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Treatment of Laser-Responsive Dermal Pigmentary Conditions in Type III-IV Asian Skin With a 755-nm Picosecond Pulse Duration Laser: A Retrospective Review of Its Efficacy and Safety

Yun Pei Koh, MBBS, Aaron Wei Min Tan, MBBS, MRCP (UK), FAMS (Dermatology), MRCPS (Glasg), and Sze Hon Chua, MBBS, MRCP (UK), FRCP (Edin), FAMS (Dermatology)*

BACKGROUND Picosecond lasers have become very popular in the treatment of hyperpigmentation.

OBJECTIVE Evaluating the efficacy and safety of picosecond 755-nm laser in treatment of nevi of Ota (NO) and Hori's nevi (HN) in Asians with Fitzpatrick skin Types III/IV.

METHODS A retrospective review of patient records at the National Skin Center, Singapore, from 2015 to 2017. Three independent blinded dermatologists assessed pre-and-post treatment photographs using the physician's global assessment (PGA) score (0-clear, 1-almost clear, 2-mild, 3-moderate, and 4-severe).

RESULTS There were 18 cases of NO and 11 cases of HN. Mean treatment sessions were 2.22 (NO; range 1–6) and 3.82 (HN; range 1–6). In the NO group, mean pre-and-post treatment PGA scores were 3.1 and 1.3, respectively (1.8 point change, *p*-value 0.0002), and average fluence used was 2.02 J/cm^2 (range: 1.02–2.38). In the HN group, mean pre-and-post treatment PGA scores were 2.6 and 1.1, respectively (1.5 point change, *p*-value 0.004), and average fluence was 2.08 J/cm^2 (range: 1.98–3.40). Eleven patients (37.9%) experienced postlaser erythema, and 1 (3.4%) patient developed transient postlaser hypopigmentation. No permanent hyper/hypopigmentation was seen.

CONCLUSION The picosecond 755-nm laser is effective in the treatment of dermal pigmentary conditions in Asians with Fitzpatrick skin Types III/IV, with minimal risk of postlaser complications, and compared with the center's past experience with the Q-switched nanosecond 1064-nm laser, results in faster and more effective pigment clearance.

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The treatment of benign epidermal and dermal pigmentation has been revolutionized by the advent of pulsed lasers and the concept of selective photothermolysis. The nanosecond (ns) Q-switched (QS) lasers have been used to treat cutaneous pigmentation since 1989[1]. However, they have been associated with a higher risk of dyspigmentation and scarring in the Asian population.[2,3]

Picosecond lasers operate within the subnanosecond range (10^{-12} seconds). They provide a greater photomechanical effect and less heat diffusion into neighboring structures, hence may theoretically lead to improved clinical outcome and decreased thermal injury as compared to traditional nanosecond devices.

The safety and efficacy of the picosecond laser in the treatment of tattoos have been well documented in the

*All authors are affiliated with the National Skin Centre, Singapore

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literature,[4,5] even among Asian patients.[6,7] In this study, we aim to share our experience on the safety and efficacy of the picosecond laser in treating dermal pigmentary conditions such as nevi of Ota (NO) and Hori's nevi (HN) on Asian skin.

Subjects and Methods

This is a retrospective analysis of patients who underwent treatment with the picosecond 755-nm alexandrite laser at the National Skin Center, a tertiary dermatological center in Singapore, from the period of January 2015 to October 2017. Patients were screened according to the inclusion and exclusion criteria for this retrospective study. Ethics approval was sought and approved by the domain specific review board.

Patients were older than 18 years, with Fitzpatrick skin Types 3 and 4. They had facial dermal pigmentation (either NO or HN) and underwent treatment with a novel picosecond laser device. Exclusion criteria included pregnant or lactating patients, patients with a history of skin cancers, keloid formation, active or systemic infections, immunosuppression, and photosensitivity.

Patient medical records were reviewed and relevant information extracted. Data collected included demographic details, co-morbid medical history, current medical history, treatment details (such as number of treatments and laser parameters), complications and adverse effects of treatment, patient and physician subjective reported improvement, as well as photographic documentation.

Patients were treated with the picosecond 755-nm alexandrite laser (Picosure; Cynosure, Westford, MA) for their dermal pigmentary conditions using a 2 to 6 mm zoom (continuously variable) handpiece. Device settings such as spot size, fluence, and repetition rate were used according to clinical discretion. All patients were pretreated with an eutectic mixture of local anaesthetics (EMLA; AstraZeneca, Cambridge, United Kingdom) 60 minutes before treatment as part of the standardized treatment protocol. During the procedure, forced air cooling (Zimmer Cryo 6), vibratory devices, and cold compressions were used to manage procedural related pain and discomfort. Adverse events after each treatment session, if any, were specifically evaluated for and recorded. All patients received standardized postprocedure advice. Interval between each treatment was at least 2 months apart based on our center's laser treatment guidelines for dermal pigmentary conditions. As dermal pigmentary conditions are nonresponsive to topical lightning agents, patients did not receive and topical therapy such as hydroquinone and steroid either before or after laser treatment.

Standardized digital photographs under controlled lighting and fixed head positioning were taken of patients before commencement and after treatments using the Visia-CR system (Canfield Scientific, Inc., Parsippany, NJ).

Clinical outcomes were assessed by comparing pre-and-post treatment standardized photographs of patients. The assessments were performed by 3 independent qualified dermatologists who were blinded to the patient's bio data, time point of each given photograph, and all treatment details. A physician's global assessment (PGA) score was used, rating the severity of pigmentation (clear: 0; almost clear: 1; mild: 2; moderate: 3; and severe: 4). A Wilcoxon signed-rank test was used to evaluate the changes in the average global assessment scores before and after treatments. Statistical significance was defined as p value < .05.

Results

A total of 29 patients were included in the study, 4 men and 25 women, their ages ranging from 22 to 59 years (mean age 40; SD = 10.78). Eighteen patients (62%) had NO, and 11 patients (28%) had HN (Table 1). The mean number of treatment sessions recorded during this time period was 2.22 for NO (range 1–6) and 3.82 for HN (range 1–6). Average treatment parameters between the 2 groups were found to be similar. No boost was set, and this corresponded to a default pulse duration of 750 ps. In the NO group, fluence used ranged between 1.02 and 2.92 J/cm^2 (mean of 2.02 J/cm^2). In the HN group, fluence used ranged between 1.67 and 2.83 J/cm^2 (mean of 2.08 J/cm^2). As the spot size selected on the zoom handpiece determined the

TABLE 1. Patient's Treatment Details

	Naevus of Ota	*Hori's Naevus*
Male	4	0
Female	14	11
Mean (min, max)		
Age	34 (22–53)	47 (30–59)
Treatment sessions	2.22 (1–6)	3.82 (1–6)
Fluence (J/cm^2)	2.02 (1.02–2.92)	2.08 (1.67–2.83)
Spot size (mm)	3.37 (2.8–5)	3.36 (3–3.8)

fluence setting, the above fluence used corresponded to spot size range of 2.8 to 5 mm (mean of 3.37 mm) for the NO group and 3 to 3.8 mm (mean of 3.36 mm) for the HN group. All patients underwent treatment with 2 passes over each treatment area, the second pass being delivered immediately after the completion of the first pass with no interval delay. The repetition rate used was 5 to 10 Hz. Treatment end point was that of either mild erythema or mild surface whitening.

Both the NO and HN group of patients showed a statistically significant improvement in physician graded clinical outcome (Table 2). There was a decrease in clinical severity grading from 3.1 ± 0.6 to 1.3 ± 0.7 (p = .0002) in the NO group (Figures 1 and 2) and from 2.6 ± 0.5 to 1.1 ± 0.4 (p = .004) in the HN group (Figure 3). No subjects were assessed to be unchanged or worsened when compared with their pre-treatment photographs.

Patients tolerated the procedures well, with a mean pain score of 4.65 of 10 (SD = 2.00). None of the patients required postprocedural oral analgesics. Eleven patients (37.9%) experienced postlaser erythema which resolved on its own without further intervention, and 1 (3.4%) patient developed transient postlaser hypopigmentation which self-resolved after 6 months. The patient with transient hypopigmentation had Fitzpatrick skin Type III and was being treated for HN for 4 treatment sessions with a mean fluence of 2.01 J/cm^2 (1.93–2.04). No cases of transient hyperpigmentation or permanent hyper/hypopigmentation were seen in our patients.

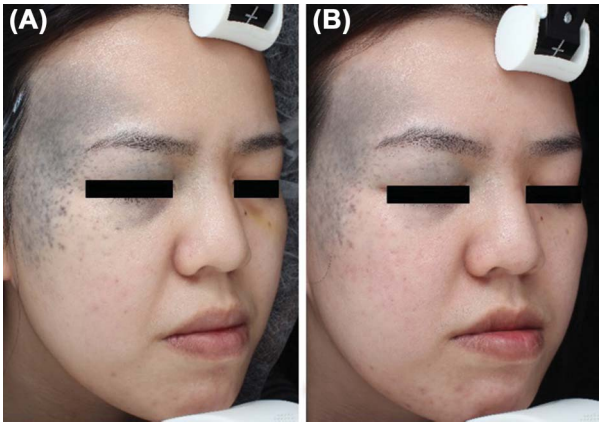

Figure 1. Before (A) and after (B). This 22-year-old female patient has had a naevus of Ota over her right temple, periorbital area, and upper cheek since childhood. She underwent 1 session of Qs-ns 1064-nm laser prior, followed by 3 sessions of picosecond 755-nm alexandrite laser. Settings: Fluence 1.98 J/cm^2, spot size 3.4 mm. There was a decrease in PGA score from 3.67 to 2.67 after 3 sessions of picosecond laser.

Discussion

Laser devices are useful in the treatment of dermal pigmentary conditions, based on the concept of selective photothermolysis. Melanosomes distributed in the dermal layer absorb short bursts emitted by the device, at an adequate energy level to break down tissue but minimizing collateral thermal damage. However, an excessive photothermal and photomechanical effect may be associated with nanosecond (ns)

TABLE 2. Pre and Post Treatment Average Physician's Global Assessment Score

	Before	*After*	p *(Wilcoxon Test)*
Naevus of Ota			
Mean ± SD	3.1 ± 0.6	1.3 ± 0.7	0.0002
Median (min, max)	3 (2–4)	1 (0.3–3)	
Hori's naevus			
Mean ± SD	2.6 ± 0.5	1.1 ± 0.4	0.004
Median (min, max)	2.7 (2–3.3)	1 (0.3–1.7)	

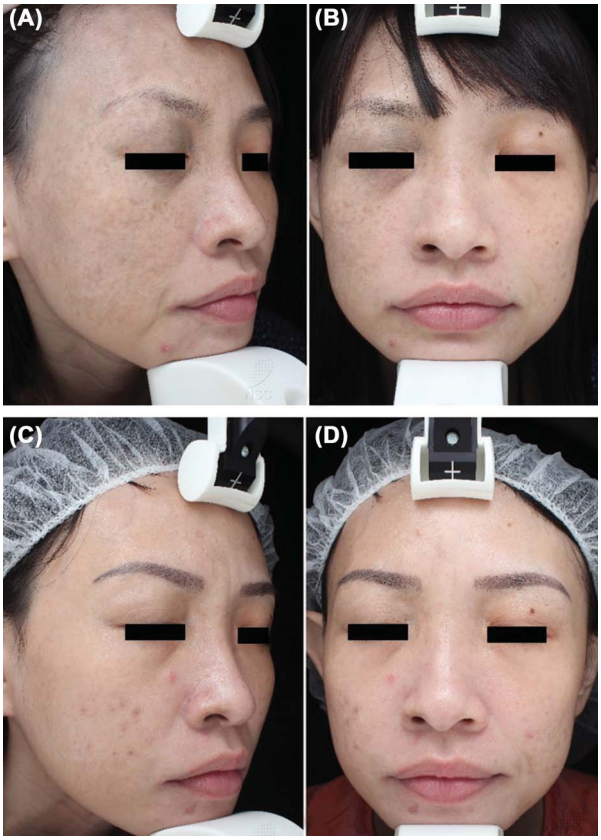

Figure 2. Before (A and B) and after (C and D). This 34-year-old female patient received 6 sessions of picosecond 755-nm alexandrite laser every quarterly to her naevus of Ota over the right forehead, temple, and cheek. Settings: Fluence 2.04 J/cm^2, spot size 3.2 mm. There was a significant decrease in PGA score from 2.67 to 1.00 after 6 sessions of picosecond laser.

Q-switched (QS) lasers. This may bring about an inflammatory response secondary to damage at the basal skin layer and superficial dermal blood vessels.[8] Melanocyte activity may be altered in the basal layer with excessive epidermal injury, resulting in subsequent dyspigmentation especially in the darker Asian skin phenotypes.[9] This gives rise to the need for a device with more optimal photoacoustic effects, particularly in this patient population.

Numerous studies have documented the safety and superiority of picosecond lasers for tattoo removal in the Asian population. Kasai[7] treated 4 Japanese patients for their multicolored tattoos with a picosecond 755-nm alexandrite laser and a picosecond Nd:YAG laser, with findings of picosecond lasers requiring less than half the number of sessions otherwise needed with ns-QS laser for treatment of black-colored tattoos. For multicolored tattoos, the picosecond laser was also found to be more efficient as compared to the conventional ns-QS laser. Lee and colleagues successfully treated 6 Korean patients with Fitzpatrick skin Type IV, using a picosecond 755-nm alexandrite laser for their black and red tattoos. Patients achieved more than 75% clearance in a shorter duration as compared to conventional ns-QS laser treatments.[6] The picosecond laser was also shown to be effective for red-colored tattoos, which was otherwise known to have diverse treatment outcomes in the literature. However, the authors report 3 of 6 patients having postinflammatory hypopigmentation after treatment and that a darker skin phenotype may have been contributory.

NO and HN are both dermal pigmentary conditions. Before the advent of ns-QS lasers, therapeutic methods such as cryotherapy and dermabrasion often induced scarring or significant textural or permanent pigmentary changes in patients. ns-QS Nd:YAG, ns-QS ruby, and ns-QS alexandrite lasers have all been shown to achieve good clinical response and have been widely accepted as the standard of care.[10] However, issues of multiple treatments and adverse events such as dyspigmentation and scarring are still associated with usage of ns-QS lasers. This is postulated to be related to photothermal damage being the main mechanism of injury in ns-QS lasers.[11]

A majority of our nevus of NO group of patients had previously undergone treatments with the ns-QS Nd:YAG 1064-nm laser with the number of treatment sessions ranging between 1 and 15 sessions. We postulate that this may be in relation to an earlier presentation of the clinical condition, as most of our patients report that the condition had been present for many years or "since childhood."

A retrospective review of 67 patients with NO treated with different QS laser modalities showed an average of 19 sessions (range 10–27, $p = .001$) required to achieve 95% clearance. Two patients (3%) experienced persistent side effects such as an atrophic scarring, although it was not mentioned how many sessions these patients underwent.[12] A recent split-face study by Ge and colleagues[13] using a picosecond 755-

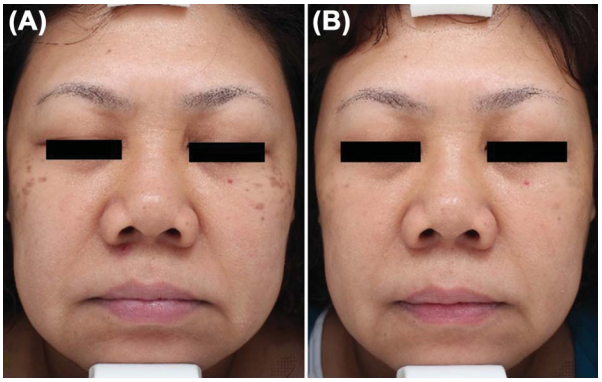

Figure 3. Before (A) and after (B). This 50-year-old female patient has had a 20-year history of Hori's naevus over her malar cheeks bilaterally. She received 6 sessions of picosecond 755-nm alexandrite laser. Settings: Fluence 2.08–2.83 J/cm^2, spot size 3.0–3.5. There was a decrease in PGA score from 3.00 to 1.67.

nm alexandrite laser versus the ns-QS 755-nm alexandrite laser for treatment of NO in skin Types III-IV showed higher efficacy and a decrease in pain scores and postinflammatory hyper/hypopigmentation in the picosecond laser–treated group.

For HN, the duration of the condition in our cohort of patients ranged from 3 to 10 years. Majority of our patients had also received prior ns-QS Nd:YAG 1064-nm laser before treatment with the picosecond 755-nm laser. In patients who achieved more than 50% improvement in average PGA scores, they received 4 or more picosecond 755-nm alexandrite laser treatment sessions, with treatment fluence ranging from 1.76 to 2.1 J/cm^2.

Polnikorn and colleagues[14] showed that only 50% of patients (6 out of 12) who underwent 3 or more sessions of ns-QS Nd:YAG laser treatment showed 50% to 75% clearance of their HN (fluence 4–6 J/cm^2, 3-mm spot size). In terms of side effects associated with ns-QS lasers, transient postinflammatory hyperpigmentation was commonly reported in majority of treated subjects by Ho and Chan.[15]

Treatment with the picosecond 755-nm alexandrite laser was well tolerated by our cohort of patients. No long-term side effects or postinflammatory hypo/hyperpigmentation were seen in our patients. This has also been reported by other studies. A retrospective comparison study by Levin and colleagues[11] of 70 patients who underwent treatment of pigmentary disorders with the 755-nm picosecond alexandrite laser and 92 patients with the ns-QS device showed similar side effects in both groups, namely edema, dyspigmentation, erythema, pain, and crust formation. These side effects resolved within 1 month without further treatment. Kung and colleagues[16] reported similar self-limiting events which resolved within 1 week to 1 month.

The limitations of this study are that this is a retrospective pilot study, involving a small cohort of patients with 2 dermal pigmentary conditions evaluated. We were not able to standardize treatment parameters or frequency of treatments due to the retrospective nature of the study. Subsequent evaluation and follow-up were not feasible due to nature of the condition and the limited data collection period of 2 years. We were also not able to account for patients who defaulted follow-up. Hence, we were unable to evaluate for recurrence. Future large prospective clinical trials on pigmentary lesions or a direct comparison between picosecond and ns-QS lasers may be required to support our findings. The current literature has also yet to establish the optimal fluence for treatment of dermal pigmentary lesions to maximize outcome and minimize side effects.

Conclusion

The picosecond 755-nm alexandrite laser is effective in the treatment of dermal pigmentary conditions (NO and HN) in Asians with Fitzpatrick skin Types III-IV, with minimal risk of postlaser complications, and compared with our center's past experience with the ns-QS 1064-nm laser, results in faster and more effective pigment clearance.

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Address correspondence and reprint requests to: Yun Pei Koh, MBBS, National National Skin Centre, 1 Mandalay Road, Singapore 308205, or e-mail: ypkoh@nsc.com.sg