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CLINICAL REPORT

# Investigating the efficacy of a fractionated 1927 nm laser for diffuse dyspigmentation and actinic changes

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## Abstract

**Objectives:** Facial actinic irregularities are frequent targets for noninvasive, energy-based treatment. These irregularities are multifactorial and driven by both intrinsic factors such as aging, genetics, and hormone exposure, and extrinsic factors, such as UV exposure. Clinically, this photodamage manifests as dyschromic skin disorders like melasma and actinic features such as solar lentigines. Fractionated 1927 nm (f1927 nm) nonablative lasers are suitable for targeting epidermal lesions and have been shown to be effective in resurfacing photoaged skin as well as addressing pigmented lesions without exacerbation. The purpose of this study was to quantify the magnitude and duration of actinic pigment and photodamage response in patients of Fitzpatrick Skin Phototypes (SPT) I–IV who underwent two treatments with a fractionated, nonablative 1927 nm thulium laser (MOXI™, Sciton).

**Methods:** The authors conducted an IRB-approved, single-center, prospective, nonrandomized study to evaluate the efficacy of f1927 nm nonablative lasers in the treatment of diffuse dyspigmentation and actinic irregularities. Patients underwent two treatments with f1927 nm nonablative laser at a 1-month interval. F1927 nm treatment and energy parameters included a pulse energy of 15 mJ, density of 15% with 15% coverage, and six total passes. The primary endpoint for this study was pigment response after treatment, measured using the VISIA Skin Imaging and Analysis System (Canfield Scientific). Pigmentary lesions measured and analyzed included spots, UV spots, and brown spots. The Physician's Global Assessment Scale was used by plastic surgeons to provide a subjective clinical assessment of melasma response. Nonparametric testing was used to assess and compare VISIA results across the study period as well as clinician evaluations. A $p$ value $\leq 0.05$ was considered statistically significant.

**Results:** Twenty-seven patients underwent two treatments with nonablative, f1927 nm laser in May and June 2022. Ninety-six percent of patients ($n = 26$) completed 1-month follow-up and 89% of patients ($n = 24$) completed 3-month follow-up. The study cohort was 100% female, with a mean ± SD age of 47.0 ± 11.5 (range: 29–74), and a mean Fitzpatrick SPT of 2.8 (range: I–IV). No serious adverse events were observed during study treatment or follow-up. Overall, analysis showed statistically significant improvements in dyspigmentation at 1 month and an increase in pigment toward baseline at 3 months. At 1 month, there was a statistically significant decrease in spots ($p = 0.002$), UV spots ($p < 0.001$), and brown spots ($p < 0.001$) compared to baseline. At 3 months,

Brown spots remained significantly improved compared to baseline ($p = 0.05$). Analysis showed 9.9% improvement in pigment on the left ($p < 0.0001$) and 7.5% improvement in pigment on the right ($p < 0.0001$) face. Right dyspigmentation remained significantly improved at 3-month follow-up ($p = 0.02$). Subjectively, clinician evaluators' mean Physician's Global Assessment Scale score was 3.4 ($p < 0.0001$) at 1-month follow-up and 3.7 ($p < 0.0001$) at 3-month follow-up, which correspond to an approximately 50% improvement hyperpigmentation when at both time points.

**Conclusion:** These results demonstrate that fractionated, nonablative 1927 nm laser treatment is an effective modality for improving clinical and subclinical photodamage. The magnitude and duration of pigment improvement are potentially influenced by the propensity for photodamage during the summer months, which may suggest the need for multiple f1927 nm treatments over time to maintain results.

**KEYWORDS**

1927nm, actinic change, diode, dyspigmentation, facial rejuvenation, fractional, hyperpigmentation, laser, melasma, nonablative, photodamage, skin laser

# INTRODUCTION

Facial actinic irregularities are frequent targets for noninvasive, energy-based treatment. These irregularities are multifactorial and driven by both intrinsic factors such as aging, genetics, and hormone exposure, and extrinsic factors, such as UV exposure.[1,2] Intrinsically, aging causes a disruption of melanocyte physiology, leading to asynchronous areas of hypo- and hyperpigmentation. Extrinsically, the accumulation of solar exposure over time both directly damages melanocytes and alters the homeostatic physiology maintained by melanocytes, keratinocytes, and endothelial cells.[3] Clinically, this photodamage manifests as dyschromic skin disorders like melasma and actinic features such as solar lentigines.

MOXI™ (Sciton) is an FDA-approved device indicated for facial cosmesis and is a nonablative, fractional thulium diode laser and emits photo-energy at 1927 nm. Ablative therapies vaporize tissue, and thus remove the superficial epidermis and dermis, while nonablative therapies maintain the epidermis and cause controlled tissue injury without complete ablation.[4] Fractionated or fractional lasers target fractions of skin, known as microscopic thermal zones (MTZ), while nonfractionated lasers cause thermal injury to all skin in its range.[4,5] The device leverages principles of selective photothermolysis, first described by Anderson et al.[6,7] whereby specific chromophores are targeted using light-based energy. This energy absorption generates heat as a byproduct, which results in a desired clinical effect in target tissues, namely hemoglobin, melanin, and water.[7,8] At 1927 nm, the maximum depth of penetration is 200 μm and nears the 1950 nm peak of water absorption, allowing for specific, maximal targeting of water in the epidermis to treat dyschromia.[9] In the case of photodamaged skin, the targeted chromophore are melanocytes present in the dermis and dermal-epidermal junction.

Fractionated 1927 nm (f1927 nm) nonablative lasers are suitable for targeting epidermal lesions and have been shown to be effective in resurfacing photoaged skin as well as addressing pigmented lesions without exacerbation.[10–17] The purpose of this study was to quantify the magnitude and duration of pigment response after two treatments with a fractionated, nonablative 1927 nm thulium laser.

# MATERIALS AND METHODS

## Study design

This is a single-center, noncontrolled prospective study conducted using a protocol approved by the University of Texas Southwestern Medical Center Investigational Review Board. Study procedures were conducted between May and June 2022. Twenty-seven women ages 29–74 with Fitzpatrick Skin Phototypes (SPT) I through IV were recruited to receive two treatments using a fractionated 1927 nm device, 4 weeks apart. All study procedures took place at the Outpatient Surgery Center at the University of Texas Southwestern Medical Center. Target subjects include patients with photodamage, actinic changes, or melasma who desired treatment for this condition. Eligible patients (Supporting Infomation: Table 1) were healthy adults aged 20–75, of Fitzpatrick SPT I–IV, deemed by investigators to have clinically significant dyspigmentation and melasma, and willing to withhold esthetic therapies that could potentially impact results to the treatment area. As such, no adjunct topical agents such as hydroquinone or retinol were prescribed to patients during the study period. Fitzpatrick SPT was determined through clinical assessment of skin response to sun exposure.[18] Exclusion criteria included known histories of inflammatory skin disease or other skin

**TABLE 1** Physician's Global Assessment Scale (PGAS).

| PGAS Score | Description |
|---|---|
| 0 | Clear, except for possible residual discoloration, 100% improvement |
| 1 | Almost clear, very significant clearance, 90% improvement; only minor evidence of hyperpigmentation remains |
| 2 | Marked improvement, significant improvement, 75% improvement. Some disease evidence of hyperpigmentation remains |
| 3 | Moderate improvement, intermediate between slight and marked improvement; 50% improvement in appearance of hyperpigmentation |
| 4 | Slight improvement, some improvement, 25% improvement; significant evidence of hyperpigmentation remains |
| 5 | No improvement; hyperpigmented condition unchanged |
| 6 | Worse; condition worse than at Week 0 |

**TABLE 2** Subject demographics.

| Subject characteristics | *N* (%) |
|---|---|
| Age (mean ± SD) | 47.0 ± 11.5 (29–74) |
| Fitzpatrick skin phototype | 2.8 |
| I | 4 (17) |
| II | 6 (25) |
| III | 5 (21) |
| IV | 9 (33) |

**TABLE 3** Total energy per f1927nm treatment.

| Treatment | Mean total energy (mJ) ± SD | Range | *p* Value |
|---|---|---|---|
| Treatment 1 | 619.1 ± 53.2 | 499–712 | 0.32 |
| Treatment 2 | 657.7 ± 63.9 | 543–812 | |

**TABLE 4** Mean pigment across study period.

| Timepoint | Mean ± SD |
|---|---|
| Baseline | 41.9 ± 18 |
| 1-month follow-up | 38.4 ± 17.4 |
| 3-month follow-up | 40.6 ± 17.7 |

pathology, systemic disease which may affect wound healing, or a recent history of isotretinoin therapy or systemic steroids. All inclusion criteria and no exclusion criteria had to be met for the subject to be eligible for enrollment. The study is registered with ClinicalTrials.gov with identifier number NCT5226104.

## Study procedure

Each patient received two f1927 nm laser treatments, approximately 4 weeks apart. Following removal of all make-up and skincare products using a gentle cleanser, a trained staff member applied a topical Benzocaine 20%–Lidocaine 8%–Tetracaine 4% to anesthetize the treatment area. After allowing 30 min for the anesthetic to take effect, the skin was cleansed and prepped with antiseptic and then dried thoroughly before treatment. Disposable eye shields were applied to each subject before the start of treatment and appropriate eye protection was worn by all present in the treatment room. One trained staff member treated each subject's face to ensure validity across subjects. Treatment parameters were standardized across patients. This included a pulse energy of 15 mJ, 15% coverage, and 6 passes completed per treatment, with a density of 2.5% per pass. At 15 mJ, the spot size was 200 μm. To account for the risks versus benefit of providing more density but potentially worsening dyspigmentation, the investigators treated at a density of 15% to offer a more incremental benefit with a lower heat factor. Following treatments, subjects were provided posttreatment instructions regarding the use of appropriate sun protection and skin care. Subjects were seen 1 and 3 months after their last treatment for follow-up.

## Photography and evaluations

The primary endpoint of the study was the degree of dyspigmentation response after treatment, assessed objectively through imaging analysis and subjectively through clinician assessment of baseline, 1-, and 3-month photographs. Objective evaluation is completed using the VISIA Skin Imaging and Analysis System (Canfield Scientific) which provides high-resolution facial images using standard, ultraviolet, and cross-polarized light. Standard light detects superficial pigment (spots), ultraviolet light detects photodamage (UV spots), and cross-polarized light detects dermal pigment and melanosis

**TABLE 5** Median change in pigment over study period.

| Timepoint | Percent change in pigment | Median difference in pigment | 95% confidence interval | *p* Value |
|---|---|---|---|---|
| Baseline versus 1 month | −8.7% | −3.65 | −4.04 to −2.62 | <0.0001 |
| Baseline versus 3 months | −3.2% | −1.25 | −2.60 to −0.57 | 0.005 |

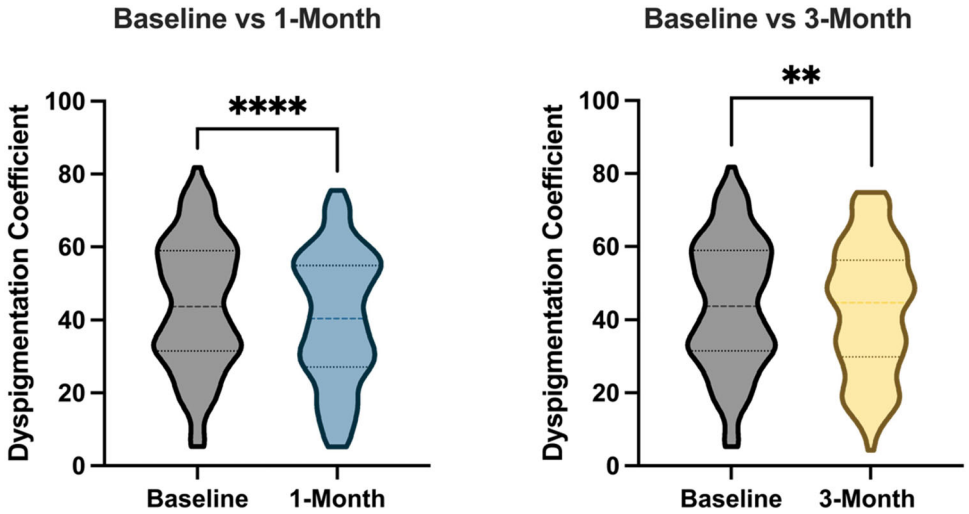


**FIGURE 1** Dyspigmentation improvement over the study period. $^{**}p < 0.01$; $^{****}p < 0.0001$.

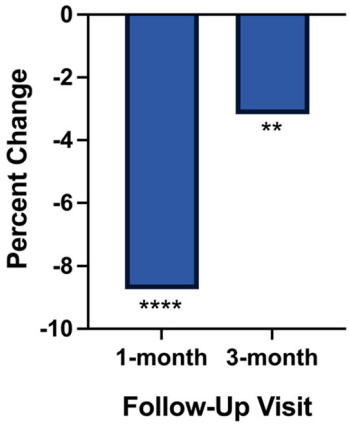


**FIGURE 2** Percent change in dyspigmentation overall. $^{**}p < 0.01$; $^{****}p < 0.0001$.

(brown spots). High-resolution photographs of the right, left, and front face were captured at baseline and 1 and 3 months after treatment. Quantification of spots, brown spots, and UV spots were measured as a "Feature Coefficient" ranging from 0 to 100, with 0 corresponding with no features and 100 corresponding with maximal features. Pigmentary lesions measured and analyzed included dyschromic skin lesions including freckles, acne scars, and dyspigmentation (spots), lesions resulting from photodamage (UV spots), and lentigines and melasma (brown spots).

Using clinical photographs, five plastic surgeons used the Physician's Global Assessment Scale (PGAS) (Table 1) to assess clinical improvement in dyspigmentation following treatment. Evaluators were trained on how to use the scale before its use. The PGAS is 6-point scale that allows trained evaluators to score changes in pigment after treatment and is considered the primary efficacy endpoint for clinical trials in melasma.[19] A score of 0 denotes complete resolution of pigment while 6 indicates worsening compared to baseline. Like prior studies, the PGAS was evaluated separately for the right and left face.[20,21]

## Statistical analysis

Statistical analysis was performed by the Bioinformatics Core Facility at the University of Texas Southwestern using R software (R Foundation for Statistical Computing). The per protocol population included all subjects who received both treatments and attended both follow-up visits to complete the study. Descriptive statistics were used in analysis of subject demographics and treatment parameters. A two-sample *t*-test was used to assess f1927 nm treatment parameters across the study period. Nonparametric statistical testing including Wilcoxon rank-sum testing was used to compare VISIA results across the study period and analyze PGAS scores. A *p* value ≤0.05 was considered statistically significant.

**TABLE 6** Pigment improvement by pigment type.

| Pigment Type | *n* | Baseline | | 1-month follow-up | | | 3-month follow-up | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Median ± SD | Range | Median ± SD | Percent change | *p* Value | Median ± SD | Percent change | *p* Value |
| Spots | 48 | 46.9 ± 11.8 | 20.7–72.6 | 41.1 ± 12.3 | −7% | 0.006 | 44.7 ± 12.0 | −3% | 0.26 |
| UV spots | 48 | 28.3 ± 9.5 | 5.3–41.2 | 22.7 ± 9.8 | −7% | <0.0001 | 23.6 ± 10.1 | −2% | 0.64 |
| Brown spots | 48 | 60.6 ± 9.9 | 38.3–81.8 | 56.4 ± 8.7 | −16% | <0.0001 | 58.5 ± 9.5 | −5% | 0.10 |

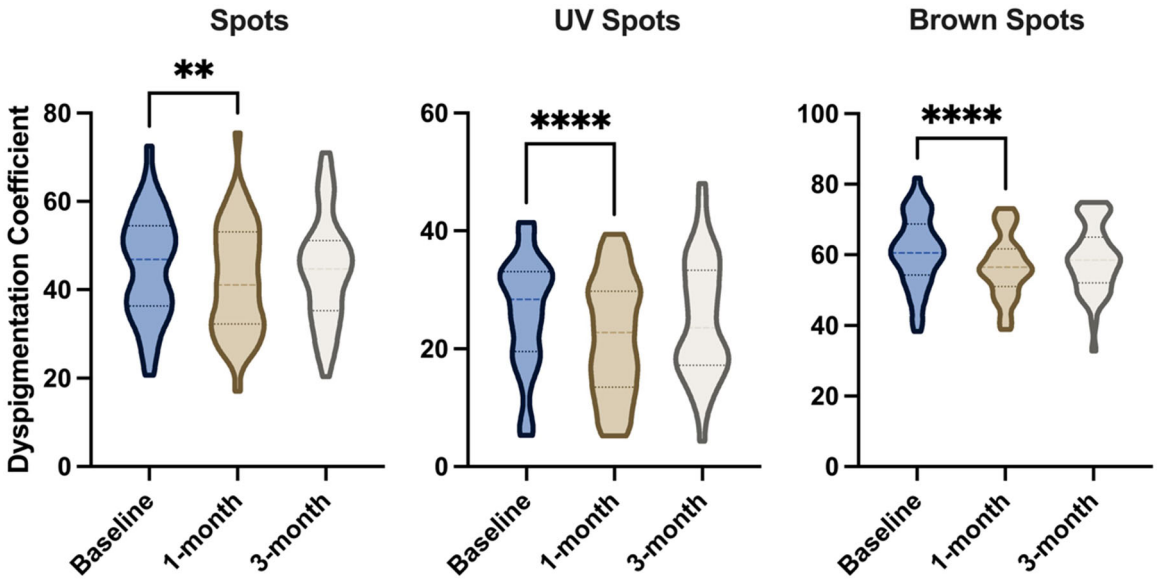


**FIGURE 3** Dyspigmentation by pigment type. $^{**}p < 0.01$; $^{****}p < 0.0001$.

## RESULTS

Twenty-seven patients underwent two nonablative f1927 nm laser treatments in May and June 2022 (Supporting Information: Video). Ninety-six percent of patients ($n = 27$) completed 1-month follow-up and 89% of patients ($n = 24$) completed 3-month follow-up. The study cohort was 100% females, with a mean ± SD age of 47.0 ± 11.5 (range: 29–74), and a mean Fitzpatrick SPT of 2.8 (range: I–IV) (Table 2). Four patients were of mixed race but were deemed eligible for study participation by clinical investigators. Twenty-four patients were included analysis per treatment protocol. Treatments lasted between 6 and 10 min.

Mean total energy (mJ) per treatment ranged from 499 to 812 mJ (Table 3). Parametric *t*-testing indicated there was no statistically significant difference between total energy used across the two treatments ($Z = -2.23$, $p = 0.32$).

Postprocedural symptoms included edema and erythema ($n = 24$) which was evident immediately following the procedure and, in most cases, subsided by 24 h. Patients also experienced superficial crusting at microthermal zones, which subsided within 5–10 days and were an indication of normal wound healing. No patients experienced post-inflammatory hyperpigmentation, hypopigmentation, or scarring as a direct result of this treatment. No serious adverse events were observed during study treatment or follow-up.

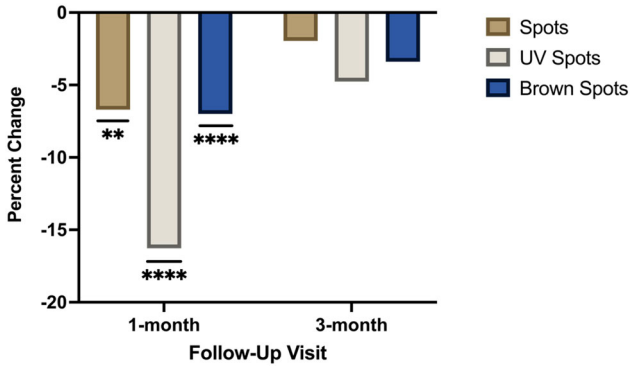


**FIGURE 4** Percent change in dyspigmentation by pigment type. $^{**}p < 0.01$; $^{****}p < 0.0001$.

### Dyspigmentation improvement overall

Overall, our cohort had a 9% improvement ($p < 0.0001$) in unwanted pigment at 1 month compared to baseline, and a 3% improvement ($p = 0.005$) at 3 months (Tables 4

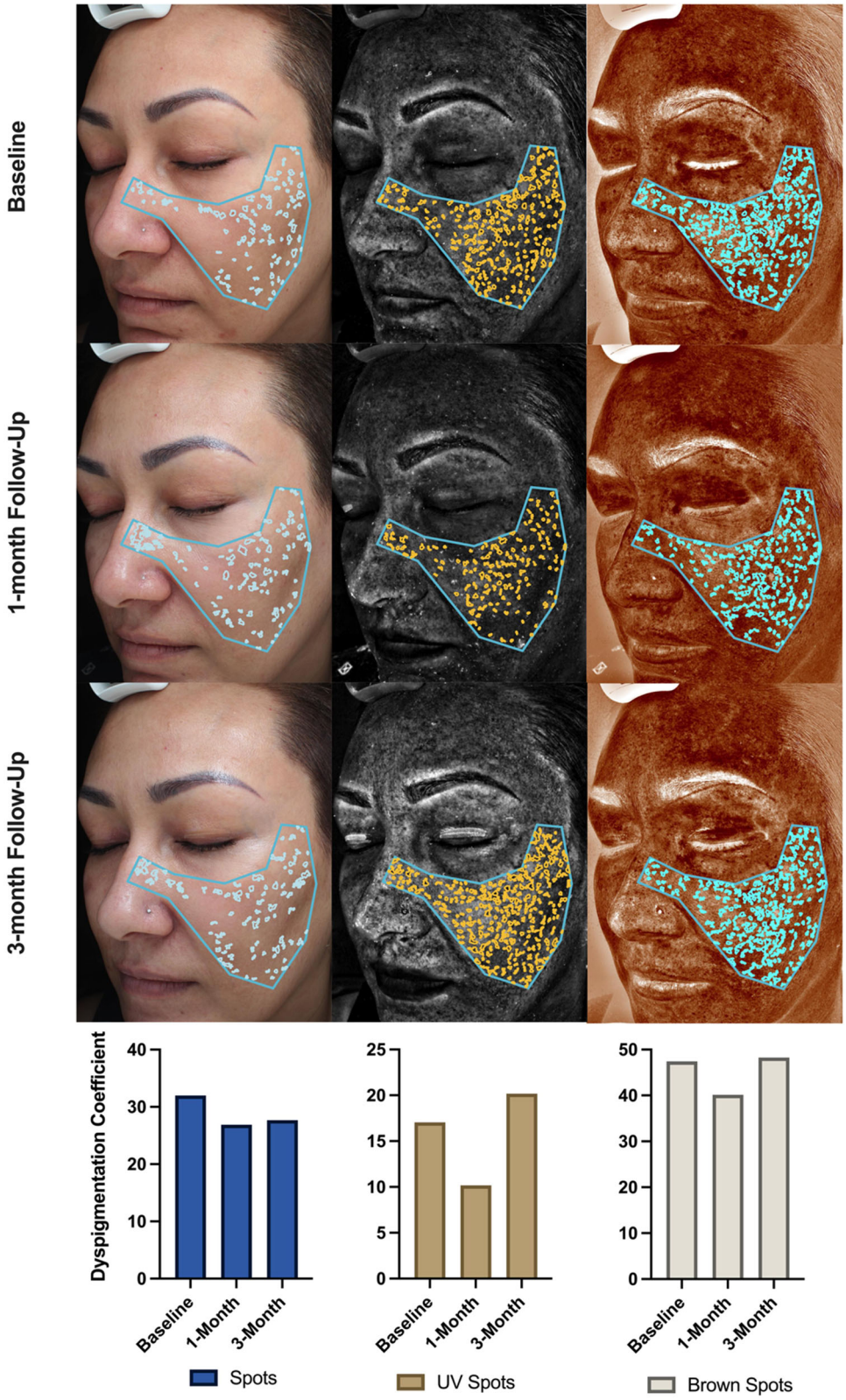


**FIGURE 5** A 47-year-old Fitzpatrick SPT IV female with VISIA imaging analysis of spots, UV spots, and brown spots. From left to right: spots, UV spots, brown spots. From top to bottom, baseline, 1 month after final f1927 nm treatment, and 3 months after final f1927 nm treatment.

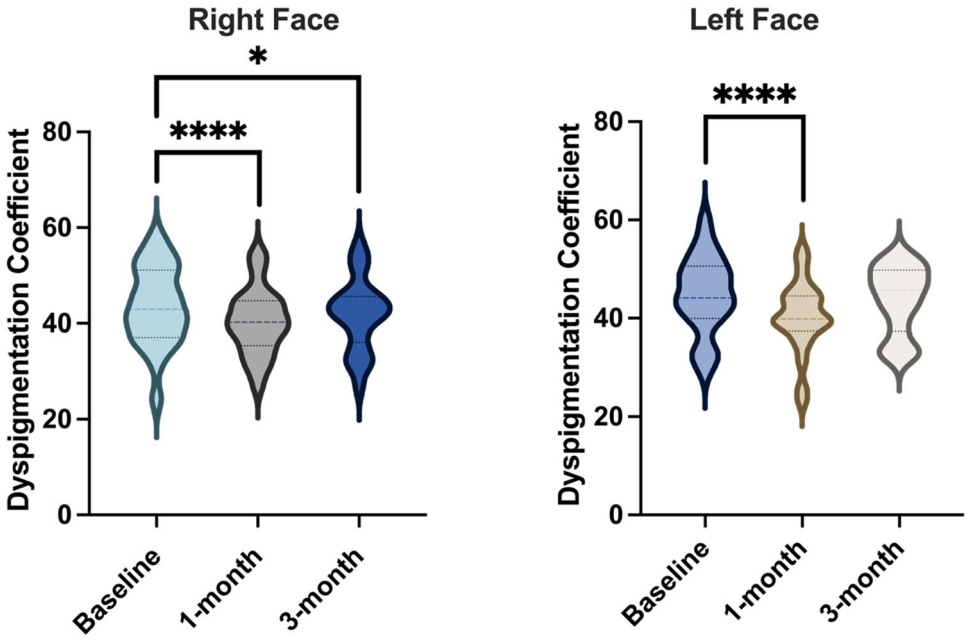


**FIGURE 6** Dyspigmentation response by location of the lesion. *$p < 0.05$; ****$p < 0.0001$.

**TABLE 7** Dyspigmentation response by location.

| | Baseline | | 1-Month | | | 3-Month | | |
|---|---|---|---|---|---|---|---|---|
| **Location** | **Median ± SD** | **Range** | **Median ± SD** | **Percent change** | ***p* Value** | **Median ± SD** | **Percent change** | ***p* Value** |
| Right | 41.8 ± 17.5 | 6.6–81.8 | 40.4 ± 17.6 | −7.5% | <0.0001* | 41.9 ± 17.4 | −3.9% | 0.02* |
| Left | 46.4 ± 17.8 | 5.3– 77.2 | 40.3 ± 17.8 | −9.9% | <0.0001* | 43.7 ± 17.6 | −2.4% | 0.21 |

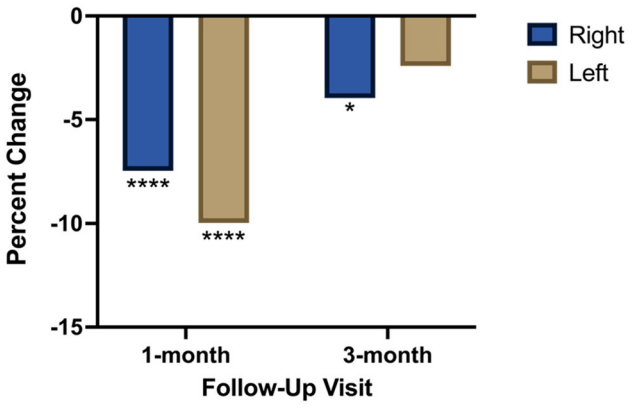


**FIGURE 7** Percent change in dyspigmentation by location. *$p < 0.05$; ****$p < 0.0001$.

and 5 and Figures 1 and 2). Maximum improvement was seen at 1-month follow-up, with improvements in dyspigmentation remaining statistically significant at 3-month follow-up.

## Pigment response according to pigment type

Analysis showed statistically significant improvements in pigmented lesions according to pigment type (Table 6 and Figures 3–5). At 1 month, there was a 7% decrease in spots ($p = 0.002$), 16% decrease in UV spots ($p < 0.001$), and 7% decrease in brown spots ($p < 0.001$) compared to baseline. At 3-month follow-up, brown spots remained improved by 3% ($p = 0.05$) compared to baseline. Spots ($p = 0.26$), UV spots ($p = 0.64$), and brown spots ($p = 0.10$) all trended upward toward baseline at 3-month follow-up without exceeding it.

## Pigment improvement according to location of lesion

Baseline pigment was greater on the left face compared to the Right (Figure 6 and Table 7); improvements were statistically significant on the right at both 1- and 3-month follow-up, and on the left at 1-month follow-up. When pigment was stratified according to location at

**TABLE 8** Dyspigmentation response by location and pigment type.

| Location | Timepoint / Pigment type | Baseline Median ± SD | Baseline Range | 1-Month Median ± SD | 1-Month Percent change | 1-Month *p* Value | 3-Month Median ± SD | 3-Month Percent change | 3-Month *p* Value |
|---|---|---|---|---|---|---|---|---|---|
| Left | Spots | 48.3 ± 12.1 | 23.5–72.6 | 42.2 ± 13.8 | −7.7% | 0.02 | 46.1 ± 13.1 | +0.8% | 0.79 |
| | UV spots | 29.4 ± 9.9 | 5.3–41.3 | 22.4 ± 10.1 | −15.9% | <0.01 | 25.8 ± 9.6 | −3.2% | 1.0 |
| | brown spots | 62.5 ± 9.1 | 42.0–77.3 | 56.3 ± 8.8 | −8.8% | <0.001 | 59.1 ± 10.1 | −4.0% | 0.07 |
| Right | Spots | 46.0 ± 11.8 | 20.7–66.4 | 42.5 ± 10.9 | −4.9% | 0.14 | 42.9 ± 10.8 | −2.3% | 0.07 |
| | UV spots | 25.4 ± 9.3 | 6.6 –41.4 | 21.6 ± 9.7 | −16.7% | <0.001 | 24.3 ± 10.8 | −6.3% | 0.28 |
| | Brown spots | 60.3 ± 10.8 | 38.3–81.8 | 57.1 ± 8.8 | −4.9% | 0.09 | 58.6 ± 9.1 | −2.3% | 0.38 |

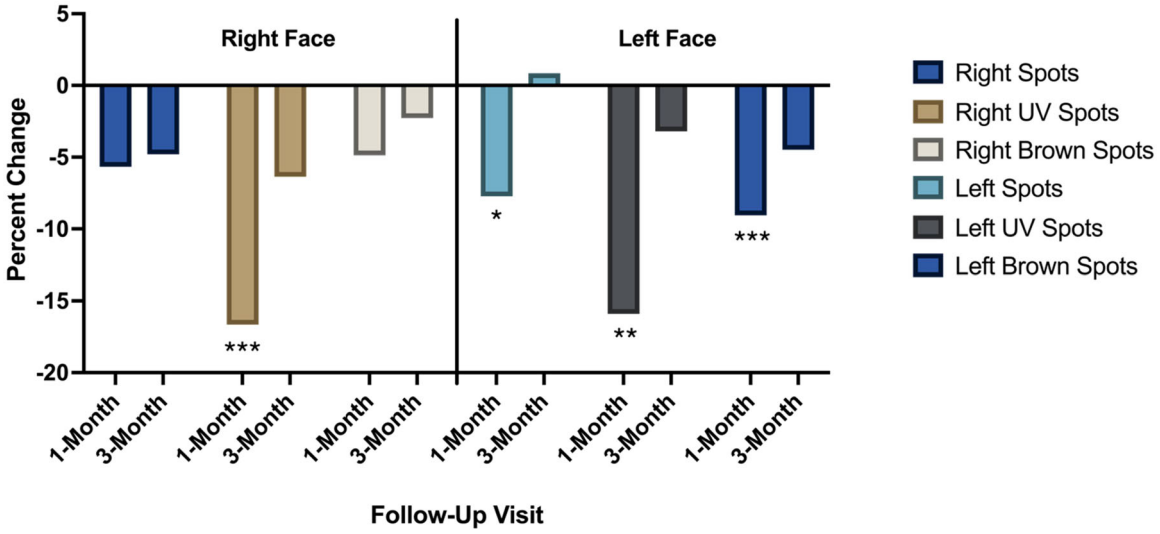


**FIGURE 8** Percent change in pigment by location and pigment type. *$p < 0.05$; **$p < 0.01$; ****$p < 0.0001$.

1-month follow-up, we found a 10% and 8% improvement in dyspigmentation on the left ($p < 0.0001$) and right ($p < 0.0001$) face, respectively (Figure 7). Like pigment type, there was a relative increase in pigment from 1- to 3-month follow-up across the entire face which approached but did not exceed baseline values. Notably, only improvements on the right remained statistically significant at 3-month follow-up ($p = 0.02$) when compared to baseline.

## Pigment improvement according to type and location

When pigment was analyzed according to both type and location, we found statistically significant improvements in spots ($p = 0.02$), UV spots ($p = 0.006$), and brown spots ($p < 0.001$) on the left and in UV spots on the right ($p < 0.001$) when comparing 1-month pigment to baseline (Table 8 and Figure 8). Like other parameters, at 3-month follow-up visits dyspigmentation remained improved from baseline but to a lesser degree compared to 1-month changes. Left spots slightly exceeded baseline values at three months, though by <1% ($p = 0.79$).

## Subjective clinician evaluation

Clinician evaluators assessed 1- and 3-month photographs to subjectively score clinical improvement (Table 9 and Figures 9 and 10). The mean Physician's Global Assessment Score of 3.4 (min: 1; max: 5) at 1-month follow-up and 3.7 (min: 1; max: 6) at 3-month follow-up corresponds to Moderate to Slight (50%–75%) improvement in dyspigmentation (Figures 11–13). These improvements were statistically significant compared to a theoretical median of 5 ("no improvement" on PGAS scale) across both time points. ($p < 0.0001$).

# DISCUSSION

The f1927 nm nonablative thulium laser has been explored as a potential treatment for acquired hyperpigmentation disorders as early as 2012.[22] To the authors' knowledge, to date, this study represents the largest prospective, full-face study using objective analysis to assess the efficacy of f1927 nm in improving the appearance of dyspigmented and photodamaged skin. Across

**TABLE 9** Physician's Global Assessment Scores.

| Follow-up visit | Right face | | | Left face | | | Overall | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean ± SD | 95% CI | *p* Value | Mean ± SD | 95% CI | *p* Value | Mean ± SD | 95% CI | *p* Value |
| 1-month | 3.45 ± 1.23 | 3.22–3.67 | <0.0001 | 3.44 ± 1.15 | 3.23– 3.65 | <0.0001 | 3.44 ± 1.14 | 3.23– 3.65 | <0.0001 |
| 3-month | 3.60 ± 1.35 | 3.35– 3.84 | <0.0001 | 3.72 ± 1.32 | 3.47– 3.96 | <0.0001 | 3.66 ± 1.28 | 3.41– 3.89 | <0.0001 |

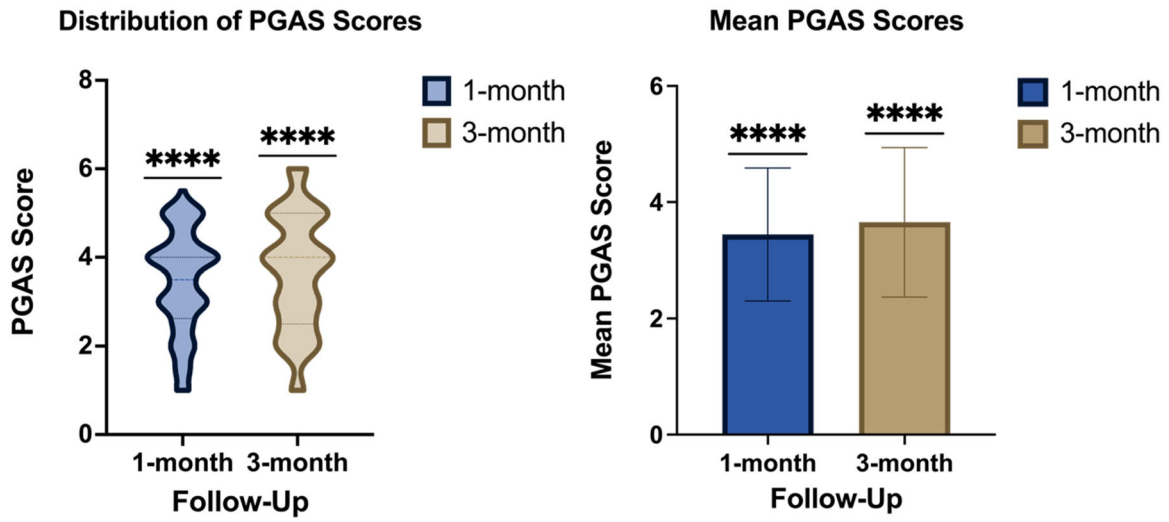


**FIGURE 9** Physician's Global Assessment Score (PGAS). ****$p < 0.0001$.

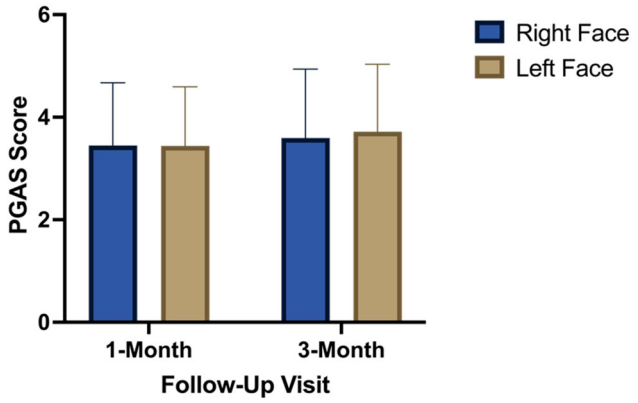


**FIGURE 10** Mean Physician's Global Assessment Score (PGAS) by side.

multiple analyses presented in this study, we found statistically significant improvements in dyspigmentation at 1-month follow-up after two f1927 nm treatments. Overall, objective imaging analysis showed that improvements in dyspigmentation were statistically significant at both 1- and 3-month follow-up. Subjectively, clinician evaluators reported statistically significant clinical improvement in dyspigmentation. The PGAS used by blinded clinician graders offers subjective grading and we consider it distinct from our objective analysis. While the scale uses percentages to help quantify changes that clinicians may observe, the scale ultimately reflects a clinician's judgment and does not necessarily mirror the numerical approximations provided by the PGAS scoring system.

As the safety and efficacy of f1927 nm photothermolysis has been previously established in the literature as safe and effective, this study differs from others in our use of serial objective assessments to quantify and explore pigment response and recurrence. Prior studies have primarily leveraged such subjective assessments as the Melasma Area Severity Index (MASI) to assess treatment efficacy (Table 10). These studies have shown that f1927 nm clinically improves melasma and similar acquired pigment disorders. One split-face study in 2013 reported objective analysis; investigators used 3 μm biopsies with resultant immunohistochemical analysis to objectively assess treatment response. Biopsies were limited to two participants at 2-month follow-up and showed a decrease in melanin without a significant change in the number of melanocytes.[21]

Our finding that pigmented and actinic lesions recur between 1- and 3 months to a statistically significant degree echoes subjective clinical findings in the literature. For example, a 2013 study by Lee et al. found a statistically significant 51% reduction in MASI scores at 1-month follow-up after 3–4 high-density f1927 nm treatments. At 3- and 6-month follow-up however, improvement decreased to 33% ($p = 0.06$) and 34%


**FIGURE 11** A 39-year-old Fitzpatrick I subject with a mean overall PGAS Score of 2.3 at 1-month follow-up and 2.9 at 3-month follow-up, consistent with marked clinical improvement and mirroring objective findings.

($p = 0.07$) improvement, respectively.[22] A 2015 study by Brauer et al. had similar findings, with blinded clinician assessment showing moderate improvement at 1-month follow-up, and mild to moderate improvement at 3 months.[16] Kurmus et al.[26] noted early improvement after f1927 nm treatment but significantly decreased MASI scores between 1- and 6-month follow-up. Despite investigations using a myriad of treatment protocols and parameters, clinically and statistically significant but temporary improvement is the prevailing prognosis after 3 months. To our knowledge, this study is the first to objectively analyze the magnitude of recurrence several months after treatment.

A closer examination of our results in the context of the theorized pathophysiology of melasma and related dyschromia—chronic UV exposure, gender and hormone exposure, genetics, and UV exposure—is necessary to understand the tendency toward recurrence.

UV exposure is a known exacerbator of dyspigmentation disorders. Prolonged UV radiation has been theorized to cause dermal inflammation, histamine release from mast cells, activate matrix metalloproteinase enzymes, and cause abnormal elastic tissue in the dermis, which collectively upregulate melanogenesis and cause basement membrane damage.[28] Objective analyses showed baseline pigment was increased on the left both overall and when stratified by pigment type. The left responded more drastically to treatment compared to the right (−9.9% vs. −7.5% at 1 month). Additionally, the rebound in pigment on the Left at 3 months exceeded that on the right (+8.4% vs. +3.8% between 1 and 3 months). Subjectively, PGAS scores were similar on the right and left at 1 month (3.45 vs. 3.44, respectively) but higher on the left at 3 months (3.60 vs. 3.72). This lateral predilection toward worsened dyspigmentation on the left aligns with a prevailing hypothesis that US drivers are chronically exposed to more UV on the left, with some studies establishing an increased predominance of left-sided photodamage, precancers, and cancers.[29,30] It should be noted that treatments were conducted during


**FIGURE 12** A 44-year-old Fitzpatrick III with a mean overall PGAS Scores of 3.7 at both 1- and 3-month follow-up, suggesting moderate clinical improvement over the study period.

May and June, with follow-ups in July and September. Historically, the mean UV index at the study site has been between 8 and 11 during the summer months, which is considered "Very High to Extreme."[18] Moreover, the literature recognizes that melasma and other sun exposure-related conditions typically worsen during the summer and improve during the winter.

The algorithmic analysis used precludes our ability to identify whether the decline in clinical improvement at 3 months was due to new dyschromic lesions versus refractory dyspigmentation in existing lesions. However, internal assessments of clinical photography suggest that the lesions themselves recurred. The histologic pathophysiology of dyspigmented lesions offers insight into its resistant to treatment its observed recurrence after several months. For example, one found no statistically significant difference in melanocyte quantity between lesional and perilesional skin, but noted that melanocytes in hyperpigmented skin were larger with prominent dendrites, and melanocytes and keratinocytes in affected skin contained increased melanosomes suggesting hyperfunctionality.[31] Other studies have shown how a disrupted basement membrane allows hyperfunctional melanocytes and melanin to spill into the dermis, outside of treatment zones of topical and laser therapy.[32–36] This hypothesis suggests chronic UV exposure induces damage to the basement membrane of the epidermis and potentially links melasma's remittance to an inciting ultrastructural insult.[36] Thus, while f1927 nm may have temporarily ablated epidermal melanin deposits leading to clinical improvement, the continued, aberrant presence of melanocytes may make subjects continually susceptible to dyspigmentation after treatment cessation.

Another contributor to pigment recurrence may lie in subjects' ongoing exposure to estrogenic hormones during child-bearing years. Interestingly, there was a statistically significant difference in the magnitude of subjects' response between those aged less than 41 years old, and those between 42 and 56 years old. Patients in our study should be considered susceptible to melasma and aberrant dyspigmentation at baseline, given their meeting eligibility to participate and 54% ($n = 13$) of our

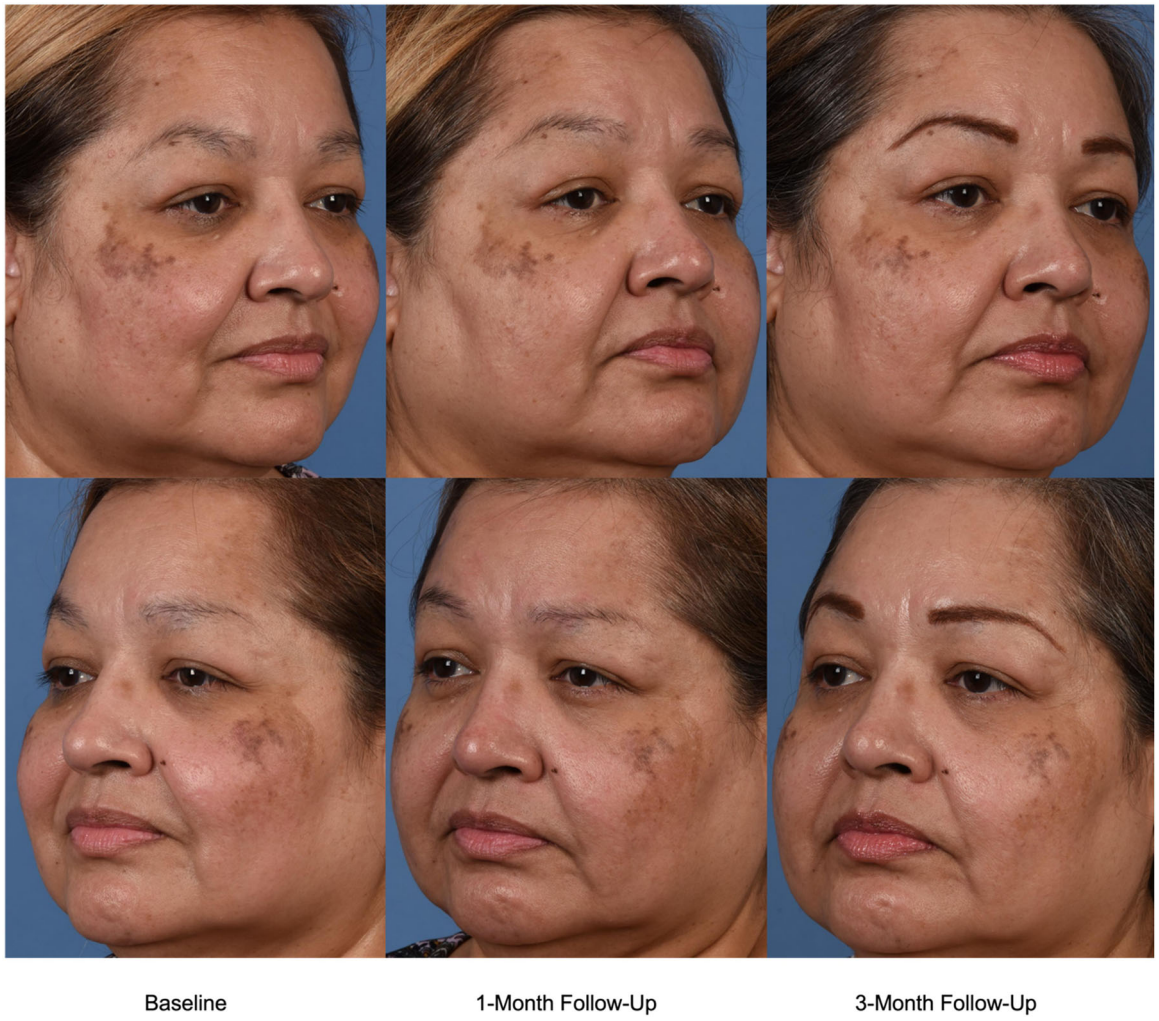


**FIGURE 13** A 58-year-old Fitzpatrick IV female, progression of dyspigmentation during the study period. PGAS Scores were 4.7 at 1 month and 4.1 at 3 months, suggesting slight improvement over the study period.

cohort being of childbearing potential and 17% ($n = 4$) taking oral contraceptive pills during the study. The use of OCPs or HRTs was not a contraindication to study participation, as the role of endogenous or exogenous hormones in melasma was not within the scope of this study. However, it is important to acknowledge the ongoing role that exposure to pro-melanotic hormones plays in patients' susceptibility to recurrence.

Our study is not without limitations. The VISIA Imaging tool used in this study is intended for clinical care, not clinical research. Treatment parameters were the same across patients, to reduce confounders and minimize the risk of laser-induced pigmentation for all patients given the range of skin phototypes treated. In clinical practice, however, practitioners may increase fluence, density, or passes in successive treatments to increase total energy delivered and maximize clinical response after seeing how individual patients respond. Additionally, patients were not on adjunct topical medications like hydroquinone and retinol to reduce potential confounders. It is important to note, however, that treatment of melasma and dyspigmentation is multifaceted and multimodal, so clinicians often combine topicals with energy-based procedures in practice. Lastly, patients' dyschromias were diagnosed clinically; most subjects in our cohort were considered to have centrofacial or malar melasma and/or photodamage or age-related actinic lesions. While clinical assessment is considered the gold standard for the diagnosis of melasma, adjunct tools such as Wood's lamps or dermoscopy may have aided in definitive rule-out of related dyschromias such as lichen planus pigmentosus or phototoxic dermatitis which may respond differently to f1927 nm treatment.[37] Additionally, these tools are also used to classify melasma's distribution within the epidermis, dermis, or both. In practice, identifying melasma's distribution may guide treatment, as targeting epidermal lesions using f1927 nm energy may not significantly impact melanin deposits in the dermis. Gathering these additional

**TABLE 10** Studies using nonablative f1927m lasers to treat acquired hyperpigmentation disorders in Fitzpatrick I–IV.

| Author, year published | Study design | *n* | Treatment parameters | No. of treatments | Subjective assessment of dyspigmentation response | Objective assessment of dyspigmentation response |
|---|---|---|---|---|---|---|
| Polder et al. (2012)[22] | Prospective | 14 | Energy: 10–20 mJ<br>Density: 20%–45%<br>6–8 passes | 3–4 treatments at 1-month intervals | MASI Score | N/A |
| Massaki et al. (2012)[23] | Retrospective | 20 | Energy: 10 or 20 mJ<br>Density: 60% | 1 treatment | MASI score | N/A |
| Lee et al. (2013)[21] | Prospective (split-face) | 25 | Energy: 10 mJ<br>Density: 30%<br>10 passes | 2–3 treatments at 1-month intervals | MASI Score | Biopsy of lesions with immunohistological analysis |
| Brauer et al. (2014)[16] | Prospective | 40 | Energy: 10 mJ<br>Density: 40%<br>4–6 passes | 2 treatments at 1-month interval | Investigator and blinded clinician assessment | N/A |
| Brauer et al. (2015)[24] | Prospective | 23 | Energy: 5 mJ<br>Density: 5%–10%<br>8 passes | 4–6 treatments at 14-day intervals | Investigator and blinded clinician assessment | N/A |
| Rho et al. (2017)[25] | Retrospective | 68 | Energy: 1.6–2.4 mJ<br>Density: 5%–10%<br>3–5 passes | 3 treatments at 2–4-week intervals | MASI score | N/A |
| Kurmus et al. (2019)[26] | Retrospective | 100 | Energy: 9-10 mJ<br>Density: 30%–50%<br>3 passes | 2 treatments at 1-month interval | MASI score | N/A |
| Wu et al. (2020)[18] | Prospective (split-face) | 20 | Energy: 20 mJ<br>Density: 30%–50%<br>8 passes | 3 treatments at 1-month interval | Global Aesthetic Improvement Scale And Quantitative Skin Aging Survey[27] | N/A |
| Vingan et al. (2023) | Prospective | 24 | Energy: 15 mJ<br>Density: 15%<br>6 passes | 2 treatments 1-month interval | PGAS score | Imaging analysis of spots, UV spots, and brown spots |

data points may have helped to better contextualize study findings. Further studies should be done to assess whether adjunct topical medications or localization of aberrant melanin can inform more specific treatment and potentially drive longer-lasting results.

## CONCLUSION

To the authors' knowledge, to date, this study represents the largest prospective study using both subjective and objective endpoints to the efficacy of f1927 nm in improving the appearance of melasma and actinic pigment.[22,23,25,38] These results demonstrate that fractionated, nonablative 1927 nm laser treatment is an effective modality for improving both clinical and subclinical pigment in patients of Fitzpatrick SPT I–IV. The magnitude and duration of pigment improvement are potentially influenced by extrinsic factors such as increased exposure to and propensity for photodamage during the summer months, which may suggest the need for multiple f1927 nm treatments over time to maintain clinical results. In real-world practice, patients with complex and multifactorial dyspigmentation would be prescribed adjunct topical medications such as hydroquinone or retinol to attenuate the risk of posttreatment recurrence. While the authors did not do so to limit the potential influence of confounders, this may have mitigated the potential for recurrence.

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## CONFLICT OF INTEREST STATEMENT

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studies outside of this submitted work. Abby Culver is a facial surgery contributing editor for *ASJ Open Forum*. Jeffrey M. Kenkel is the editor-in-chief of *ASJ Open Forum* and associate editor of *Aesthetic Surgery Journal*. John Hoopman is a shareholder and former educator for Sciton, Inc. (Palo Alto, CA, USA). The remaining author declares no conflict of interest.

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## SUPPORTING INFORMATION

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