Evolution of the Picosecond Laser: A Review of Literature

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BACKGROUND Picosecond pulse duration lasers (PS) have altered the field of dermatology. PS were initially used in tattoo removal, to optimize efficacy and reduce side effects with nanosecond domain lasers. More recently, they have been demonstrated to be effective in the treatment of pigmentary disorders, acne scarring, and photoaging.

OBJECTIVE In this article, we critically analyze the published data on the many uses of picosecond lasers in dermatology.

MATERIALS AND METHODS A systematic review of PubMed was conducted using the following search terms: "picosecond," "picosecond laser," "picosecond laser dermatology," "picosecond laser pigment/pigmentation," and "picosecond laser tattoo removal." Articles ranged from 1988 until 2017.

RESULTS Forty-one articles were identified, and 27 met inclusion criteria for review. Indications for the PS included a variety of dermatologic applications include tattoo removal, benign pigmented lesions/pigmentary disorders, acne scarring, and photoaging. Most studies demonstrated safe and effective treatment.

CONCLUSION The development of the picosecond pulse duration is a breakthrough innovation in laser technology, changing the scope of laser treatment. Encouraging findings in tattoo pigment clearance spurred the use of PS in a wider array of dermatologic issues. The increasingly positive results and low incidence of adverse effects further substantiates PS efficacy for a variety of dermatologic uses.

The authors have indicated no significant interest with commercial supporters.

Lasers and light-based technologies first appeared in the early 1960s with studies performed by Goldman and colleagues.[1] Early lasers used for tattoo removal and treating pigmented lesions were the argon and CO_2 lasers.[2] These lasers were not selective and produced considerable side effects.[3] A paradigm shift in laser therapy occurred in the 1980s with the description of selective photothermolysis by Drs. Anderson and Parrish. The theory of selective photothermolysis allows for targeting specific chromophores by selecting an appropriate wavelength. As a result, there is target destruction, and collateral damage is minimized by choosing a pulse duration that is less than or equal to the target's thermal relaxation time (TRT).[7,8] Until recently, quality-switched (Q-switched) nanosecond lasers have been the workhorse lasers in the field of tattoo removal and treating pigmented lesions. They utilize the concept of selective photothermolysis to target tattoo pigments while also having a photoacoustic/photomechanical effect to aid in breaking up the targeted pigment particles. Relative to other chromophores, tattoo pigments have a very short TRT of 10 nanoseconds.[4–6] Therefore, delivering the energy within even shorter pulse durations, measured in picoseconds, may enhance the efficacy of lasers in tattoo removal.

In the late 1990s, picosecond lasers finally became clinically available, helping to test this key concept. Ho and colleagues evaluated the efficacy of picosecond lasers initially through computer simulations, using a

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1,064-nm wavelength and graphite as the standard pigment particle.[10] These simulations revealed that it is primarily a photomechanical effect, rather than photothermal, that leads to the successful elimination of pigment tattoo particles. The rapid rise in temperature leads to a pressure wave that exceeds the tensile strength of the pigment particles, causing it to shatter into smaller fragments. Ho and colleagues found an optimal pulse duration range of 10–100 picoseconds, which allows for effective pigment destruction and clearance with little collateral heating or damage.[10]

The development of the picosecond laser has advanced the field of tattoo removal. A majority of studies comparing picosecond and nanosecond lasers have shown greater effectiveness in tattoo pigment clearance with no increase in adverse effects from picosecond lasers.[12,13] However, the small observed difference between the 2 lasers in tattoo removal needs further evaluation to substantiate these initial findings. Since 2012, picosecond lasers have been FDA approved for laser tattoo removal and treatment of benign pigmented lesions.[2,5] However, the applications of picosecond lasers continue to expand beyond exogenous and endogenous pigment removal to acne scarring, photoaging, rhytides, and more. Promising results have been shown in a wide array of data, albeit many small, single-center studies. The following literature review and critical analysis reviews the current data available for picosecond lasers to further elucidate its role in dermatology.

Methods

A review of all the published literature on picosecond laser use in dermatology through PubMed was performed up until March 2017. The following terms were searched: "picosecond" combined with "laser," "dermatology," "pigment/pigmentation," and "laser tattoo removal." Inclusion criteria were (1) article is a case study, review of literature, case report, or commentary and (2) the use of picosecond lasers was discussed in the article. Exclusion criteria were nonhuman (2 articles), non-English language, and articles that did not discuss picosecond laser removal (Figure 1).

Results

The PubMed search for "picosecond" yielded 5,078 articles. A more focused set of articles was found when using the following more specific search terms: "picosecond laser" (1982), "picosecond laser skin" (49), "picosecond laser pigment" (17), "picosecond laser dermatology" (38), "picosecond laser tattoo"

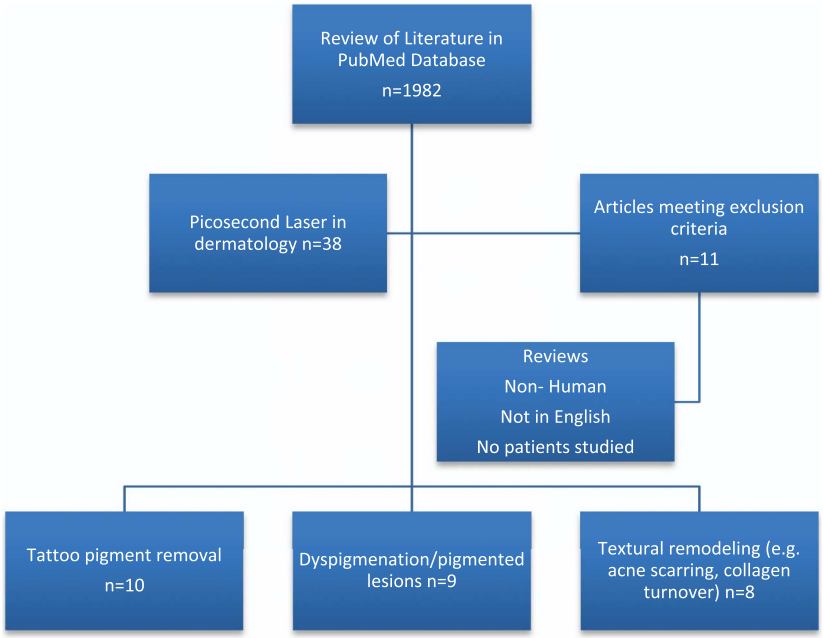

Figure 1. Search strategy.

TABLE 1. Clinical Studies of Picosecond Laser for Tattoo Removal, Pigmented Lesions, and Novel Dermatologic Uses

Use	*Author(s)*	*Year*	*Design*	*No. and Type of Subject*	*Target or Chromophore*	*Clinical End Points*	*Adverse Effects*	*Treatment Settings*	*Industry Sponsored (Y/N)*
Tattoo removal	Ross et al[11]	1998	Intratattoo comparison study	16 pts	11 multicolored tattoos (black, red, and green); 5 black only	12/16 tattoos with PS showed significantly more lightening than NS	Pinpoint bleeding, edema, hypopigmentation, and scarring in NS	PS pulse duration; or an Nd:YAG QS laser, spot size 1.4 mm, and a 3.5-mm settings: fluence 0.65 J/cm^2, spot size 1.4 mm, and a 10-NS pulse duration, fluence 0.65 J/cm^2, 4 treatment sessions	N
	Brauer et al[14]	2012	Case series	10 pts	Blue and green tattoo pigment	11/12 tattoos 75% clearance at 1-month follow-up after 1 treatment; 12th tattoo required 2 treatments	Pain (mean pain score for treatment: 1.08 on 10-point scale)	755-nm laser, pulse duration of 750–900 PS, repetition 5 Hz, spot sizes 3.0–3.6 mm, fluence from 2.0 to 2.83 J/cm.^{2}	Y
	Saedi et al[15]	2012	Prospective trial	15 pts	Black and blue tattoo pigment	12/15 patients had greater than 75% clearance 1–2 treatments; 3 had 75% in 3–4 treatments.	Pain (mean pain score 4.5/10), swelling, postinflammatory hypopigmentation 3/15, postinflammatory hyperpigmentation 2/15, blistering	755-nm laser, pulse duration of 500–900 picoseconds, spot size 2.5–3.5 mm, and a pulse, fluence 2.1–4.1 J/cm^2	Y
	Alabbdulrazzaq et al[17]	2015	Case series	6 pts	Multicolored tattoos that contain yellow pigment	1 subject complete clearance in 1 treatment; 5 subjects 2–4 treatments to achieve 75% clearance	Pain (mean pain score 1.3/10), edema, erythema, pain, blisters (3/6), and transient hypopigmentation (1/6)	Frequency-doubled 532-nm Nd:YAG PS, pulse duration of 450–500 picoseconds settings were spot size of 2.5–3.3 mm and fluences 1.1–1.4 J/cm^2	N
	Au et al[21]	2015	Randomized controlled trial	26 pts	Blue-black tattoos	81 patients treated with picosecond plus AFR did not experience blistering vs 26 PS alone (statistically significant)	81/95 patients blistered after PS alone; 6/81 did not blister after PS plus AFR	Alexandrite PS laser with spot size 2.94–3.31, fluence of 2.67–3.37 J/cm^2, or combination of PS laser–fractionated CO_2 laser setting of fractional CO_2 was 10–60 mJ, coverage of 15% to 40%.	Y
	Bernstein et al[18]	2015	Prospective clinical study	21 pts	Black (31), green (8), red (6), blue (2), purple (2), and yellow (2) tattoos	Overall average clearance 79% in average 6.5 treatments	Edema, erythema; rarely transient pigment alteration	1,064 nm with a pulse duration of 450 PS, and 532-nm pulse duration of 350 ps. Spot size 2–10 mm fluences of up to 11 J/cm^2 (1,064 nm) to 5.5 J/cm^2 for (532 nm)	Y
	Pinto et al[20]	2016	Randomized single-blinded clinical trial	21 pts with 30 black tattoos	Comparison of efficacy and safety between PS and NS lasers for tattoo removal	After 2 sessions, no clinical difference between PS and NS (both >25% improvement). However, statistically significant decrease in painfulness on visual analog scale: 3.8 for PS and 7.9 NS	No statistically significant difference in adverse side effects seen: hypopigmentation/hyperpigmentation, bleeding, or bullae formation. No scars were formed in PS-treated side.	PS pulse duration; ND:YAG or Nd:YAG QS laser, spot size 3–8 mm (QS) and 2–10 mm (PS), fluence 2–12 J/cm^2 (QS) and 2–12.5 J/cm^2 (PS), NS pulse duration 5 NS (NS) and 450 PS (PS)	N
	Lee et al[16]	2016	Case report	6 pts	Black- or red-colored tattoos	75% improvement after 1 to 5 treatments	Persistent hypopigmentation in 50% (3/6) of patients at 3-month follow-up	755-nm laser, pulse duration of 550–750 picosecond, fluence of 2.68–5.25 J/cm^2, and spot size of 2~3 mm, repetition rate 5 Hz	N
	Friedman[19]	2016	Case report	1 pt	Effect of picosecond laser on multicolored tattoo	75% and 90% improvement in the black and red areas, respectively, after 3 treatments	No adverse side effects were noted	1,064-nm domain: fluence of 0.5–0.6 J/cm^2; repetition 3 Hz; spot size of 10 mm. Red tattoo 532 nm with a fluence mean of 0.25–0.3 J/cm^2, repetition 1 Hz, and spot size of 9–10 mm.	N

TABLE 1. (Continued)

Use	Author(s)	Year	Design	No. and Type of Subject	Target or Chromophore	Clinical End Points	Adverse Effects	Treatment Settings	Industry Sponsored (Y/N)
Management of dermal pigment	Chestnut et al[22]	2015	Case series	3 pts	Nevus of Ota	All showed significant lightening and cosmetic improvement. No repigmentation at 2- to 7-month follow-up	Mild transient erythema and edema resolved in 2 days	Picosecond pulse duration of 450–500 picoseconds, fluences of 2.08–2.83 J/cm^2, spot size of 3–4 mm	N
	Rodrigues and Bekhor[27]	2015	Case series	3 pts	Minocycline-induced pigmentation	Clearance of pigment within 1 session for 2 patients and third patient has significant lightening after 2 treatments	Transient erythema at treatment site	755-nm alexandrite picosecond laser fluence of 2.8–3.0 J/cm^2 and spot size of 3 mm	N
	Wu et al[31]	2015	Prospective clinical study	20 pts	Photoaging of décolletage	At 1 and 3 months, significant improvements in dyspigmentation, keratosis, and texture noted	Transient erythema and pain was 3.7 on 10-point visual analog scale	755-nm alexandrite PS laser with fluence of 0.71 J/cm,^{2} spot size of 6 mm, repetition rate of 10 Hz for 4 treatment sessions	N
	Chan et al[23]	2016	Prospective clinical study	15 pts	Pigmented lesions in Asian patient population	6/13 (46%) of Asian patients had 50% improvement in pigmentation in benign pigmented lesions maintained 6 months after treatment	Transient erythema and hypopigmentation, pain, and swelling. No evidence of postinflammatory hyperpigmentation noted.	N/A	N
	Moore et al[28]	2016	Case report	1 pt	Minocycline-induced postsclerotherapy pigmentation	Complete clearance of pigment in 2 treatments	No adverse effects were noted	755-nm PS alexandrite laser fluence; 2 J/cm^2, repetition rate 2 Hz, spot size 4 mm	Y
	Bae et al[25]	2016	Case series	2 pts	Paradoxical darkening after Q-switched laser tattoo removal	Black paradoxical pigmentation and red tattoo pigment were significantly improved at 1 month (1–2 treatments)	No adverse effects were noted	QS frequency-doubled Nd:YAG setting 3 J/cm^2 fluence, spot size 3.4 mm, and other half picosecond frequency-doubled Nd:YAG laser fluences 0.3–1.2 J/cm^2 and spot sizes 2.5–4 mm	N
	DiGiorgio et al[29]	2016	Case report	1 pt	Argyria	Significant improvement in pigmentation at 1 week with near 100% return to baseline pigmentation	Transient edema for 3–4 days was noted, but no blistering or scarring	755-nm PS alexandrite laser fluence. 1.59–2.08 J/cm^2, spot size 3.5 and 4 mm	N
	Levin et al[39]	2016	Retrospective chart and photographic review	42 pt (17 pts treated with pico-second laser)	Safety and efficacy of picosecond lasers for pigmentary disorders in skin of color	Visual analog score of 2.44 (approx. 50% clearance) for picosecond-treated pigmentary disorders at follow-up	For picosecond lasers, there was transient erythema, pain, dyspigmentation, and hypopigmentation. Several nanosecond lasers had permanent dyspigmentation	N/A	N
	Oshiro et al[24]	2016	Retrospective chart and photographic review	10 pts	Pigmented lesions in Asian patient population (6 nevus of Ota, 4 Mongolian spots)	All patients achieved 25%–94% clinical improvement.	Transient hyperpigmentation was noticed in patients treated with PS 755 nm and severe transient erythema/edema but no hyperpigmentation with PS 1,064-nm Nd:YAG	N/A	N
	Vanaman-Wilson et al[30]	2017	Case report	1 pt with infraor-bital discolora-tion in skin type IV	Use of picosecond lasers with DLA in skin of color for pigment disorder around the eye	Near-complete clearance after one session at 3-month follow-up	Patient tolerated the procedure well. No dyspigmentation or scarring noted at follow-up.	755-nm alexandrite with DLA pulse duration 550 PS, fluence 0.57 J/cm^2 repetition rate 1 Hz, spot size 6 mm,	N
	Guss et al[26]	2017	Retrospective chart and photographic review	6 pts with solar lentigines (255 lesions) in skin type IV	Use of picosecond lasers for solar lentigines in skin of color	5/6 patients had greater than 50% improvement in only one session. Majority of lesions (78%) with >75% improvement.	Only 2 lesions with dyspigmentation but rest no dyspigmentation or scarring noted at follow-up.	532-nm Nd:YAG PS laser fluence 0.65 J/cm^2, spot size 4.50 mm, and repetition rate 1.67 Hz	N

TABLE 1. (Continued)

Use	Author(s)	Year	Design	No. and Type of Subject	Target or Chromophore	Clinical End Points	Adverse Effects	Treatment Settings	Industry Sponsored (Y/N)
Novel Applications (Acne scarring, photoaging)	Brauer et al[32]	2015	Prospective clinical study	20 pts	Acne scarring	Meanmasked assessment scores at 1 and 3 months were 1.5, 1.4, respectively (0 = 0–25%, 3 = 75%). Mean improvement in scar vol. 24.3%	Mean pain score was 2.83/10. Only transient erythema and edema.	755-nm PS alexandrite laser: pulse duration of 750 PS, fluence 0.71 J/cm^2, spot size of 6 mm, and repetition rate 5 Hz	Y
	Haimovic et al[34]	2016	Retrospective chart review	56 pts skin type IV-VI	Safety of picosecond lasers with DLA in skin of color for scars, pigment disorders, and striae	Clinical satisfaction was not evaluated. 46 patients treated with picosecond lasers with DLA developed transient erythema (n = 7), hyperpigmentation (n = 6), edema (n = 3), and scabbing (n = 1)	Transient erythema, edema, scabbing, and hyperpigmentation. Hyperpigmentation in 3 patients lasted up to 3 months (all treated lesions on lower extremities)	755-nm PS alexandrite laser with DLA: pulse duration of 750–850 PS, fluence of 0.71 J/cm^2, and spot size of 6 mm.	N
	Ge et al[35]	2016	Prospective clinical study	10 pts	Use of picosecond lasers with DLA in skin of color for acne scarring and photoaging	Blinded review showed improvement in GPS 2.67–1.44 and APS 2.78–1.89	Patient tolerated moderate treatment pain. No dyspigmentation or scarring noted on follow-up	755-nm PS alexandrite laser with DLA: pulse duration of 750–850 PS, fluence of 0.4–0.71 J/cm^2, and spot size of 6–8 mm, and repetition rate 2.5–5 Hz	N
	Tanghetti[33]	2016	Prospective clinical study	11 pts	The effect of PS lasers with DLA on the skin histology	Laser energy created intraepidermal cavities that stimulate epidermal repair mechanisms	Transient side effects of petechiae without permanent scarring	755-nm PS alexandrite laser with DLA: fluence of 0.25–0.71 J/cm^2, and spot size of 6–10 mm.	Y
	Khetarpal et al[36]	2016	Prospective clinical study	20 pts	Use of picosecond lasers with DLA for photoaging with compressed treatment interval	Blinded review showed 93% in overall improvement. Patient improvement was rated with a validated scoring system: rated 1.5 at 1 month and 1.4 at 3 months (0 = 0%–25% and 3 = >75% improvement).	Side effects were minimal with the most common being transient erythema, swelling, and pain. No scarring or permanent hyperpigmentation/ hypopigmentation was noted.	755-nm PS alexandrite laser with DLA: pulse duration of 750 PS, fluence of 0.71 J/cm^2, and spot size of 6 mm, and repetition rate 10 Hz	Y
	Saluja[38]	2016	Prospective clinical study	20 pts	Safety and efficacy of picosecond lasers for skin tightening and textural improvement of off the face application	Improvement in A–A average was 1.05 and 1.40 at 1.3 months (baseline 3.10). Physician 50% extremely satisfied and satisfied at 3 months for décolletage and 70% satisfied for hand at 3 months	No adverse events were noted in the study population	755-nm PS alexandrite laser with DLA: fluence of 0.71 J/cm^2, and spot size of 6 mm, and repetition rate 10 Hz, 4 treatments	Y
	Weiss et al[37]	2017	Prospective clinical study	40 pts	Use of picosecond lasers with DLA for treatment of rhytides	Improvement in wrinkle scale average of 1.97 (pre- vs post-treatment). Physicians and patients were extremely satisfied at 6 months 97.4% and 42.1%, respectively	All adverse effects were transient (erythema and edema). No permanent adverse effects.	755-nm PS alexandrite laser with DLA: pulse duration of 750 PS, fluence of 0.71 J/cm^2, and spot size of 6 mm, and repetition rate 10 Hz, 4 treatments	Y

A–A, Alexiades–Armenakas Scale; AFR, ablative fractional resurfacing (CO_2 laser); APS, Asian pigmentation scale; DLA, diffractive lens array; GPS, global photoaging scale; N, No; N/A, not applicable; NS, nanosecond laser; PS, picosecond laser; Pt, Patient; Y, Yes.

(25), and "picosecond laser pigmentation" (17). Twenty-seven articles met the inclusion criteria and were reviewed (Table 1). The laser treatment parameters and goals can be divided into the following categories: tattoo removal, pigmentation, and novel applications (Table 1).[11–29]

Tattoo Removal

Ross and colleagues performed the first comparative intratattoo study in human subjects. Each tattoo segment was treated using either an Nd:YAG Q-switched laser (Model YG501; Quantel Technologies, Santa Clara, CA) at settings of 0.65 J/cm^2, spot size 1.4 mm, and a 35-picosecond pulsed duration; or an Nd:YAG Q-switched laser (Model NY82–10; Continuum, Santa Clara, CA) at the following settings: fluence of 0.65 J/cm^2, spot size 1.4 mm, and a 10-nanosecond pulsed duration. In 12 of 16 tattoos, the picosecond laser treatment site, in comparison with the nanosecond laser, showed significant lightening on blinded evaluation after 4 treatments.[15] There are several noncomparative studies demonstrating the efficacy of picosecond lasers in the treatment of darker tattoo pigments. Bauer and colleagues reported a case series of 10 patients with 12 blue and/or green tattoos that were treated with a 755-nm alexandrite picosecond laser (PicoSure; Cynosure, Inc., Westford, MA). Eleven of the 12 patients had greater than 75% clearance with either 1 or 2 treatments at one-month follow-up.[14] Saedi and colleagues evaluated the efficacy and safety of a picosecond 755-nm alexandrite laser (PicoSure; Cynosure, Inc) to treat blue and/or black tattoos. Twelve patients were treated at the following settings: fluences of 2.1 to 4.1 J/cm^2, spot size between 2.5 and 3.5 mm, and a pulse duration of 500 to 900 picoseconds. There was greater than 75% clearance in the tattoos with an average of 4.25 treatments. All side effects from the treatment were mild and transient in nature.[15] A similar study, involving 6 Korean patients (skin type IV), used the same device to treat black and red tattoos. After 1 to 5 treatments, all patients had greater than 75% improvement. However, 50% of patients had post-treatment hypopigmentation.[16]

A recent randomized, single-blinded, split-tattoo comparative study between 1,064-nm nanosecond (MedLite C6; Hoya-ConBio, Inc., Fremont, CA) and picosecond lasers (PicoWay; Syneron Candela, Corp., Wyland, MA) was performed by Pinto and colleagues, involving 21 patients with 30 black tattoos of various ages. After 2 treatments, spaced 6 weeks apart, there was a 36% and 37% improvement seen with the picosecond and nanosecond laser, respectively. This difference did not reach statistical significance. However, there was a significant decrease in pain in the picosecond-treated sites.[20]

Success in treatment of green, blue, and black tattoos spurred evaluation of a 532-nm picosecond laser to remove more difficult pigments, including red and yellow. In a small study, 6 patients with red and yellow tattoos were treated with the frequency-doubled 532-nm Nd:YAG picosecond laser. The settings used were fluences between 1.1 and 1.4 J/cm^2, spot size of 2.5 to 3.3 mm, and pulse duration of 450 to 500 picoseconds at every 6 to 8 weeks (4 treatment sessions). The results showed that patients reached 75% clearance in 2 to 4 treatments.[17] In a larger study, 21 patients with multicolored tattoos were treated with an Nd:YAG picosecond domain laser (PicoWay; Syneron Candela, Corp). Thirty-one tattoos were treated. Black, blue, green, and purple ink were treated with the 1,064-nm laser, whereas red and yellow pigments were treated with the 532-nm laser. Blinded-scaled evaluation showed an average 79% clearance score after 6.5 treatments. Tattoo pigment clearance varied by color, with black and purple showing the most improvement.[18]

There is a paucity of data about the use of 532-nm picosecond lasers for tattoo removal in skin of color due to higher risk of melanin absorption at that wavelength. Friedman evaluated the use of an Nd:YAG picosecond laser (PicoWay; Syneron Candela, Corp) in a black and red tattoo on a single patient with skin type VI. The black tattoo was treated in the 1,064-nm domain with the following parameters: fluence mean of 0.5 to 0.6 J/cm^2; repetition 3 Hz; and spot size of 10 mm. The red tattoo areas were treated with the 532 nm with a fluence mean of 0.25 to 0.3 J/cm^2, repetition 1 Hz, and spot size of 9 to 10 mm. After 3 treatments, at 3-week intervals,

improvements of 75% and 90% clearance were noted for the black and red tattoo pigments, respectively. Side effects were minimal and transient, including mild erythema and edema.[19]

Finally, a retrospective review on adjuvant ablative fractional resurfacing use to decrease the occurrence of bullae after picosecond laser tattoo removal was performed. Patients were treated with either the picosecond alexandrite laser alone with fluence of 2.67 to 3.37 J/cm^2 and spot size 2.94 to 3.31 (n = 81) or the combination of picosecond laser with fractionated CO_2 laser (n = 21) setting of fractional CO_2 were 10 to 60 mJ, with a coverage of 15% to 40%. Bullae occurred in 26/81 patients (32%) treated with picosecond alone, whereas no bullae developed in any member of the combination group.[21]

Management of Epidermal and Dermal Pigment

After tattoo removal, treating endogenous pigmentation is the second most studied application of picosecond lasers in dermatology. Six studies have been published thus far, the first of which evaluated the use of a 755-nm picosecond for the clearance of a nevus of Ota in a small case series (n = 3) in 2015. Treatment parameters included fluences of 2.08 to 2.83 J/cm^2, spot size of 3 to 4 mm, and pulse duration of 450 to 500 picoseconds. All patients achieved significant lightening and were satisfied with the results in 2 to 3 treatments. No repigmentation was noted on follow-up (2–7 months).[22]

Only 2 studies have investigated the use of picosecond lasers in the treatment of photoaging and pigmented lesions in an Asian population. Chan and colleagues retrospectively analyzed 13 patients treated with a 755-nm picosecond laser (PicoSure; Cynosure, Inc). The following lesions were treated: nevus spilus (n = 1), nevus of Ota (n = 4), the Horii macules, café-au-lait patches (n = 5), lentigines (n = 1), and the Becker nevus (n = 1). Six of 13 patients had at least 50% improvement in pigmentation in 1 to 8 treatments. Adverse effects included transient erythema, post-treatment crust formation, pain, and swelling, with no hyperpigmentation or recurrence appreciated at 6-month follow-up.[23]

A similar study by Oshiro and Sasaki evaluated picosecond lasers for the treatment of nevi of Ota (n = 6) and Mongolian spots (n = 4). Seven patients were treated with a 755-nm alexandrite picosecond laser (PicoSure; Cynosure, Inc), whereas 3 patients were treated with a1064-nm Nd:YAG picosecond laser (Enlighten; Cutera, Brisbane CA and PicoWay; Syneron Candela, Corp). After 3 treatment sessions at varying intervals in all patients, the 1,064-nm laser achieved a 50% to 94% improvement in 3 lesions and the 755-nm laser achieved mostly 50% to 94% improvement at 3-month follow-up. Transient hyperpigmentation occurred in the 755-nm group, and transient erythema/edema without pigment alteration in the 1,064-nm laser group.[24]

The use of picosecond lasers in the skin of color for treatment of pigmentation disorders was undertaken by 2 retrospective reviews. Guss and colleagues analyzed 6 patients with 255 solar lentigines who underwent a single treatment with the 532-nm Nd:YAG picosecond laser (PicoWay; Syneron Candela, Corp). Treatment parameters were as follows: mean fluence of 0.65 J/cm^2, pulse duration of 375 picoseconds, spot size to 4.50 mm, and a repetition rate of 1.67 Hz. At follow-up, 201/255 (78.82%) showed greater than 75% improvement. Only 2 lesions had subsequent lasting hyperpigmentation.[26] In the second review, Levin and colleagues compared the safety and efficacy of the Q-switched ruby and Nd:YAG lasers (n = 25) with that of the 755-nm alexandrite picosecond lasers (n = 17) for pigmentary disorders in skin of color, namely nevus of Ota and solar lentigines. Eight patients with facial pigmentary lesions treated with the picosecond laser achieved a score of 2.44 (50% clearance) on a visual analog scale. Fifty percent of patients (n = 10) were satisfied to completely satisfy with the picosecond laser treatment results. All adverse effects with the picosecond laser were transient.[39]

Several additional studies investigated the use of picosecond lasers in less common pigmentary disorders. A small case series (n = 3) compared the 755-nm alexandrite picosecond laser (fluence range of 2.8–3.0 J/cm^2 and spot size of 3 mm) and the Q-switched Nd:YAG nanosecond laser in the treatment

of minocycline-induced pigmentation. Two patients achieved complete clearance with a single picosecond laser treatment, and the third required only 2 treatments.[27] Similarly, a case of minocycline-induced postsclerotherapy pigmentation was treated with the 755-nm alexandrite picosecond laser (PicoSure; Cynosure, Inc). Two treatments, with a fluence of 0.71 J/cm^2 and spot size of 6 mm, resulted in complete pigment clearance.[28] In addition, 2 patients with paradoxically darkening of red tattoos after previous laser tattoo removal were treated with a 532-nm and 1,064-nm Nd:YAG picosecond laser (Cynosure, Inc). Both black paradoxical darkening and red tattoo pigment were significantly improved at 1-month follow-up.[25] The picosecond laser also demonstrated success in the management of recalcitrant argyria. The patient had significant improvement immediately after treatment and near 100% return to baseline at 1 week.[29] Finally, the use of picosecond lasers for the novel application of treating under eye hyperpigmentation in a patient with skin type IV was recently published. The patient underwent 2 to 4 passes in one treatment session with the 755-nm alexandrite picosecond laser (PicoSure; Cynosure, Inc) with diffractive lens array (DLA) (Figure 2). This handpiece delivers highly concentrated energy beams within the treatment window, at regular spaced density. A majority of the treated area are exposed to low fluence energy where up to 10% of the treated area receives higher fluence levels.[34] This is similar to density of microthermal zones of fractional nonablative resurfacing. At 3-month follow-up, the patient had near-complete clearance of the infraorbital discoloration with no dyspigmentation or scarring.[30]

Novel Applications of Picosecond Lasers

The more recently investigated and sought after applications of the picosecond lasers include the treatment of photoaging and scarring. Studies involving photoaging have shown benefit beyond dyspigmentation, both on and off the face. The first study was a prospective open-label trial of 20 subjects evaluating a picosecond laser in the treatment of photoaging in the décolletage. All patients were treated with a 755-nm alexandrite picosecond laser with DLA (PicoSure; Cynosure, Inc) using the following parameters: fluence of 0.71 J/cm^2, spot size of 6 mm, and frequency of 10 Hz for 3,500 pulses. At 1 month, there was significant improvement in most photoaging categories (dyspigmentation, rhytides, texture, and keratosis) except erythema. At 3 months, all categories were still significantly improved from baseline except rhytides after 4 treatment sessions.[31] Ge and colleagues evaluated the use of the 755-nm alexandrite picosecond laser with DLA for improvement of facial photoaging, as well as acne scarring, using a split-face protocol in 10 patients. The blinded evaluation at 2-month follow-up showed an improvement in the Global Photoaging Scale (2.67–1.44) and an improvement in pigmentation (2.78–1.89 on the Asian Pigmentation Scale). Physicians also noted improvement in skin tightening. Only transient erythema,

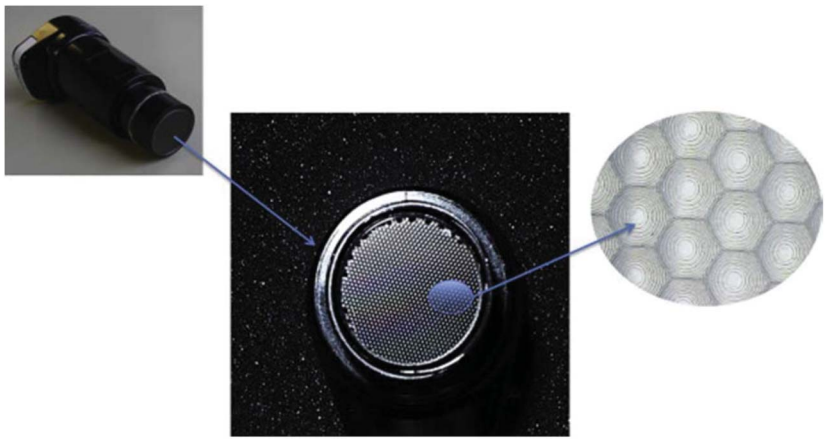

Figure 2. Reprinted with permission from Elsevier from Haimovic A, Brauer JA, Cindy Bae YS, and Geronemus RG. Safety of a picosecond laser with diffractive lens array (DLA) in the treatment of Fitzpatrick skin types IV to VI: A retrospective review. *J Am Acad Dermatol* 2016;74:931–6. Copyright American Academy of Dermatology, Inc. All permission requests for this image should be made to the copyright holder.

edema, and moderate treatment-associated pain were noted as side effects.[35]

One of the original topics investigated beyond pigment removal was the treatment of acne scarring with a picosecond laser using DLA. Analogous to fractionation in other laser devices, the DLA is used on the picosecond laser to provide a focal increase in fluence while maintaining overall reduction in treatment energy density.[29,32,34–36] Notably, Khetarpal and colleagues prospectively demonstrated the safety of a shortened treatment interval (every 2–3 weeks) using the 755-nm picosecond alexandrite laser with DLA for the treatment of photoaging in 20 patients. Patient satisfaction was 81% at the 3-month follow-up and 93% of physicians were extremely satisfied and satisfied. Similar minimal side effects were seen.[36]

Weiss and colleagues investigated the utility of the 755-nm picosecond laser with DLA for the treatment of facial wrinkles, specifically. Forty female subjects were treated with a fluence of 0.71 J/cm^2, spot size of 6 mm with DLA, pulse duration of 750 picoseconds, and repetition rate 10 Hz (Cynosure, Inc). Fitzpatrick wrinkle score showed on average an improvement of 1.97 points from baseline. At 6-month follow-up, the treatment physician was extremely satisfied 97.4% of the time, whereas the 42.1% of patients were extremely satisfied. Histology of the treated areas showed increased collagen and elastin. There were no permanent side effects noted. The investigators proposed that the photomechanical and photothermal effects on collagen turnover are critical for the treatment of photoaging.[37]

Saluja further evaluated the efficacy and safety of "off the face" applications of the picosecond laser with DLA, specifically skin texture and tightening. Twenty female subjects were prospectively treated with the 755-nm alexandrite picosecond laser to the hands (n = 10) and décolletage (N = 10) with identical parameters (Cynosure, Inc). For the décolletage, a reduction to 1.05 on the A–A scale was achieved, from a baseline of 3.10. This was maintained at 3 months with a score of 1.4 on the A–A scale. Investigators noted a 70% improvement of the hands at 3 months. No adverse effects were noted during the study.[38]

Several studies investigated the use of picosecond lasers with DLA for the treatment of scars. Brauer and colleagues studied 20 patients with facial acne scarring, including rolling (94%), boxcar (24%), and ice pick (18%). Patients were treated with the 755-nm alexandrite picosecond laser at the following treatment parameters: fluence of 0.71 J/cm^2, spot size of 6 mm, pulse duration of 750 picoseconds, and repetition rate of 5 Hz (Cynosure, Inc). Mean masked assessment scores of 1.5 and 1.4 of 3 were achieved at 1 and 3 months, respectively (with 0 representing 0%–25% improvement and 3 representing >75% improvement). Three-dimensional volumetric analysis revealed a mean scar volume improvement of 24.3% by the sixth treatment. Histologic evaluation showed increased elastic fibers and collagen in treated areas.[32] Tanghetti studied the specific mechanism of collagen and elastic tissue stimulation and melanin clearance after picosecond laser treatment with DLA. Vacuoles, termed laser-induced optical breakdown (LIOB), were identified through the histologic and confocal imaging and are believed to stimulate repair mechanisms. Melanin absorption of picosecond laser beams leads to the formation of plasma that results in photothermal and mechanical effects. Greater melanin concentration and/or higher fluence show a theoretical proportional relationship because of earlier LIOB formation during treatment.[33]

Haimovic and colleagues specifically analyzed the safety of the 755-nm picosecond laser with DLA in the treatment of acne scars (hypertrophic and atrophic), striae, and pigmented lesions in 56 patients of skin types IV to VI. Clinical satisfaction was not evaluated. Ten patients were lost to follow-up, and transient adverse effects included erythema (n = 7), hyperpigmentation (n = 6), edema (n = 3), and scabbing (n = 1). With respect to hyperpigmentation, it was more likely to be seen in lower-extremity laser treatments.[34]

Discussion

The early success of picosecond lasers in exogenous pigment removal has spurred evaluation of its use in the treatment of unwanted endogenous pigmentation. Published studies in pigmented lesions range from nevus of Ito, congenital nevus, nevus spilus, nevus of

Ota, the Horii macules, café-au-lait patches, lentigines, and the Becker nevus.[21–23,25,26] In addition, picosecond has been used for other types of pigmented conditions including argyria, paradoxical darkening after laser tattoo removal, and minocycline-induced hyperpigmentation.[24,26–29]

An emerging indication for the picosecond laser includes that of photorejuvenation, encompassing improvement in dyspigmentation, rhytides, skin texture, and skin tightening.[30,34–37] Multiple studies have now demonstrated statistically significant improvement in the various facets of photoaging of the face, décolletage, and hands.[30,34–37] As a result, in 2014, the FDA gave clearance for picosecond laser with DLA in the treatment of wrinkles and acne scarring in most skin types (I–IV).[11]

Laser use in dermatology, particularly in the treatment of pigment or pigmentary disorders, has been associated with possible consequences of hypopigmentation or hyperpigmentation, scarring, erythema, and edema. The preponderance of data reviewed in the literature has shown that picosecond lasers are safe to treat a wide array of conditions. However, appropriate treatment settings (e.g., fluence, spot size, pulse duration, and wavelength) needed to be used to prevent possible adverse effects.

A retrospective chart review of 42 patients showed that picosecond lasers only had transient side effects such as erythema, edema, and transient pigmentary alteration, in contrast to the nanosecond lasers, which did have a few instances of permanent dyspigmentation.[39] The safety of the picosecond lasers notably extends to patients of skin types IV–VI as well, which several studies investigated. A retrospective review involving 56 patients of skin types IV–VI, treating a variety of conditions, observed only transient adverse effects including erythema, edema, scabbing, and hyperpigmentation.[34] However, more studies are needed to establish a robust safety profile with picosecond laser's novel use.

Picosecond laser use for tattoo removal has been successful, as shown in the literature; however, this is a niche market. To expand on this market, clinicians and laser companies have explored other uses in photorejuvenation, scarring, and dermal pigment to recoup the lasers' high associated costs. Picosecond lasers can be a promising treatment modality for management of difficult to treat pigment conditions; however, most studies conducted at this time are small and lack an adequate comparator.

Picosecond laser published data do show improved patient- and physician-rated results in comparison with nanosecond lasers. However, in the head to head studies by Pinto and colleagues, there was no significant difference between the two. Based on the commentary by Ross, it seems that, at the present time, picosecond lasers for tattoo removal perform better in a few select scenarios. He states that these cases are 750-picosecond alexandrite versus 50-nanosecond alexandrite lasers (even at higher nanosecond fluences), yellow pigment tattoos treated with low-energy green-light picosecond laser, and successively treated tattoos clearing faster with picosecond lasers.[41] With respect to all non–tattoo-related removal, there has yet to be a large enough pool of data to make critical assessment on picosecond versus nanosecond lasers. A global view of the picosecond laser literature demonstrates a trend toward superiority in comparison with nanosecond lasers for tattoo removal, dermal pigment management, and other treatments, but the difference is not definitive. The paucity of well-designed randomized clinical trials limits definitive statements on picosecond laser superiority over nanosecond pulse duration lasers.

Conclusion

Picosecond laser use for tattoo pigment removal has exhibited notable success, and the use for other entities is expanding. Applications have now extended beyond tattoo removal to acne scarring, benign pigmented lesions, other dyspigmentation, and photoaging.[16,19,23,25,34,35,40] In the small studies available, patient satisfaction and clinical results have been encouraging for these challenging conditions. These results have been associated with fewer side effects, even in darker skin types, and the need for fewer treatments.[9,10] More robust clinical studies are needed to appropriately evaluate picosecond pulse duration laser role in dermatology.

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