The Treatment of Melasma with Fractional Photothermolysis: A Pilot Study

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BACKGROUND. Melasma is a common pigmentary disorder that remains resistant to available therapies. Facial resurfacing with the pulsed CO_2 laser has been reported successful but requires significant downtime, and there is a risk of adverse sequelae.

OBJECTIVE. To determine if melasma will respond to a new treatment paradigm, fractional resurfacing.

METHODS. Ten female patients (Fitzpatrick skin types III–V) who were unresponsive to previous treatment were treated at 1- to 2-week intervals with the Fraxel laser (Reliant Technologies, Palo Alto, CA, USA). Wavelengths of 1,535 and 1,550 nm were both used, and 6 to 12 mJ per microthermal zone with 2,000 to 3,500 mtz/cm^2 were the treatment parameters. Four to six treatment sessions were performed. Responses were evaluated according to the percentage of lightening of original pigmentation. Two physicians evaluated the photographs, and each patient evaluated her own response.

RESULTS. The physician evaluation was that 60% of patients achieved 75 to 100% clearing and 30% had less than 25% improvement. The patients' evaluations agreed, except for one patient, who graded herself as 50 to 75% improved as opposed to the physician grading of over 75%. There was one patient with postinflammatory hyperpigmentation and no patient with hypopigmentation. No downtime was necessary for wound healing.

CONCLUSIONS. Fractional resurfacing affords a new treatment algorithm for the treatment of melasma that combines decreased risk and downtime with significant efficacy. This treatment modality deserves further exploration to maximize benefits.

RELIANT TECHNOLOGIES LOANED THE FRAXEL LASER FOR THE STUDY. RICHARD E. FITZPATRICK, MD, IS A PAID CONSULTANT FOR RELIANT AND A STOCKHOLDER.

MELASMA IS a common pigmentary condition characterized by ill-defined brown macules of the face. The majority of cases are seen in the sun-exposed portion of the face in women, although 10% of the cases are seen in men. A variety of etiologies, including genetic factors, sun exposure, oral contraceptives, pregnancy, and phototoxic drugs, may play a role in the pathogenesis of this condition.[1] Histologically, three patterns of pigmentation are recognized: an epidermal type, in which the pigment is deposited in the basal or suprabasal layer; a dermal type, in which melanin-laden macrophages are in the superficial and mid-dermis; and the mixed type, characterized by features of both the epidermal and the dermal type.[1]

Traditional therapies for melasma include the judicious use of sunscreens, discontinuation of hormonal therapy, and the use of topical agents such as hydroquinone, topical retinoids, and topical steroids. Although the use of glycolic acid peels as an adjunct therapy has gained much popularity in the past few years, there are conflicting reports as to the efficacy of this modality.[2,3]

The use of lasers and intense pulsed light source in the treatment of melasma has also been controversial. The use of a 510 nm pigmented lesion dye laser in the treatment of melasma was disappointing.[4] Taylor and Anderson reported on the ineffective treatment of melasma and postinflammatory hyperpigmentation in eight subjects using the Q-switched ruby laser.[5] The use of intense pulsed light source for the treatment of melasma was recently investigated by Wang and colleagues.[6] These investigators treated 17 patients with the intense pulsed light source (Vasculight, ESC Santa Clara, CA, USA) during four sessions at 4-week intervals using various filters along with hydroquinone. Only the control group, composed of 16 patients, received hydroquinone therapy. They reported a 39.8% improvement in the relative melanin index in the treatment group compared with 11.6% improvement in the control group at week 16. However, the authors reported excellent to good (51–100%) improvement in only 35% of the patients.

Recently, there have been a few reports on the successful treatment of melasma by using resurfacing lasers. Nouri and colleagues used a combination of pulsed CO_2 laser alone versus in conjunction with the Q-switched alexandrite laser in limited test spot areas in a small number of patients and reported on the resolution of the pigment in the test areas in both groups.[7] However, certain patients developed a ring of hyperpigmentation around the areas of clearing. Angsuwarangsee and Polnikorn conducted a split-face study comparing the combined ultrapulse CO_2 laser and Q-switched alexandrite laser versus the alexandrite

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laser alone in the treatment of refractory melasma in six Asian subjects and followed the patients for 6 months.[8] They reported a statistically significant reduction in Melasma Area and Severity Index (MASI) scores on the side treated with combination therapy and an insignificant reduction on the side treated with the Q-switched alexandrite laser.[7] There have also been anecdotal reports of successful treatment of melasma using the ultrapulse CO_2 laser, as well as the observation of resolution of melasma when the primary indication for CO_2 resurfacing has been photodamage. As a result of these observations in our own experience, several patients with melasma as the sole indication have been treated successfully with the ultrapulse CO_2 laser, with excellent long-term results. The primary downside to this treatment, however, has been the downtime for initial healing and the universal occurrence of postinflammatory hyperpigmentation lasting as long as 9 months. Similarly, erbium resurfacing may also cause improvement in melasma but was associated with significant postinflammatory hyperpigmentation.[9]

Fractional photothermolysis (Fraxel laser treatment, Reliant Technologies, Palo Alto, CA, USA) is a new concept in laser resurfacing in which the skin is resurfaced fractionally at one time. This is accomplished by the placement of numerous microscopic zones of thermal damage in the epidermis and dermis surrounded by islands of normal tissue.[10] Since this laser system resurfaces the skin 15 to 20% at one time and does not cause full epidermal wounds, healing time is minimized. We postulated that the new treatment algorithm of fractional treatments offered by the Fraxel laser may be successful in avoidance of adverse sequelae associated with CO_2 resurfacing and may improve melasma in the same manner as the CO_2 laser. Thus, we investigated the use of Fraxel laser technology in the treatment of melasma as a pilot study.

Methods

Ten female patients (Fitzpatrick skin types III–V) with the clinical diagnosis of melasma were enrolled in the study (Table 1). An explanation including the risks, benefits, and potential complications was given to the patients, and written informed consent was obtained. All patients had been previously treated with at least topical agents. A significant number of patients also had undergone peels and other laser treatments (see Table 1).

Anesthesia was achieved with a topical 30% lidocaine gel for 1 hour prior to each treatment. A blue dye (FD&C No. 1), which serves as a guide marker for the intelligent optical tracking device of the laser handpiece, was used to demarcate the areas of laser treatment. The patients were treated with the Fraxel laser at four to six sessions, and each session was 1 to 2 weeks apart. The settings of 2,000 to 3,500 mctz/cm^2 were used at energy levels ranging from 6 to 12 mJ per microthermal zone. Initially, a prototype laser with a wavelength of 1,535 nm was used, which was later substituted with the current commercially available laser with a wavelength of 1,550 nm. Patients were instructed to apply Aquaphor ointment immediately posttreatment followed by a few days of the application of a bland moisturizer.

Patients were instructed to avoid the use of bleaching agents during the course of treatment. They were also instructed to exercise sun protection and wear a broad-spectrum sunscreen. Patients who had active labial herpes simplex virus did not receive laser treatment until their lesions had resolved.

The patients were evaluated by two assessors (C.K.R. and R.E.F.), who compared detailed before and after pictures. The patients' improvement was rated according to four categories: 0%, 1 to 25%, 26 to 50%, 51 to 75%, and 76 to 100%. At the 3-month follow-up, the patients were asked to report on their level of improvement according to the same scale. The patients also rated their overall level of satisfaction with the laser treatment according to the following scale: very satisfied, satisfied, slightly satisfied, and unsatisfied. They also reported on average pain scores from a scale of 1 to 10, with 1 describing mild pain and 10 describing severe bee sting–like pain.

Table 1. Patient Demographics

Patient	*Sex*	*Age (yr)*	*Location*	*Skin Type*	*Previous Therapy*	*Duration (yr)*
E.S.	F	42	Cheeks	IV	OTC HQ	12
S.S.	F	51	Cheeks, forehead	V	HQ, peels, RA	20
G.M.	F	56	Forehead, cheeks, chin	V	OTC HQ	6
K.H.	F	36	Cheeks	III	Microdermabrasion, IPL, HQ	5
J.M.	F	36	Forehead, cheeks	III	HQ 15%, IPL	10
S.C.	F	44	Entire face	V	HQ	2
C.F.	F	53	Forehead, cheeks	V	HQ	6
M.S.	F	58	Mandible, neck	III	$UPCO_2$ laser, alexandrite laser, IPL, peels, HQ, RA	38
M.A.	F	60	Cheeks	IV	Triluma, Sciton laser	25
S.R.	F	47	Jawline, neck	III	HQ, RA	16

HQ = hydroquinone; IPL = intense pulsed light; OTC = over the counter; RA = Retin A; $UPCO_2$ = ultrapulse carbon dioxide.

Results

All 10 patients completed the study. All participants were females with a mean disease duration of 14.5 years. The average age of the study population was 45 years. There were four patients with skin type III, two patients with skin type IV, and four patients with skin type V (see Table 1). Treatment areas included the cheeks, forehead, chin, and neck.

Side effects were limited to sunburn-like erythema, which lasted 1 to 3 days. Rarely, at high densities, the patients had small linear abrasions each about 2 to 3 × 8 to 16 mm, which healed uneventfully. In a few cases, these abrasions or crusts appeared 3 to 5 days after treatment. By 7 days, the patients had returned to normal, except some rare residual erythema. Although facial edema is a rare side effect that we have encountered while treating at aggressive settings, no patient had significant edema at the above settings. Patients reported an average pain score of 6.3 on a scale of 1 to 10, with 10 signifying pain similar to a bee sting. Patients described the pain as a hot brush or rod against their skin. There was no incidence of scarring. We did observe one case of hyperpigmentation in one patient who was of Hispanic origin (type V). Interestingly, four other Hispanic patients who were also treated did not develop any hyperpigmentation. One such patient of Hispanic origin (type V) had 75 to 100% clearing according to both investigator and patient assessments. There was no incidence of hypopigmentation. All patients returned to work or normal activity immediately, and no patient needed to take time off from work. Some patients had difficulty with complete removal of the blue dye after the treatment. We discovered that baby wipes do an effective job of removing most of the residual blue dye. If any residual dye was left on the skin, the patients reported that it would usually disappear by the next day.

Sixty percent of patients were assessed to have 75 to 100% clearing of their melasma according to the evaluator assessment (Figure 1). Fifty percent of patients also rated themselves as having 75 to 100% improvement (Figure 2). Of note was 100% clearing of melasma on bilateral cheeks in an Asian patient with type IV skin without any evidence of hyperpigmentation or hypopigmentation (Figures 3 and 4). There was also one Hispanic patient (skin type V) who had 75 to 100% improvement according to both the evaluator and the patient assessments (Figure 5). All patients had at least been treated with topical agents. It is noteworthy that three patients were previously treated with intense pulsed light, without significant improvement. One patient whose facial melasma had cleared with CO_2 resurfacing but still had residual melasma on the neck had 50 to 75% improvement according to the patient after six treatment sessions with the Fraxel laser. The one patient who did not respond to Fraxel laser treatment also had not responded to multiple sessions of 10- to 20-micron erbium laser peels (Sciton, Inc., Palo Alto, CA, USA), which, in our experience, is somewhat helpful for treatment-resistant melasma. The patients were also asked to rate their level of satisfaction with the laser treatment according to the following four categories: very satisfied, satisfied, slightly satisfied, and unsatisfied. Sixty percent (6 of 10) were very satisfied, 30% were slightly satisfied, and 10% were unsatisfied.

Of the nonresponder (n = 1) or the ones with minimal improvement (n = 2) (1–25%), all were of Hispanic origin. However, one Hispanic patient had 75 to 100% clearance after five sessions, without any evidence of hyperpigmentation (see Figure 5).

Coincidentally, all patients expressed improvement in skin texture even after one to two treatments (Figure 6). This, however, was not assessed formally by the investigators. We treated patients' melasma on the neck in two patients without any adverse sequelae (see Figure 7).

Discussion

This study is the first report of fractional photothermolysis in the treatment of melasma and treatment of large

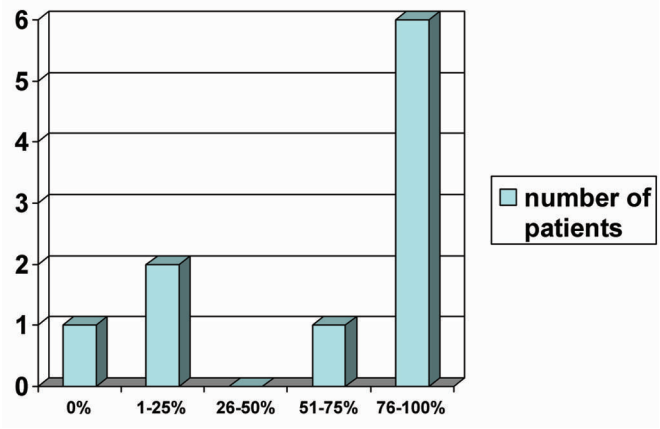

Figure 1. Percentile improvement in melasma as assessed by the evaluators.

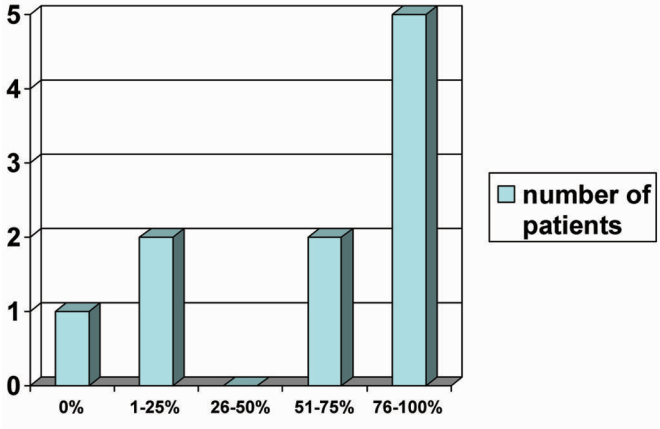

Figure 2. Percentile improvement in melasma as assessed by the subjects.

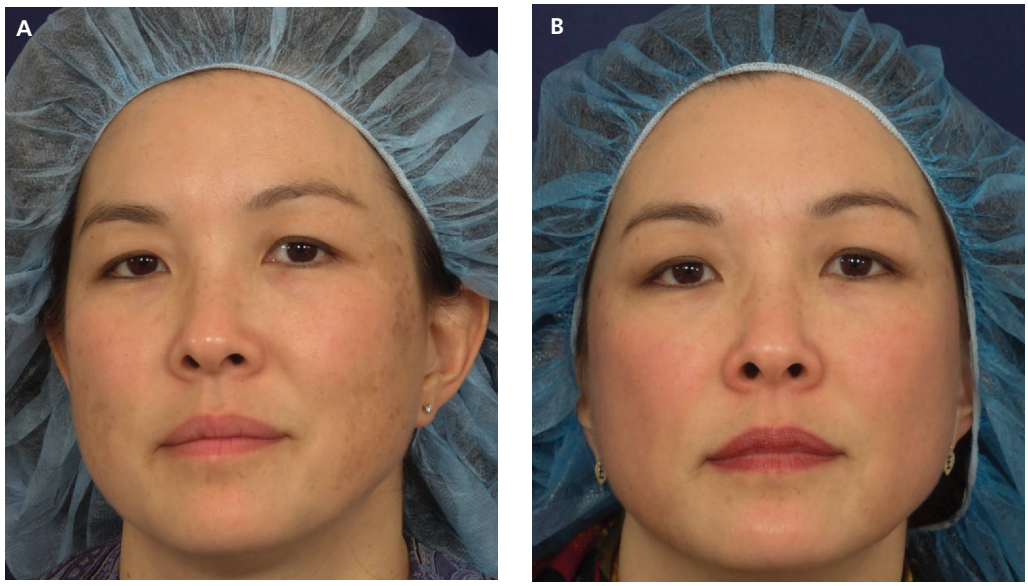

Figure 3. (A) Melasma on the face of an Asian patient after one treatment (preoperative picture not available). (B) Complete resolution of melasma after five treatment sessions with the Fraxel laser.

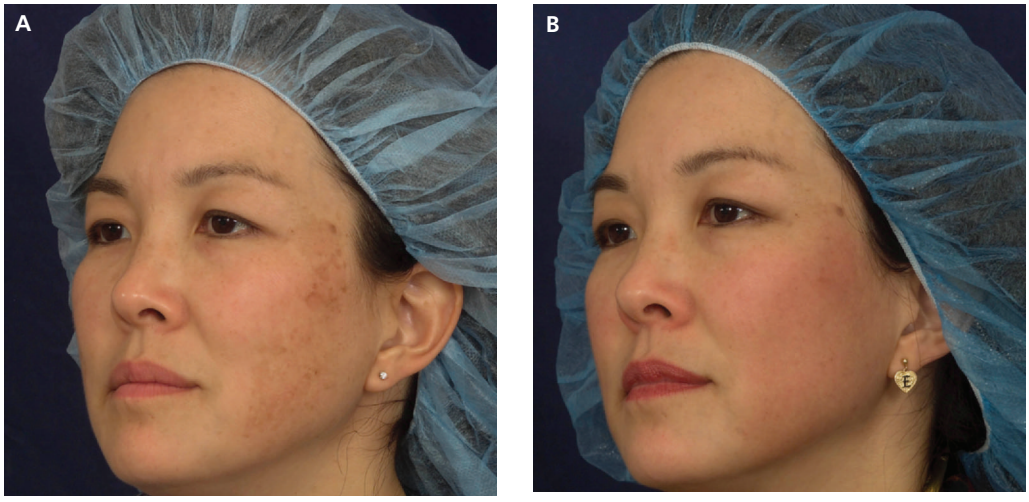

Figure 4. (A and B) Side profiles of the same patient.

anatomic surface areas such as the full face or neck. We have long known that CO_2 laser resurfacing causes significant improvement in or complete resolution of melasma. This notion was recently confirmed in various studies.[7,8] A natural extension of this thought process is that a fractional approach to resurfacing should cause significant improvement in melasma. Thus, we undertook evaluating this concept in a pilot open-label study in 10 patients.

Fractional photothermolysis is a new concept in laser applications in which the laser treatment results in the placement of numerous microscopic zones of thermal damage, leaving the majority of the skin tissue intact. The remaining untreated skin serves as a reservoir for healing. The depth and diameter of each microthermal zone are determined by the energy setting. An energy level of 6 mJ per microthermal zone corresponds to a diameter of 80 microns and a depth of 360 microns in each microthermal zone as assessed through histologic evaluation. Similarly, an energy level of 10 mJ per microthermal zone corresponds to a diameter of 110 microns and a depth of 500 microns in each microthermal zone (Reliant Technologies, personal communication March 2001). What proportion of the surface area is treated depends on the densities used and the number of passes.

Fraxel laser treatment is currently approved by the US Food and Drug Administration for improvement of periorbital rhytids, lentigines, and dyspigmentation. In the periorbital study to establish the safety and efficacy of fractional photothermolysis recently published by Manstein and colleagues, the investigators reported improvement in periorbital rhytids in 96% of patients and an average 0.9 improvement in Fitzpatrick wrinkle scores in 30 subjects.[9] The forearm part of the study established the sequence of

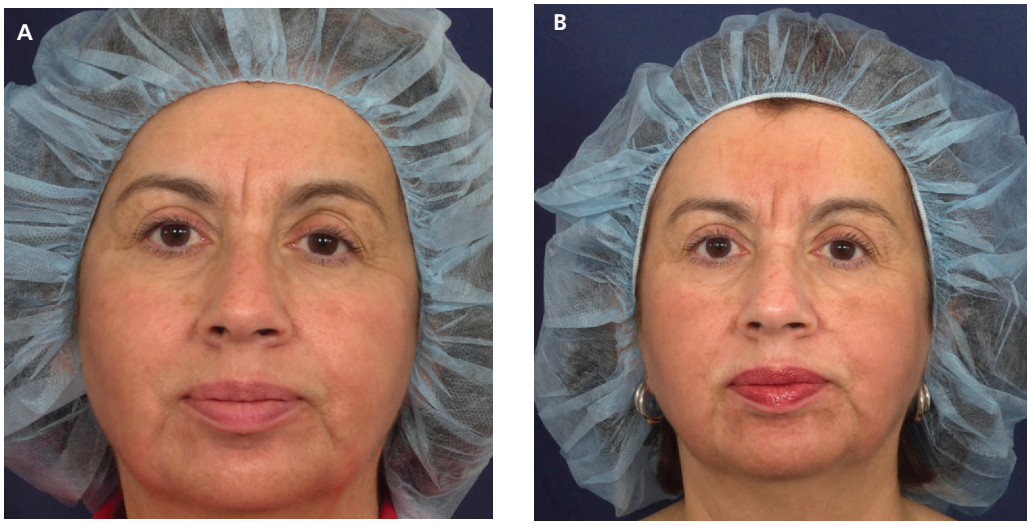

Figure 5. (A) Melasma in a patient with type V skin pretreatment. (B) Improvement in melasma after five treatment sessions.

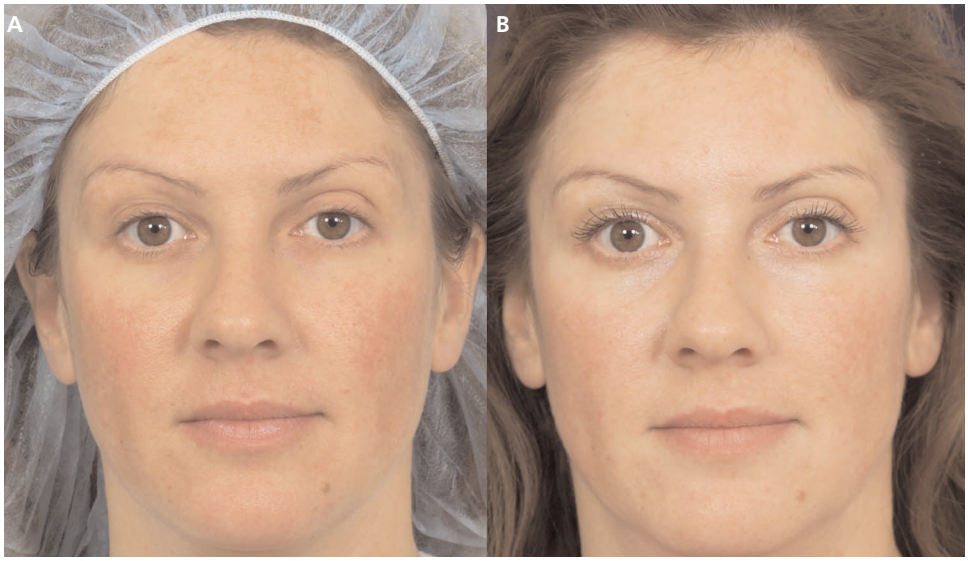

Figure 6. (A) Melasma on the cheeks and forehead before treatment. (B) Significant reduction in melasma after six treatment sessions.

events subsequent to the placement of microthermal zones characterized by columns of denatured epidermis and dermis. The microepidermal necrotic debris (MEND) describes "a spheroid or button-shaped collection of necrotic debris located just below an intact stratum corneum overlying each dermal wound,"[10] which is extruded at about 1 week postexposure. The area right below the MEND is characterized by a column of denatured collagen.

The advantages to this fractional approach to resurfacing are numerous, from both a theoretical and a practical perspective. First and foremost, patients do not have open wounds, and, as such, downtime is minimized. Second, anatomic areas that would generally be highly prone to complications of scarring with traditional resurfacing lasers, such as the neck, chest, and hands, can be safely treated. Third, potential complications associated with open wounds, such as infection and hyper- or hypopigmentation, are minimized. Fourth, one can potentially treat deeper dermal pathology. Traditionally, with CO_2 laser resurfacing, one ablates tissue approximately 200 to 400 microns during multiple-pass procedures. Treatment that is any deeper risks the complication of scarring. With Fraxel laser treatment, one can penetrate tissue much deeper safely because entire epidermal and dermal ablation has not been achieved. This has potential therapeutic implication for dermal melasma.

This pilot study describes the first report of improvement in melasma through a fractional approach to resurfacing. According to the patient improvement scores, 50% of patients in this study deemed their melasma to be 75 to 100% improved. This was in agreement with the evaluator assessment of melasma having improved 75 to 100% in 60% of the patients. The nonresponder and the ones with slight improvement ($n = 2$) were all Hispanic patients with

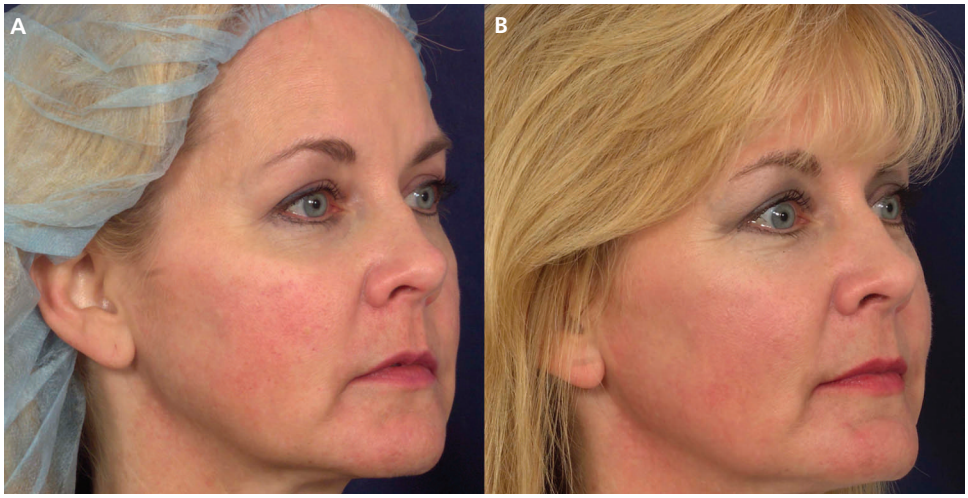

Figure 7. (A) Melasma on the cheeks and neck of a patient before treatment. (B) Significant reduction in dyspigmentation following five treatment sessions.

type V skin. It may be that melasma in this group of patients is fueled by factors that are not yet fully understood. It may be that these patients had dermal melasma and that a protocol to target deeper dermal melanin would have been more effective. Of interest is the low incidence of pigmentary changes associated with this laser compared with traditional resurfacing techniques. However, one needs to keep in mind that hypopigmentation as an adverse sequela of CO_2 laser resurfacing can appear as long as 6 to 24 months post-treatment. Therefore, longer follow-up in our series of patients is necessary to conclude that delayed pigment loss does not occur with fractional resurfacing. We advise against the use of this laser in patients with active labial herpes simplex virus because we have observed this condition to exacerbate in one patient treated for other indications. Prophylactic suppression when treating patients known to have this infection is advised.

The subjects rated the pain associated with this laser treatment at 6.3 on a scale of 1 to 10. All patients in this series were able to tolerate the procedure with only topical anesthetics. In our experience, in patients who require more than topical numbing, nerve blocks, especially in the perioral region, can be helpful. The use of cooled air devices to decrease pain can be considered, but the issue of whether cooling can, in effect, decrease the diameter and depth of each microthermal zone at a particular energy setting needs further investigation.

One shortcoming of this pilot study is that we did not categorize the patients according to melasma type either with a biopsy or Wood's light examination. However, as a pilot study, we were only trying to answer the question of whether this treatment approach can treat melasma at all. It may be that by categorizing patients, the treatment protocol can be adjusted to treat that specific type of melasma more effectively. The small number of patients treated invites larger-scale studies for further evaluation of this subject matter.

One other major pitfall with the treatment of melasma with any therapeutic modality is the notion that melasma has a high tendency to recur. As this was a pilot study, we did not have long-term follow-up; longer follow-ups are needed to assess the long-term efficacy of our results. Potential refinement of the number of sessions and treatment parameters need further evaluation to maximize the therapeutic efficacy of this new laser technology in the treatment of melasma.

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