# Treatment of Pigmentary Disorders in Patients With Skin of Color With a Novel 755-nm Picosecond, Q-switched Ruby, and Q-switched Nd:YAG Nanosecond Lasers: A Retrospective Photographic Review

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**Background and Objectives:** Laser procedures in skin of color (SOC) patients are challenging due to the increased risk of dyspigmentation and scarring. A novel 755 nm alexandrite picosecond laser has demonstrated effectiveness for tattoo removal and treatment of acne scars. No studies to date have evaluated its applications in pigmentary disorders. The purpose of this retrospective study was to evaluate the safety profile and efficacy of the picosecond alexandrite laser compared to the current standard treatment, Q-switched ruby and neodynium (Nd):YAG nanosecond lasers, for pigmentary disorders in SOC patients.

**Study Design/Materials and Methods:** A retrospective photographic and chart evaluation of seventy 755 nm alexandrite picosecond, ninety-two Q-switched frequency doubled 532 nm and 1,064 nm Nd:YAG nanosecond, and forty-seven Q-switched 694 nm ruby nanosecond laser treatments, in forty-two subjects of Fitzpatrick skin types III–VI was conducted in a single laser specialty center. The picosecond laser was a research prototype device. Treatment efficacy was assessed by two blinded physician evaluators, using a visual analog scale for percentage of pigmentary clearance in standard photographs. Subject assessment of efficacy, satisfaction, and adverse events was performed using a questionnaire survey.

**Results:** The most common pigmentary disorder treated was Nevus of Ota (38.1%), followed by solar lentigines (23.8%). Other pigmentary disorders included post-inflammatory hyperpigmentation, congenital nevus, café au lait macule, dermal melanocytosis, Nevus of Ito, and Becker's nevus. Clinical efficacy of the Q-switched nanosecond lasers and picosecond laser treatments were comparable for lesions treated on the face with a mean visual analog score of 2.57 and 2.44, respectively, corresponding to approximately 50% pigmentary clearance. Subject questionnaires were completed in 58.8% of the picosecond subjects and 52.0% of the Q-switched subjects. Eighty four percent of subjects receiving Q-switched nanosecond laser treatments and 50% of the subjects receiving alexandrite 755 nm picosecond laser treatments felt satisfied to completely satisfied. Side effects observed in subjects treated with the alexandrite 755 nm picosecond laser were similar to those commonly observed and reported with the nanosecond Q-switched technology. All side effects were temporary, resolving within one month, and no long-term complications were noted. All patients who were very satisfied with their picosecond laser treatment for Nevus of Ota noted a delayed improvement only after 3 months.

**Conclusion:** The 755 nm alexandrite picosecond, 694 nm ruby, 532 nm, and 1064 nm neodynium:YAG nanosecond lasers appear to be safe and effective modalities for removal of pigmentary disorders in skin of color patients with no long-term complications if used appropriately. This study demonstrates the potential of the 755 nm alexandrite picosecond laser in further clinical applications beyond tattoo removal. While the Q-switched lasers were effective, promising results were also observed using an early version of the novel picosecond laser for the removal of pigmentary lesions in SOC patients. As we continue to improve our understanding of the 755 nm picosecond laser, this device may prove to be a safe and effective alternative to the Q-switched lasers for the treatment of facial pigmented lesions in patients with skin of color. Lasers Surg. Med. 48:181–187, 2016.


**Key words:** picosecond; pigment; nanosecond; skin

## INTRODUCTION

A person's skin color is one of the most recognizable phenotypes. Historically, skin color differences have been

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Accepted 16 November 2015
Published online in Wiley Online Library (wileyonlinelibrary.com).
DOI 10.1002/lsm.22454

associated with political, economic, and social status. As such, individuals afflicted with disorders of pigmentation often experience negative emotional and psychological consequences [1]. Pigmentary disorders occur more frequently in darker-skinned, or "skin of color" (SOC), patients due to the higher prevalence of congenital disorders of pigmentation, such as nevus of Ota, and acquired pigmentary dermatoses, such as solar lentigines, and melasma. It is currently estimated that 37% of the United States population is non-Caucasian, and this figure is projected to rise to 48% by the year 2050 [2–5]. With this dynamic demographic shift, the management of common dermatologic disorders seen in SOC patients will become increasingly important.

The introduction of selective photothermolysis revolutionized the landscape for laser therapy by allowing for precise tissue targeting, thus ameliorating the risk of dyspigmentation and scarring associated with earlier therapies such as depigmenting agents, cryotherapy, and dermabrasion [6–9]. Despite the transformative advances in laser technology over the past 45 years, however, the treatment of pigmentary disorders in SOC patients has been slow to progress. While the Q-switched lasers, fractional photothermolysis, and other non-ablative laser therapies have become well-established modalities for melanin-directed therapy, there remains a paucity of studies involving SOC patients, who continue to be at increased risk of adverse events with these procedures due to increased epidermal melanin content and reactive fibroblast responses. This limited experience, combined with the greater technical challenges posed by more heavily pigmented skin, has predisposed to inadequate treatment, recurrence of lesions, and disappointing outcomes.

More recently, the novel picosecond laser has been shown to be efficacious for tattoo removal [10,11]. Brauer and colleagues demonstrated the successful treatment of green and/or blue tattoos using the picosecond 755 nm alexandrite laser with 75% clearance of pigment after one to two treatments [11]. These promising results have been attributed to more rapid heating and greater fragmentation achieved by the ultra-short picosecond pulses [10]. Given the success of tattoo removal with the picosecond laser, we hypothesized that the picosecond laser could be an alternative treatment for pigmentary disorders. In this study, we performed a retrospective chart and photographic review to evaluate the efficacy and safety profile of various lasers used for the treatment of pigmentary disorders in SOC patients, including the current standard-of-care treatment with the Q-switched ruby and Nd: YAG lasers and the newer alexandrite picosecond laser.

## MATERIALS AND METHODS

The chart records of subjects who were treated with either the 755 nm alexandrite picosecond (Picolase, Cynosure, Westford, MA), 694 nm ruby nanosecond (Sinon, Alma Lasers, Buffalo Grove, IL), frequency doubled 532 nm and 1064 nm Nd:YAG nanosecond (Spectra, Lutronic, Fremont, CA), lasers for pigmentary disorders in a laser surgery clinic specializing in the treatment of pigmentary disorders from January 2011 to December 2013 were screened against eligibility criteria. Inclusion required Fitzpatrick skin types III through VI, the treatment of pigmentary disorders with either the 755 nm alexandrite picosecond, 694 nm ruby, 532 nm, and 1064 nm Nd:YAG nanosecond lasers, and appropriate quality photographic documentation pre-laser treatment and post-laser treatment. Exclusion criteria were Fitzpatrick skin types I through II and poor quality photographic documentation. Verbal consent was obtained for patients who underwent a phone questionnaire. The Essex Institutional Review Board, Essex, New Jersey, approved the study protocol.

Information from the patient's medical record was extracted, which included the age of patient at time of procedure(s), condition(s) for which the procedure(s) was performed, procedure(s) performed, settings of the procedure(s) performed, duration and number of times the procedure(s) was performed, complication(s), and clinical photograph before and after each procedure. Clinical outcomes were evaluated using side-by-side comparisons of clinical photographs taken pre-treatment and after the last treatment. These photographs were evaluated by two blinded, independent physicians using a visual analog scale consisting of six levels of treatment response according to percentage of pigmentary lightening, with grade 0 corresponding to no change; grade 1, 1–24% improvement; grade 2, 25–49% improvement; grade 3, 50–74% improvement; grade 4, 75–99% improvement; and grade 5, 100% improvement or complete clearance.

A phone questionnaire was performed to collect information about basic demographic information, prior skin conditions, pre-operative diagnosis, complication(s), duration of complication(s), perspective of the laser treatment, and patient satisfaction. A seven-point Likert scale was used to rate the subjects level of agreement to the various statements regarding subject satisfaction of the laser treatment.

Statistical analysis was performed using Fisher's exact and Wilcoxon rank sum tests. Fisher's exact test was used to compare categorical variables including demographics, distribution of Fitzpatrick skin types, and satisfaction scores. Wilcoxon rank sum test was used to for comparison of mean number of treatments and VAS scores between the picosecond and nanosecond laser treatment groups.

## RESULTS

### Clinical Characteristics of the Patients

The clinical characteristics of the subjects are summarized in Table 1. A total of 42 patients (6 males and 36 females) were studied. The mean age at time of laser treatment was 37.1 years (range 1–71 years) overall. However, the mean age of the subjects who received the Q-switched laser (62.5 years) was higher than that of the picosecond subjects (24 years). Seventeen subjects (40.5%) received treatment with the 755 nm alexandrite picosecond laser, while eight (19.0%), ten (23.8%), and seven (16.7%) subjects received treatment with the Q-switched frequency doubled 532 nm Nd: YAG

**TABLE 1. Subject Demographics and Clinical Characteristics**

| | Picosecond | QS nanosecond | *P*-value |
|---|---|---|---|
| Number of subjects (%) | 17 (40.5) | 25 (59.5) | 1.00 |
| Male | 2 (11.8) | 4 (16.0) | |
| Female | 15 (88.2) | 21 (84.0) | |
| Mean age (years) at time of laser treatment | 24 (7.41) | 62.5 (18.34) | 0.07 |
| Fitzpatrick skin types (%) | | | |
| III | 8 (47.1) | 8 (32.0) | 0.63 |
| IV | 3 (17.6) | 8 (32.0) | |
| V | 6 (35.2) | 8 (32.0) | |
| VI | 0 (0.0) | 1 (4.0) | |
| Indications (%) | | | |
| Nevus of Ota | 6 (35.2) | 10 (40.0) | |
| Solar lentigines | 1 (5.9) | 9 (36.0) | |
| Post-inflammatory hyperpigmentation | 1 (5.9) | 3 (12.0) | |
| Congenital nevus | 2 (11.8) | 1 (4.0) | |
| Café-au-lait macule | 2 (11.8) | 1 (4.0) | |
| Dermal melanocytosis | 2 (11.8) | 1 (4.0) | |
| Nevus of Ito | 1 (5.9) | 0 (0.0) | |
| Becker's nevus | 2 (11.8) | 0 (0.0) | |
| Distribution of lesions (%) | | | |
| Face | 8 (47.1) | 22 (88.0) | 0.001 |
| Trunk | 5 (29.4) | 0 (0.0) | |
| Upper extremities | 0 (0.0) | 1 (4.0) | |
| Lower extremities | 4 (23.5) | 2 (8.0) | |
| Mean number of treatments (SD) | 4.12 (2.23) | 5.46 (4.62) | 0.68 |
| Mean total duration of treatment in weeks (SD) | 18.21 (21.89) | 120.57 (115.97) | 0.03 |

nanosecond, Q-switched 694 nm ruby nanosecond, and Q-switched 1,064 nm Nd: YAG nanosecond lasers, respectively.

The most common Fitzpatrick skin type was type III in both the picosecond and QS groups (47.1–32%), followed by type V (35.2–32%), type IV (17.6–32.0%), and VI (0–4%). The distribution of skin types did not differ significantly between the two groups ($P = 0.63$). In both the picosecond and nanosecond groups, more than half of the subjects had Fitzpatrick skin types IV or V. Sixteen patients (38.1%) had a nevus of Ota and this was the most commonly treated pigmentary disorder. Other pigmentary disorders included solar lentigines (23.8%), post-inflammatory hyperpigmentation (9.5%), congenital nevus (7.1%), café-au-lait (7.1%), dermal melanocytosis (7.1%), Becker's nevus (4.8%), and nevus of Ito (2.3%). The face was the most common site of involvement in both the picosecond and QS groups (47.1% and 88.0%).

The mean number of treatments was similar between the two groups. Patients treated with the picosecond laser underwent an average of 4.12 treatments while those treated with the nanosecond lasers received an average of 5.46 treatments ($P = 0.68$). The mean total follow-up time was longer in the QS group at 120.57 weeks compared to that in the picosecond group at 18.21 weeks ($P = 0.03$).

For the subjects who received treatment with the 755 nm alexandrite picosecond laser, a research prototype device was used. Therefore, parameters were variable, with pulse duration ranging from 750 to 900 picoseconds, spot size from 2.5 to 6 mm, and energy density range from 0.71 to 4.07 J/cm$^2$.

## Clinical Efficacy and Safety Profile Assessment

Clinical efficacy of the Q-switched nanosecond lasers and picosecond laser treatments were comparable. Responses varied based on site of involvement, with facial lesions responding more favorably when compared to lesions located elsewhere. Twenty-three patients underwent Q-switched treatments for pigmented lesions on the face, with a mean visual analog scale (VAS) score of 2.57, corresponding to approximately 50% pigmentary clearance. In the eight patients who received the picosecond treatment for facial lesions, the mean VAS score was 2.44. Of the pigmented lesions treated, nevus of Ota was the most responsive to treatment. The mean VAS score for nevus of Ota was 2.80 in ten patients for the Q-switched laser and 2.25 in six patients for the picosecond laser. For lesions on the trunk and extremities, mean VAS score was 0.72 for the picosecond laser and 2.33 for the Q-switched nanosecond laser group (Table 2). No recurrences were observed in our patients, however, follow-up time was limited.

Questionnaire surveys were completed by ten (58.8%) of the picosecond and thirteen (50%) of the nanosecond laser subjects. Patient satisfaction was higher in the subjects

**TABLE 2. Clinical Response by Site of Involvement or Clinical Indication**

| | Picosecond laser | | Q-switched nanosecond lasers | | |
|---|---|---|---|---|---|
| Site or clinical indication | Number of patients | Mean VAS | Number of patients | Mean VAS | *P*-value |
| Face | 8 | 2.44 | 22 | 2.57 | 0.95 |
| Extremities or trunk | 9 | 0.72 | 3 | 2.33 | 0.0051 |
| Nevus of Ota | 6 | 2.25 | 10 | 2.8 | 0.48 |
| Overall | 17 | 1.53 | 25 | 2.54 | 0.0056 |

who received the Q-switched laser treatment compared to the subjects who received the picosecond treatments, with 84% of the subjects receiving Q-switched treatments feeling satisfied to completely satisfied and 50% of the subjects receiving the picosecond treatments feeling satisfied to completely satisfied ($P = 0.17$). The mean VAS score for the subjects, who received greater than the median number of treatments for their respective group was 3.0 for the picosecond laser group and 2.46 for the nanosecond laser group ($P = 0.30$). The weighted kappa statistic for interobserver variability between the two blinded physician observers was 0.89 (95% confidence interval 0.82–0.96).

Anticipated complications were mild to moderate in severity and included edema, dyspigmentation, erythema, pain, and crust formation in both treatment groups. In the Q-switched nanosecond treatment group, 16% (4/25) of the subjects experienced permanent dyspigmentation; all affected subjects had Fitzpatrick skin types V or VI. On the other hand, all side effects in the 755 nm picosecond laser treatments were temporary and resolved within four weeks of treatment. Of note, in three patients treated with the picosecond laser, transient hyperpigmentation post-procedure was followed by improvement to complete resolution of the pigmentary lesion at 3 months follow-up without any interval treatment (Fig. 1).

## DISCUSSION

The treatment of pigmentary disorders in skin of color (SOC) patients remains challenging due to the increased risk of side effects associated with treating SOC patients with laser therapies. Owing to the potential for adverse effects and the relative lack of evidence on laser therapies in this population, treatment courses are often prolonged and frustrating, and clearance is often incomplete. Given these challenges, further investigations into optimal treatment modalities and parameters for pigmentary disorders in ethnic skin patients are warranted. To date, however, studies on this topic remain limited.

To our knowledge, this is the first retrospective study to demonstrate efficacy of the 755 nm picosecond laser not only for the treatment of pigmentary disorders, but specifically in SOC patients. Significant pigmentary reduction was achieved with few treatments for pigmentary lesions located on the face (Fig. 2). We did not see a favourable response for pigmented lesions located on the extremities or trunk with the picosecond laser. This may be attributable to the type of lesions treated in these locations for the patients in the picosecond laser group. Two of the nine patients (22%) in this group underwent treatment for congenital nevi, a pigmented lesion that is notably difficult to treat due to the histologic depth of the melanocytes [12]. Meanwhile, lesions on the extremities or trunk in the Q-switched nanosecond laser group consisted of superficial pigmentary disorders such as lentigines, which are known to respond well to Q-switched nanosecond technologies and require fewer treatments as compared to congenital nevi [13]. Another contributing factor was likely the lack of familiarity with and suboptimal settings used for the picosecond laser due to novelty of the laser when employed, as a few patients did experience marked improvement even in non-facial locations (Fig. 3). The picosecond laser appeared most consistently effective for treatment of nevus of Ota, with similar efficacy noted with both the picosecond and Q-switched lasers. Chestnut and colleagues have also found success with recalcitrant nevus of Ota with the picosecond 755 nm alexandrite laser [14].

Q-switched lasers have widely been considered the standard of care for the removal of pigmentary lesions. Based on the concept of selective photothermolysis, the photothermolytic effect of lasers is achieved when chromophores are irradiated at preferentially absorbed wavelengths for a duration less than or equal to their thermal relaxation times. The short duration of Q-switch lasers allows for targeted thermal damage of melanosomes [15]. Because the Q-switched lasers rely primarily on photothermal damage as the main mechanism of injury, however, adverse reactions from thermal damage to surrounding structures, including dyspigmentation and scarring, can occur, particularly in darker skinned patients.

Due to the recent discovery of safe and successful tattoo removal with the novel picosecond laser, this device has unsurprisingly piqued the interest of dermatologists for a potential use in the treatment of pigmentary disorders. Prior studies have demonstrated that exogenous tattoo pigment particles are more effectively cleared from the skin with picosecond laser pulses compared to the nanosecond pulses [16]. While the precise mechanism has not been fully elucidated, it has been theorized that high-energy picosecond energy generates an intense shock wave that leads to fragmentation of targets *via* a photomechanical, rather than photothermolytic, effect. Thus, the fragmentation of tattoo pigment, rather than its selective heating, is thought to be responsible for the increased safety and efficacy associated with the picosecond laser [17].

Indeed, the 755 nm picosecond laser compared favorably to the Q-switched lasers in this study. The picosecond treatments demonstrated a more favorable safety profile,

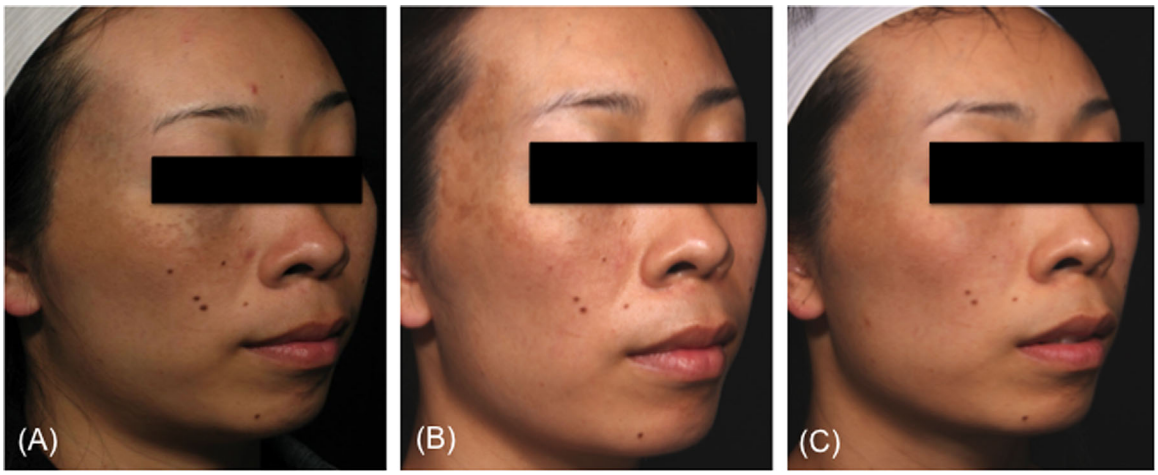


Fig. 1. A 31-year-old woman with Fitzpatrick skin type III who underwent treatment of a nevus of Ota in the right periorbital region at (**A**) baseline; (**B**) 1-month follow-up after five treatments with 755 nm Alexandrite picosecond laser (2.83 J/cm2, 3 mm, 900 picoseconds) with no pigmentary clearance and temporary hyperpigmentation; (**C**) 3-month follow-up without any interval treatment demonstrating grade 4 pigmentary clearance (greater than 75%).

with only temporary adverse reactions and no undesired long-term complications noted. In contrast, permanent dyspigmentation was noted in several subjects who underwent the Q-switched nanosecond laser treatments. This study also found similar efficacy between the Q-switched and picosecond laser groups for facial lesions, the majority of which consisted of nevus of Ota in the picosecond laser group. Thus, it appears that clearance of melanin may be achieved not only via photothermolytic, but also photomechanical means, and this may decrease the risk for adverse effects.

Finally, of interest, three of our subjects who received the picosecond laser treatments were observed to experience initial apparent exacerbation followed by delayed improvement at three months following their treatment rather than at their one-month follow-up (Fig. 1). While the reason for this remains unclear, a possible theory is that rapid heating with the picosecond pulse duration results in photomechanical rupture of melanosomes, leading to immediate apparent worsening due to aggregation of melanin particles, but subsequent delayed clearance corresponding to phagocytosis of pigment by dermal macrophages and fibroblasts. If this proves true, the picosecond laser may emerge as a safer device for SOC patients, for whom thermal damage to surrounding pigment presents as an important barrier to treatment. Furthermore, electron microscopy studies investigating the effects of the picosecond and nanosecond lasers on tattoo pigment particles have shown that laser irradiation results in the formation of enlarged bubble-like particles, with the shorter picosecond pulse generating a greater proportion of altered particles [16]. This phenomenon may also help explain the transient exacerbation of pigmentation with subsequent delayed clearance noted with the picosecond laser.

Limitations to our study, include the small sample size as well as the study design as a retrospective chart review, lending to recall and selection bias. As the 755 nm

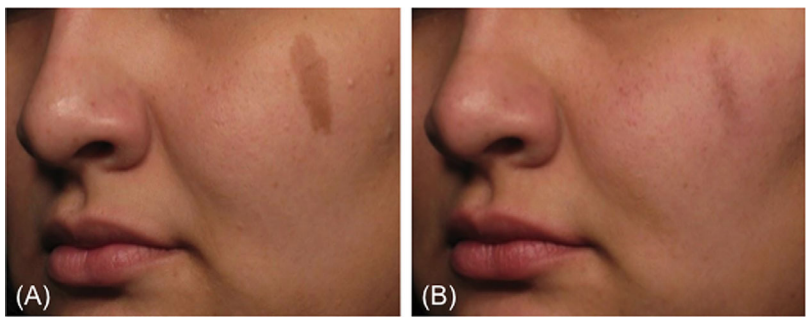


Fig. 2. A café-au-lait macule in a Fitzpatrick skin type III patient (**A**) at baseline and (**B**) after a single treatment (1.59 J/cm$^2$, 2.5 mm, 750 picoseconds) demonstrating grade 3 (greater than 50%, less than 75%) pigmentary clearance.

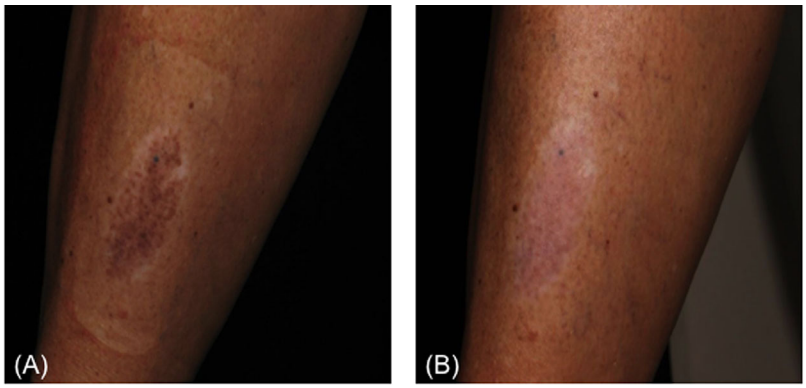


Fig. 3. A previously treated congenital nevus in a Fitzpatrick skin type V patient (**A**) at baseline and (**B**) at 3-month follow-up after eight treatments (0.71–1.02 J/cm$^2$, 5–6 mm, 750–900 picoseconds) demonstrating grade 4 (greater than 75%) pigmentary clearance.

alexandrite picosecond laser used in this study was a research prototype device, varied parameters were used and enrollment was limited to a small number of participants. Thus, our outcomes and comparisons should be interpreted as preliminary observations. Additionally, the Q-switched 755 nm nanosecond laser was not included in this review and as a result, the observed effect may not be fully attributable to pulse duration alone. Lastly, while our results suggest that the picosecond laser is safe in patients with skin types III to V, the safety of this laser for skin type VI remains unknown due to the lack of skin type VI subjects in the picosecond group. Future studies, such as a prospective, split lesion study with larger groups of participants that includes a direct comparison between the 755 nm nanosecond and picosecond lasers, and with longer follow-up time should be considered to further validate our findings. The most recent clinical model has been modified to include enhancements such as a better quality beam profile, higher quality standardized photography, shorter pulse width options, and the addition of the diffractive lens array. Thus, the current study may have underestimated the effect of the potential utility of picosecond laser.

To conclude, we demonstrate that multiple laser devices are available to treat pigmentary disorders in darker-skinned patients effectively, including the 532 nm double-pulsed Nd: YAG, 694 nm ruby, 1,064 nm Nd:YAG Q-switched nanosecond lasers, and now, the novel 755 nm alexandrite picosecond laser. Notably, the picosecond laser demonstrated promising results, with similar efficacy and minimal adverse risk even with an early prototype of the device. Our results, suggest that the picosecond laser has a more favorable safety profile to the Q-switched nanosecond lasers due to the lack of permanent dyspigmentation. While the results of this study are preliminary and broad application to pigmentary disorders requires further investigation, the 755 nm picosecond laser appears particularly efficacious for the treatment of nevus of Ota. With the active, ongoing advancement of picosecond technology, the 755 nm alexandrite picosecond laser may prove to be a safe and effective alternative to the Q-switched lasers in patients with skin of color. As picosecond lasers continue to evolve, we eagerly await the results of further studies on treatment of pigmentary disorders in darker-skinned patients, a patient population that has historically been challenging to treat with laser devices.

## ACKNOWLEDGMENT

We gratefully acknowledge and are indebted to the Research Department at the Laser & Skin Surgery Center of New York.

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