Short-pulsed laser for the treatment of tattoos, pigmented lesions, scars and rejuvenation

Emil A Tanghetti, MD;[1] Kristina Andrea Hoffmann, MD;[2] and Klaus Hoffmann, MD[2]

Abstract

This review describes the use of picosecond lasers for the treatment of tattoos, pigmented lesions, scars, and their use in rejuvenation. These devices have delivered enhanced efficacy for the treatment of tattoos and pigmented lesions when compared to the older 40-50 nanosecond devices. The fractional delivery with the picosecond devices have opened up a new method of rejuvenation for photodamaged skin and the treatment of scars. The delivery of these high-energy short pulses have created zones of injury in the skin referred to as areas of laser-induced optical breakdown. These areas of damage appear to produce cytokines and chemokines which result in epidermal and dermal repair and remodeling. The dual use of these devices with the flat and the fractional optics have made these devices useful in many ways that have been unanticipated.

Semin Cutan Med Surg 36:148-154 © 2017 Frontline Medical Communications

In western culture, tattoos have become a common form of expression. Their prevalence has dramatically increased over the last 2 decades, often lead by sports figures and individuals in the art world. As with all forms of expression, the individuals and times change. These forms of body art can become dated, out of fashion, and a significant social problem for many. The intended permanence of this ink in the skin poses a challenge to its removal. Nonspecific destructive methods such as excision, salabrasion, dermabrasion, and ablative carbon dioxide (CO_2) lasers have resulted in significant scarring and an appearance that is often unattractive.

An understanding of a tattoo ink in the skin is important in developing a strategy for its removal. India ink is a common agent used in tattoos. It is largely placed in the papillary and reticular dermis with various needling techniques. After a number of days, the ink is taken up by macrophages and histiocytes which then migrate to the perivascular areas of the dermis. In these cells, the ink is contained in granules which are 400 to 4,000 nm in diameter. These granules are made up of loosely packed particles generally in the range of 40-100 nm in diameter (Figure 1). These data suggest that the ink could be targeted as granules as large as 4,000 nm to particles as small as 40 nm.

[1]Center for Dermatology and Laser Surgery, Sacramento, California.
[2]Department of Dermatology, Center of Laser medicine NRW, Bochum, Gemany.

Disclosures: Dr Tanghetti reports other from Cynosure, during the conduct of the study. Dr KA Hoffman has nothing to disclose. Dr K Hoffman reports personal fees and other from Cynosure, from Cutera, during the conduct of the study.

Correspondence: Emil A Tanghetti, MD; et@dermatologyandlasersurgery.com

The development and commercialization of the quality-switched Ruby, the neodymium yttrium aluminum garnet (Nd:YAG) and the Alexandrite laser in the 1990's with nanosecond technologies provided a practical and affordable means to remove tattoos with acceptable downtime and side effects. The pulse durations of these devices are in the 6-100 nanosecond ranges. All 3 wavelengths are absorbed by black ink. The Ruby and Alexandrite lasers are also absorbed by green and blue. The Nd:YAG with 532 nm light is absorbed by red, and to a lesser extent, yellow. To effectively treat most colors, the practitioner is best configured for success with an Nd:YAG and an Alexandrite or Ruby laser. These devices are in a range that rapidly heats the inks in the skin resulting in rapid steam formation both heating and fragmenting these granules and particles. The energies required to achieve clearance do result in unwanted side effects when used in the nanosecond domain. Due to the characteristics of the pulse duration, there can be unwanted heating of the tattoo ink that could result in textural change and hypopigmentation. Also, total clearance of professional, heavily inked tattoos or tattoos over tattoos are difficult to achieve. Even with pulses in the nanosecond domain there is a significant difference in the pulse durations between a 5 ns and a 50 ns device (10 x shorter at 5 ns) which will result in better thermal confinement and less unwanted side effects.

The potential benefits of pulse durations shorter than those in the nanosecond domain were suggested by Jacques.[1] It was postulated that picosecond or femtosecond pulses would not only lead to delivery of heat, but also a rapid delivery of acoustic energy which would cause tensile stress leading to fragmentation of the tattoo particles. A simple analogy would be the heating of a cold glass pan where it is placed in a cold oven and both are heated gradually. However; when a cold glass pan is placed in a hot oven, there is a very rapid temperature change which can lead to rapid fracturing and breakage of the glass (Figure 2). This concept was explored with experimental picosecond and femtosecond devices in animals and later in humans with proof that these devices could clear ink.[2,3] Based upon these findings, providers encouraged individuals in industry to build a commercial device with picosecond pulse widths. Modeling data by Ho suggested that a pulse duration of 10-100 picosecond would be ideal to treat graphite ink particles.[4] However, Ross et al cautioned that the creation of a superficial plasma might pose some limitations for the deeper delivery of the energy generated by these devices.[3]

The first commercial picosecond laser was an Alexandrite manufactured by Cynosure with a pulse duration of 750 picoseconds. The most dramatic finding was the rapid clearance of blue and green ink which was previously difficult to clear after many treatments with the 40-50 ns Alexandrite lasers.[5] Practitioners could finally deliver near complete clearance of blue and green ink, in just a few treatments (Figure 3). This study demonstrated greater than 75% clearances after 1 to 2 treatments with two-thirds of patients achieving complete clearances with fluences of 2.0-2.83 J/cm^2.[5]

1085-5629/13$-see front matter © 2017 Frontline Medical Communications
https://doi.org/10.12788/j.sder.2017.032

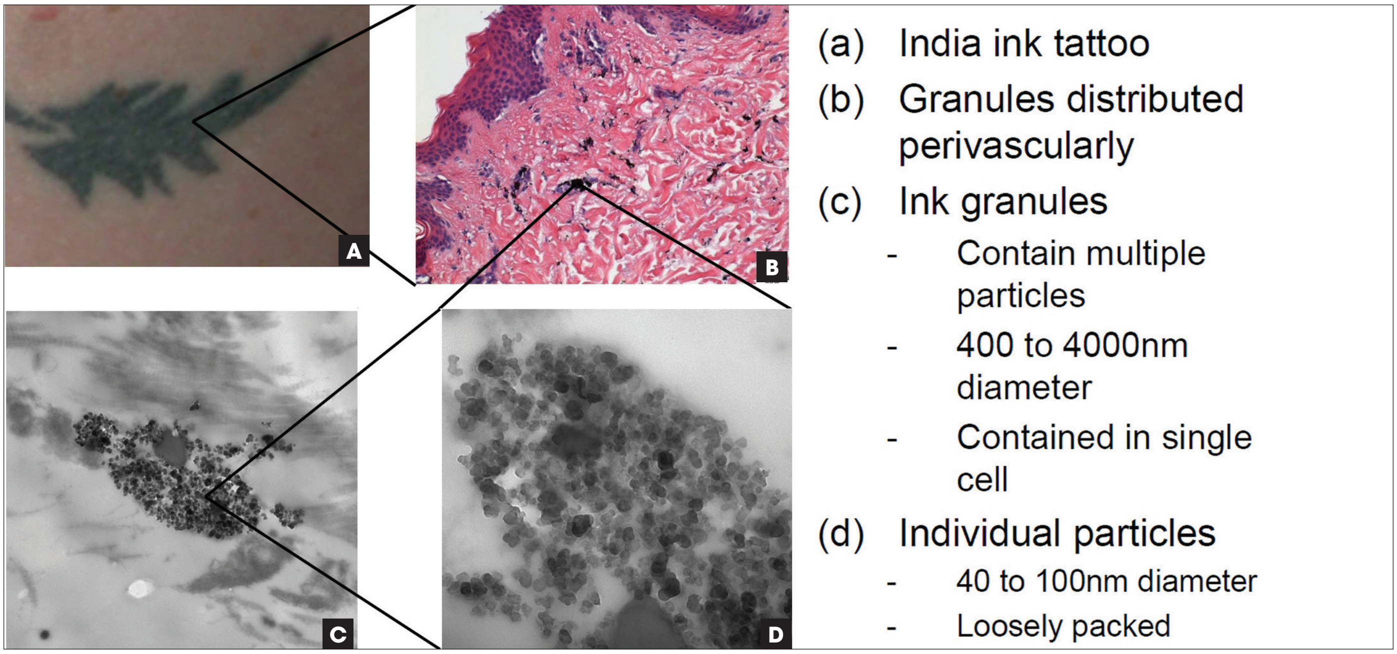

FIGURE 1. Tattoo ink in the skin. Electron microscopy. Courtesy of H. R. Jalian, MD

An early comparative study with this new commercially produced picosecond Alexandrite (Picosure, Cynosure, Inc, Westford, Massachusetts) was presented by Sierra in 2012.[6] This device was compared to two commercially available nanosecond devices: the Alexandrite laser (Accolade, Cynosure, Inc, Westford, MA; at 50 ns) and an Nd:YAG 1064/532 nm (RevLite, Cynosure, Westford, MA; at 5 ns). The picosecond device used in this study was able to achieve similar clearances than the other two devices operating at the manufacturer's suggested optimal treatment parameters with half the number of treatments and at a significantly lower fluence (Figure 4).

In a recent study performed by Pinto et al with a 450 picosecond 1064 nm Nd:YAG versus a 5 ns 1064 nm Nd:Yag, there was no significant difference with 2 treatment sessions in tattoos which had been previously treated [7]. Unfortunately, only two treatments were administered. In another study by Kono that was conducted with the 450 picosecond 1064 nm Nd:YAG 50 ns Alexandrite and a 50 ns Nd:YAG, there was greater black pigment clearance on the side treated with picosecond device after 4 treatment sessions (Figure 5).[8,9] Another commercially available picosecond 1064 nm Nd:YAG laser (Enlighten, Cutera, Brisbane, California) also has a 2 ns pulse duration option which is recommended for heavily inked tattoos in the first few treatments followed in later sessions by 750 ps pulse duration. Picosecond lasers also enable the provider to treat tattoos at significantly lower fluences than nanosecond devices with less discomfort. All these data suggest that the picosecond devices are an improvement over the longer-pulse nanosecond lasers especially as the ink particles size diminishes with more treatments, and that 755 nm picosecond devices may be more effective than nanosecond lasers. From a practical view, a picosecond device may not deliver dramatically greater clearance of tattoos in comparison to 2-6 ns devices. However, our experience and that from the literature would suggest that picosecond lasers do offer a dramatic difference in results over 40-50 ns devices.

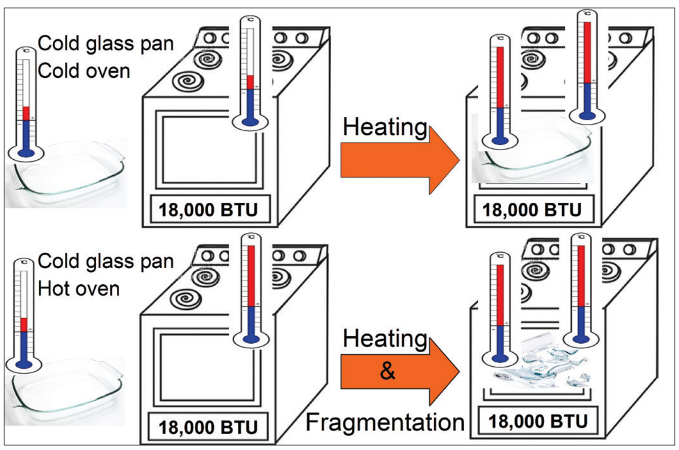

FIGURE 2. Heating and fragmentation example

Challenges to treating tattoos

The proper treatment of tattoos is more challenging than generally believed. The issue at hand is the lack of a *"Standard-tattoo."* Neither the process of injecting the ink into the skin, nor the tattoo dye itself is in any form standardized. In Europe, through legislation passed by the European Union, an index displaying which substances are not to be used in tattoo dyes exists. In the United States, a comparable list has not been developed.

The tattoo artist places the ink in the skin with various needles which in themselves can be of different size, grind and thickness. With a special tattoo gun, the artist can set up the frequency at which the needle is supposed to penetrate the skin as well as the depth into which the ink is injected. The pressure applied onto the skin, the retention time of the needle at a specific location as well as several other factors determine how much pigment is injected and into which depth of the skin they are placed. Appropriate aftercare is essential. If the tattoo is not properly treated, there is a risk of infection

FIGURE 3. Courtesy of R. Saluja, MD

and scar formation. Most tattoo artists, as well as their customers, are typically unaware of the contents of the color being used; yet, it is easy to understand that among the population wishing to have a tattoo removed, this information can be very important. Tattoo dyes consist of binders, solvents and excipients in addition to the pigment. The tattoo pigment (dye) constitutes less than 30% of what the artist is transferring from the ampulla into a vial then into the skin. There is a strong suspicion that the excipients play a major role in the process of the pigment integration in the skin.

Applying the evidence: how we treat patients

When we see patients at our institutions, one of the most crucial questions is whether it is an amateur or professional tattoo. Tattooists working professionally are usually more precise with the amount of pigment injected and the depth of placement. The age of the tattoo is also very important. Older tattoos generally fade with time and may require less treatment sessions. During the process of degradation of a colorful tattoo, cleavage products form where the injected dye splits and the tattoo fades. The ink particles are recognized as a foreign body and are engulfed by macrophages and other inflammatory cells, which are distributed perivascularly in the dermis. This entire process results in an altered faded appearance of the tattoo.

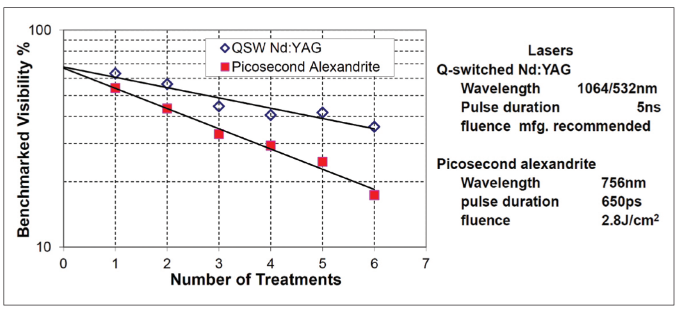

FIGURE 4. Clinical Results – Benchmarked visibility percentage graded by blinded evaluators comparing split treatment clinical photos vs digitally processed pretreatment photos with 0, 20, 40, 60, 80 and 100% pigment removed digitally

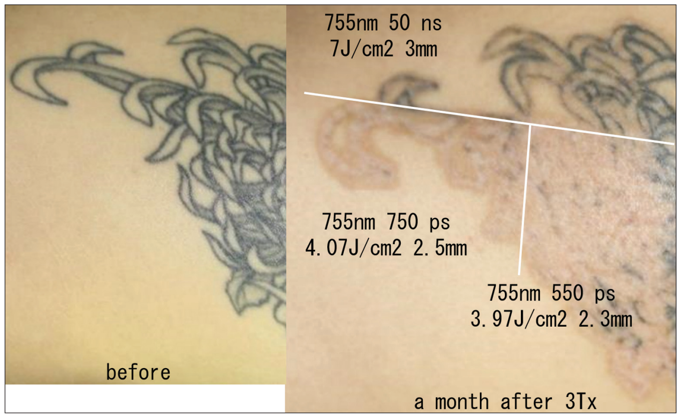

FIGURE 5. 755 nm alexandrite laser (TriVantage TM by Candela Corporation) using the 50 ns vs 755 nm alexandrite laser (Picosure TM by Cynosure Corporation) using the 550-750 psec. Courtesy of Taro Kono MD

Before initiating treatment, it is important to determine if the tattoo is a cover-up over an older preexisting tattoo. These can be challenging to treat, especially when the added ink is done by a professional where the placement of the ink is done densely and sometimes more deeply. If a variety of wavelengths are available, it would be ideal to administer a series of test spots prior to a complete treatment session.

Squares of 1 cm² (1 cm x 1 cm) are treated. Four weeks later we judge the effect of the test session and recommend the best wavelength for further treatments. If we feel that the ink is more deeply situated, we often prefer to use a 1064 nm wavelength due to the increased depth of penetration and the higher energy available with our device. Overall, we stress to our patients that several treatment sessions are necessary and that the effects are unpredictable. This sets the stage for a realistic and ultimately content patient after treatment.

Since each patient has a different threshold for pain, the level of discomfort experienced will be different from patient to patient. While topical anesthetics help minimize the pain, it is important that they do not alter the penetration of light through the skin. They must be thoroughly removed and the area cleaned before tattoo removal. We often use forced cool air as an adjunct to tattoo removal primarily for its anesthetic properties. We also use the local infiltration of anesthetics with epinephrine to help reduce the pain and diminish bleeding. Generally, we treat at 4-week intervals. However, waiting for 2 to 3 months can be helpful in its own right due to the continued removal of ink in the skin during the healing process. In our practice, we have found that our picosecond lasers result in less tissue damage than our older nanosecond devices, and as a consequence are much better tolerated.

Fractional delivery of picosecond pulses

During the commercialization of the first picosecond Alexandrite laser for tattoo treatments, the Cynosure team responsible for this device developed a diffractive lens array to deliver the short-pulsed, high energy in a fractional manner. The developers hoped that it would be useful as a rejuvenation tool. In our own practice with the Alexandrite laser with diffractive lens array, many of us noted skin lightening, scar pigment and texture improvement, pore size reduction and improvement in photodamage. These initial findings were

FIGURE 6. Brazilian Skin Type:IV MI:27 - 6 mm fractional optic

validated in clinical studies by Brauer demonstrating improvement in acne scars.[10] These investigations included patients of all skin types demonstrating safety and efficacy in these individuals. The darker skin types including skin types IV, V, and VI responded well to multiple passes and sessions without the postprocedural dyspigmentation that was all too common with the other ablative and nonablative devices.[11] In addition to improvements to the acne scars, a gradual lightening of the skin was appreciated when treating darker skin types (Figure 6). When studied in Asian patients, similar improvement in scars, tone, texture, pore size, and pigmentation were observed.[12] The minimal down time and the absence of postprocedural dyspigmentation made this particularly appealing in the Asia-Pacific region.

Furthermore, McDaniel and Weiss investigated this device on patients with photodamage and demonstrated improvement in fine wrinkles, mottled hyperpigmentation, lentigines, skin tone, and texture.[13] Generally, improvement is noted over 4 to 5 treatment sessions. The posttreatment profile of this device is particularly appealing to patients who require minimal down time. The series of photos as seen in (Figure 7) by McDaniel is an accurate representation of the mild postprocedural erythema that usually lasts for a few hours. There is generally mild discomfort associated with this procedure, sometimes requiring only topical anesthesia.

The use of the picosecond Alexandrite with the diffractive lens array has been also used as a rejuvenation tool in areas that are very sensitive and prone to scarring with more aggressive lasers. Recent studies have demonstrated significant improvement in photodamage involving the neck and chest regions with this device and optic.[14,15] In particular, improvement of dyspigmentation, texture, and fine wrinkles are seen after a series of 3 to 5 treatments at monthly intervals. Saluja has successfully used the picosecond lens array for the treatment of photodamage of the hands with notable improvement in dyspigmentation and texture (Figure 8).[15] These studies validate the efficacy and safety of this device in the treatment of conditions of many anatomic areas.

The clinical improvements seen with the 755 nm picosecond laser and the defractive lens array appear to be well-correlated with the production of new collagen, elastic tissue, and mucin in the dermis. This was observed in skin biopsies performed 3 months after 6 treatment sessions.[10] The histologic studies performed by

FIGURE 7. Clinical appearance with the picosecond Alexandrite and the defractive lens array

FIGURE 8. Focus lens array

FIGURE 9. Intra-epidermal vacuole in skin with FST III, MI = 23 measuring approximately 60 microns in diameter. Biopsy performed 10 minutes posttreatment.

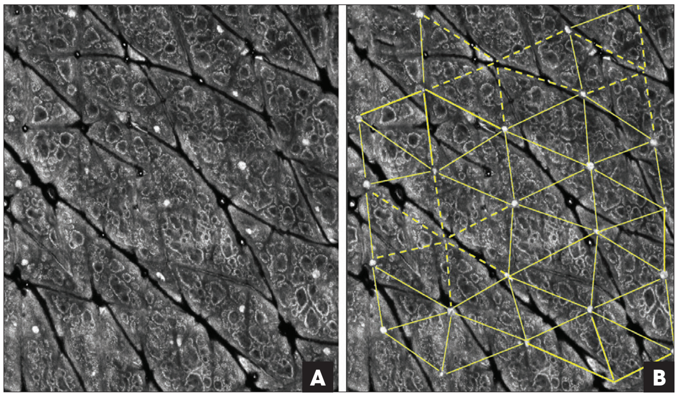

FIGURE 10. (A) Approximately 40 microns below the skin surface small vacuoles are seen in the epidermis corresponding to the vacuoles noted on microscopic examination. **(B)** Connecting these spaces reveals a grid pattern of the fractional optic with similar pitch.

Tanghetti provided some clues to the type of injury that is responsible for the clinical improvement seen with the Alexandrite laser and a defractive lens array.[16] Immediately following the treatment with this device and optic there are circular voids observed in the epidermis measuring 40-60 microns in diameter (Figure 9). They are centered in the granular layer of the epidermis. The surrounding keratinocytes are intact. The basement membrane and the stratum corneum are preserved. At 24 hours after the treatment, this space is occupied by cellular debris which stains positively for melanin suggesting that melanin is the target of this device. When studied with a confocal microscopy, these vacuoles are observed in a pattern that corresponds to the treatment grid of the fractional diffractive lens array (Figure 10).

This diffractive lens array consists of individual lenses with 500 micron center to center lens distance which results in the delivery of the short-pulsed laser energy in a low-fluence background and high-energy micro spots. Approximately 70% of the fluence is delivered in these high-energy zones and 30% in a low-energy background (Figure 11). This high-powered, short-pulsed delivery of laser light appears to result in a localized area of plasma formation by the absorption of this 755 nm energy by melanin. This process is confined to a very small portion of the epidermis and results in a very localized area of heating with the formation of a small steam ball, thereby producing the voids seen on histology (Figure12).

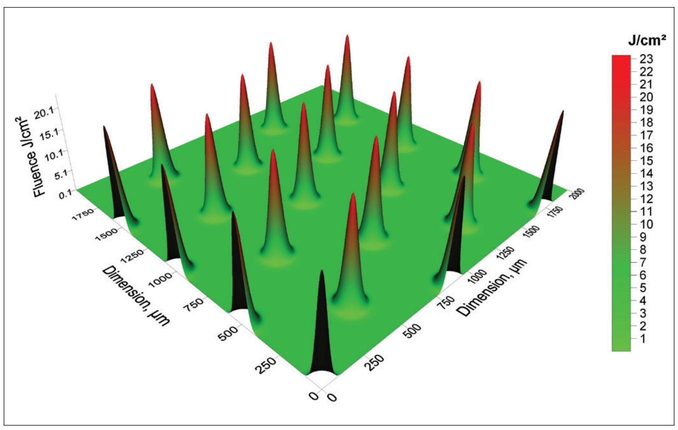

FIGURE 11. Fluence distribution in the treatment plane on the skin surface. Treatment spot size 6 mm, average fluence setting 0.71 J/cm²

In an attempt to better understand the physiological consequences of this unique injury to the skin, Tanghetti and Tartar studied the thermal signatures of the picosecond Alexandrite with the diffractive lens array over a 24-hour period. There was no significant temperature rise by pulsing with 4 consecutive passes or 4 passes with 1 minute between each pass when evaluated with a thermal camera.[17,18] However, beginning 15 minutes and peaking at 1 hour, there was a significant temperature elevation of 5.6 degrees centigrade from baseline which dissipated over 24 hours. The histology of a localized epidermal injury with notable delayed temperature rise all suggest that a well-placed epidermal injury can produce a number of chemical mediators which could be responsible for the temperature elevation as well as the delayed production of collagen and elastic tissue that has been described with the use of this device. It is not surprising that dermal remodeling can occur without dermal wounding since Kang and others have reported improvements with long-standing acne scars with the use of a topical retinoid.[18]

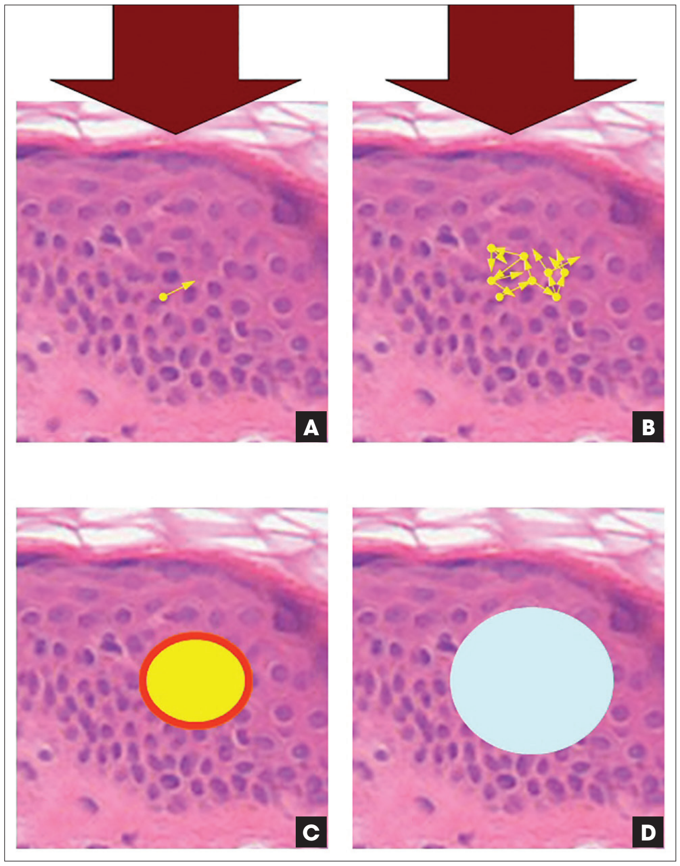

FIGURE 12. Process of vacuole formation in the epidermis: (**A**) A high-intensity portion of the laser beam created by the diffractive lens array irradiates a region of the skin. A seed electron is ejected from an absorber (melanin); (**B**) The number of free electrons grows in an avalanche process. Electron plasma density increases absorbing energy from the beam; (**C**) The laser beam terminates leaving a hot plasma ball. The plasma ball rapidly heats the surrounding tissue above boiling temperature; (**D**) Steam expansion creates a vacuole in the epidermis

TABLE. Wavelength comparison chromophore effects

Wavelength, nm	532			1064			755		
Melanin abs, cm^{-1}	555			50			3.0		
Blood abs, cm^{-1}	235			3.2			54:1		
Melanin: Blood abs, ratio	2.4:1			16:1					
Epid. Melanin %	2%	15%	43%	2%	15%	43%	2%	15%	43%
LIOB Thresh, J/cm^2	2.8	2.7	2.6	31	30	29	9.5	9.1	8.8
Blood Team rise, °C	172	105	40	28	25	22	7.8	6.5	4.8

Abbreviations: abs, absorption; Epid, Epidermal; LIOB, laser-induced optical breakdown.

- Modeling calculation for LIOB threshold fluence and corresponding blood temperature rise for capillaries near the dermal/epidermal junction.
- Melanin and blood absorption at 755nm offer the best compromise and lead to the lowest blood temperature rise at the LIOB threshold fluence or higher

The introduction of a family of picosecond Nd:YAG lasers with wavelengths at 532 nm and 1064 nm provided an opportunity to investigate the delivery of this energy to the skin in a fractional manner. There is significant absorption of energy by melanin at these 2 wavelengths. Our team first worked on a comparison of 755 nm, 532 nm and 1064 nm picosecond laser light delivered to the skin with a diffractive lens array.[19] We found that there was persistent erythema with areas of petechial hemorrhage lasting for several days with 532 nm and 1064 nm compared to the transient erythema lasting 24 hours or less with 755nm. The histological examination demonstrated focal areas of epidermal necrosis in the form of a vacuole with scattered areas of superficial dermal vascular damage with extravasation of red blood cells. This was noted across all skin types with the 532 nm and the 1064 nm diffractive lens. This was in contrast to the regularly spaced epidermal vacuoles with the absence of dermal hemorrhage at 755 nm.

These investigations were repeated with a direct histological and clinical comparison of a 532 nm and 1064 nm picosecond device using a holographic diffractive optic to the picosecond 755nm laser with a diffractive lens array.[20] At the manufacturers' recommended settings with both devices there was erythema and superficial hemorrhage observed with 532 nm and 1064 nm lasting for several days at the higher settings. This was in contrast to the short-lived erythema lasting less than 24 hours with the 755 nm system. The histologies revealed epidermal voids with all 3 wavelengths, but with the absence of dermal hemorrhage with the 755 nm system.

Both of these comparative studies strongly suggest that there is a preferential absorption of 755 nm light by melanin when compared to hemoglobin. We have tabulated the relative melanin and hemoglobin absorption as well as the threshold for vacuole formation (laser induced optical breakdown, LIOB) at different concentrations of epidermal melanin and compared this to blood temperature rise (Table). The preferential absorption of melanin to hemoglobin becomes apparent with a 54 to 1 ratio at 755 nm, 16 to 1 at 1064 nm and 2.4 to 1 at 532 nm. At the energy to create an LIOB, the characteristic epidermal vacuole, 755 nm can achieve this endpoint with the lowest temperature rise in the superficial vasculature.

Conclusion

This review demonstrates that the new high-energy, short-pulsed commercially available picosecond lasers at 755 nm, 532 nm and 1064 nm are an important addition to our therapeutic tool chest. These shortened pulse durations have permitted practitioners to obtain enhanced clearances of tattoos with less textural changes and scarring due to the photomechanical properties of the picosecond relative to the longer nanosecond pulses. The fractional delivery of energy of this high-energy, short-pulse laser light has opened up a new avenue of treatment by the creation of a unique epidermal injury which appears to result in both epidermal and dermal remodeling through factors generated during and after treatment. This type of treatment is particularly well suited for individuals with darker skin types with high epidermal melanin content who are prone to dyspigmentation with other more invasive devices.

References

1. Jacques SL. Role of tissue optics and pulse duration on tissue effects during high-power laser irradiation. *Appl Opt*. 1993;32(13):2447-2454.
2. Kilmer S. Picosecond and femtosecond laser treatment of tattoo ink. Abstract presented at: *American Society of Laser Medicine and Surgery*, April 15-17, 1996.
3. Ross V, Naseef G, Lin G, et al. Comparison of responses of tattoos to picosecond and nanosecond q-switched neodymium: YAG lasers. *Arch Dermatol*. 1998;134(2):167-171.
4. Ho DD, London R, Zimmerman GB, Young DA. Laser-tattoo removal - a study of the mechanism and the optimal treatment strategy via computer simulations. *Lasers Surg Med*. 2002;30(5):389-397. https://doi.org/10.1002/lsm.10065.
5. Brauer JA, Reddy KK, Anolik R, et al. Successful and rapid treatment of blue and green tattoo pigment with a novel picosecond laser. *Arch Dermatol*. 2012;148(7):820-823. https://doi.org/10.1001/archdermatol.2012.901.
6. Sierra R, Mirkov M. Tattoo Treatment: A new technology for an old problem. Paper presented at: *LaserInnsbruck 2012;* September 12-15, 2012; Innsbruck, Austria.
7. Pinto F, Große-Bűning S, Karsai S, et al. Nd:YAG (1064-nm) picosecond vs. Nd:YAG (1064-nm) nanosecond laser in tattoo removal: a randomized controlled single-blind clinical trial. *Br J Dermatol.* 2017;176(2):457-464. https://doi.org/10.1111/bjd.14962.
8. Kono T, Shek S, Chan H, Groff W, Imagawa K, Miyasaka M. Comparison study of a 532/1064 picosecond laser vs a 532/1064 nanosecond laser in the treatment of multicolored tattoos in Asians [abstract 38A]. *Lasers Surg Med*. 2016;48(suppl 27):14. https://doi.org/10.1002/lsm.22485.
9. Kono T, Shek S, Chan H, Groff W, Imagawa K, Miyasaka M. Comparison study of a 532/1064 Picosecond laser vs a 532/1064 nanosecond laser in the treatment of black tattoos in Asians [abstract 38B]. *Lasers Surg Med*. 2016;48(suppl 27):1-92. https://doi.org/10.1002/lsm.22485.

10. Brauer JA, Kazlouskaya V, Alabbulrazzaq H, et al. Use of a Ppicossecond pulsed duration laser with specialized optic for treatment of facial acne scarring. *JAMA Dermatol*. 2015;151(3): 278-284. https://doi.org/10.1001/jamadermatol.2014.3045.
11. 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. https://doi.org/10.1016/j.jaad.2015.12.010.
12. Ge Y, Guo L, Wu Q, Zeng R, Lin T. A prospective split-face study of the picosecond Alexandrite laser with specialized lens array for facial photoaging in Chinese. *J Drugs Dermatol*. 2016;15(11):1390-1396.
13. McDaniel D. Treatments of facial photodamage and rhytides using a picosecond pulsed Alexandrite laser with specially designed focus optic [abstract 30]. *Lasers in Surgery and Medicine*. March 2014;46 (suppl 25)30.
14. Wu DC, Goldman MP. Evaluation of the safety and efficacy of the picosecond Alexandrite laser with specialized lens array for treatment of the photoaging décolletage. *Lasers Surg Med*. 2016;48(2):188-192. https://doi.org/10.1002/lsm.22427.
15. Saluja R. Evaluation of the safety and efficacy of a low fluence, picopulsed, Alexandrite laser in a pico-toning technique with a diffractive lens optic for the treatment of photodamage and textural improvement in "off the face" applications. *J Drugs Dermatol*. 2016;15(11):1398-1401.
16. 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. https://doi.org/10.1002/lsm.22540.
17. Tanghetti EA, Tartar DM. Comparison of the cutaneous thermal signatures over twenty-four hours with a picosecond Alexandrite laser using a flat or fractional optic. *J Drugs Dermatol.* 2016;15(11):1347-1352.
18. Patel MJ, Chien AL, Audibert F, Rueda MJ, Kerrouche N, Kang S, et al. Improvement in atrophic acne scars by topical adapalene (0.3% gel) [abstract P8622). *J Am Acad Dermatol.* May 2014;70;5(suppl 1), AB8
19. Tanghetti E. Clinical and histological cutaneous effects of picosecond 532nm, 755nm and 1064nm with the flat and fractional optic. American Society for Laser Medicine & Surgery presentation. March 30 – April 3, 2016. Boston, MA.
20. Tanghetti E. The comparative cutaneous and histological changes of skin types I-VI over 24 hours using the fractional holographic optic with picosecond 532nm, 1064nm, and the diffractive lens array with picosecond 755nm. American Socitey for Laser Medicine & Surgery presentation. April 5 – April 9, 2017. San Diego, CA