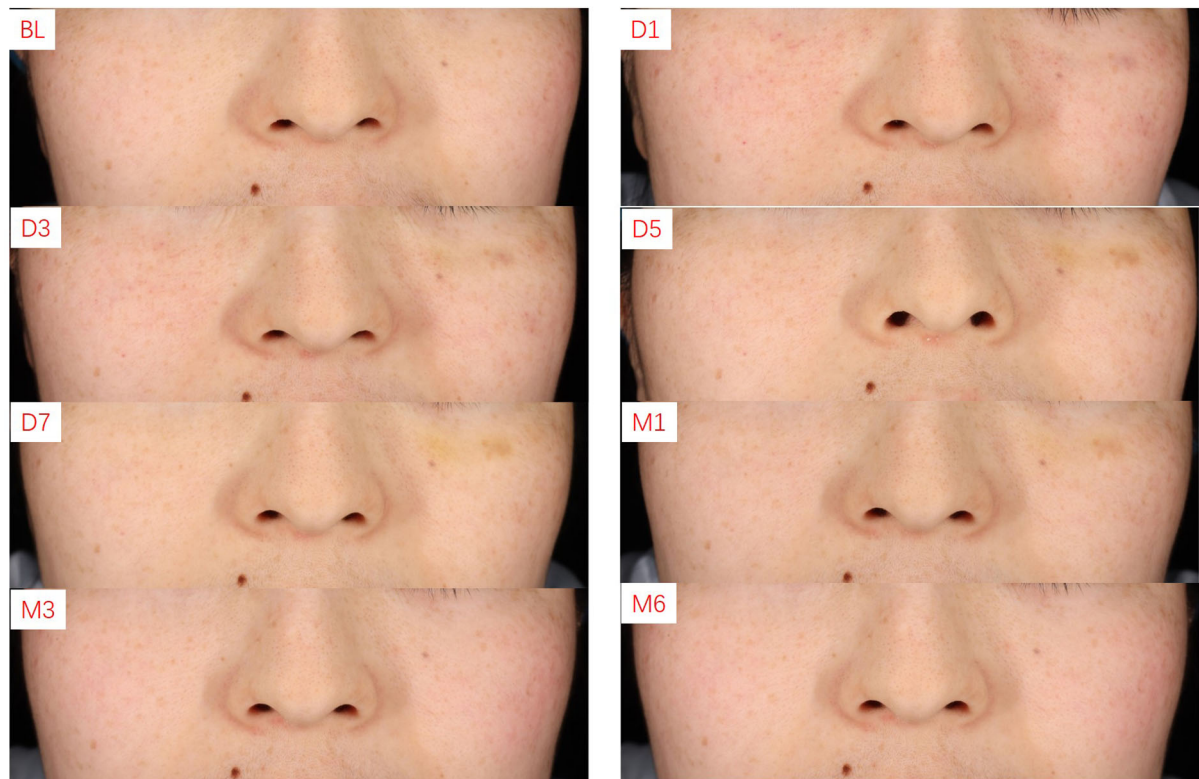


Fig. 1 VISIA images of a female at different time points before and after MFRS treatment. Images were collected prior to laser treatment (BL = baseline), and at D1 (day

1), D3 (day 3), D5 (day 5), D7 (day 7), M1 (month 1), M3 (month 3), and M6 (month 6) after treatment. MFRS microneedle fractional radiofrequency system

Table 1 Patient demographics and adverse events

Total no. of volunteers	20
Sex	
Male	4
Female	16
Age (years)	
Mean \pm SD (range)	35.80 \pm 7.40 (26–52)
Fitzpatrick skin type	
III	14
IV	6
Facial cosmetic conditions	
Loose skin	9
Loose skin combined with melasma	5
Loose skin combined with seborrheic keratosis	4
Acne-inflamed erythema and scars	5
Enlarged pores	6
Adverse events	
Bleeding during treatment	20
Erythema	20
Edema	20
Pinpoint purpura	7

in the subjective perception of skin sensitivity were observed. We evaluated the clinical self-assessment of skin sensitivity with the Sensitive Scale 10-item version (SS-10) developed by Laurent Misery et al. in 2014 [8]. The score for each question ranges from 0 to 10 points, with a total score of 100 points. Irritability, heat, tautness, itching, flushing, and redness were observed before treatment.

During the first week after each treatment, some patients showed several discomforts such as mild skin irritation, burning, heat, tightness, pain, flushing, and erythema. After about 1 week, the symptoms of all patients improved

and showed no significant difference from those before treatment (Table 2). These results suggest that the MRFS treatment does not increase sensitivity in facial skin. Table 2 shows the quantitative perceptions of the patients' subjective skin sensitivity over time. We also observed that post-treatment photographs showed no exacerbation of melasma after the MFRS treatment.

Facial Skin Sensitivity Before and After RF Therapy

Red Areas of the Face

The red areas of the face were quantitatively analyzed using the VISIA Skin Analysis System (Fig. 2) at BL and at the end of the follow-up of five patients. The red area improved significantly in three patients and improved moderately in two patients with post-inflammatory erythema and scars (Fig. 3).

Measurements of TEWL

Readings of TEWL obtained from the zygomatic region at different time points were statistically analyzed (Fig. 4). On D1, the facial TWEL mean value was 13.17 ± 1.52 , which was not significantly different from the BL ($p = 0.22$). On D3, the facial TWEL mean values were 13.83 ± 1.59 , which were significantly higher than the BL ($p < 0.01$). At D5, D7, M1, M3, and M6, there were no significant differences in water loss before and after treatment. At D5 and D7, the TWEL value gradually decreased to BL level, and there was almost no difference in TWEL values at all the time points.

Measurements of Epidermal and Dermal Thickness and Density

Changes in epidermal and dermal thickness and density at different time points after the second MFRS treatment were detected using high-frequency ultrasonography (Fig. 5). The researchers obtained readings from the chin region and analyzed the results. The thickness of the epidermis and dermis before and after treatment was 115.70 ± 42.49 (115.80 ± 37.47) μm and 1628.67 ± 98.67 (1664.40 ± 90.66) μm ,

Table 2 Quantified perceptions of changes in subjective skin sensitivity of patients over time^a

Factors	BL	D1	D3	D5	D7	1st month	3rd month	6th month	F	Pb	Fc	Pc
Skin irritability	0.23 (0.80)	2.85 (2.53)	2.08 (1.90)	1.15 (1.23)	0.46 (0.75)	0.15 (0.36)	0.00 (0.00)	0.00 (0.00)	8.56	0.00	1.66	0.17
Burning	0.00 (0.00)	2.15 (2.34)	1.38 (2.27)	0.54 (1.08)	0.15 (0.53)	0.08 (0.26)	0.00 (0.00)	0.00 (0.00)	5.12	0.00	0.8	0.53
Sensations of heat	0.15 (0.36)	2.54 (2.93)	1.23 (2.29)	0.38 (0.92)	0.23 (0.58)	0.15 (0.36)	0.08 (0.27)	0.08 (0.27)	4.71	0.00	0.39	0.85
Taurness	0.08 (0.27)	2.85 (2.41)	2.85 (2.74)	2.23 (2.83)	1.84 (2.77)	1.38 (2.24)	0.61 (1.39)	0.15 (0.53)	3.36	0.00	2.42	0.06
Itching	0.08 (2.27)	0.92 (1.14)	0.85 (1.61)	0.85 (2.11)	0.46 (1.34)	0.77 (2.67)	0.77 (2.267)	0.77 (2.67)	1.43	0.20	0.85	0.50
Pain	0.00 (0.00)	2.92 (3.22)	1.00 (1.75)	0.77 (1.19)	0.31 (0.61)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	6.40	0.00	3.10	0.02
General discomfort	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.08 (0.27)	1.00	0.44	1.00	0.41
Flushes	0.08 (0.27)	3.46* (3.48)	2.08 (2.13)	1.23 (1.42)	0.46 (0.93)	0.08 (2.27)	0.00 (0.00)	0.00 (0.00)	7.83	0.00	2.22	0.08
Redness	0.15 (0.36)	2.38 (3.27)	1.38 (1.64)	0.69 (0.99)	0.23 (0.42)	0.00 (0.00)	0.00 (0.00)	0.08 (0.27)	4.77	0.00	1.59	0.19
Overall skin sensitivity	0.84 (1.83)	2.00 (2.91)	1.31 (1.98)	0.77 (1.48)	0.69 (1.49)	0.46 (0.93)	0.46 (0.93)	0.23 (0.58)	1.39	0.22	0.44	0.78

^aValues represents the mean value of scores (standard deviation in parentheses)

^b $P > 0.01$ represents the scores without difference between follow-up and baseline

^c $P > 0.01$ represents the scores without difference between after D7 follow-up and baseline

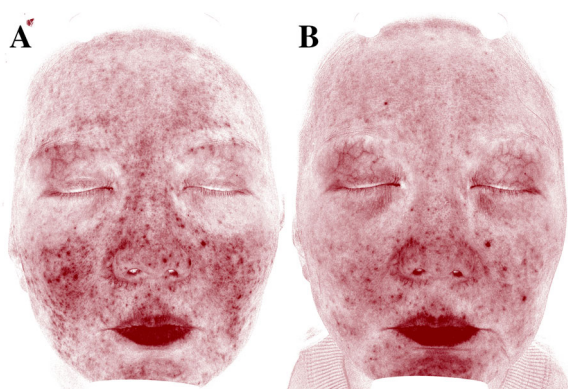


Fig. 2 Representative VISIA images of acne-inflamed erythema. The areas shown are the red areas before (A) and after (B) treatment

respectively. The densities of the epidermis and dermis before and after treatment were 114.83 ± 56.07 (114.60 ± 56.93) and 15.83 ± 3.73 (15.60 ± 6.25), respectively. Six months after treatment, there were no significant differences in epidermal thickness and density compared to BL. An increase in dermis thickness and density was observed, but the differences were not significant.

Pigment Changes Before and After RF Therapy

Measurements of the Melanin Index

To assess whether the RF therapy can induce or worsen melasma, we measured the melanin index (MI) of 20 patients at BL, M1, M3, and M6

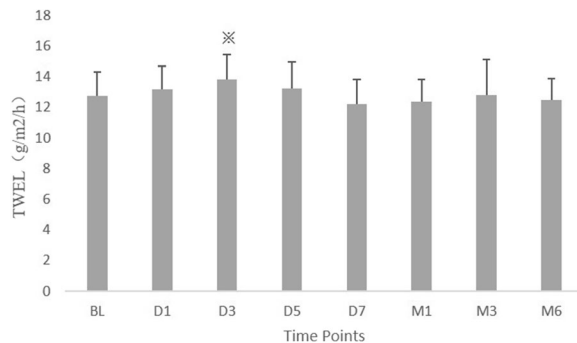


Fig. 4 Changes in transdermal water loss rate (TEWL) at different time points after and before MRFS treatment. (* $p < 0.05$)

after treatment (Skintel™ Melanin Reader) including nine patients with melasma (Fig. 6). The mean MI of BL was 24.16 ± 1.52 , and that of M1, M3, and M6 was 23.90 ± 2.02 , 24.57 ± 1.42 and 24.77 ± 2.12 , respectively ($p > 0.05$). The average MI of BL of patients with melasma was 24.90 ± 1.43 , and the values at M1, M3 and M6 were 23.90 ± 1.43 , 23.70 ± 2.23 and 23.4 ± 1.60 , respectively ($p > 0.05$). There were no significant differences in MI on M1, M3, and M6 after treatment, compared to BL. MRFS did not aggravate melasma. MRFS therapy did not lead to hyperpigmentation or aggravated melasma in patients with or without melasma.

Measurements of MASI

The MASI developed by Kimbrough–Green et al. was used to assess the area and severity of

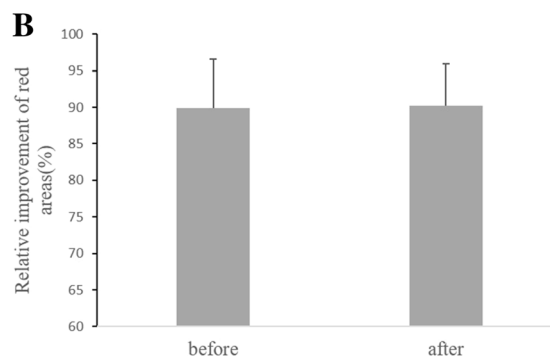
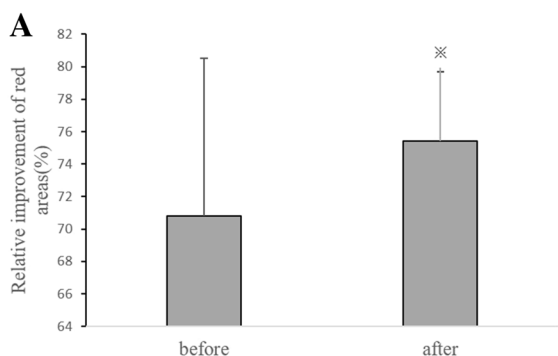


Fig. 3 Facial red area before and after MRFS treatment. Statistical analysis shows (A) the red area of acne-related erythema and (B) the remaining 15 volunteers. (* $p < 0.05$)

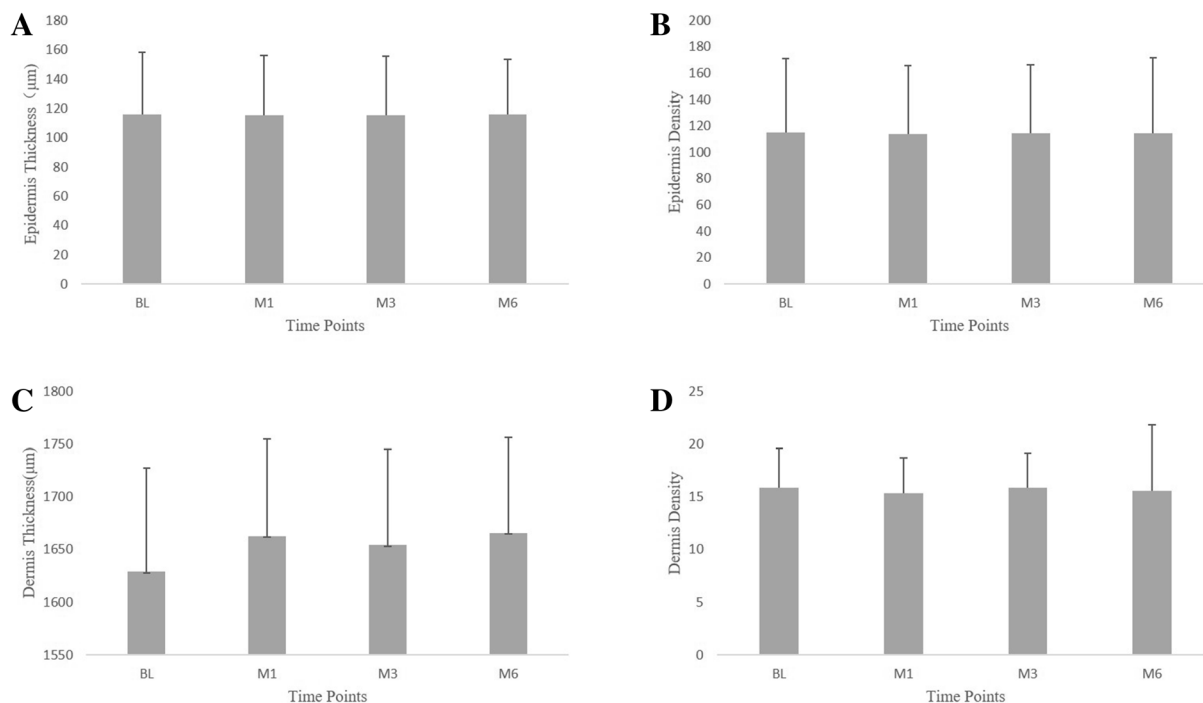


Fig. 5 A–D Comparison of thickness and density of the epidermis and dermis before and after MFRS treatment. (* $p < 0.05$)

melasma before and after the MFRS treatment in nine patients. The MASI score was 7.47 ± 0.50 before treatment and 7.58 ± 0.58 after treatment. There was no statistical difference between the two ($p = 0.55$). MFRS treatment did not cause irritation of melasma.

DISCUSSION

Acne, scarring, enlarged pores, loose skin, and photoaging are the most common facial cosmetic skin conditions and are considered major aesthetic problems. Minimally invasive treatments with quick recovery that do not lead to pigmentation, scarring, skin infection, and other side effects are currently preferred.

MFRS is an emerging aesthetic technique for treating facial lesions, such as acne, scarring, photoaging, enlarged pores, and skin laxity [9, 10]. During wound healing, denatured collagen is replaced by new dermal tissue, elastin and collagen are increased, and new elastin and collagen are gradually remodeled [11]. Hence, it

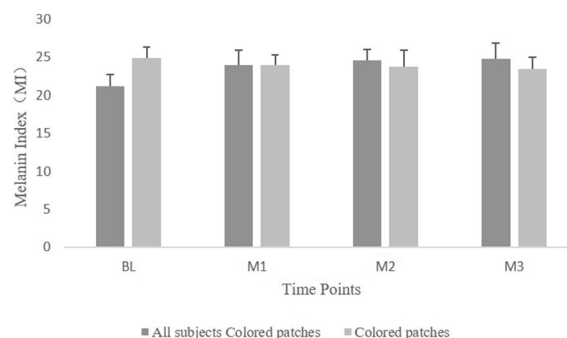


Fig. 6 Melanin index changes at different time points on the same site before and after treatment. (* $p < 0.05$)

can treat acne scars, enlarged pores, skin relaxation, and photoaging [12, 19].

Since ablative fractional CO_2 laser treatment of acne scars may damage skin barrier function, resulting in adverse reactions such as pigmentation and flushing, the incidence of microbial infection and inflammatory injury also increases correspondingly [13]. MFRS treatment has a quick recovery, short downtime, and it rarely causes pigmentation or skin infection.

In our study, according to photographic analysis, ultrasonography, and VISIA results, we found that facial cosmetic conditions improved significantly after MFRS treatment. Additionally, MFRS treatment did not affect skin sensitivity based on the SS-10. Based on the results of the MASI and the MI, the treatment did not irritate or aggravate melasma.

The MI and MASI score were used to objectively evaluate the melasma change process after MFRS treatment, and the results showed that there was no exacerbation of melasma in either the 1-week recovery period or the follow-up period. In the recovery period, the patients had different degrees of erythema, edema, or purpura, which returned to BL 1 week later. Kwon et al. found the combination of MFRS and Nd:YAG laser safe and effective for the treatment of melasma and has a significantly improved therapeutic effect [14]. They also found that Nd:YAG laser alone may lead to an increase in the incidence of hyperpigmentation and hypopigmentation. The possible reason is that Nd:YAG laser can gradually reduce epidermal pigmentation, and MFRS can stabilize melanin activity by interfering with potential pathogenic targets.

In a previous study of 27 patients with moderate facial photoaging, MFRS was effective in improving wrinkles, skin firmness, and skin tone. Most patients were satisfied with the treatment, but there were varying degrees of adverse effects, such as tolerable pain, mild bleeding, mild erythema, edema, and needle-like purpura. Throughout the procedure, none of the patients experienced significant or permanent adverse effects such as hyperpigmentation, hypopigmentation, or scarring [15]. The reason is that MFRS energy is concentrated near the electrode tip located in the dermis. Therefore, the skin is not affected by a high temperature, and the energy is not diffracted or absorbed by the skin melanin, hence, there is only a small risk of damage to the activated epidermal melanocytes. Therefore, MFRS causes less hyperpigmentation and shows a lower burning rate compared to other treatment [16].

A study comparing non-insulated micro-needle radiofrequency alone with non-insulated microneedle radiofrequency in

combination with polynucleotides for the treatment of melasma reported that the MI and erythema indices were lower than those at BL [17]. The treatment was well tolerated by the patient. Similar to our study, no exacerbation or recurrence of melasma was observed. Moreover, invasive bipolar pulsed microneedle radiofrequency combined with polynucleotides was not superior to microneedle radiofrequency alone in the treatment of melasma. In our study, no reduction of melasma was observed, possibly because there were only two MFRS treatments in our study, which was less than those in other studies [18].

Whether laser treatment induces skin sensitivity is also one of the key indicators observed in this prospective study. It has been documented that carbon dioxide laser resurfacing may induce skin sensitivity in sensitive areas of susceptible individuals, resulting in unpleasant sensations such as burning, pain, itching, or tingling. However, it has not been reported whether repeated use of ablative lasers increases skin sensitivity in real-world populations [19, 20]. It is currently believed that sensitive skin is related to impaired function of the epidermal barrier, which can lead to various kinds of discomfort [21]. Studies have shown that TEWL, epidermal and dermal structures, and the red area of the face are related to barrier function [22]. In this study, we measured TEWL values and the thickness and density of the epidermis and dermis to assess changes in the skin barrier function comprehensively. The results showed that facial water loss gradually increased from D1 to D3 after MFRS treatment. One week after treatment, TEWL gradually decreased to BL level, and at M6, there was no significant difference in TEWL compared with BL level. A possible reason is that, immediately after MFRS treatment, the epidermis is damaged to varying degrees, and the dermal tissue swells, leading to rapid water loss. Subsequently, with the gradual decrease in dermal swelling, the epidermis slowly returned to normal; thus, skin water loss was controlled and normalized. MFRS treatment might damage the skin barrier only in the early stage but resolves in 1 week without affecting skin sensitivity. Also, the sensitivity scale developed by Misery et al. (2014), a self-

scoring questionnaire, was used to subjectively evaluate the sensitive skin condition of the participants before and after MFRS treatment. The results showed no difference in the sensitivity scores before and after treatment, suggesting that MFRS treatment did not irritate the skin barrier and did not cause skin sensitivity.

High-frequency ultrasonography was used to measure the thickness and density of the epidermis and dermis before and after the MFRS treatment, which showed no significant difference despite an observed increase in thickness and density of the dermis. On the contrary, Alavi et al. [9] found that MFRS significantly increased the density and thickness of the epidermis and dermis, which may be due to radiofrequency affecting collagen synthesis in the dermis. The differing results between the two studies may be related to the number of MFRS treatments, courses of treatment, and follow-up intervals.

This study had some limitations. Facial histologic analysis is hardly conducted in patients on aesthetic consultation. Because of the relatively small sample size, we did not perform any correlations with the indices measured with each other or with demographic data of patients. In addition, the MFRS treatment data available are small due to the absence of a control group, relatively small sample size and insufficient follow-up period. The side effects of MFRS treatment require further follow-up studies with larger sample sizes and more treatment sessions.

CONCLUSIONS

In conclusion, MFRS is a safe and effective treatment for facial cosmetic conditions since it does not cause skin sensitivity or melasma exacerbation.

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Authorship. All authors meet the International Committee of Medical Journal Editors' criteria for authorship, take responsibility for the integrity of the work, and have given their approval for this version to be published.

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Disclosures. Xiujuan Wu, Zhen Zhang, Jian Zhu, Sheng Lu, Chen Chen, Xianglei Wu, Xue Wang and Zongfeng Zhao have nothing to disclose.

Compliance with Ethics Guidelines. This study was approved by the Ethics Committee of the Ninth People's Hospital affiliated with Shanghai Jiao Tong University (SH9H-2019-T127-2). All the enrolled patients signed an informed consent form before treatment and for the publication of figures. This study complied with the ethical guidelines of the 1975 Declaration of Helsinki.

Data Availability. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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