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ORIGINAL RESEARCH REPORT

A retrospective analysis of the management of freckles and lentigines using four different pigment lasers on Asian skin

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Abstract

Background: The risk of post-inflammatory hyperpigmentation (PIH) is increased during freckles and lentigines treatment in Asians. *Objective*: To determine the effectiveness and safety of using 595-nm long pulsed dye laser (LPDL), 755-nm LP Alexandrite laser, 532-nm QS Nd:YAG laser and 532-nm LP potassium-titanyl-phosphate (KTP) laser for the treatment of freckles or lentigines in Asian patients. *Methods*: This is a retrospective study of 40 Chinese patients, who were divided into four groups based on treatment modality using four different pigment lasers. Each patient attended between 1 and 4 treatments (mean of 1.8), at 4–6 weeks intervals, depending on clinical response. Lesional clearance and PIH were assessed by two independent clinicians. *Results*: Statistically significant improvement of global and focal facial pigmentation was found after treatment with LPDL, QS Nd:YAG and LP KTP lasers. No significant improvement was found after LP Alexandrite laser. PIH risk was 20% after LP Alexandrite treatment, 10% with QS Nd:YAG, and absent after LPDL and LP KTP treatment. *Conclusion*: A long pulse laser and small spot size appear to reduce the risks of lentigines treatment in darker skin types.

Key Words: *freckles, lentigines, asian, oriental and lasers*

Introduction

Freckles and solar lentigines are common and early signs of photoaging, which are major cosmetic concerns among Oriental patients. Freckles tend to appear during childhood and adolescence and are relatively uniform in distribution, size and colour. Histologically, they are characterised by epidermal hypermelanosis without an increase in melanocyte numbers. In contrast, lentigines increase in number and prevalence with age. They tend to vary in size and colour and are non-uniformly distributed. The number of melanocytes and degree of epidermal hypermelanosis are both increased with elongation of epidermal rete ridges seen (1).

With the advent of lasers, safe and effective treatment options for epidermal pigmentation have become more varied for different Fitzpatrick skin types. Different factors need to be considered when choosing pigment specific lasers for darker skin types.

Q-switched (QS) lasers have long being recognised to be effective in the treatment of freckles and lentigines. They are traditionally the treatment of choice for light-skinned patients with minimal complications seen. However, studies using QS Nd:YAG, QS ruby and QS Alexandrite lasers for pigmented lesions in Asians have reported a post-inflammatory hyperpigmentation (PIH) risk of approximately 10–25% (2–4).

Long-pulsed (LP) lasers, with their millisecond pulse widths, have been found to be equally effective in dark-skinned individuals without the high risk of PIH seen with QS devices (4,5). This can be explained by the fact that LP lasers, with their longer pulse width, cause melanin destruction only by photothermolysis. In contrast, QS lasers utilise high-energy nanosecond radiation, which exhibit both photothermal and photomechanical effects. The undesirable photomechanical effect induces damage to surrounding oxyhaemoglobin and melanin, resulting in

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inflammation of superficial vessels, altered activity of melanocytes and subsequent PIH.

There has been increasing use of vascular lasers for the removal of freckles and lentigines. Five hundred and ninety-five-nanometer long pulsed dye laser (LPDL) targets both haemoglobin and melanin. In order to reduce the risk of bruising and subsequent PIH with this device, diascopy during laser therapy is frequently used. This involves compression and emptying of dermal vessels using the glass window on the hand-piece, thus resulting in minimal vascular damage and PIH. Studies carried out by Kono (6–8) have supported the use of LPDL as an effective and safe modality for treating lentigines in Asians.

In order to shed more light on the efficacy and safety of different lasers on darker skin types, a retrospective analysis of our clinical data was carried out on Oriental patients who had freckles or lentigines treated using 595-nm LPDL, 755-nm LP Alexandrite laser, 532-nm QS Nd:YAG laser and 532-nm LP KTP laser.

Method

The study is a retrospective analysis of 40 female Chinese patients who underwent laser treatments for management of freckles and lentigines at a private centre by a single clinician. They were selected from 197 previously treated patients who presented to the clinic between the end of 2004 and early 2008 for treatment of freckles and lentigines, representing 20.3% of the total cohort.

The patients analysed can be divided into four groups based on the laser treatment they had received, with 10 patients in each group. The four different laser modalities used were 595-nm LPDL (VBeam Perfecta, Candela Corporation, Wayland, MA, USA), 755-nm LP Alexandrite laser (GentleLASE, Candela Corporation, Canton, MA, USA), 532-nm QS Nd:YAG (MedLite C3, Hoya ConBio Inc., Fremont, CA, USA) and 532-nm LP KTP laser (Gemini, Iridex Corporation, CA, USA).

As per routine practice, each patient would have had a detailed history and examination to determine the clinical diagnosis prior to a discussion about the available treatment options and associated risks. The treatment would have been carried out after informed consent was obtained, either at first presentation or at a later date. Topical anaesthetic (lidocaine 2.5% and prilocaine 2.5%, EMLA®) would have been applied under cling-film occlusion for 1 hour to sites targeted for laser treatment. In patients treated with 595-nm LPDL, the clinical end point would be defined as the lowest fluence that can achieve an ash-grey appearance without purpura. In the LP Alexandrite and 532-nm LP KTP groups, an ash-grey appearance would also be regarded as the desired clinical endpoint. For the 532-nm QS Nd:YAG laser, the ideal endpoint would be immediate whitening without bleeding. Immediately post procedure, a potent topical steroid cream (mometasone furoate, 0.1% cream, Schering-Plough, USA) would be applied to the irradiated areas for up to 3 days. Patients would be warned to avoid direct sunlight. Microcrusts over the irradiated pigmented lesions would typically appear 1–2 days after treatment and would shed over the subsequent 3–4 days.

The patient demographics and parameters used for each laser are shown in Table I. Each patient attended between 1 and 4 treatments at 4–6 weeks intervals, depending on their clinical response.

Digital photographic imaging under the same conditions (light source, room, camera) using a Canfield Visia CR system (Canfield, NJ, USA) have been used to assess all patients before and after each treatment session. This system allows for consistent

Table I. Patient characteristics and laser parameters used.

	595-nm LPDL	755-nm LP Alexandrite	532-nm QS Nd:YAG	532-nm LP KTP
No. of patients	10	10	10	10
Sex *N* (%)	Female: 10 (100%)	Female: 10 (100%)	Female: 10 (100%)	Female: 10 (100%)
Age				
Range	27–49	33–48	24–45	28–49
Mean (Standard)	39.6 (6.7)	42.0 (4.6)	36.0 (6.5)	40.1 (6.4)
Fitzpatrick	III: 9 (90%)	III: 6 (60%)	III: 9 (90%)	III: 8 (80%)
Skin type	IV: 1 (10%)	IV: 4 (40%)	IV: 1 (10%)	IV: 2 (20%)
Laser parameters	Energy range: 11–13 J/cm^2 Spot size: 7 mm Pulse width: 1.5 ms No cooling, 7 pl	Energy range: 20–35 J/cm^2 Spot size: 10 mm Pulse width: 3 ms Pulse rate: 1.5 Hz No cooling	Energy: 0.6 J/cm^2 Spot size: 2 mm Pulse rate range: 5–10 Hz No cooling	Energy range: 12–14 J/cm^2 Spot size: 2 mm Pulse width: 2 ms Pulse rate: 1.0 Hz Aim Beam 5 Contact cooling window and cooling gel used
Mean number of treatments	1.7	1.6	1.8	2.0
Mean length of follow-up (months)	2.9	1.5	2.2	2.2

positioning of the patient's head and images taken had a 6.1-megapixel resolution. Side by side clinical photographs, pre- and post-treatment, were reviewed by an independent clinician blinded to the sequence of images and treatment type.

The overall facial pigmentation of each patient before and after treatment was scored using a visual analogue scale (VAS) numbered 0–9, with 0 representing no pigmentation and 9 representing very dark pigmentation. The colour intensity of specific pigmented lesions was also scored using a VAS numbered 0–4, ranging from absent to severe. The Wilcoxon Signed Ranks test and Mann–Whitney test were used to analyse the data. The investigator global assessment was recorded and consisted of the following grading system: 0 = worsening, 1 = no change, 2 = mild improvement, 3 = moderate improvement and 4 = marked improvement. Lastly, the incidence of PIH, as seen from the digital images, was assessed.

Results

The characteristics of the patients are shown in Table I; all patients were female with a clinical diagnosis of freckles and lentigines. The ages of the patients ranged from 24 to 49 years (mean age = 39.4), and 32 were Fitzpatrick skin type III with the other 8 being skin type IV. Representative responses to the four different lasers used are shown in (Figure 1).

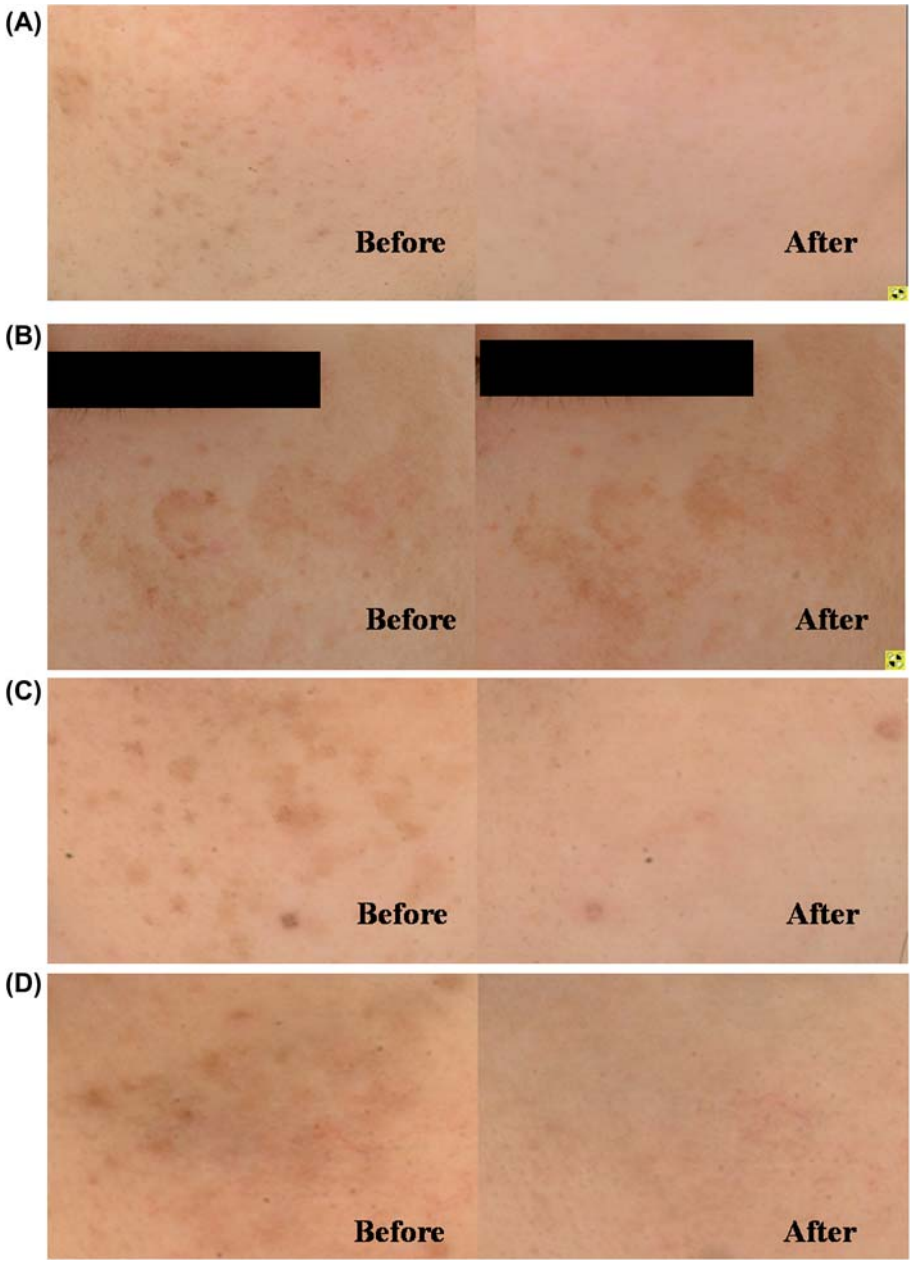

Figure 1. Representative treatment outcomes with the four different lasers. (A) Marked improvement after two treatments of 595-nm LPDL. (B) Moderate improvement after three treatments of 755-nm LP Alexandrite laser. (C) Marked improvement after two treatments of 532-nm QS Nd:YAG. (D) Marked improvement after two treatments of 532-nm LP Nd:YAG.

The mean number of treatments for the entire cohort was 1.7 for 595-nm LPDL, 1.6 for 755-nm LP Alexandrite laser, 1.8 for 532-nm QS Nd:YAG and 2.0 for 532-nm LP KTP laser. The mean length of follow-up was 2.9, 1.5, 2.2 and 2.2 months for the four respective groups.

The results from the visual analogue score grading for changes to global and focal hyperpigmentation are shown in Table II. There was a statistically significant improvement in overall facial pigmentation, when comparing endpoint VAS to baseline VAS, for patients treated with 595-nm LPDL, 532-nm QS Nd:YAG and 532-nm LP KTP laser ($p < 0.01$, $p < 0.05$, $p < 0.01$, respectively). There was no significant improvement in the patients treated with 755-nm LP Alexandrite laser ($p > 0.05$). When comparing the different groups, a significant difference was found between 532-nm LP KTP and 755-nm LP Alexandrite laser only ($p < 0.05$).

The results for colour intensity of specific pigmented lesions treated by the different laser groups mirrored the previous results. There was a significant improvement from baseline for patients treated with 595-nm LPDL, 532-nm QS Nd:YAG and 532-nm LP KTP laser ($p < 0.01$, $p = 0.01$, $p < 0.01$ respectively). There was no significant improvement in the patients treated with 755-nm LP Alexandrite laser ($p > 0.05$). Similarly, a significant difference was found between 532-nm LP KTP and 755-nm LP Alexandrite laser groups only ($p < 0.05$).

The investigator global assessment shows the responses seen with the different laser therapies at the follow-up after the last treatment (Figure 2). General improvement (mild, moderate or marked) was seen in 100% of patients treated with 532-nm LP KTP, 90% of patients treated with 595-nm LPDL, 80% of patients treated with 532-nm QS Nd:YAG and 70% of those treated with 755-nm LP Alexandrite laser. Moderate to marked improvement in pigmentation was found in 70%, 60% and 50% of patients treated with LP KTP laser, 532-nm QS Nd:YAG laser and 595-nm LPDL, respectively. It was found that 755-nm LP Alexandrite was associated with the highest proportion of patients (20%) having worsening of pigmentation post-treatment.

PIH risk after each treatment was found to be highest in the 755-nm LP Alexandrite and 532-nm QS Nd:YAG laser treated groups, with 20% and 10% documented, respectively. Patients treated with 595-nm LPDL and 532-nm LP KTP had the lowest risk of PIH, with none documented in this study.

Discussion

Skin of colour is differentiated by the amount and epidermal distribution of melanin. Larger melanocytes produce more melanin and widely dispersed melanosomes absorb and deflect UV light more efficiently, conferring significant photoprotection to darker skinned individuals (9). However, significant photodamage in the form of epidermal atypia and atrophy, dermal collagen and elastin damage and pigmentary disorders can occur in skin of colour (10). Other investigators have similarly observed that pigmentary changes occur earlier and with a greater incidence than skin wrinkling in Asians (11,12).

These superficial pigmentary changes in Asian skin can often be a challenge to treat as the risk of PIH is recognised to be greater in melanin-rich skin after laser therapy (2–4). Several factors contribute to the development of PIH, including increased melanocytic activities, dermal melanophages and haemosiderin deposition secondary to haemorrhage. The severity of PIH is also related to the degree of inflammation and the extent of disruption of the dermal–epidermal junction.

Over the last few decades, there has been a plethora of lasers available to treat superficial pigmentation. Clinicians are also increasingly looking to laser devices with multiple uses as cost and space saving solutions. As there has been relatively little research on the treatment of superficial pigmentation

Table II. Mean improvement in VAS for global and focal hyperpigmentation.

Laser	Region	Mean Baseline (Std)	Mean End point (Std)	Improvement in VAS
595 nm LPDL	Overall facial pigmentation	5.4 (1.0)	3.7 (1.3)	1.7
	Color intensity of specific pigmented lesions	2.6 (0.5)	1.5 (0.6)	1.1
755 nmLP Alexandrite	Overall facial pigmentation	5.4 (1.1)	4.8 (1.2)	0.6
	Color intensity of specific pigmented lesions	2.5 (0.4)	1.9 (1.0)	0.6
532 nmQSND:YAG	Overall facial pigmentation	5.4 (0.9)	3.6 (1.8)	1.8
	Color intensity of specific pigmented lesions	2.6 (0.5)	1.3 (0.9)	1.3
532 nm LP KTP	Overall facial pigmentation	5.8 (1.0)	3.9 (1.0)	1.9
	Color intensity of specific pigmented lesions	2.8 (0.5)	1.4 (0.6)	1.4

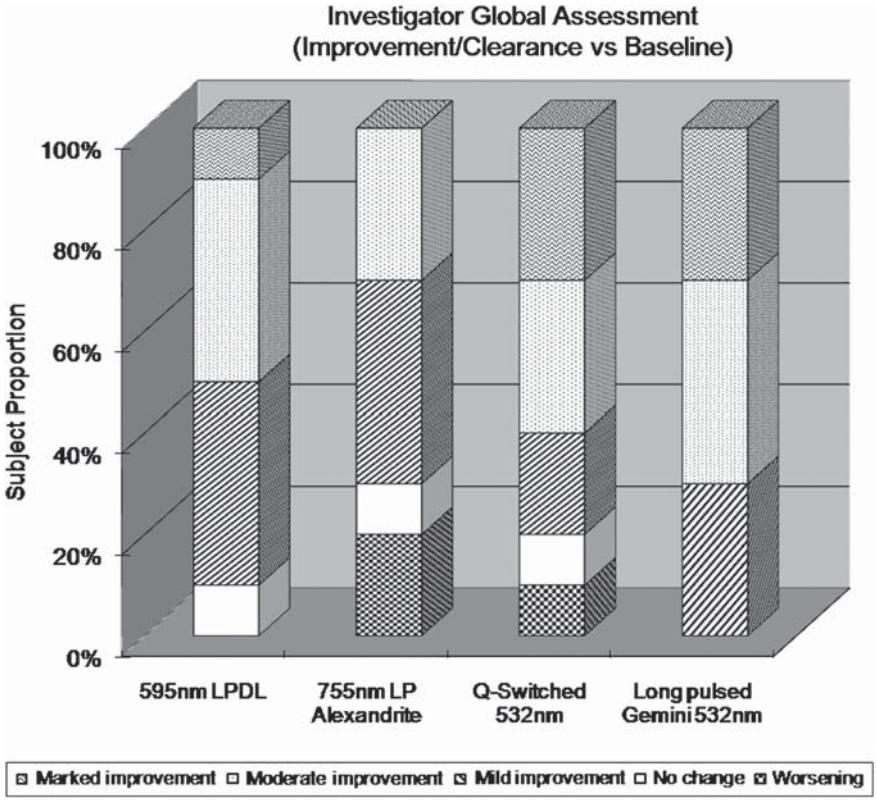

Figure 2. Distribution of patient responses to different laser therapies.

using different lasers in Asian skin, we carried out the first retrospective analysis comparing 595-nm LPDL, 755-nm LP Alexandrite laser, 532-nm QS Nd:YAG and 532-nm LP KTP laser in the treatment of freckles and lentigines in Fitzpatrick Type III and IV skin.

Our results showed significant global and focal improvement of superficial pigmentation with the use of 595-nm LPDL, 532-nm LP KTP lasers and 532-nm QS Nd:YAG. Although a large majority of patients in these groups showed improvement, 532-nm QS Nd:YAG was associated with a 10% risk of PIH. Despite previous promising results in Type II skin (13), 755-nm LP Alexandrite laser, failed to deliver significant results and was also associated with the highest risk of PIH (20%) in our current study. There did not appear to be any risk of PIH in patients treated with 595-nm LPDL and 532-nm LP KTP laser. It thus appears that the long pulsed lasers, which utilise a more gentle heating approach, are effective in targeting melanin-rich epidermal lesions with minimal photomechanical effects. QS devices, on the contrary, cause acute and abrupt destruction of melanocytes by generating acoustic waves that lead to secondary photomechanical damage of surrounding pigmented cells and superficial vessels, resulting in a higher incidence of PIH (14).

From our experience, the contrast between lesional and non-lesional skin is an important consideration in determining clinical outcome and PIH. The beam spot size used may also influence the risk of PIH. Larger spot sizes may lead to inadvertent treatment of unaffected skin, when the lesion treated is smaller than the spot size available, especially when contrast between lesional and non-lesional skin is low.

For patients with low contrast between lesional and non-lesional skin, there have been reports that the LP Alexandrite laser offered less clearance of these lighter coloured lentigines compared to darker coloured lentigines, due to less amount of chromophore available for uptake of laser energy (13,15). It was noted that moderate lesion darkening and perilesional erythema foreshadowed a good outcome. However, this end point may be delayed by several minutes, unlike the immediate whitening seen with QS devices (13). The large 10-mm spot size and relatively high fluence used with the Alexandrite laser also present a significant risk of injury to the surrounding normal skin, especially if the lesions treated are relatively small, leading to subsequent PIH. These factors could explain the disappointing results seen with the LP Alexandrite laser in our study.

Although the 595-nm LPDL uses a fairly large spot size of 7 mm and high fluence to achieve effective results, an additional compression window allows for visualization and compression of dermal vessels during treatment in order to reduce the risk of vascular damage and any subsequent PIH. The effectiveness

of such simple diascopy is supported by our promising results with 595-nm LPDL, and also previous results from Kono et al., who conducted three different studies involving the use of 595-nm LPDL, repeatedly demonstrating the effectiveness and safety of using 595-nm LPDL with compression for the treatment of lentigines in Asians, when compared to IPL and QS Ruby laser (6–8).

For the 532-nm LP KTP, a small 2-mm spot size is used, allowing for accurate targeting of lesional skin. The energy can also be safely increased with little risk of damage to surrounding normal skin. In addition, the LP KTP has a compression contact cooling window to minimise vascular damage and treatment involves the use of cooling gel to further protect surrounding normal skin.

PIH risk for patients treated with 532-nm QS Nd:YAG was found to be 10%, which is in concordance with previous studies (2–4). From our experience, QS Nd:YAG can sometimes result in dramatic improvement in superficial pigmentation after 1–2 treatments, especially in patients with low contrast lesions.

Other common pigment lasers such as the QS Ruby were not included in our current study. However, it is likely that its nanosecond pulse width is a potential risk for photomechanical damage, and its longer 694-nm wavelength may also result in damage to follicular melanocytes, leading to permanent hypopigmentation. In addition, QS Ruby devices utilise large spot sizes (3 or 6 mm), and this can once again result in inadvertent treatment of melanin rich skin if the target lesion is small. A previous study investigating the use of QS Ruby for the treatment of facial lentigines in Asian skin has also reported a high risk of PIH (22.2%) (6).

One of the concerns regarding the use of long pulsed lasers for the treatment of cutaneous pigmented lesions is the potential for thermal diffusion from the epidermis to the dermis, and the subsequent risk of scar formation. To prevent such occurrences, the pulse duration used should be shorter than the thermal relaxation time of the epidermis, which was estimated to be about 10 ms for a 100-μm thick epidermis (16,17). In our study, 1.5–3 ms were the pulse durations used for the long pulsed lasers, which yielded satisfactory clinical outcomes with no scarring seen.

With a follow-up of around 60–90 days, our study provides a good picture of short term efficacy but not the long term therapeutic effects. Being a retrospective study, a selection bias may exist and future larger prospective studies are recommended. Our current results show that superficial pigmentation requires repeated laser treatments for a satisfactory clinical outcome. Re-exposure to the sun and hormonal changes can all contribute to new or recurrence of freckles and lentigines. Regular laser treatments, in combination with use of a daily broad-spectrum sunscreen and bleaching creams (such as hydroquinone, retinoids, kojic acid and azelaic acid) are effective management strategies.

In conclusion, our study has shown that for treatment of freckles and lentigines in Fitzpatrick type III and IV skin, 595-nm LPDL and 532-nm LP KTP appear to be more effective with less complications compared to 532-nm QS Nd:YAG and 755-nm LP Alexandrite laser. A long pulse laser and small spot size are therefore important in reducing the risk of lentigines treatment in darker skin types.

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