Lasers in Surgery and Medicine 51:8–13 (2019)

Efficacy and Safety of Picosecond 755-nm Alexandrite Laser With Diffractive Lens Array for Non-Ablative Rejuvenation in Chinese Skin

Heidi Wat, BSc, MD,[1] Samantha Yee-nam Shek, MBBS,[2] Chi Keung Yeung, MD, FRCP,[2] and Henry Hin-lee Chan, MD, PhD, FRCP[2,3]*

[1]*Division of Dermatology, Department of Medicine, University of Alberta, Edmonton, Alberta, Canada*
[2]*Division of Dermatology, Department of Medicine, The University of Hong Kong, Hong Kong SAR, China*
[3]*Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts*

Background and Objectives: The picosecond alexandrite laser with diffractive lens array (DLA) offers the dual advantages of a picosecond pulse duration and the fractionated delivery of laser energy. This study explores the efficacy and safety of the DLA for treatment of multiple aesthetic concerns associated with photoaging of the face including skin texture irregularities, dyspigmentation, enlarged pore size, rhytides, and skin laxity.

Methods: This prospective, evaluator-blinded trial enrolled Fitzpatrick skin type III–IV patients with mild to moderate signs of facial photoaging. Patients received six full face treatments at 4 week intervals for a total of 107 treatments. Standardized photography was obtained at baseline and at 1, 2, and 3 month follow-up visits. Two independent blinded evaluators rated each of the five signs of photoaging on a 10-point visual analog scale (VAS) at each follow-up visit compared to baseline. A global aesthetic improvement score was also assigned at each follow-up visit. Secondary outcomes included patient-rated pain and heat sensation on a 10-point VAS, and overall satisfaction. Adverse events were noted after each treatment and at each follow-up visit.

Results: A total of 18 Chinese patients age 35–59 completed the study. A statistically significant improvement in skin texture and dyspigmentation scores was noted at the 1 month follow-up that was sustained at 3 months. No significant improvements were observed in pore size, rhytides, or skin laxity. The mean pain score was 5.1 ± 2 and mean heat sensation was 3.6 ± 2.1. Expected transient erythema and edema occurred in 95.3% (102/107) and 1.9% (2/108) of treatments, respectively, and resolved in hours. No incidences of post-inflammatory hyperpigmentation (PIH) were noted at the 1, 2, and 3 month visits.

Conclusion: The 755-nm picosecond laser with DLA is a safe and effective non-ablative modality for targeting facial skin texture irregularities and dyspigmentation in Chinese skin. Patients tolerated the treatment well with adverse effects limited to transient erythema and edema. Lasers Surg. Med. 51:8–13, 2019. © 2018 Wiley Periodicals, Inc.

Key words: picosecond; Asian; rejuvenation

INTRODUCTION

Chronic exposure to ultraviolet radiation results in visible signs of photoaging including dyspigmentation, textural irregularities, sallow complexion, rhytides, and skin laxity. A broad range of energy modalities has been applied to target these photoaging concerns. Treating skin of color requires taking into account the unique characteristics of pigmented skin and its response to laser energy.

Darker skin types have a higher melanin content due to the presence of larger melanocytes and unique melanosome aggregation and reactivity patterns.[1–3] This higher melanin content confers greater protection against ultraviolet damage[2] and delays the onset of rhytides and fine lines, but manifests as pigmentary aberrations with age.[4,5] Similarly, the increased melanin content may interfere with laser wavelengths due to its broad absorption spectra and serve as heat sinks that both decrease therapeutic efficacy and promote adverse sequela through nonspecific thermal injury.

Picosecond lasers represent a significant advancement from their nanosecond (quality switched, QS) predecessors. The 755 nm picosecond alexandrite laser (Picosure™, Cynosure, Boston, MA) was the first device in this class that was approved by the United States Food and Drug Administration (FDA) in 2012 for the treatment of tattoos and pigmented lesions. This technology confers several theoretical advantages over traditional laser modalities. By delivering short pulses of energy in the range of 500–

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

*Correspondence to: Henry H. Chan MD, PhD, FRCP, Hong Kong Dermatology and Laser Center, 11/F Silver Fortune Plaza, 1 Wellington Street, Central, Hong Kong SAR, China.
E-mail: hhlchan@hkucc.hku.hk

Accepted 31 July 2018
Published online 28 August 2018 in Wiley Online Library (wileyonlinelibrary.com).
DOI 10.1002/lsm.23014

750 picoseconds, it creates a greater degree of photomechanical damage and reduces the degree of non-specific photothermal effects thereby enhancing the specificity of energy delivered to target molecules. When used in conjunction with the diffractive lens hand piece, it offers the added benefits of fractionation. In this setting, a unique mechanism of tissue injury induces optical breakdown in the epidermis and papillary dermis, which may confer superior healing characteristics.[6]

The diffractive lens array (DLA) is comprised of densely packed hexagonal microlenses that function to redistribute the laser beam into peaks of high fluence surrounded by a low fluence background. The hexagonal lenses are spaced 500 μm apart (measured center to center) and are able to focus 70% of the total energy toward only 10% of the total treatment area thereby creating high energy peaks. The remaining 30% of energy is distributed to 90% of the remaining surface area creating a low fluence background. As a result, the device delivers a fixed fluence to spot size where the average fluence is inversely proportional to spot size. This laser system has previously been reported to be effective for rejuvenation of the décolletage,[7] acne scarring,[8] peri-ocular rhytides,[9] infraorbital pigmentation,[10] hyperpigmentation associated with venous stasis,[11] and pigmented lesions.[12]

The picosecond alexandrite laser used with the DLA theoretically combines both the advantages of fractionated energy delivery and a picosecond pulse duration thereby making it suitable for treating pigmented skin types. Brauer *et al*. demonstrated in a retrospective review that this device was effective for the treatment of acne scars, pigmented lesions, and stria in Fitzpatrick skin types IV–VI.[13] Wu *et al*. demonstrated that a single treatment with picosecond neodymium-doped yttrium aluminum garnet (Nd:YAG) laser was effective for clearing solar lentigines in Fitzpatrick skin types III–IV.[12] This prospective study aims to determine the safety and efficacy of the picosecond alexandrite laser with the DLA in treating common signs of photoaging including skin texture irregularity, dyspigmentation, enlarged pore size, rhytides, and skin laxity in Chinese skin.

MATERIALS AND METHODS

Study Design

Ethics approval for this protocol was granted from the Western Institutional Review Board® (WIRB®, Washington). This prospective, evaluator-blinded clinical trial investigated the efficacy and safety of picosecond 755 nm alexandrite laser (Picosure®, Cynosure, Westford, MA) with a diffractive Focus Lens Array (DLA) for addressing photoaging concerns in Asian skin. Healthy Chinese male and female subjects between 35 and 60 years of age with baseline presence of mild to moderate photodamage were recruited to the study. Exclusion criteria included active dermatological disease on the face, history of poor wound healing, and keloidal scar formation, pregnancy or lactation, presence of baseline tan, and the use of topical or oral retinoids in the 8 months prior to trial commencement. Patients with documented photosensitivity, taking photosensitizing medications, or received previous laser, chemical peel or filler treatments in the past 6 months were also excluded.

Intervention

Each patient received six treatments spaced 4 weeks apart. All treatments were performed by a single non-evaluating investigator. Initially, subjects received treatment settings of a 0.4 Joules/cm^2 (J/cm^2) fluence, 8 mm spot size, 5 Hz pulse rate, and a total of four passes to the entire face. Those who tolerated these treatment parameters were later treated with stronger settings consisting of a 0.71 J/cm^2 fluence, 6 mm spot size, 10 Hz pulse rate, and a total of four passes to the entire face. Topical anesthesia was achieved with 4% lidocaine applied for 30 min prior to each treatment. No forced air cooling was necessary during the procedure. Patients received a cooling pad and a petrolatum-based ointment immediately following each treatment.

Investigator-Evaluated Outcomes

Standardized photography was obtained at baseline and during each follow-up visit using the Canfield VISIA®-CR system (Canfield Scientific, Parsippany, NJ). Photographs were captured with standard lighting, cross-polarization, parallel polarization, and ultraviolet light at right lateral 37°, left lateral 37°, and frontal views.

Primary outcomes included improvement in the five photoaging parameters compared to baseline as well as global aesthetic improvement. Two blinded, non-treating evaluators independently rated skin texture, pigment, pore size, rhytides, and skin laxity on a 10-point Visual Analog Scale (VAS). Global aesthetic improvement was graded as Excellent (75–100% improvement), Good (50–74% improvement), Moderate (25–49% improvement), Slight (> 0–24% improvement), No change, or Worsened. Ratings were performed at baseline and at 1, 2, and 3 month follow-up visits. The composite score was based on an average of the two independent blinded assessments. Scores that had a greater than 20% discrepancy were discarded and reassessed.

Patient-Evaluated Outcomes

Secondary outcomes included subjective measures of pain, heat sensation, and overall patient satisfaction. Subjects rated pain and heat sensation on a 10-point VAS after each treatment, and overall satisfaction on a 10-point VAS at the completion of six treatments.

Statistical Analysis

Statistical analyses were performed using SPSS 25.0 software (SPSS Inc, Chicago, IL). Two-tailed, non-parametric statistical tests were employed. The Friedman test was used to test for differences between baseline and 1, 2, and 3 month follow up scores (multiple groups). Statistical significance was defined as $P < 0.05$. The Wilcoxon signed rank test with Bonferroni correction was used to compare differences between two groups

(baseline compared to 1 month, baseline compared to 2 months, etc.) for each of the aesthetic measures that showed a significant difference between the four assessment time points on the Friedman test. Statistical significance was defined as $P \leq 0.008$.

RESULTS

Twenty patients with Fitzpatrick skin type III–IV were enrolled in the study. Eighteen patients completed all follow-up assessments. Patients were predominantly female (17 female, 1 male) with a mean age of 47.3 (range 35–59). Patient demographics are summarized in Table 1. Initial treatments were performed using treatment parameters of 0.4 J/cm^2 fluence, 5 Hz repetition rate, 8 mm spot size, and four passes. After subjects tolerated the initial treatments, the settings were increased to 0.71 J/cm^2 fluence, 10 Hz repetition rate, 6 mm spot size, and four passes. A total of 107 treatments were performed. Of these, 19.6% (21/107) utilized the lower settings and 81.3% (87/107) the higher. One patient was lost to follow-up and one withdrew participation due to a mild allergic dermatitis unrelated to the laser treatments. The dermatitis responded to 2 weeks of topical corticosteroid application.

Skin Texture, Dyspigmentation, Rhytides, Pore Size, and Skin Laxity

Analyses of VAS scores at follow-up compared to baseline are summarized in Table 2. At 1 month follow-up, there were significant improvements observed in skin texture ($P = 0.003$), dyspigmentation ($P = 0.000$), and rhytides ($P = 0.008$) compared to baseline, but not in pore size and skin laxity. This improvement persisted at the 3 month follow-up for skin texture ($P = 0.002$) and dyspigmentation ($P = 0.000$), but not for rhytides ($P = 0.034$).

At 1 month follow-up, 88.9% of patients had up to a four point improvement in pigmentation and this improvement persisted in the same percentage at 3 months (Fig. 1–3). For skin texture, 61.1% of patients had up to a three point improvement, which also persisted in the same percentage at 3 months (Figs. 4 and 5). Of all parameters analyzed, the greatest degree of improvement was seen in pigmentation as evidenced by 44.4% of patients achieving a 3–4 point improvement at both 1 and 3 month follow ups (Table 3).

Global aesthetic improvement was rated as Moderate to Good for 55.6% of patients at 1 and 3 months (Table 3). The mean patient satisfaction score was 7.5 out of 10 at 3 month follow-up (Table 4).

TABLE 1. Patient Demographics

Total patients	18
Gender	
F	17 (94.4%)
M	1 (5.6%)
Mean age (SD, min–max)	47.3 ± 6.81 (35, 59)
Skin phototype (I–VI)	
III	2 (11.1%)
IV	16 (88.9%)
Glogauaging skin classification	
I = mild	0
II = moderate	11 (61.1%)
III = advanced	7 (38.9%)
IV = severe	0
Total treatments	107
Pulses per treatment	1450 ± 462.58 (745, 2,613)
Anticipated effects	
Erythema	102/107 (95.3%)
Edema	2/107 (1.9%)

TABLE 2. Investigator-Evaluated Outcomes

Objective improvement Score (VAS)[a]	*P*-value[b]
Skin texture	
Baseline vs. 1 month follow-up	0.003*
Baseline vs. 3 month follow-up	0.002*
Dyspigmentation	
Baseline vs. 1 month follow-up	0.000*
Baseline vs. 3 month follow-up	0.000*
Pore size	
Baseline vs. 1 month follow-up	0.010
Baseline vs. 3 month follow-up	0.034
Rhytides	
Baseline vs. 1 month follow-up	0.008*
Baseline vs. 3 month follow-up	0.034
Skin laxity	
Within group analysis**	0.392

[a]10-point visual analog scale, VAS (0 absent, 10 worst).
[b]Wilcoxon signed rank test with Bonferroni correction.
*Statistical significance defined as $P \leq 0.008$.
**No significance difference shown on Friedman test, therefore, no subsequent analysis performed.

Adverse Effects

Adverse events were mild and self-limited. Transient erythema was noted after 95.3% (102/107) of treatments and edema after 1.9% of treatments (2/107), which both resolved within 2–3 hours of treatment. No instances of post-inflammatory hyperpigmentation (PIH) were observed. The mean patient reported pain score was 5.1 ± 2.0 and heat sensation was 3.6 ± 2.1 out of 10 (Table 4).

DISCUSSION

This is the first prospective, evaluator-blinded trial evaluating the safety and efficacy of the 755-nm picosecond laser used with DLA for addressing multiple signs of photoaging in the Chinese population. The results demonstrate that a series of six treatments delivered at 4 week intervals was effective for improving skin texture and dyspigmentation. Clinical benefit was detectable as early as 1 month and was sustained at 3 month follow-up. At 1 month and 3 month follow-up, 55.6% of patients were rated to have a Moderate to Good global aesthetic improvement (25–74% improvement from baseline).

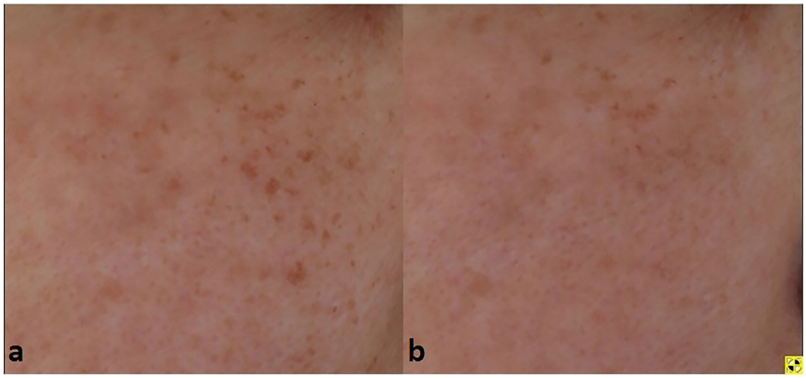

Fig. 1. Ephelides. (**a**) Baseline, (**b**) 3 month after sixth treatment (755 nm, 0.71 J/cm^2, 10 Hz, 6 mm, 4 passes); global assessment: moderate (25–49% improvement).

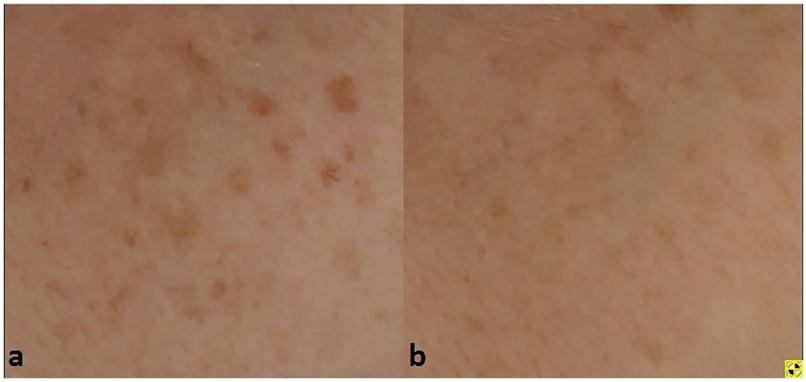

Fig. 2. Ephelides. (**a**) Baseline, (**b**) 3 month after sixth treatment (755 nm, 0.71 J/cm^2, 10 Hz, 6 mm, 4 passes); global assessment: slight (>0–24% improvement).

The first study utilizing the DLA system for treatment of photodamage demonstrated promising results in lighter skin types.[7] Interestingly, an increasing amount of evidence suggests that picosecond laser has an important role to play in the treatment of skin of color due to the potentially increased safety profile over other longer-pulsed lasers.[10,12,13] The reason for this increased safety profile may be due to a unique mechanism of action. With the DLA system, discrete zones of ionized plasma are generated at focal depths within the epidermis and dermal-

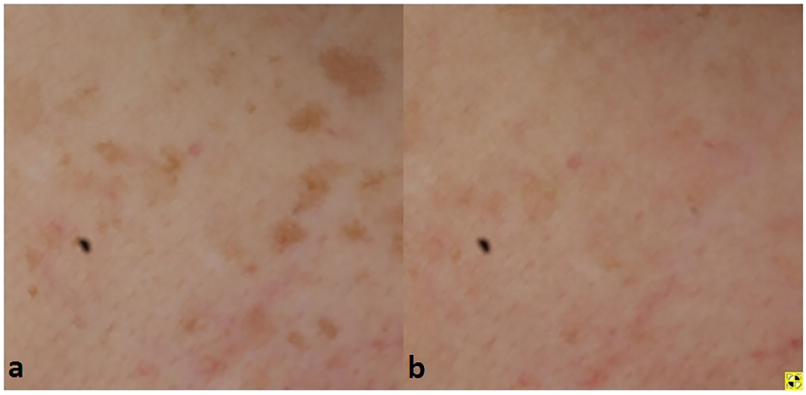

Fig. 3. Ephelides. (**a**) Baseline, (**b**) 3 month after sixth treatment (755 nm, 0.71 J/cm^2, 10 Hz, 6 mm, 4 passes); global assessment: moderate (25–49% improvement).

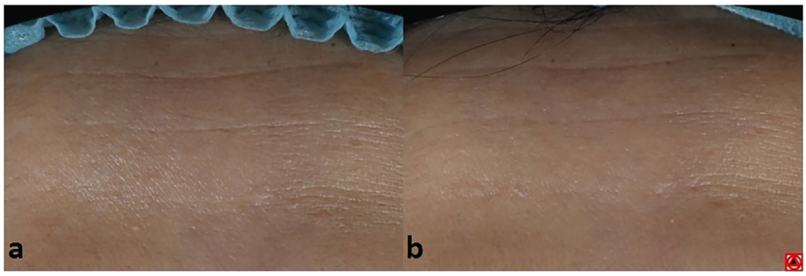

Fig. 4. Rhytides. (**a**) Baseline, (**b**) 3 month after sixth treatment (755 nm, 0.71 J/cm^2, 10 Hz, 6 mm, 4 passes); global assessment: slight (>0–24% improvement).

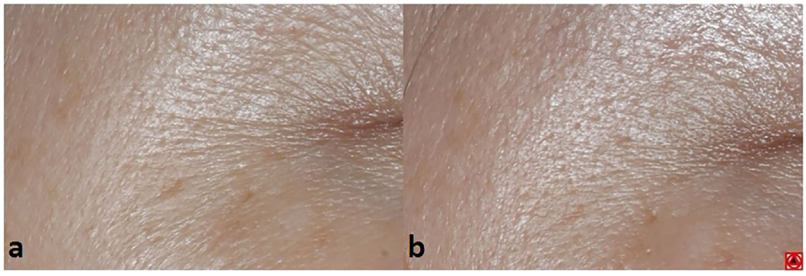

Fig. 5. Rhytides. (**a**) Baseline, (**b**) 3 month after sixth treatment (755 nm, 0.71 J/cm^2, 10 Hz, 6 mm, 4 passes); global assessment: slight (>0–24% improvement).

epidermal junction (DEJ), which resolve into vacuolated structures known as laser induced optical breakdown (LIOB). These vacuoles accumulate tissue debris consisting of hemoglobin and melanin that eventually transeliminate through the epidermis and are shed. Importantly, all surrounding tissue structures appear to be undamaged by this process and a significant neocollagenesis and neoelastinogenesis response is stimulated.[6] This is in contrast to traditional fractional photothermolysis, which creates full thickness columns of thermal damage, thus theoretically leading to a greater degree of disruption at the DEJ. Clinically, this may translate to a decreased risk for PIH in skin of color.[12] Our previous work with the 1,550-nm fractionated erbium doped laser (Fraxel Re:store, Solta Medical, Hayward, CA) in Chinese skin revealed a PIH rate of 6–18%.[14] In this study, there was no incidence of PIH observed suggesting that the safety profile of this system is superior.

Limitations of this study include absence of a control arm, small sample size, and the lack of a validated assessment score. The development of validated assessment scores, larger patient numbers, and the use of a

TABLE 3. Objective Scores in Global Aesthetic Improvement, Skin Texture, and Dyspigmentation

	1 Month	2 Months	3 Months
Global aesthetic improvement*			
Excellent (75–100%)	0	0	0
Good (50–74%)	7 (38.9%)	3 (20.0%)	2 (11.1%)
Moderate (25–49%)	3 (16.7%)	4 (26.7%)	8 (44.4%)
Slight (>0–24%)	6 (33.3%)	6 (40.0%)	6 (33.3%)
No change	2 (11.1%)	2 (13.3%)	2 (11.1%)
Worsen	0	0	0
Physician assessment (0–10 VAS)			
Skin texture			
3-point	2 (11.1%)	1 (6.7%)	0
2-point	3 (16.7%)	3 (20.0%)	4 (22.2%)
1-point	6 (33.3%)	4 (26.7%)	7 (38.9%)
No improvement	7 (38.9%)	7 (46.7%)	7 (38.9%)
Pigment			
4-point	2 (11.1%)	2 (13.3%)	2 (11.1%)
3-point	6 (33.3%)	6 (40.0%)	6 (33.3%)
2-point	6 (33.3%)	3 (20.0%)	3 (16.7%)
1-point	2 (11.1%)	2 (13.3%)	5 (27.8%)
No improvement	2 (11.1%)	2 (13.3%)	2 (11.1%)

*Percentage improvement compared to baseline.

TABLE 4. Patient-Evaluated Outcomes

Patient satisfaction*	
1 month ($n = 18$)	7 (6, 10)
2 month ($n = 16$)	7 (5, 10)
3 month ($n = 18$)	7.5 (6.5, 10)
Mean pain score** (SD, min–max)	5.1 ± 2.0 (0, 9)
Mean heat level** (SD, min–max)	3.6 ± 2.1 (0, 8)

SD, standard deviation.
*Rated on a 0–10 point scale visual analog scale, VAS (0 extremely unsatisfied, 10 extremely satisfied).
**Rated on a 0–10 point visual analog scale, VAS (0 no pain, no heat sensation; 10 severe pain, severe heat sensation).

comparative device or split-face trials are required to provide stronger clinical recommendations.

CONCLUSION

In conclusion, the 755-nm picosecond alexandrite laser with DLA is an effective and safe option for targeting skin texture irregularities and dyspigmentation in Chinese patients. A series of six treatments at 4 week intervals may be required. Most notably, this approach may be desirable for patients where the risk of PIH is significant or poorly tolerated.

REFERENCES

1. Szabo G, Gerald AB, Pathak MA, Fitzpatrick TB. Racial differences in the fate of melanosomes in human epidermis. Nature 1969;222(5198):1081–1082.
2. Tadokoro T, Kobayashi N, Zmudzka BZ, et al. UV-induced DNA damage and melanin content in human skin differing in racial/ethnic origin. FASEB J 2003;17(9):1177–1179.
3. Taylor SC. Skin of color: biology, structure, function, and implications for dermatologic disease. J Am Acad Dermatol 2002;46(2 Suppl Understanding):S41–S62.
4. Nouveau-Richard S, Yang Z, Mac-Mary S, et al. Skin ageing: a comparison between Chinese and European populations. A pilot study. J Dermatol Sci 2005;40(3):187–193.
5. Tsukahara K, Fujimura T, Yoshida Y, et al. Comparison of age-related changes in wrinkling and sagging of the skin in Caucasian females and in Japanese females. J Cosmet Sci 2004;55(4):351–371.
6. Tanghetti EA. The histology of skin treated with a picosecond alexandrite laser and a fractional lens array. Lasers Surg Med 2016;48(7):646–652.
7. Wu DC, Fletcher L, Guiha I, Goldman MP. Evaluation of the safety and efficacy of the picosecond alexandrite laser with specialized lens array for treatment of the photoaging decolletage. Lasers Surg Med 2016;48(2):188–192.
8. Brauer JA, Kazlouskaya V, Alabdulrazzaq H, et al. Use of a picosecond pulse duration laser with specialized optic for treatment of facial acne scarring. JAMA Dermatol 2015; 151(3):278–284.
9. Weiss RA, McDaniel DH, Weiss MA, Mahoney AM, Beasley KL, Halvorson CR. Safety and efficacy of a novel diffractive lens array using a picosecond 755nm alexandrite laser for treatment of wrinkles. Lasers Surg Med 2017;49(1):40–44.
10. Vanaman Wilson MJ, Alkhonizi S, Wu DC. Successful treatment of under-eye pigmentation in skin type IV with a picosecond alexandrite laser with diffractive lens array. Dermatol Surg 2017;43(8):1095–1097.
11. Wu DC, Goldman MP. Successful treatment of chronic venous stasis hyperpigmentation of the lower limbs with the picosecond alexandrite laser. Dermatol Surg 2018;44 (6):881–883.
12. Guss L, Goldman MP, Wu DC. Picosecond 532 nm neodymium-doped yttrium aluminium garnet laser for the treatment of solar lentigines in darker skin types: safety and efficacy. Dermatol Surg 2017;43(3):456–459.
13. Haimovic A, Brauer JA, Cindy Bae YS, Geronemus RG. Safety of a picosecond laser with diffractive lens array (DLA) in the treatment of Fitzpatrick skin types IV to VI: A retrospective review. J Am Acad Dermatol 2016;74(5): 931–936.
14. Chan NP, Ho SG, Yeung CK, Shek SY, Chan HH. The use of non-ablative fractional resurfacing in Asian acne scar patients. Lasers Surg Med 2010;42(10):710–715.