

Successful Treatment of Freckles Using a 730-nm Picosecond Laser: A Prospective Study

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Objective: Freckles are common hyperpigmented diseases that commonly occur in Caucasians and Asians. Freckles often cause cosmetic and even psychosocial concerns. Various lasers with different wavelengths have been used to treat pigmented spots. This study aims to evaluate the efficacy and safety of a novel 730-nm Ti: Sapphire picosecond laser in the treatment of freckles in Chinese patients.

Methods: A total of 12 patients with freckles were enrolled. Patients underwent one laser treatment and were followed-up after eight weeks. Images were captured before treatment and at the eight-week follow-up, which were independently examined by two physicians to assess the treatment efficacy, including the lesion clearance rate and global aesthetic improvement scale. Patients recorded their pain and other adverse effects. Ex vivo human foreskins were treated with 730 nm picosecond lasers for one pass with a 3.75 J/cm² and then stained with hematoxylin and eosin (H&E).

Results: The average clearance rate as 74.46% and the mean GAIS as 4.13 ± 0.61. The pain scores were averaged at 3.08 ± 0.79. One patient exhibited hyperpigmentation (8.33%) and another patient developed hypopigmentation (8.33%) by the 8-week follow-up visit. A large number of uniform vacuoles were observed in the epidermal basal layer and the dermal papillae in the ex vivo foreskins, immediately after the treatment with 730-nm Ti: Sapphire picosecond laser. The vacuoles were uniformly sized, principally with 20–40 µm diameter.

Conclusion: The 730-nm Ti: Sapphire picosecond laser is safe and effective for treating freckles.

Keywords: freckles, 730-nm picosecond laser, Ti: Sapphire, GAIS, VAS

Introduction

Freckles (ephelides) are multiple scattered brown macules observed on the face, arms, and back, easily causing cosmetic and even psychosocial concerns. Freckles are mainly observed in Caucasians and Asians. They appear during childhood and intensify in adolescence. Their occurrence is related to heredity and sun exposure. The lesions become darker in summer and lighter in winter.¹ The short pulse picosecond lasers have been clinically available since the late 1990s. These lasers remove pigment particles and tattoos effectively, owing to their primary photomechanical and minimal photothermal effects. New laser devices and wavelengths are being assessed owing to their growing popularity and employment.² A 730-nm picosecond laser was successfully applied to several pigment disorders and tattoos.^{3,4} Here, we conducted a novel, prospective clinical study to evaluate the efficacy and safety of a 730-nm picosecond laser in the treatment of freckles. And this study was innovatively conducted to investigate changes in the skin upon treatment with 730-nm Ti: Sapphire picosecond laser through ex vivo human histological analysis.

Materials and Methods

Patients

A total of twelve (ten female and two male) patients were enrolled. This prospective study was approved by the institutional ethics committee of the Institute of Dermatology, Peking Union Medical College, Chinese Academy of Medical Sciences (2018-KY-012) and carried out in accordance with the Declaration of Helsinki. All subjects were over 18 years of age and their informed consent and authorization for images was obtained from the study participants prior to the study commencement. The patient inclusion criteria were as follows: diagnosed with freckles, 18–60-year age range, and Fitzpatrick III or IV skin types. Patients were instructed to follow the schedule and record their post-treatment responses. Patients who had received laser treatment within the past year and were suffering from other photosensitive diseases were excluded. Informed consent specifically stated that patients were prohibited from having laser treatment on freckles in the melasma area.

Laser Therapy

The apparent pigmented macules were chosen as treating area. After cleansing the face, the participants were treated using a 730-nm Ti: Sapphire picosecond laser (Picoway®; Syneron Candela, Corp., Wayland, MA) that delivered a 250 ps pulse and a moderate whitening endpoint reaction on each pigmented macule without anesthesia. The VISIA system (Canfield Scientific, Parsippany, NJ) was used to capture the images before treatment and at the eight-week follow-up.

Ex vivo human foreskins were collected after circumcision and treated with 730 nm picosecond lasers for one pass with a 3.75 J/cm^2 fluence on a 2 mm spot. Subjects were over 18 years of age, and their informed consent was obtained from the study participants prior to study commencement. The foreskin specimens were fixed in formalin and stained with hematoxylin–eosin staining (H&E).⁵ The experiments were repeated three times.

Clinical Assessment

Two physicians who were not involved in this research independently assessed the treatment efficacy using these collected images. Treatment efficacy was evaluated using the lesion clearance rate and global aesthetic improvement scale (GAIS). The lesion clearance of each patient was calculated as the number of macules before treatment minus that after treatment and then divided by the number of macules before treatment.⁶ The GAIS was used to evaluate the aesthetic improvement scale: worsening (score 1), no change (score 2), light improvement (score 3), moderate improvement (score 4), and significant improvement (score 5).⁷ A mean score was used when the patient scores differed. The patients recorded the pain during the laser treatments using the visual analog scale (VAS) (from 0 (no pain) to 10 (hardest to bear)) and the duration of their erythema, edema, and scabs. The presence of hyperpigmentation, hypopigmentation, and/or scars was also noted.

Statistical Analysis

The data were analyzed using IBM SPSS software (version 23.0; IBM Corp., Armonk, NY, USA). Quantitative data are summarized as mean $\pm$ standard deviation, and qualitative data are presented as percentages.

Results

Patient Demographics

A total of twelve (ten female and two male) patients were enrolled for one treatment and the eight-week follow-up (Table 1). The Fitzpatrick skin type IV patients were predominant. The mean age was 31.17 ± 7.80 years and the age ranged between 21 and 47 years. One of the subjects with freckles had melasma on cheeks, which was not considered as treating area. The mean energy fluence was $3.43 \pm 0.78 \text{ J/cm}^2$ (range 1.8–4.0 J/cm^2 , median 3.75 J/cm^2) and the spot sizes were 2–3 mm during the treatment.

Table 1 Patient Demographics

No. of patients	12
Gender	
Male	2 (16.67%)
Female	10 (83.33%)
Age (y)	31.17 ± 7.80 (21–47)
Fitzpatrick skin type	
III	1 (8.33%)
IV	11 (91.67%)
Accompanied with melasma	
Yes	1 (8.33%)
No	11 (91.67%)

Table 2 Efficacy and Adverse Events

Clearance rate	74.46% (52–86.50%)
GAIS	4.13 ± 0.61
VAS	3.08 ± 0.79
Adverse events	
Erythema	Mild, 1–3 day
Edema	Mild, 1–3 day
Scab	5–10 day
Hyperpigmentation	1/12 (8.33%)
Hypopigmentation	1/12 (8.33%)
Scar	0

Clinical Efficacy and Safety Evaluation

The physicians examined the pre- and post-treatment images and calculated the average clearance rate as 74.46% and the mean GAIS as 4.13 ± 0.61 (Table 2). Figure 1 depicts the facial freckle reduction after 730-nm picosecond laser treatment. The pain scores were averaged at 3.08 ± 0.79 . Moreover, mild erythema and edema persisted for 1–3 days after laser therapy. The scabs were shed in 5–10 days. One patient exhibited hyperpigmentation (8.33%) and another patient developed hypopigmentation (8.33%) by the 8-week follow-up visit. These patients did not exhibit any scarring (Table 2).

Skin Histopathological Examination

A large number of uniform vacuoles were observed in the epidermal basal layer and the dermal papillae in the ex vivo foreskins, immediately after the treatment with 730-nm Ti: Sapphire picosecond laser (3.75 J/cm^2 fluence) on 2 mm spots (Figure 2). Melanin absorbed the laser energy and the resulting photothermal and photomechanical effects caused vacuole formation. The vacuole formation may be consistent with the skin whitening immediately after laser treatment. The vacuoles were uniformly sized, principally with 20–40 μm diameter, indicating the relatively uniform laser energy distribution.

Discussion

The pigmentary skin disease patients exhibited successful freckle reduction and improved appearance after one laser treatment session. The Q-switched double-frequency Nd: YAG 532-nm laser, Q-switched 694-nm ruby laser, and Q-switched 755-nm alexandrite laser were moderately successful in freckle treatment and pigment removal.^{6,8} These Q-switched lasers, whose pulse width is measured in nanoseconds, mostly exerted photothermal effect. The photothermal conduction potentially affects the surrounding normal melanocytes and thereby resulted in unwanted dyspigmentation.



Figure 1 Female patient (29 years) before (a and b) and eight weeks (c and d) after the 730-nm picosecond laser treatment.

The picosecond lasers were preferred owing to their shorter pulse duration and primary photomechanical effects. They removed the pigments with lesser hyperpigmentation.⁹

The picosecond double-frequency Nd: YAG 532-nm and picosecond alexandrite 755-nm lasers were widely used to treat pigmentary diseases.⁴ The picosecond double-frequency Nd: YAG 532-nm lasers penetrate the superficial layer and the energy absorbed by normal melanocytes led to the hyperpigmentation in dark-skinned patients.⁴ Therefore, the double-frequency Nd: YAG 532-nm laser was administered in the light skinned patients for the epidermal hyperpigmented treatment. A 755-nm

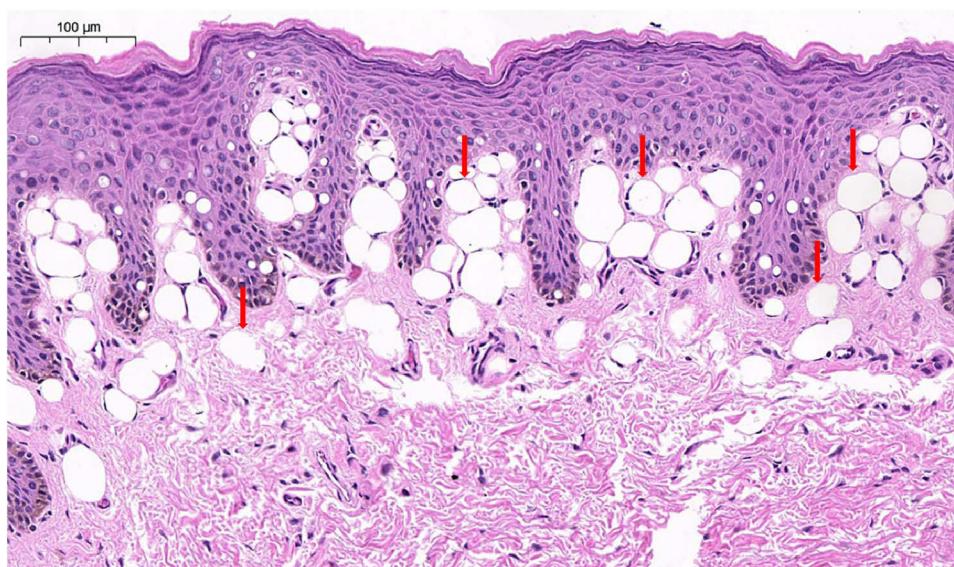


Figure 2 Histological characteristics of the ex vivo foreskin upon one round 730-nm picosecond laser treatment (3.75 J/cm^2 fluence on a 2 mm spot). Relatively uniform-sized vacuoles (red arrow) were observed in the epidermal basal layer and dermal papillae. ($\times 200$).

picosecond laser was preferred in the dark-skinned patients for treating dermal pigmentary diseases and epidermal disorders. However, theoretically, the absorption of pigments by the 755-nm laser is weaker than that of the 532-nm laser.⁴ A novel wavelength laser, which exhibited stronger pigment absorption and lesser unwanted pigmentation should be employed in the freckle or lentigenes treatment. We hypothesized that the 730-nm picosecond laser would be consistent with the said characteristics, owing to its shorter wavelength (than the 755-nm laser) and stronger absorption by melanin. Thus, the 730-nm wavelength laser efficiently reduced epidermal pigments, such as the freckles.^{3,4}

The Ti: Sapphire laser wavelengths range from 690 to 1050 nm.⁹ The novel 730-nm wavelength Ti: Sapphire picosecond laser was explored in pigmentary disease treatment and tattoo removal.^{3,4,10} The 730-nm picosecond lasers cleared the black, green, blue, purple, red, and yellow pigments by 70%, 77%, 83%, 83%, 26%, and 8%, respectively.³ A 21-year-old patient's freckles were lightened by 75–94% in one treatment session, whereas a 49-year-old patient's freckles and melasma were lightened by 50–74%.⁴ A large-scale and prospective research on dark-skinned people is lacking. In addition, Mohamed et al showed that 577-nm yellow diode laser was an effective and safe device in the treatment of freckles for four treatment sessions at 2-week intervals.¹¹

Here, we examined the efficacy and safety of freckles in dark-skinned patients. The 730-nm picosecond laser effectively treated the freckles and can be explored as a novel and effective choice. The post dyspigmentation was similar to published studies¹² and the patients obtained normal condition after several months, so it may suggest that the 730-nm picosecond laser is safe for treating freckles. Moreover, several uniform-sized vacuoles were observed in the epidermal basal layer and dermal papillae post 730-nm laser treatment, indicating the relatively uniform laser energy distribution within the laser spot, suggesting that this laser treatment may be safe and effective in treating hyperpigmented disorders.

Conclusion

The 730-nm Ti: Sapphire picosecond laser is a novel, effective and safe option for freckle treatment in Chinese patients.

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Disclosure

The authors report no conflicts of interest in this work.

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