Treatment of Melasma With the 1,927-nm Fractional Thulium Fiber Laser: A Retrospective Analysis of 20 Cases With Long-Term Follow-Up

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Background: Melasma is a common acquired symmetrical hyperpigmentation that is often recurrent and refractory.

Objectives: To investigate the efficacy and safety of a single administration of high-density fractional thulium fiber laser (1,927 nm) for the treatment of refractory melasma in 20 patients.

Materials and Methods: A retrospective chart and photographs review of 20 women (Fitzpatrick skin type II–IV) with clinical diagnosis of melasma treated with the 1,927-nm fractionated thulium laser at 10 or 20 mJ/cm², with 60–70% surface area coverage. Four investigators independently evaluated Melasma Area Severity Index (MASI) scores before, 4 weeks, 3–6 months, and 6–12 months after treatment.

Results: Mean MASI scores decreased dramatically from 13.2 ± 5.4 before treatment to 8.5 ± 3.5 at 4 weeks after laser treatment (P = 0.004). Patient assessment revealed that 12 of the 20 subjects had more than 50% clearance of their melasma. Recurrence was reported by 7 out of 15 patients who were successfully followed-up (mean 10.2 months). Two patients developed postinflammatory hyperpigmentation that subsided with topical bleaching after 3 months.


Key words: melasma; fractional laser; thulium laser

INTRODUCTION

Melasma is an acquired, usually symmetric facial hypermelanosisis appearing as irregular light-brown to dark-brown macules and patches on the face, predominantly on the forehead, malar areas, and chin. It is particularly observed in women with Fitzpatrick skin types III to V [1], especially Asian and Hispanic women, although all skin types can be affected. Genetic factors, sun exposure, oral contraceptives, pregnancy and phototoxic or photoallergic drugs or cosmetics may play a role in the pathogenesis of this condition [2]. However the etiology and pathogenesis are not yet fully understood as recent studies have shown that the underlying basis for melasma may be more complex than originally thought [3,4].

Treatment modalities in use for this condition include broad-spectrum (ultraviolet A + ultraviolet B) sunscreens, hydroquinone, topical retinoids, corticosteroids, azelaic acid, kojic acid, chemical peels, and various laser modalities. More recently, short-sequence oligopeptides have been reported to show inhibitory activity against tyrosinase with therapeutic potential for the treatment of skin hyperpigmentation disorders [5]. The efficacy of these topical treatments is only moderate and therefore melasma is still considered as a continuing challenge in terms of treatment outcome. The use of lasers and intense pulsed light source in the treatment of melasma has been proposed as a treatment alternative based on the fact that these treatment modalities have been associated with relatively low occurrence of postinflammatory hyperpigmentation (PIH) and varying degrees of success, although frequent melasma recurrence is seen with laser treatments. More specifically, ablative laser resurfacing, including carbon dioxide laser and erbium-doped yttrium aluminum garnet laser resurfacing have been reported successful [6,7], but require significant downtime and, in some instances, resulted in scarring and long-lasting PIH [6]. Nonablative fractional (NAF) laser therapy at 1,550 nm is approved by the FDA for the treatment of melasma, periorbital rhytides, pigmented lesions, skin resurfacing,
acne, and surgical scars [8]. This newer technology creates thousands to hundreds of thousands of microscopic treatment zones (MTZs) in the dermis and epidermis, sparing the surrounding tissue [9]. Among the current lasers in use, fractional laser appears to be the most effective for melasma, although a long-term risk for PIH and need for maintenance therapy is present. The new addition to the 1,550 nm erbium-doped fractional device is the 1,927 nm thulium fiber laser (Fraxel re:store Dual, Solta Medical, Inc., Hayward, CA) with a greater ability of targeting epidermal processes such as pigmentation disorders and less risk of causing problematic PIH as it targets water instead of pigment. In the present retrospective study we evaluate the long-term efficacy of 20 subjects previously treated with a single administration of high-density fractional thulium fiber laser (1,927 nm) for the treatment of refractory melasma.

PATIENTS AND METHODS

A retrospective chart and photographs review of 20 women with clinical diagnosis of melasma treated with high-density fractional thulium laser by two physicians within one practice between October 2009 and September 2011 was performed. Patient charts were reviewed for demographic data such as age, sex, skin phototype, past treatments, and disease duration (Table 1). Exclusion criteria for our retrospective analysis included pregnancy or nursing, active labial herpes simplex, localized or systemic infection, history of keloid formation. The treated area was thoroughly cleansed with a mild soap before each session and a topical anesthetic cream (combination of lidocaine 2.3% and tetracaine 7%) was applied to the treatment site for 1-hour preprocedure. The anesthetic cream was removed immediately before laser surgery using wet gauze. Patients underwent treatment with the 1,927-nm fractionated thulium laser at 10 or 20 mJ/cm², with 60–70% surface area coverage, total energies from 1.72 to 4.42 kJ. A cooling device (Zimmer Elektromedizin Cryo 5 device, Zimmer Medizin Systems, Irvine, CA) was used to relieve pain and discomfort during treatment.

Patients were instructed to avoid sun exposure for 10 days after the laser treatment and wear a broad-spectrum sunscreen. High-potency corticosteroid cream (clobetasol propionate cream 0.05%) was used over the melasma area, immediately after the laser treatment, twice daily for 1–3 days. Digital photographs of the melasma were recorded using a digital camera (15 megapixels, Canon EOS T3, Tokyo, Japan) at baseline and at each follow-up visit. Patients were advised to start topical 4% micronized hydroquinone over remaining melasma area 1 month after the procedure in order to maintain efficacy achieved with the laser treatment. Patients were asked to return according to the recommended follow-up regimen by the senior author: 1 and 4 weeks after the procedure. Subjects were subsequently contacted to return for long-term follow-up visits at 3 to 6 months and 6 months to 1 year after laser treatment.

Four investigators independently evaluated Melasma Area and Severity Index (MASI) scores based on clinical photographs before, 4 weeks, 3–6 months, and lastly 6–12 months after treatment. According to the MASI score determined by Kimbrough-Green and colleagues [10], the whole face is divided into four areas: the forehead, right malar, left malar, and chin, corresponding to 30%, 30%,

TABLE 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Skin type</th>
<th>Duration (years)</th>
<th>Pretreatment history</th>
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<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>36</td>
<td>III</td>
<td>5</td>
<td>Tretinoin, HQ, IPL</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>44</td>
<td>IV</td>
<td>20</td>
<td>HQ, chemical peel</td>
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<tr>
<td>3</td>
<td>F</td>
<td>38</td>
<td>IV</td>
<td>8</td>
<td>HQ</td>
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<td>42</td>
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<td>Tretinoin, HQ</td>
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<td>5</td>
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<td>44</td>
<td>II</td>
<td>5</td>
<td>HQ</td>
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<td>6</td>
<td>F</td>
<td>41</td>
<td>III</td>
<td>3</td>
<td>Chemical peel</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>45</td>
<td>III</td>
<td>10</td>
<td>HQ, IPL</td>
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<td>F</td>
<td>46</td>
<td>II</td>
<td>10</td>
<td>Tretinoin</td>
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<tr>
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<td>50</td>
<td>IV</td>
<td>7</td>
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<td>32</td>
<td>III</td>
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<td>20</td>
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<td>34</td>
<td>III</td>
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<td>None</td>
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</table>

Mean 41.1 7.2

HQ, hydroquinone; IPL, intense pulsed light.
calculated according to the following equation:

\[
\text{MASI} = 0.3(DF + HF) \cdot AF + 0.3(DMR + HMR) \cdot AMR \\
+ 0.3(DML + HML) \cdot AML + 0.1(DC + HC) \cdot AC
\]

where D is darkness, MR is right malar, ML is left malar, and C is chin.

Patients were required to evaluate their subjective satisfaction at 4 weeks after treatment and during follow-up using a quartile grading scale: grade 1, less than 25% clearance; grade 2, 26–50% clearance; grade 3, 51–75% clearance, and grade 4, more than 75% clearance of their melasma.

Recurrence, defined as increase of pigment or enlargement of the melasma area from the last visit, was evaluated for all patients. In order to avoid any bias due to patient dropout, those patients who failed to make their follow-up visits were called to reassess their subjective satisfaction with the treatment and to verify any degree of recurrence of their melasma. Patients were able to request additional treatment if they felt that their melasma had recurred after 6 months of follow-up.

For statistical analysis, difference in MASI values before and after therapy was tested using paired t-test. Data are expressed as means ± standard errors, and \( P < 0.05 \) was considered to be statistically significant.

RESULTS

Table 1 summarizes patient characteristics and Figure 1 shows changes in mean MASI score over time. All subjects included in our review were women, with an average age of 41.1 years (range 30–51). Four of the 20 women (20%) were skin type II and the remaining 16 of the 20 patients (80%) were skin types III and IV. Most of the patients had been previously treated with at least topical agents. A significant number of patients had undergone chemical peels, intense pulsed light and/or other laser treatments with little or no improvement or recurrence of their condition. The average duration of melasma was 7.2 years. Patient assessments revealed that 12 of the 20 subjects (60%) had more than 50% clearance of their melasma at 4 weeks after the single laser treatment session. Eleven patients completed the 3- to 6-month follow-up and eight patients were able to complete the 6- to 12-month post-treatment follow-up for physician assessments. Mean MASI scores decreased dramatically from 13.2 ± 5.4 before treatment to 8.5 ± 3.5 at 4 weeks after laser treatment (\( P = 0.004 \)), achieving 35% improvement from the baseline MASI score. By 3- to 6-month follow-up the average MASI score of 7.7 ± 4.4 was significantly lower, representing a 45% reduction in mean MASI score from baseline (\( P = 0.004 \)). Interestingly, the mean MASI score continued to decrease with time to 6.1 ± 5.6 (\( P = 0.002 \)) at the 6- to 12-month follow-up visit, achieving 53.8% improvement from baseline MASI score. In patient’s self-evaluation, a mean grade of 2.75 was observed for clinical improvement at 4 weeks after the laser procedure, with nine patients (45%) indicating more than 75% clearance (Fig. 2). Two patients thought they had poor clearance (less than 25%) of their melasma and two patients with skin type IV experienced worsening of the melasma attributed to PIH that subsided with topical bleaching after 3 months. Clinical examples of patients treated with a high-density fractional 1,927-nm thulium laser are presented in Figures 3 and 4. Fifteen of the 20 patients were successfully contacted and were able to assess their clinical improvement during follow-up (average 10.2 months) and reported an average grade of clinical clearance of 2.0. Partial recurrence of their melasma was reported by 5 of the 15 patients (33.3%) and 2 of the 15 (13.3%) reported total recurrence of their melasma. Two patients received an additional treatment session 7 and 12 months after their initial treatment since they had noted partial recurrence of their melasma.

Moderate post-treatment erythema and edema were noted immediately after treatment which subsided within 24–72 hours (Fig. 5); peeling, that occurred between 3 and 7 days postprocedure, was also reported by all of the patients. None of the patients noted any long-term adverse effects such as scarring or hypopigmentation.

![Fig. 1. MASI scores pre- and post-Tx.](image-url)
DISCUSSION

Melasma is a common pigmentary disorder that can cause significant negative impact on the patient’s quality of life [11–13]. This disorder can pose a substantial therapeutic challenge because of its refractory and recurrent nature. Therapeutic options for this condition, besides rigorous sun protection, included topical preparations, such as bleaching agents [14], corticosteroids [15], retinoids [16], combination formulation [17], in addition to physical modalities, such as chemical peels [18,19], dermabrasion [20], intense pulsed light [21], and ablative and nonablative laser treatments [22–24]. While topical medications with triple combination products containing hydroquinone, a retinoid, and a fluorinated steroid are still considered as a first-line treatment for melasma [25], long-term application, slow response, limited effects, and undesirable recurrence are still major disadvantages [17,26].

The use of lasers and light therapy for pigment is based on the theory of photothermolysis introduced by Anderson...
and Parrish [27] that states that when a specific wavelength of energy is delivered over a period of time shorter than the thermal relaxation time of the target chromophore, heat and injury are limited to the target, with less damage to the surrounding skin. Melanosomes have a short relaxation time, ranging from 50 to 500 nanoseconds whereas the absorption spectrum of melanin is broad [28], allowing a variety of lasers and light sources to be used for cutaneous pigmentary disorders.

The Q-switched lasers, which deliver nanosecond pulse durations and can selectively target melanosomes, were some of the first type of lasers used for the treatment of pigmented skin lesions [25]. However, Taylor and Anderson [24] noted no improvement and, in some cases, PIH in eight subjects with melasma and PIH refractory to other treatments using the Q-switched ruby laser. The Q-switched Nd:YAG (1,064 nm) laser has a longer wavelength and penetrates deeper into the skin, which makes this laser generally safer in darker skin types as it produces less injury to the epidermis than the lasers with shorter wavelengths. Wattanakrai et al. [29] have recently studied the use of low-fluence Q-switched Nd-YAG (1,064 nm) for the treatment of facial melasma in 22 Asians. After five treatments at 1-week intervals, Q-switched 1,064-nm Nd:YAG laser produced only temporary improvement and side-effects such as rebound hyperpigmentation and even hypopigmentation occurred in 4 of the 22 and 3 of the 22 patients, respectively. We feel that the melanosome is not the correct target in melasma but rather the full epidermis and, to some extent, the superficial papillary dermis in order to eliminate the dysfunctional melanosomes in both the epidermis and superficial dermis. In addition, the nanosecond pulses of Q-switched lasers are also too traumatic with their photoacoustic effects and much more prone to cause PIH in our experience.

Resurfacing lasers, such as erbium:YAG laser and pulsed CO₂ laser have also been reported for melasma treatment. Manaloto and Alster [30] evaluated the erbium:YAG laser in 10 patients with Fitzpatrick skin type II to V and refractory melasma and found that there was improvement immediately after the procedure, but all patients had PIH by 3–6 weeks post-treatment. Nouri et al. [22] used a combination of pulsed CO₂ laser alone versus in conjunction with the Q-switched Alexandrite laser in test spot areas in eight patients with Fitzpatrick skin types IV to VI with dermal melasma. The authors found resolution of the pigment in the test areas in both groups, however, some patients developed peripheral hyperpigmentation around the areas of clearing. Therefore, given the risks of PIH in addition to the downtime for initial healing associated with the CO₂ and erbium:YAG resurfacing lasers, the use of these lasers has been limited for patients with melasma.

With NAF laser therapy, recovery is relatively fast and, theoretically, the resulting inflammation and dyspigmentation is less of a risk. Goldberg et al. [31] evaluated the histologic and ultrastructural changes associated with the 1,550-nm erbium-doped fractional laser in 10 patients with epidermal melasma. Post-treatment lesional skin showed a decrease in the number of epidermal melanosomes on light microscopy and fewer enlarged melanocytes on electron microscopy. The authors also suggested that NAF laser therapy may delay repigmentation due to decreased number of melanocytes noted after three epidermal turnover cycles.

Previous reports have demonstrated the efficacy and safety of the 1,550 nm erbium-doped fiber laser in the treatment of melasma. Rokhsar and Fitzpatrick [32] were the first to report improvement of melasma through a NAF laser therapy. The authors evaluated 10 patients, Fitzpatrick skin phototypes III to V, treated with four to six sessions with fractionated 1,550-nm erbium-doped laser (6–12 mJ/MTZ with 2,000–3,500 MTZ/cm²). The physician evaluation was that 60% of patients achieved 75–100% clearing of melasma; one patient developed PIH. Katz et al. [33] also reported greater than 50% clinical improvement in eight (Fitzpatrick skin type II–IV) patients with melasma treated with two to seven sessions (6–40 mJ/MTZ with 9–29% surface area coverage) at 3- to 8-week intervals. Five of the eight patients were able to maintain their clinical improvement for an average of 13.5 months after the last treatment session. However, there are recent reports [34,35] showing limitations in terms of efficacy of NAF laser therapy, with modest efficacy and high recurrence rates. Lee et al. [35] reported the results of 25 Asian patients with melasma who were treated with four monthly sessions of NAF laser therapy (15 mJ/MTZ, 1,000 MTZ/cm²) and followed up to 24 weeks after treatment completion. Although a physician assessed 60% of patients as improved, and 44% of subjects assessed themselves as improved at 4 weeks after the last treatment session, only 34.8% of patients assessed themselves as improved 24 weeks after treatment. Furthermore, the authors believe that although NAF laser therapy with the 1,550-nm erbium-doped laser is an option for the treatment of refractory melasma, with possibility of long-term remission, there is still a risk of PIH. Indeed one of the original subjects reported in the pilot study of Rokhsar and Fitzpatrick [32] returned approximately 2 years post-treatment with PIH not only in the areas of melasma but in all areas previously treated. It should be noted that this complication occurred 2 years following treatment and 2 months after a 2 weeks beach vacation. Karsai et al. [34] conducted a controlled single-blinded trial in 51 patients who received a broad-spectrum sunscreen either alone or in combination with four sessions of 1,550-nm NAF treatment (15 mJ/1048 MTZ/cm²) at 3-week intervals. The authors found that the percentage of subjective improvement was the same in both groups. The MASI corroborated the patient’s subjective estimate both in terms of the degree of improvement and the lack of a group difference.

The 1,927-nm wavelength has a higher absorption coefficient for water than the 1,550-nm and at maximal settings can achieve up to 70% surface area coverage per treatment. Moreover, at its maximum energy of 20 mJ, this laser produces a cutaneous injury zone up to a penetration depth of over 200 μm in the papillary dermis.
suggested a semi-ablative action, but closer to nonablative rather than ablative lasers. Therefore, the fractionated 1,927-nm thulium laser might be particularly beneficial in the treatment of epidermal conditions, such as lentigines, dyspigmentation, and actinic keratosis. Our results demonstrate the safety and efficacy of high-density single treatment session using the 1,927-nm fractional thulium laser in the treatment of facial recalcitrant melasma. It is important to note that marked improvement (>75% clearance) was observed by 9 of 20 patients (45%) at 4 weeks after a single laser treatment. Of interest is the relatively low incidence (10%) of pigmentary changes, particularly PIH, even though high surface area coverage was used and the majority of the patients (80%) were skin types III and IV. Although the use of high-potency corticosteroids to reduce the incidence of PIH still needs further studies to evaluate this effect, we believe that their use can be beneficial during the immediate post-treatment period to shut down the inflammatory cascade.

According to patient’s self-evaluation, 13.3% of patients (2/15) revealed total recurrence, while partial recurrence was reported by 33.3% (5/15) of patients during follow-up (average 10.2 months). However, some degree of clearance was still present, as demonstrated by the average grade of 2.0 (26–50% clearance) for clinical improvement reported by subjects. Physician’s evaluation pointed out 53.8% improvement of MASI scores at 6–12 months of follow-up compared to baseline. As opposed to patient’s own assessments which were mildly worse during follow-up (average 10.2 months) compared at 4 weeks (2.0 vs. 2.75), the mean MASI score assessed at 6–12 months was slightly lower than the mean MASI score at 4 weeks (6.1 ± 5.6 vs. 8.5 ± 3.5), although it did not reach statistical significance. We believe that the MASI scores are more reliable and accurate as a measure outcome for melasma. We find that in general patient self-assessment tends to be more pessimistic as there is no “before photo” for comparison. However, it is possible that the high number of patients lost to follow-up (9 out of 20 patients at 3–6 months and 12 out of 20 patients at 6–12 months), a main limitation in our study, might had contributed to this optimistic outcome. In addition, the use of topical bleaching agents restarted 1 month after laser treatment could also have contributed to those lower MASI scores found at 6–12 months of follow-up. Because the majority of patients had used a bleaching agent before the laser treatment with no change in pigmentation, we believe that the use of bleaching cream in this study was useful in preventing the recurrence of melasma although we did not have a control for hydroquinone.

Another limitation of our study is that we were not able to categorize the patients according to melasma type. It is possible that poor responders (n = 2) were patients with dermal or mixed type melasma as the fractional 1,927-nm thulium laser has been shown to penetrate up to superficial dermis only [36,37]. However, as a retrospective analysis, we were trying to determine if this treatment approach, using high-density coverage of this new wavelength laser, can treat melasma effectively and safely.

One other major difficulty of the treatment of melasma is the high rate of recurrence with any therapeutic method. Therefore, longer follow-up in our series of patients is necessary as additional recurrence is to be expected especially if the patient gets any sun exposure. The Thulium laser showed to be a useful tool to treat melasma, but it has no direct impact on the pathogenesis of this condition like all the former lasers and clearly it is not yet the definitive treatment for melasma. However, it can be a very useful laser as part of the overall regimen when used as a single high-density treatment as shown in this retrospective review. A reasonable success rate associated with a low incidence of PIH has been demonstrated.

In contrast to the NAF laser therapy using the 1,550-nm wavelength [32–35] where four to six treatment sessions are needed for effective treatment, we were able to achieve acceptable results in a single treatment session. If desired by the patient, lower densities (30–40%) can be used for faster clearance of crusting, but then multiple treatment sessions are likely to be necessary.

Our study shows that high-density coverage fractional 1,927-nm thulium laser treatment followed by topical hydroquinone proved to be a safe and effective treatment modality for melasma, with quick response, low incidence of PIH and long-term remission. Further prospective large-scale studies are warranted to statistically analyze recurrence rates and rates of PIH.

REFERENCES


