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10.3109/14764172.2012.738909

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OBJECTIVE: Our objective was to assess the efficacy and safety of the Er:YAG laser (2,940 nm) using the “ablative” fractional resurfacing mode to treat photodamaged facial skin.

METHODS: A total of 29 Korean patients were treated for photodamaged facial skin using a fractional Er:YAG laser. The number of treatment was mean 2.3 sessions at two-week intervals. Independent investigators assessed the efficacy using standardized photographs. The patients’ satisfaction rate was also evaluated.

RESULTS: For dyspigmentation, 62.5% of the treated patients showed improvement greater than 26%. Regarding wrinkles, 50% of the treated patients showed improvement greater than 26%. All patients showed various degrees of improvement in skin laxity. Assessing the overall features, 62.5% of the study subjects showed improvement greater than 26%, and most of them (91.7%) reported that their subjective satisfaction rate was above “slight satisfaction”.

Downtime accounted for approximately one week in most patients.

CONCLUSIONS: A fractional Er:YAG laser can deliver an effective and minimally invasive treatment for photodamaged facial skin in Asians.

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Short title: A fractional Er:YAG laser for photodamaged skin

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Key words: erbium-doped yttrium aluminium garnet; fractional photothermolysis; photodamaged skin

INTRODUCTION

Laser resurfacing has been used as a treatment for photodamaged facial skin. Traditional ablative laser resurfacing with the 10,600 nm carbon dioxide laser or 2,940 nm erbium-doped yttrium aluminium garnet (Er:YAG) laser, has been used to treat photodamaged skin (1). Such ablative lasers improve photodamaged skin, i.e. fine wrinkles, some coarse wrinkles, and dyschromia. However, traditional ablative laser resurfacing has limitations which result in significant downtime with notorious persistent erythema and complications such as hypertrophic scarring, infection, and post-inflammatory hyperpigmentation (PIH).

Fractional photothermolysis (FP) has been introduced as a way to overcome the limitations of traditional ablative resurfacing (2). FP is a new technique for the treatment of skin lesions in which an array of microscopic thermal wounds (microscopic treatment zones) is induced into the skin in order to stimulate a therapeutic response deep in the dermis. This new modality of laser skin resurfacing was developed to provide a successful clinical response comparable to traditional ablative resurfacing but with shorter downtime and fewer complications (3,4). FP is composed of non-ablative laser devices and ablative laser devices. The original prototype, non-ablative FP at a wavelength of 1,550 nm, has been found to be effective for the treatment of melasma, mild to moderate rhytides, acne scars, surgical scars, and even poikiloderma of Civatte (5). However, this “coagulative” approach is both time-consuming and painful, and the results are not always predictable. Several reports have confirmed that the efficacy of ablative FP surpasses that of the original prototype non-ablative FP, and has only slightly longer downtimes and similar low adverse events profiles. However, the carbon dioxide fractional laser can cause adverse events such as PIH which is common in Asian skin, and can also cause severe pain. Recently, “ablative” FP using the Er:YAG laser (2,940 nm) has been introduced as a novel means of providing treatment that would be as effective as traditional ablative approaches while avoiding their high downtime and risks (Table. I) (2,3,5-7). However, there have been no reports of fractional Er:YAG laser treatment for photodamaged skin in Asians.

The aim of this study was to investigate the efficacy and safety of fractional Er:YAG laser resurfacing to treat photodamaged facial skin in Asians.

MATERIAL AND METHODS

Patients

Twenty-nine patients (one male, 28 females) were enrolled in this study. Study subjects ranged in age from 29 to 67 years (mean, 41.6 years). All patients presented with photodamaged facial skin, i.e. dyspigmentation, fine wrinkles, or skin laxity. All subjects had Fitzpatrick Skin Type III or IV. None of the patients had undergone skin resurfacing within the previous three months. The exclusion criteria included photosensitivity, use of photosensitizing medications, history of abnormal scarring, and use of isotretinoin during the previous year. All patients were provided with a detailed description of the purpose and possible outcomes of treatment and gave written informed consent to participate in the study and to give their permission for clinical photographs to

be taken. Written informed consent was obtained as part of our Institutional Review Board-approved protocols respecting the Declaration of Helsinki's guidelines, and the study was approved by the Institutional Review Board of the Asan Medical Center (Seoul, Korea).

Technique

In all patients, treatments were carried out using a topical anesthetic cream (EMLA[®], AstraZeneca, UK) applied to the face under occlusion 30 minutes before treatment. Fractional ablative photothermolysis treatment was carried out using a 2,940 nm Er:YAG laser (ACTION[™], Lutronic, Korea) with 250 μ s pulse width. The fractional mode of this device ablates both the epidermis and upper dermis forming vertical microablative columns in the dermis (MAC, microbeam diameter of 250 μ m, density 100 spots/cm²) with variable micro-pulse energy (1~14 mJ) by dividing pulsed light into an array of microbeams (lens array). In addition to the single shot mode, each microbeam can be repeatedly shot from twice to ten times using the 'multi shot' mode and the user can select from 9 x 9 mm or 12 x 12 mm fractional hand piece tips. For this study, the 12 x 12 mm fractional handpiece was used. Five percent skin coverage is achieved with a single pass. According to unpublished data provided by the manufacturer in a micropig model, at 14 mJ an approximate penetration depth of 80 μ m was achieved per single shot.

Each patient underwent full-face fractional rejuvenation with one or two passes during each treatment session with energies that varied from 12 to 14 mJ. More severely photodamaged regions such as the periorbital area, were treated with a further one or two passes. Twenty patients underwent one treatment session, while the other eight underwent a total of four to six sessions at two-week intervals.

Evaluation

The study subjects returned for follow-up at post-treatment days two, three, and seven and at four and eight weeks so that we could monitor their recovery, improvement, and any subsequent sequelae. Standardized digital photographs were taken using a Robo Skin Analyzer CS50 (Inforward Inc., Japan) at baseline and again at four to eight weeks after the last treatment. Using these photographs, independent investigators evaluated the clinical improvement of dyspigmentation, wrinkles, laxity, and the overall skin improvement using the following 5-point scale: 0 = 0%, no improvement; 1 = 1 – 25% improvement; 2 = 26 – 50% improvement; 3 = 51 – 75% improvement; and 4 = 76 – 100% improvement. We also evaluated the patients' subjective

satisfaction rate using the following 5-point scale: Unsatisfied = 0%, no improvement or worse; Slightly satisfied = 1 – 25% improvement; Satisfied = 26 – 50% improvement; Very satisfied = 51 – 75% improvement; Totally satisfied = 76 – 100% improvement.

During the study, all patients were asked to report any adverse symptoms, e.g. erythema, edema, pain, crusting, infection, pigmentary change, and scarring.

RESULTS

Of the 29 study subjects, 24 (0 male, 24 females) completed the study (Table. II), and five were lost to follow-up. No patient withdrew from this study because of any treatment-related, severe adverse event. The number of treatment sessions ranged from one to six (mean, 2.3).

Efficacy

We assessed the efficacy of fractional Er:YAG laser treatments using independent and blinded assessment of standardized photographs at eight weeks after the last treatment session. As only three patients were unavailable at eight weeks after their last treatment, we evaluated the photographs and subjective satisfaction rate at either two weeks or twelve weeks after the last treatment. Representative clinical photographs of the study subjects demonstrating the improvement of their photodamaged facial skin are seen in Figure 1. As for dyspigmentation, five subjects (20.8%) showed 51 – 75% improvement; ten (41.7%) showed 26 – 50% improvement; seven (29.2%) showed 1 – 25% improvement; and two patients (8.3%) showed no improvement. Regarding wrinkles, most patients (83.3%) rated their improvement as 1 – 50% and only one patient (4.2%) showed no improvement. All patients showed various degrees of improvement in skin laxity. Assessing the overall improvement in the skin condition, one patient (4.2%) showed 76 – 100% improvement; five (20.8%) showed 51 – 75% improvement; nine (37.5%) showed 25 – 50% improvement; eight (33.3%) showed 1 – 25% improvement; and only one study subject (4.2%) showed no improvement. Most patients (91.7%) reported a subjective satisfaction rate of above “slightly satisfied”. Two patients were unsatisfied with the treatment result (Figure 2).

Safety

In all patients, the initial reactions to treatment consisted of erythema, minimal edema and microcrust formation in the treated areas; they also reported

a burning sensation or mild pain. However, the burning sensation or pain was mild and gradually subsided within two days. Erythema lasted between three and ten days (mean, 4.8 days). Overall, erythema was mild without long-lasting downtime. Edema also resolved within one week (mean, 4.8 days/ range, 2 to 7 days). All patients presented with microcrust formation which usually lasted for 1 week and then gradually disappeared. Some patients reported an itching sensation and skin dryness, neither of which required additional treatments except for humectants. In three patients, herpes simplex infection occurred. No permanent side effects were noted such as post-inflammatory hyperpigmentation, hypopigmentation or scarring.

Representative examples of downtime-related side effects are seen in Figure 3.

DISCUSSION

Hantash et al. (8) first reported on a prototype of a novel AFP (fractionated CO₂ laser) device for use in human skin in vivo in 2007. With the ablative approach, histologically one can see ablated micro-columns varying in thickness and depth depending on the pulse width and wavelength used⁹. Owing to the ablative character of the procedure, the stratum corneum is mostly absent, contrary to the situation in non-ablative fractionated technology (9). Re-epithelialization of the coagulation zones occurs rapidly, within 48 hours (9). With AFP, immunohistochemical studies indicated a prolonged wound remodeling response for at least 3 months after treatment. With this prolonged stimulation of wound repair induced by AFP, Hantash et al. (9) theorized that greater clinical improvements in skin texture and wrinkling could be achieved with AFP than with NAFP. Significantly greater degrees of improvement in the cutaneous signs of photo-aging have been demonstrated in preliminary studies using fractionated CO₂ laser technology than the original generation of nonablative FP devices.

Weiss et al. (10) reported a comparative split-face trial with half treated using fractionated CO₂ laser and the other half treated using a 1,550 nm, non-ablative, fractional erbium glass (Er:glass) laser. Significantly greater improvement in periorbital rhytides (75% improvement) was observed in the 10 patients treated with the fractionated CO₂ laser than in those treated with the 1,550 nm Er:glass laser (25% improvement) on blinded photographic analysis.

In addition to fractional CO₂ lasers, fractional Er:YAG lasers were also introduced as an ablative fractional laser. In contrast to CO₂ lasers (10,600 nm), the Er:YAG laser has a technical benefit because its wavelength of 2,940 nm is

much closer to the absorption maximum of water (3,000 nm), thus allowing for high precision yet superficial skin ablation (3). However, with the selection of appropriate parameters, the biophysics of CO₂ and Er:YAG laser–tissue interaction can create similar tissue reactions and cosmetic results (3).

Lapidoth et al. (5) reported on the efficacy of an ablative fractionated Er:YAG laser used to improve the appearance of photo-aging. Twenty-eight patients were treated for mild to moderate actinic damage. Two months after treatment, these patients rated their improvement as excellent in 75% of the cases (n = 21) and good in the remaining 25% (n = 7). Upon follow-up six to nine months after treatment, all patients reported continuance of the results seen during the initial follow-up.

Lomeo et al. (7) reported the results of a split-face comparative trial of fractional Er:YAG and fractional CO₂ laser resurfacing in 10 patients. Half of each patient's face was treated with the fractional Er:YAG laser with the opposite half treated using a fractional CO₂ laser. There was significantly greater improvement in skin texture and color on the side treated with the fractional CO₂ laser than on the side treated with the fractional Er:YAG laser. The Er:YAG treated side had a shorter average downtime after treatment (3.4 vs 4.5 days) as a result of the shorter duration of crusting. Patient satisfaction was slightly greater for CO₂ laser resurfacing despite the prolonged downtime following treatment (3.8/5 vs 3.4/5).

Ross et al. (6) published the results of a study comparing the efficacy of a 2,940 nm fractional Er:YAG laser with that of a standard ablative Er:YAG laser for the treatment of facial rhytides and dyspigmentation. The improvement in moderate to severe periorbital and perioral rhytides after one treatment using a fractional Er:YAG laser was approximately 50% from the baseline. On comparative analysis, traditional Er:YAG laser resurfacing demonstrated wound-healing times equivalent to those of fractional Er:YAG, although preliminary data demonstrated that areas treated with fractional Er:YAG demonstrated significantly greater improvement in wrinkle reduction.

A recent study by Karsai et al. (3) evaluated profilometric measurements of wrinkle depth and the Fitzpatrick wrinkle scores in 28 patients who were randomly assigned to receive a single treatment on each side of the periorbital region, i.e. one side using a fractional CO₂ laser and the other side using a fractional Er:YAG laser. They concluded that a single treatment with either laser demonstrated comparatively equal improvement in rhytids (20% and 10% reduction in wrinkles and the Fitzpatrick scores, respectively).

One of the significant advantages of nonablative FP is the low incidence of adverse events; a recent study by Graber et al. (11) found that 7.6% of 961

patients treated with 1,550 nm erbium-doped laser developed complications, of which the most common were acneiform eruptions (1.87%) and herpes simplex virus outbreaks (1.77%). All experienced adverse events were temporary and did not result in any long-term or significantly severe sequelae such as scarring. A study was performed to compare a non-ablative fractional 1,550 nm Er:glass laser and ablative fractional CO₂ laser in the treatment of acne scars, which reported a mostly comparable safety data rate between non-ablative and ablative fractional lasers (12).

Fractional ablative laser treatment also has the advantage of only 7 to 14 days of downtime. One report indicated that, whereas most patients treated with Er:YAG FP devices will have a downtime of anywhere from 1–3 days, those treated with CO₂ FP devices may have 3–7 days' downtime (9). Erythema and edema are common, and desquamation may follow for several days afterward (9). Our present study also showed that there was a downtime of approximately one week in most of our patients. Physician must keep in mind, however, that with multiple passes, the ablative damage accumulates, and this increases the thermal damage and consequently also the healing times.

Some recent studies have reported on the efficacy of Er:YAG laser ablation as a transdermal drug delivery system. Fang et al. (13) reported that the Er:YAG laser showed the greatest enhancement of 5-aminolaevulinic acid (ALA) permeation in vitro compared to other delivery system such as microdermabrasion, iontophoresis and electroporation. Hsiao et al. (14) also showed that Er:YAG laser pretreatment increased the transdermal flux of vitamin C derivatives in mice models. Although another ablative laser, i.e. the carbon dioxide laser, also increases skin permeability, the Er:YAG laser has the advantage of its wavelength-related water absorption characteristics (2,940nm) so that incident Er:YAG energy is almost completely absorbed in the water in the epidermis and very superficial dermis, limiting thermal damage to that superficial target, and does not cause the underlying thermal damage that can be produced by the longer wavelength (10,600 nm) of the CO₂ laser (14). Therefore, we suggest that fractional Er:YAG laser resurfacing combined with topical whitening agent application can be more effective for improving photodamaged skin than fractional Er:YAG laser resurfacing alone. It is our experience in several cases that fractional Er:YAG laser plus whitening agents more effectively improved pigmentary lesions (data not shown). However, in order to evaluate the efficacy and safety of the combined treatment, we need to perform a randomized, controlled study with a large sample size.

DISCUSSION

Our present study demonstrated that the fractional Er:YAG laser can be effective for the treatment of photodamaged facial skin in Asians. It is worth noting that persistent hyperpigmentation, hypopigmentation, and scarring did not occur in any of our patients, although our follow-up period was relatively short. The other limitations of our study were the gender imbalance (only 1 patient was male, and he failed to complete the study), the small sample size, and because it was a pilot study, there was no control group. Further studies will be required to compare the efficacy of fractional Er:YAG lasers and other devices for treating photodamaged skin. In conclusion, we suggest that fractional Er:YAG laser treatments can be an effective and minimally invasive way to treat photodamaged facial skin in Asian women.

Conflict of interest

There is no conflict of interest.

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Figure Legends

Figure. 1. A 34-year-old woman before (A) and after (B) one treatment session. Settings were 12mJ / 2passes. A 57-year-old woman before (C) and after (D) one treatment session. She was treated with 2 passes full-face at 12mJ over her face and 4 further passes at 14mJ over severely wrinkled areas such as the periorbital area.

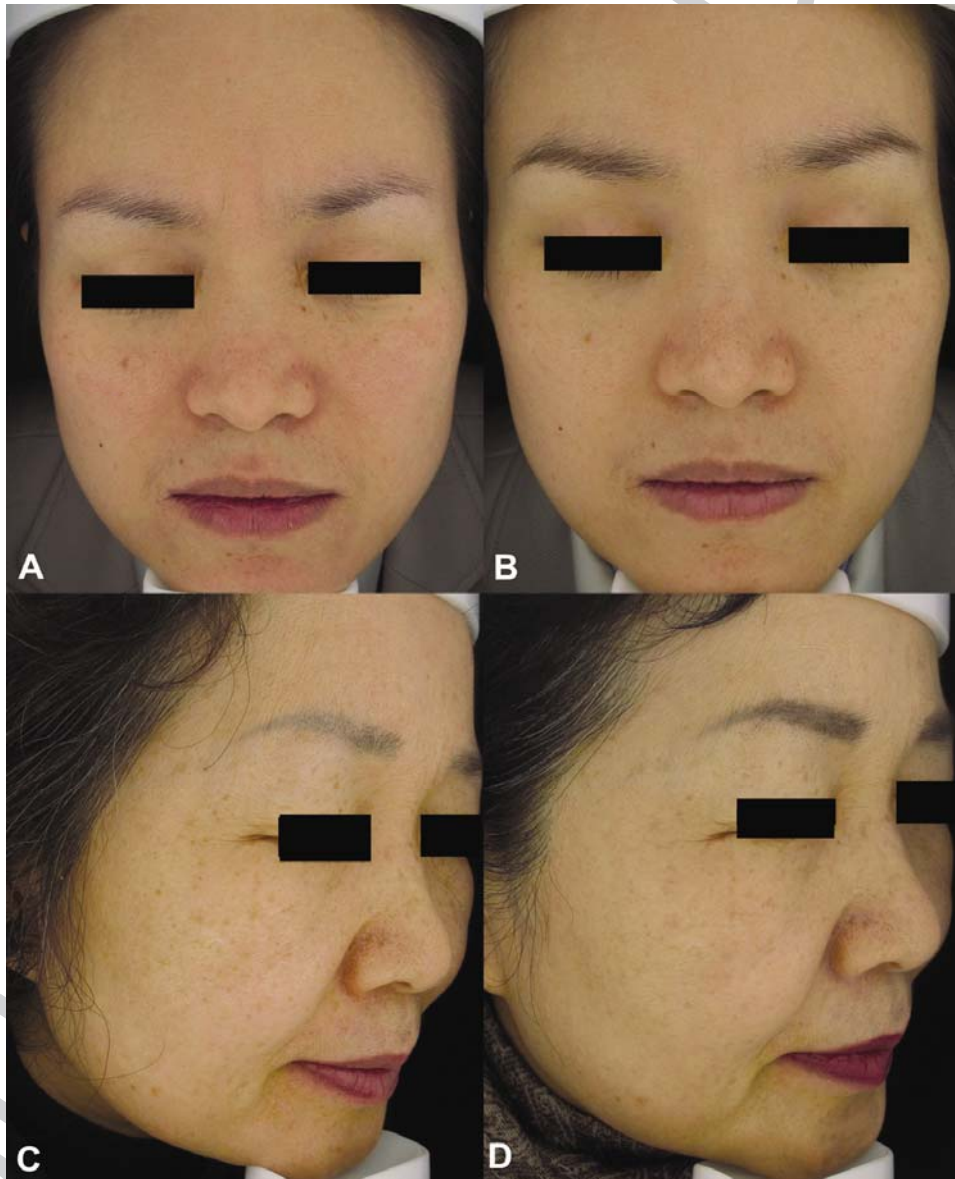


Figure. 2. Clinical improvement based on standardized photographs (A. dyspigmentation, B. wrinkles, C. laxity, D. overall features), and the subjective satisfaction rate (E).

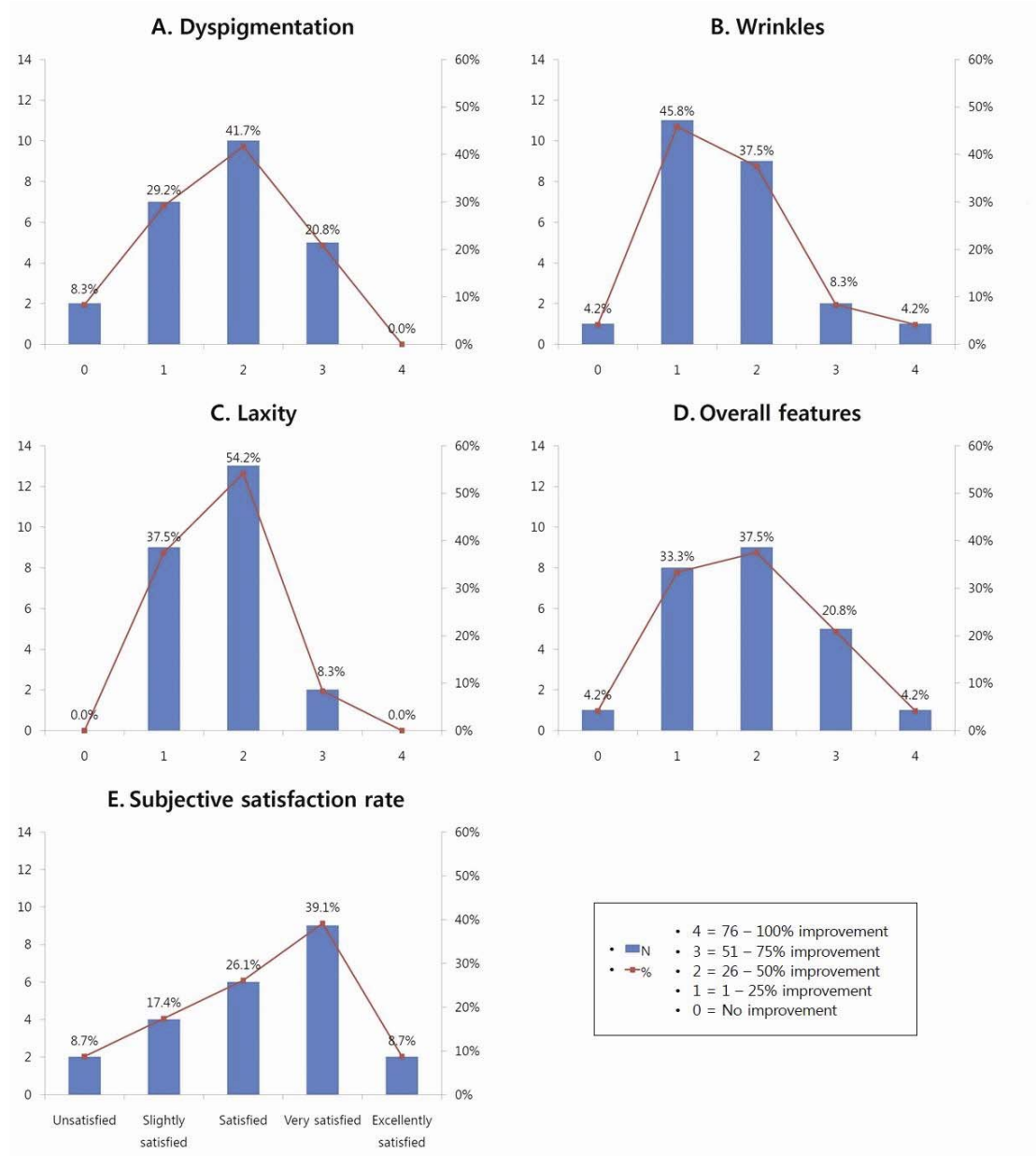


Figure. 3. A 34-year-old woman before (A) and after (B-D) one treatment session with 2 passes at 14mJ. On the day after the treatment, she presented with significant erythema and edema (B). Three days after the treatment, her erythema and edema subsided and bronzed skin was observed due to microcrust formation (C). Four weeks after the treatment, she showed clinical improvement without any sequelae (D).

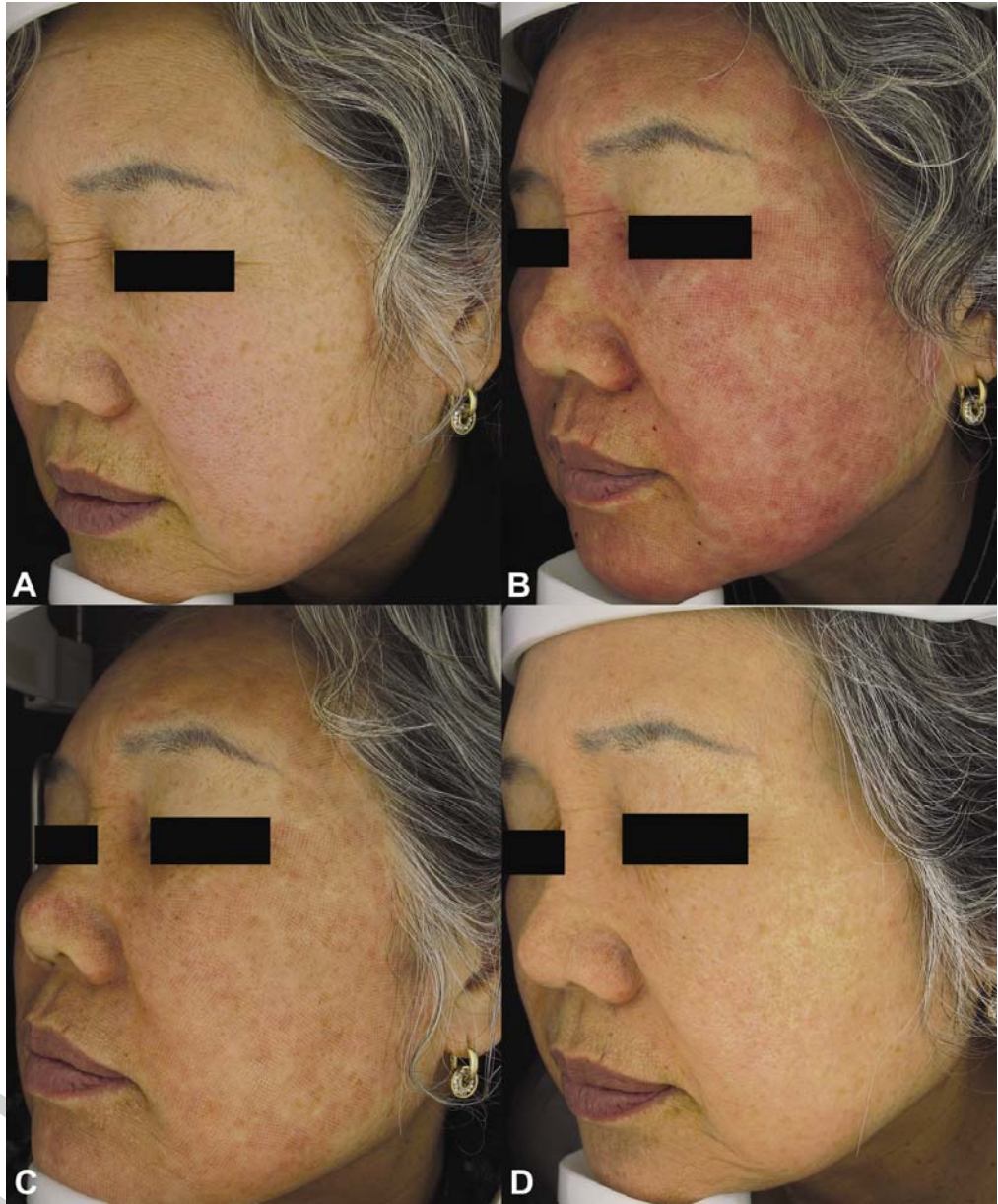


Table I

Fractional Er:YAG laser treatments for photodamaged facial skin.

Author	Subjects	Treatment devices & setting	Results
Lapidoth, et al (5)	Israel & Brazil, Fitzpatrick skin type II-IV	Pixel, Alma Lasers Ltd, Caesarea, Israel Setting: 2-4 stacked passes were performed for a penetration of 20 μm (evaporative) 30 μm (thermal) (1 st pass), 35 + 40 μm (2nd pass), 50 + 45 μm (3rd pass), 60 + 50 μm and (4th pass); and a microzone diameter of 150 μm , mean	Two months after treatment, all patients showed clinical improvement greater than 50%.

3.2 sessions			
Lomeo, et al (7)	Italy (Fitzpatrick II-III)	Half of the face was treated with the fractional Er:YAG (MCL 30 Dermablade ,Asclepion, Jena, Germany) versus half treated with a fractional CO ₂ laser (Mixto Sx, Slim Evolution, Lasering, Modena, Italy). Setting: Density 17% (Er:YAG) and 20% (CO ₂)	All patients showed improvement in skin texture and color on both treated sides. A slightly higher improvement score on the CO ₂ side (+15%). The Er:YAG side had a shorter average downtime period (3.5 vs 4.5 days).
Ross, et al (6)	U.S (Fitzpatrick skin type I-	2,940-nm fractional Er:YAG laser compared with a	Wrinkle improvement in the perioral and periorbital areas was approximately 50% after on treatment.

	III)		standard ablative Er:YAG laser in the treatment of facial rhytides and dyspigmentation. Setting: density of 400–920 microbeams/cm ²
Karsai, et al (3)	German (Fitzpatrick skin type I-III)	MCL 30 Dermablate, Asclepion, Jena, Germany Setting: total fluence 60J/cm ² , six stacked pulses, density 20%, single sessions	Wrinkle depth and Fitzpatrick score were reduced by approximately 10%.
Goldberg, et al (2)	U.S (Fitzpatrick	DermaSculpt, HOYA ConBio,	All patients recorded some clinical improvement in their treated skin; half

skin type I- Fremont, CA, USA reported over 50% improvement.

III) Setting: 15-30mJ

per microspot,

density 8 – 21%, 6

sessions

Our Korea ACTION, Lutronic, 62.5% of subjects showed an improvement

present (Fitzpatrick Seoul, Korea) greater than 26%

study skin type Setting: 10-14mJ

III-IV) per microspot,

density: 5-10%

, mean 2.3

sessions

JUST ACCEPTED

Table IIPatient characteristics (study-completed, $n = 24$).

	Count n , %
Average age (range), years	42.4 (32-67)
Female	24 (100%)
Male	0 (0%)
Number of treatment sessions (mean, 2.3 sessions)	15 (62.5%)
1 session	1 (4.2%)
2 sessions	0 (0%)
3 sessions	1 (4.2%)
4 sessions	3 (12.5%)
5 sessions	4 (16.6%)
6 sessions	