Solar lentigines and ephelides removal in Asians using a combination of a novel 670 nm picosecond and 1,064 nm laser

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Background: Picosecond (PS) lasers have evolved over the years, and several new wavelengths have been adopted for more efficient and safe treatment of various skin conditions. We specifically studied the 670 nm wavelength for its high melanin–hemoglobin ratio, effectiveness, and safety in laser–unfriendly Asian skin.

Objective: This study evaluated the effectiveness, safety, and patient satisfaction following treatment of solar lentigines and ephelides with a combination of a novel 670 nm PS and 1,064 nm wavelength laser in a series of Asian patients.

Methods: This retrospective study evaluated 30 patients who underwent treatment for solar lentigines and ephelides. A PS laser of wavelength 670 nm and 660 PS pulse width was adopted at a spot size of 2.0–3.5 mm, fluence of 0.7–0.8 J/cm², and repetition of 2.0–3.3 Hz. Treatment intervals ranged from 3–5 weeks for a total of 3–6 sessions. Skin pigmentations in the patients were documented with a high–resolution camera and the results were assessed by physicians. In addition, patient satisfaction was evaluated.

Results: Thirty patients (27 females, 3 males), aged 21–66 years, with Fitzpatrick skin type III or IV were treated and evaluated. It was observed that 100% of the patients achieved at least good results (>50% improvement), 80% achieved good results (>75% improvement), and 40% achieved clinical clearance (>90% improvement). The average downtime with mild redness was 2–3 days and transient darkening of pigmentation (crème brulée reaction) was observed for 5–7 days. Higher–contrast lesions demonstrated better responses. The post–inflammatory hyper– and hypopigmentation rates were 3.3% and 6.67%, respectively.

Conclusion: PS laser is effective for the treatment of solar lentigines and ephelides. The 670 nm wavelength is beneficial in improving the efficacy and safety of the PS laser treatment, which is especially important in Asian skin that is prone to laser complications.

Keywords: Asian; freckles; hyperpigmentation; laser; pigment

Introduction

Picosecond (PS) laser is a novel dermatological laser that exerts a significant selective photomechanical effect, which is “Less Irritating” while being “More effective” (LIME) than traditional lasers in terms of clinical and histological aspects,

as demonstrated by a pilot study [1]. There are several new wavelengths. Among the different wavelengths, 670 nm has been reported to have a favorable melanin–hemoglobin ratio (Fig. 1). This property aids in targeting melanin problems in a specific manner, while preventing damage to the vascular structures. Theoretically, this property induces less edema,

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Fig. 1. The melanin-hemoglobin absorption ratio of the 670 nm wavelength is higher than that of the contemporary wavelengths including 755 nm and 785 nm (Courtesy, Beard et al.).

irritation, and inflammation, resulting in a LIME procedure, in addition to having other advantages of the PS technology. The 670 nm wavelength is longer than the 532 nm wavelength, which can bypass the functional epidermal melanin layer more effectively; therefore, is safer for darker skin types. Pigmentation is an important and common sign of aging in Asian skin [2], and solar lentigines and freckles are the two most common entities. However, skin fairness and whiteness are considered important in the expression of beauty in Asian cultures [3]. Therefore, one of the most important treatments for aging in the Asian population is pigment removal. As Asian skin has a high concentration of functional melanin layer in the epidermis, laser treatment is associated with epidermal complications, including erythema, burns, as well as hyper- and hypopigmentation [4]; therefore, a LIME laser procedure is required. Considering this requirement, the PS laser with a new generation 670 nm wavelength would be the most suitable option. This study focused on the 670 nm wavelength for its high melanin-hemoglobin ratio, effectiveness, and safety in laser-unfriendly Asian skin. Moreover, this is the first of the two studies using this novel wavelength of 670 nm to treat skin pigmentation in Asians.

Materials and methods

Study design and subjects

This retrospective study recruited 30 patients with a clinical diagnosis of solar lentigines and ephelides from June 2018 to May 2019 at the Medaes Medical Centre, Hong Kong. Among them, 27 were females and three were males (Table 1). Sun screening and melanin stabilizers, including arbutin, licorice, and 2% hydroquinone were used to prevent reactivation of the

Table 1. Summary of parameters of the study subjects

Variable	Value
Total no. of patients	30
Sex (n)	
Female	27
Male	3
Age range (yr)	21–66
No. of treatments studied (range)	3–5
Skin types	Fitzpatrick type III and IV
Highest 670 nm fluence (range)	0.7–0.9 J/cm ²
Highest 1,064 nm fluence (range)	0.7–1.0 J/cm ²

pigment. Patients received 3 to 5 treatments in total at intervals of 3–5 weeks. Follow-up was performed after 3 months for reassessment. All skin conditions were photographed using a single-lens reflex camera under the same settings. The assessment was done by the patient and physician based on a 5-category scale and the outcomes were categorized as poor (0%–25%), fair (26%–50%), good (51%–75%), excellent (76%–90%), and clinically cleared (>90%).

Laser device and settings

The Enlighten IIITM system (Cutera Inc., Brisbane, CA, USA) with 532/670/1,064 nm wavelengths was used. The pulse duration for the 532/1,064 nm wavelengths was 750 PS, while that for the 670 nm wavelength was 660 PS. The treatment involved two phases during the same session. The first phase was spot treatment using the 670 nm wavelength at a fluence of 0.7–0.9 J/cm² and spot size of 2.5–3.5 mm at the target lesions. The second phase was general 1,064 nm PS toning of the whole face at a fluence of 0.7–1.0 J/cm² and spot size of 7–10 mm with shot counts from 1,500–5,000. All make-up was removed before the treatment by washing the face, and a topical anesthetic cream (4% lignocaine) was applied for 30 minutes. During the treatment, no frosting was considered an endpoint. The only endpoint was mild delayed erythema that occurred approximately 1 minute after the laser treatment; however, occasionally no specific endpoint was required. After the treatment, a moisturizing cream and 1% hydrocortisone were applied.

Statistical analysis

Statistical analysis was performed to compare the data before and after treatment at 1st, 2nd, 3rd, and thereafter treatments by IBM SPSS ver. 27 (IBM Corp., Armonk, NY, USA), using Pearson correlation 2-tailed test; and statistical significance was set at 0.05.

Results

Efficacy and general response

Regarding the clearance rate of freckles and solar lentigines, 100% of the patients (30 out of 30) achieved at least good results (>50% improvement), 80.0% (24 out of 30) achieved excellent results (>75% improvement), and 40.0% (12 out of 30) achieved clinical clearance (>90% improvement) (Table 2). The average downtime was 2 to 3 days post-treatment and transient darkening of pigmented lesions (crème brulée reaction, CBR) was observed for 5 to 7 days.

Contrast of the lesion

Based on further analysis and correlations of different parameters, we found that the improvement in pigmentation was related to the contrast of the lesions. Higher lesion contrast was associated with better outcomes of the 670 nm PS laser treatment ($p=0.001$; Table 3).

Post-inflammatory hyperpigmentation

The post-inflammatory hyperpigmentation (PIH) rate was

Table 2. Clinical improvement according to the 5-category scale

Degree of improvement	Frequency	Percentage (%)
Poor (0%–25%)	0	0
Fair (26%–50%)	0	0
Good (51%–75%)	6	20.0
Excellent (76%–90%)	12	40.0
Clinically cleared (>90%)	12	40.0

Table 3. The frequency of different degrees of contrast lesions treated and their correlation with the clinical outcome

Lesion contrast	Frequency	Percentage (%)	Remark
Low	4	13.3	Higher contrast lesions were associated with better improvement ($p=0.001$)
Medium	11	36.7	
High	15	50.0	

Table 4. The occurrence frequencies of ripple response and PIH after 3 months

Variable	Frequency	Percentage (%)
Ripple response occurrence		
No	21	70.0
Yes	9	30.0
PIH more than 3 months		
No	29	97.7
Yes	1	3.3

PIH, post-inflammatory hyperpigmentation.

defined as a hyperpigmentation rate of 3.3% after 3 months of treatment (Table 4). Furthermore, it was related to a higher value of the highest 670 nm laser fluence ($p=0.008$; Table 5). Based on the data analysis, only one patient, who was treated with the 670 nm laser fluence that reached 0.9 J/cm^2 , demonstrated PIH for more than 3 months after the treatment.

Ripple response

Regarding transient hyperpigmentation for less than 3 months, we considered the reaction as a “ripple response,” and it was observed in 33.3% of the patients (10 out of 30). It is a pale, smoky based darkening of the complexion around the laser-treated area. This response was commonly found to occur in the Asian skin type. The ripple response was not statistically related to the highest fluence of the 670 nm PS laser ($p=0.538$) and the intensity of erythema after the treatment ($p=0.188$). In this study, 10.0% of the patients with ripple response developed PIH (1 out of 10); however, the rate of PIH was not high ($p=0.129$; Table 4).

Hypopigmentation

The occurrence rate of hypopigmentation was 6.67% (2 out of 30) (Table 6). It was not statistically related to the high fluence of the 670 nm or 1,064 nm laser ($p=0.867$, $p=0.065$, respectively). However, hypopigmentation only occurred with higher fluence of the 1,064 nm laser (at 3.0 J/cm^2 and 2.5 J/cm^2 in this study).

Erythema

The associated erythema was relatively mild. The severity score ranged from 2 to 5 out of 9 (Table 7). Furthermore, it

Table 5. The correlation between the fluence of the 670 nm picosecond laser and occurrence of PIH

Fluence	Frequency	Percentage (%)	Occurrence of PIH 3 months after treatment	Remark
0.70 J/cm^2	14	46.7	0	Higher fluence was related to higher rate of PIH ($p=0.008$)
0.80 J/cm^2	15	50.0	0	
0.90 J/cm^2	1	3.3	1	
Total	30	100	1	

PIH, post-inflammatory hyperpigmentation.

Table 6. The occurrence frequency of treatment-induced hypopigmentation

Hypopigmentation	Frequency	Percentage (%)
No	28	93.3
Yes	2	6.7

was not related to the ripple effect ($p=0.188$), PIH ($p=0.435$), or hypopigmentation ($p=0.814$). The erythema usually resolved within 2 to 3 days.

Other complications

The patients did not report any burns, blistering, or intolerable pain.

Discussion

Freckles and solar lentigines are common benign pigimentary disorders seen in Asians, which represent an important sign of aging. However, to date, the treatment of these disorders has been sub-optimal. Although freckles and solar lentigines are a simple pathology that are relatively easy to treat, past treatments using traditional quality-switched (QS) lasers resulted in significant skin irritation and caused adverse effects, such as burns, hypopigmentation, and PIH, with an occurrence rate of 10%–47% [1,5]. These are of particular concern in the Asian skin type with more concentrated epidermal functional melanin, which can lead to complications such as laser burn and hyper/hypopigmentation. The situation has improved with the evolution of PS lasers.

PIH occurred in only 4.65% of the patients by using the 532 nm PS laser. Histologically, the PS laser was shown to result in minimal disruption of the epidermal-dermal junction (EDJ) compared to the significant disruption following use of QS laser (Fig. 2) [1]. Nonetheless, the 532 nm laser has a suboptimal melanin-hemoglobin ratio and extremely shallow penetration properties, and the treated skin remains prone to functional epidermal melanin-related complications.

Properties of the 670 nm laser and its importance

The 670 nm wavelength has a high melanin-hemoglobin ratio and deeper penetration property than the 532 nm wavelength. The 670 nm wavelength is safer and more specific for melanin lesions, which potentiates its efficacy in the context of PS lasers. This means that the energy of the laser is preferentially delivered to the target melanin to exert a photomechanical effect instead of damaging vessels and surrounding tissues. Therefore, even at a relatively higher fluence, the increased amount of energy exerts a greater therapeutic effect on the target melanin, while the unwanted energy to the surrounding tissue remains

Table 7. The post-laser clinical erythema severity scores and their respective frequencies

Erythema severity score (0–9)	Frequency	Percentage (%)
2	4	13.3
3	13	43.3
4	11	36.7
5	2	6.7

Fig. 2. Histological findings after QS/PS Nd:YAG laser treatment (H&E stain). (A) After QS laser treatment with disruption of the epidermal-dermal junction (EDJ) (arrows). (B) After PS laser treatment without disruption of the EDJ. QS, quality-switched; PS, picosecond; Nd:YAG, neodymium-doped yttrium aluminum garnet. Cited from the article of Negishi K, et al. (*Lasers Surg Med* 2018;50:851–8) [1] with original copyright holder's permission.

Fig. 3. Before (A) and after (B) skin condition of a patient with freckles.

Fig. 4. Before (A) and after (B) skin condition of a patient with solar lentigines.

minimal. This results in efficient laser treatment with a wider safety margin (Fig. 1). And the treatment results of freckles and solar lentigines are satisfactory (Fig. 3, 4).

These properties, namely increased melanin specificity, efficiency, and a wider safety margin, make the 670 nm PS laser theoretically optimal for the treatment of benign pigmented lesions in Asians. Clinically, we observed that the treatment efficacy was favorable, with minimal adverse effects. The PIH rate observed in this study was 3.3%, which was even lower than that of the 532 nm PS laser (4.65%), as demonstrated by Negishi et al [1].

New concepts of no frosting endpoint, crème brûlée reaction, and ripple response

There is a new concept that no frosting is required to be considered an endpoint for a satisfactory result, because the PS laser exerts a predominantly photomechanical effect which generates significantly less heat energy. Therefore, there is minimal redissolution of gas in the EDJ to cause disruption of the architecture and lead to frosting. Considering the minimal injury to the skin structure, crust formation will not occur as compared to the QS laser. The cracked and cytoplasmically externalized

melanin will then be removed by the lymphatic system or be eliminated with normal upward turnover of the keratin layer (Fig. 5). The turnover elimination gives rise to a very thin and darkened pigment layer that lasts for approximately 5 to 7 days and subsequently flakes off. As the turnover layer is thin and does not involve severe disruption of the EDJ, it has been described as the CBR. Normal-colored skin without hypopigmentation was observed after resolution of the CBR.

Melanogenesis is more reactive in the Asian skin type and commonly occurs after insults, including light treatment, acne vulgaris, or any injury that leads to inflammation. This makes the Asian skin laser-unfriendly. The specific high melanin-hemoglobin ratio of the 670 nm laser and its use in conjunction with the PS technology resulted in relatively lesser insult and inflammation. The rate of PIH was low at 3.3% compared to 4.65% for the 532 nm laser and 10%–47% for the QS lasers [1,5]. However, due to the Asian skin type, a transient smoke-like pigmentation persisted around the laser treatment area (Fig. 6) in 30% of the patients, which has been described as the “ripple response” for the first time in this study. The intensity of this pigmentation was very pale and was not restricted to the point of original freckles or solar lentigines, but occurred a few mil-

Fig. 5. Mechanism of pigment elimination in the skin. As there is no thermal killing of keratinocytes, there is no crust formation after picosecond laser treatment. The upward turnover of the keratinocyte melanin gives rise to a thin layer of pigmentation, like a thin layer of caramel on a crème brûlée.

Fig. 6. Before treatment (A), smoky based darkening of tone in the laser treated area; the “ripple response” (B); resolution of the ripple response pigmentation in 1 month (C).

limeters to centimeters away. The same condition has been observed at other wavelengths, such as in the 532 nm laser. Moreover, the ripple response was transient and lasted for less than 1 to 3 months, and the severity was relatively mild. Therefore, it may be considered that the condition was a mild over-reaction of the functional melanocytes that caused transient melanin overproduction in the brief period following mild inflammation induced by the laser. The ripple response subsided effectively after application of melanin stabilizers and PS laser toning, and could be prevented by applying 1% hydrocortisone, which reduces inflammation.

Complications of the 670 nm laser

The various properties of the 670 nm PS laser make it relatively gentle for the Asian skin type and cause fewer complications. Apart from lower PIH rates and lack of crust formation, the 670 nm laser was associated with a low hypopigmentation rate of 6.7% and mild erythema. Considering that the erythema was relatively mild, it was not practically a complication, which explains why the degree of erythema was not statistically associated with PIH or hyperpigmentation.

In conclusion, the 670 nm wavelength is efficacious along with the PS laser technology for the treatment of solar lentigines and ephelides, resulting in minimal adverse effects, including PIH and hypopigmentation. Furthermore, the patient satisfaction rate was high, and there was no requirement to reach the frosting endpoint, as in traditional laser treatments. A higher-contrast lesion was found to exhibit a better response. The

injury to the EDJ was minimal; therefore, only the CBR was observed without any wound or crust formation. The “ripple response” may occur for a brief period with mild severity.

Conflicts of Interest

The author has nothing to disclose.

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