Laser Treatment of Professional Tattoos With a 1064/532-nm Dual-Wavelength Picosecond Laser

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BACKGROUND Picosecond-domain laser pulses improve the photomechanical disruption of tattoos.

OBJECTIVE This study evaluates the efficacy and safety of a novel, dual-wavelength, 1,064/532-nm, picosecond-domain laser for tattoo clearance.

MATERIALS AND METHODS This was a prospective, self-controlled, clinical study of 34 subjects with 39 tattoos treated at 2 sites with an interval of 4.8 ± 1.6 weeks and up to 10 treatments (mean, 7.5). Blinded evaluation and investigator assessment of serial digital images was performed to evaluate treatment efficacy in the 36 tattoos that received at least 3 treatments. Investigators also assessed efficacy before each treatment visit up to 10 treatments. Safety and tolerability was evaluated for all 39 tattoos that underwent at least 1 treatment.

RESULTS Blinded evaluation demonstrated that lightening of tattoos was achieved in all subjects, with 86% (31 of 36 tattoos) showing at least a 50% clearance after 3 treatments. Adverse events were few and transient in nature. Patient satisfaction and treatment tolerability were high.

CONCLUSION Treatment of single-colored and multicolored tattoos with this novel 1,064/532-nm picosecond laser is highly safe and effective.

The authors have indicated no significant interest with commercial supporters. Equipment for this study was provided by Syneron Medical.

Nanosecond-domain Q-switched lasers have been used for tattoo removal for several decades.[1,2] Poor absorption of laser wavelengths by particular ink colors and the inability to sufficiently fragment smaller particles of tattoo ink has made laser tattoo removal a cumbersome process sometimes, requiring upwards of 10 or even 20 treatment sessions, or resulting in incomplete tattoo removal.[3]

Tattoo ink fragmentation and removal relies, in part, on the ability of a particular ink or chromophore to strongly absorb the laser wavelengths. The 3 main commercially available laser wavelengths include the 694-nm ruby laser,[3,5–11] the 755-nm alexandrite laser,[3,5–7,12–14] and the 1,064-nm and 532-nm neodymium-doped, yttrium-aluminum-garnet (Nd:YAG) laser,[3,5–7,15–18] but these wavelengths are not well absorbed by all the colored ink pigments used in tattoo application today. The ruby and alexandrite lasers target black, blue, and green pigments, and the Nd:YAG laser, with its 2 emitted wavelengths, targets black and blue pigments with the 1,064 nm and red, pink, and orange pigments with the 532 nm wavelengths.[5]

The fragmentation of larger tattoo ink particles into smaller ones is required for efficient phagocytosis by macrophages, which carry the ink away to draining lymph nodes, resulting in tattoo lightening. Photomechanical disruption of the ink by the explosive generation of high-pressure waves, termed a photoacoustic effect, results in the fragmentation of the ink particles. Greater photoacoustic effects are achieved with shorter pulse durations. Nearly 20 years ago,

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Ross and colleagues[20] demonstrated faster clearance of tattoo ink with picosecond compared with nanosecond pulses. Recent innovations in laser technology produced commercially feasible picosecond-domain lasers, and clinical studies confirmed their ability to achieve improved clearance of multicolored tattoos.[2–4]

Q-switched nanosecond lasers produce pulses measured in the billionth of a second (10^{-9} seconds), and picosecond lasers produce pulse durations 100 times shorter, measured in the trillionth of a second (10^{-12} seconds). According to the theory of selective photothermolysis,[21] selective destruction of skin chromophores requires that a preferentially absorbed wavelength of light be delivered in a pulse duration shorter than the thermal relaxation time of the target (the time it takes the object to lose heat to the surrounding tissue). Nanosecond-domain pulses produce partially photothermal and partially photomechanical effects on tattoo ink in tissue.[3] Most tattoo particles fall in the range of 40 nm to 300 nm in size, which can be effectively targeted with nanosecond laser pulses.[19,20] However, as these larger particles are reduced in size by each laser treatment, further fragmentation becomes less efficient. The ideal pulse duration producing photomechanical disruption of tattoo ink should be shorter than what is termed the stress relaxation time of the target, which is in the picosecond range. Pulverizing ink particles into even smaller granules increases the efficiency of phagocytosis for faster tattoo lightening.[20]

A prospective, self-controlled, clinical study performed at 2 sites in the United States evaluated a novel picosecond-domain Nd:YAG laser with a potassium titanyl phosphate frequency-doubling crystal for the clearance of decorative tattoos of varying colors.

Materials and Methods

Device Description

A picosecond-domain, 1,064/532-nm Nd:YAG laser with a frequency-doubling crystal (PicoWay; Syneron Candela, Corp., Wayland, MA) approved now by the now Food and Drug Administration was used for treatment in this study. The laser delivers up to 400 mJ pulses at 1,064 nm with a pulse duration of 450 picoseconds, and pulses of up to 200 mJ of energy at the 532 nm wavelength with a pulse-duration of 375 picoseconds. Spot sizes from 2 to 6 mm with maximum fluence of 1.9 J/cm^2 for the 532-nm and 8.5 J/cm^2 for the 1,064-nm handpieces were used for treatment.

Study Design

This was a prospective, self-controlled, clinical study performed at 2 sites in the United States that evaluated tattoo removal in 34 subjects with 39 tattoos of single or multiple colors. The study was approved by an Institutional Review Board (Essex Institutional Review Board, Inc., Lebanon, NJ) for the treatment of human subjects.

The primary study end points were the global percent tattoo clearance, which was evaluated over the entire treatment area independent of tattoo color, and the treatment safety, reflected in the number and type of adverse events that occurred. The study efficacy success criterion required a global percent tattoo clearance of at least 50% after 3 treatments (average clearance grade, ≥3) by at least 85% of subjects, as agreed upon by at 2 of the 3 blinded evaluators. The secondary end point of the study was defined as a global percent tattoo clearance of at least 75%, as assessed by the study investigators.

Tattoos were treated for up to 10 sessions with an interval of 4 ± 2 weeks. All tattoos were considered independent of body location. Tattoos were assessed at each treatment visit, by the study investigators and subjects, and at 4, 8, and 12 weeks following the last treatment session.

The number of treatments performed for each tattoo depended on the degree of tattoo clearance. Both the 532 nm and 1,064 nm wavelengths could be used on the same tattoo, and treatment parameters were chosen according to the subject's skin type and degree of tattoo clearance.

All subjects were asked to rate the level of discomfort or pain perceived immediately following each treatment using a numerical 0 to 10 scale (0 = no pain/discomfort; 10 = worst/intolerable pain). In addition, subjects completed a 3-point questionnaire at each follow-up visit, assessing their comfort level following treatment and improvement of the tattoo appearance. Subjects' treatment satisfaction levels were recorded using a 5-point scale, 0 = unsatisfied, 1 = no opinion, 2 = slightly satisfied, 3 = satisfied, and 4 = very satisfied. The percentage of subjects electing not to use any anesthesia for the procedure was noted.

Digital photographs (D80; Nikon Corporation, Melville, NY) of targeted tattoos were taken in a standardized manner at baseline visit and at each treatment and follow-up visits for comparison at the end of the study. Study photographs from each visit were collated and randomized prior to the blinded assessments. After all subjects completed the third treatment, each of the photographic images taken at baseline and after the third treatment were evaluated by the blinded physicians to assess tattoo clearance. If there was a complete response in the tattoo (i.e., more than 95% of the tattoo removed, as assessed by the study investigator) before the fourth treatment, the blinded physician compared the last study visit photographs to those captured at baseline.

The independent blinded dermatologists and the study investigators compared each baseline and post-treatment tattoo image using a 5-point grading scale with 1 = poor response (0%–24% lightening), 2 = fair response (25%–49% lightening), 3 = good response (50%–74% lightening), 4 = excellent response (75%–94% lightening), and 5 = complete response (≥95% lightening). Subjects also used this 5-point grading scale to evaluate tattoo clearance at the 4, 8, and 12 weeks of follow-up visits.

Baseline Demographics and Characteristics

A total of 34 subjects at 2 sites with 39 tattoos received picosecond laser treatment (mean, 7.5 treatments; range, 1–10 treatments). The majority of subjects were women (*n* = 19; 56%) and Caucasian (*n* = 25; 74%), and the mean age was 34.6 ± 11.1 years (range, 19–67 years). The treated tattoos were located on the arms or shoulders (*n* = 18; 46%), back (*n* = 6; 15%), abdomen (*n* = 5; 13%), legs (*n* = 4; 10%) or ankles (*n* = 3; 8%), neck (*n* = 2; 5%), and chest (*n* = 1; 3%). The majority of treated tattoos were professional (*n* = 37; 95%). Of the 39 treated tattoos, 56% had 1 color and 44% were multicolored with 1 to 5 tattoo colors (Table 1).

Treatment Procedure/Parameters

A total of 291 treatment sessions were performed on the 39 tattoos. The mean number of treatments performed was 7.5 (range, 1–10). Just prior to each treatment, a topical anesthetic cream (56%, 162/291) or local injection of anesthetic (36%, 106/291) or both (6%, 18/291) was administered to ensure patient comfort. Five treatments (2%, 5/291) for 2 subjects were performed without anesthesia upon patient request.

The treatment parameters used for each of the wavelengths at different spot sizes are summarized in Table 2. The choice of the treatment parameters used was guided by the Fitzpatrick skin type of the subject. Test spots of increasing fluence were used to achieve the desired end point of skin whitening, while also testing for paradoxical darkening that may occur with some tattoo pigments (i.e., titanium dioxide and ferric oxide pigments).

Results

Blinded Reviewer Evaluation Results

A total of 36 tattoos underwent at least 3 picosecond laser treatments and were evaluable for blinded assessment after the third treatment. Two subjects with a total of 3 tattoos were lost to follow-up before

TABLE 1. Number of Tattoos (*n*) Containing Various Tattoo Ink Colors

Color	*n*
Black	38
Green	6
Red	12
Blue	6
Purple	2
Yellow	4
Orange	1

TABLE 2. Treatment Parameters

Wavelength	*532 nm*		*1,064 nm*	
Beam Spot Size Diameter (mm)	*Treatment Fluence (J/cm^2)*	*N*	*Treatment Fluence (J/cm^2)*	*N*
2			7.2 6.1–8.5	7
3	1.5 0.9–1.9	14	4.7 3.0–6.0	117
4	1.5 0.8–1.9	88	2.8 1.6–3.3	180
5	1.2 0.7–1.7	2		
6	0.45 0.3–0.8	10	1.0 0.7–1.5	13

N = number of treatments performed.

the third treatment session due to non–study-related reasons. The study results met the primary end point of the study, with 86% (31 of 36) of the tattoos showing at least a 50% clearance after 3 treatments, as agreed upon by at least 2 of 3 blinded evaluators (Figure 1). After 3 treatment sessions, 3 tattoos (8%) were ranked as "complete response" (≥95% clearance); 8 tattoos (22%) had excellent clearance (75%–94% clearance), and 20 (56%) tattoos had good clearance (50%–74% clearance).

Investigator Assessment Results

Subjects could receive up to 10 treatments, but treatment was terminated once excellent to complete clearance was achieved. For tattoos that were assessed to have complete (≥95% clearance; Grade 5) or excellent (75%–95% clearance; Grade 4) responses and did not undergo additional treatments, the last investigator assessment for these subjects was carried forward for the remaining of the study treatment visits (until treatment 10).

In the secondary efficacy end point analysis in which study investigators used a 5-point scale to assess global percent tattoo clearance of at least 75% (excellent to complete response) at each visit following the first treatment, 28% (10/36) of tattoos achieved 75% or greater clearance after 3 treatments, 66% (24/36) after up to 6 treatments, and 92% (33/36) after up to 10 treatments.

Comparison of Blinded Evaluator and Study Investigator Assessments

Of note, the blinded evaluator assessments and the study investigator assessments for tattoo clearance after 3 treatments were consistent, with 30% (11/36) and 28% (10/36) of subjects, respectively, achieving excellent to complete (≥75%) tattoo clearance post 3 treatments.

Patient Self-Assessment Results

A total of 23 subjects provided self-assessments at the 4-week follow-up, 20 subjects at the 8-week follow-up, and 13 subjects at the 12-week follow-up after the final treatment. No additional treatments were performed at follow-up visits. At 4 weeks following the last treatment, all 23 subjects noted lightening of their tattoos, with 35% (8/23) and 39% (9/23) reporting

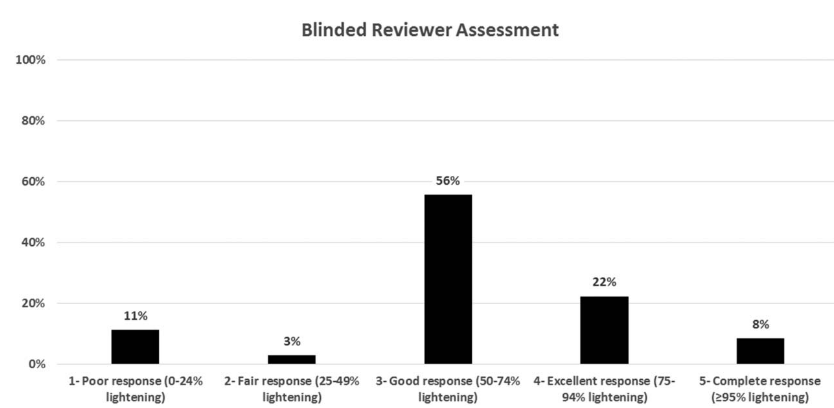

Figure 1. Blinded reviewer assessments for tattoo clearance following 3 picosecond laser treatments.

a good or excellent response, respectively. Similar positive outcomes were seen with 96% (22/23), 95% (19/20), and 85% (11/13) of subjects satisfied to very satisfied with their treatment outcomes at 4, 8, and 12 weeks, respectively.

Safety

A total of 291 treatment sessions were performed for the 39 tattoos that underwent at least 1 treatment. Immediate treatment effects were reported by the treating physician and included mild to moderate edema (98%, 286/291), erythema (95%, 276/291), pinpoint bleeding (9%, 27/291), and purpura (24%, 70/291). Mild to moderate crusting (35%, 103/291) and blistering (10%, 28/291) were reported by the subjects but resolved without intervention prior to the following treatment.

There were 16 adverse events (5%, 16/291) reported by the subjects during the course of the study. There were 8 cases of mild to moderate pruritus, 4 cases of a mild textural change in the treated sites, 1 case of mild soreness, 1 case of prolonged erythema, and 1 case of mild hyperpigmentation. Topical hydrocortisone cream was prescribed for pruritus (3 of the 8 cases) and 4% hydroquinone for the 1 case of hyperpigmentation. There was 1 case of severe pruritus and bulla formation, which completely recovered without any intervention. Scarring was not observed.

Pain Assessment

Using a Numerical 0 to 10 point scale, subjects assessed their pain or discomfort level immediately following laser treatment, recording the pain they perceived for treated tattoo. In total, 288 pain level assessments (assessments were not provided for 3 treatments) were made from the first to 10th treatment session with a mean score of 2.9 ± 2.8. There was none to minimal discomfort/pain in 50% (144/288) tattoo treatments, mild discomfort in 20% (57/288), moderate discomfort in 24% (69/281), and 6% (17/288) with severe pain.

Discussion

This study demonstrates that the dual-wavelength Nd:YAG picosecond laser removed single-colored and multicolored tattoos with a high degree of safety and efficacy. The majority (86%, 31/36) of the treated tattoos showed at least 50% clearance, and 30% (11/36) of tattoos showed at least 75% clearance after 3 treatments, by blinded evaluator assessment. The study investigator assessment revealed that the rate of achievement of at least 75% tattoo clearance increased with additional laser treatments and that a majority of tattoos (66%, 24/36) showed at least 75% clearance after the sixth treatment. At the end of the study, 100% of the treated tattoos showed 50% or more clearance and 92% (33/36) of the treated tattoos showed at least 75% clearance.

A total of 23 subjects provided self-assessments at the 4-week follow-up, 20 subjects at the 8-week follow-up, and 13 subjects at the 12-week follow-up after the final treatment. At the 4-week follow-up, all 23 subjects saw improvements in their tattoos, with 35% (8/23) and 39% (9/23) reporting a good or excellent response, respectively. Patient satisfaction was very positive, with 96% (22/23), 95% (19/20), and 85% (11/13) of subjects reporting to be "satisfied" to "very satisfied" at the 4, 8, and 12-week follow-ups, respectively. Laser treatments were very tolerable, with 70% (201/288) of treatments associated with none to mild discomfort.

In this clinical study of 34 subjects with 39 tattoos treated at least once, the number of treatments for each tattoo depended on the degree of clearance/response of the tattoo to treatment. Two key factors that play a role in tattoo clearance are the number of treatment sessions and the time interval between treatments. In this study, there was an average of 7.5 treatments for the 39 tattoos (up to 10 treatments were performed), with an average interval between treatments of 4.8 ± 1.6 weeks. The majority (92%, 33/36) of the treated tattoos showed at least 75% clearance (excellent to complete response), after an average of 7.5 treatments (Figures 2 and 3). Bernstein and colleagues[1] conducted a parallel study in 21 subjects with 31 tattoos, using a slightly different protocol consisting of fewer treatments (up to 7) and with slightly longer treatment intervals of 7.8 ± 1.1 weeks. Blinded assessment of the 31 tattoos revealed 79% removal on average after an average of 6.5 treatments. Black and red pigments

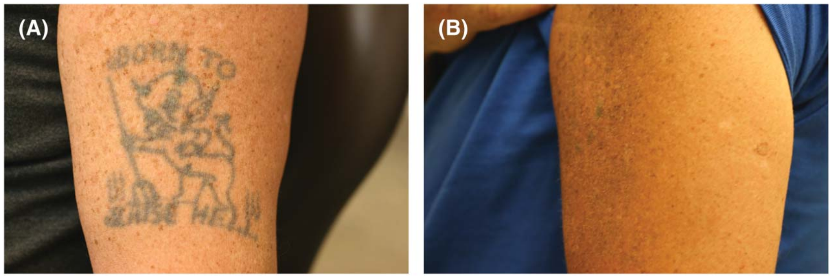

Figure 2. Tattoo before (A) and after (B) 6 treatment sessions with a 532/1,064-nm picosecond laser.

were removed very effectively, with an average 92% clearance of black ink after an average of 6.5 treatments. Both studies supported previous studies with picosecond lasers that demonstrated more rapid clearance of tattoos with fewer treatments than that reported with nanosecond laser treatment.[2,20,22,23]

Tattoo ink removal is dependent on several factors: the degree of absorption by the wavelengths of light available, the ability to generate sufficiently high fluence to fracture the tattoos, the use of pulses sufficiently close to the stress relaxation time of the ink particles, and efficiency of phagocytosis and immune clearance of the ink particles. Picosecond lasers have a pulse duration that is approximately 100 times shorter than traditional nanosecond Q-switched lasers, and it more closely matches the stress relaxation time for tattoo ink particles. It is conceivable that the profound photomechanical disruption that occurs at these ultrashort pulse durations is so great that it may be possible to fragment tattoo ink pigments that are poorly absorbed with commercially available laser wavelengths. This may allow for improved clearance of difficult-to-treat colors, such as yellow, lavender, purple, light blue, and the like. Ross and colleagues[20] compared picosecond and nanosecond laser pulses in a split tattoo study design in 16 consecutive subjects with 16 black tattoos. A 1,064 nm Nd:YAG laser was used with a fluence of 0.65 J/cm^2, a 1.4-mm spot size, and a pulse duration of either 35 picoseconds or 10 nanoseconds. After 4 laser treatments spaced 4 weeks apart, the picosecond pulses produced greater lightening in 12 of the 16 subjects.

Additional clinical studies with picosecond lasers showed that excellent responses were achieved with fewer treatments than those reported with nanosecond lasers. A picosecond-domain 755-nm alexandrite laser device used to treat 12 green and/or blue tattoos demonstrated at least a 75% clearance after 1 or 2 treatments.[22] In another recent clinical study,[23] multicolored tattoos containing yellow pigment in 6 subjects were treated with a frequency-doubled Nd:YAG 532-nm picosecond laser (2.5–3.3 mm spot, 450–500 picoseconds, 1.1–1.4 J/cm^2). Treatments were performed at 6 to 8 weeks intervals, with the final follow-up performed at 2 months after the last treatment session. One patient achieved a complete clearance at the treated site after 1 treatment, and 5 subjects achieved more than 75% clearance after 2 to 4 treatments.

Amateur tattoos have been previously reported to respond more quickly and with fewer treatment sessions when compared to professional tattoos.[10,13] In the present study, only 2% of treated tattoos were

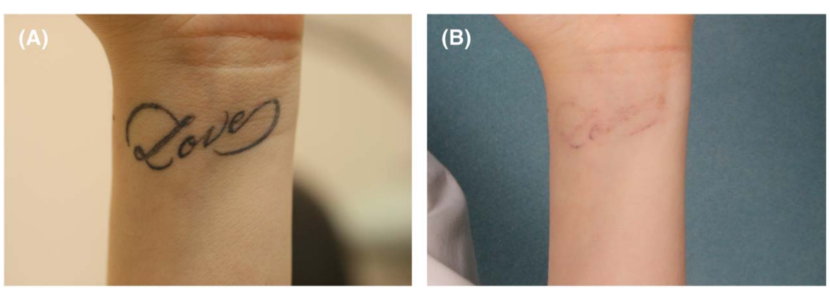

Figure 3. Before (A) and after (B) 4 treatment sessions with a 532/1,064-nm picosecond laser.

amateur, and 98% were professionally applied, and they presented a wide array of single color and multicolor tattoos, providing a realistic evaluation of device performance. The 2 wavelengths of the device are designed to address the varying absorption rates of different ink colors, that is, the 1,064 nm wavelength is more effective for black, blue, and green inks, and the 532 nm wavelength is more effective for brown, red, orange, and yellow pigments. The results of the present study demonstrate the high safety and efficacy of this 532/1,064-nm picosecond laser for the removal of decorative tattoos of varying colors and high patient satisfaction with treatment.

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