

Rosacea Treatment Using the New-Generation, High-Energy, 595 nm, Long Pulse-Duration Pulsed-Dye Laser

Eric F. Bernstein, MD^{1*} and Albert Kligman, MD, PhD²

¹Laser Surgery and Cosmetic Dermatology Centers, Bryn Mawr, Pennsylvania

²S.K.I.N., Inc., Conshohocken, Pennsylvania

Background and Objectives: Rosacea results from sun-induced hyper-vascularity of exposed facial skin, often accompanied by acneiform papules and pustules. The pulsed-dye laser has an unparalleled safety record and emits an ideal wavelength for treating the abnormal vessels that occur in rosacea patients. In this study we investigate the ability of the long pulse-duration pulsed-dye laser to improve rosacea.

Study Design/Materials and Methods: Twenty subjects with rosacea were treated with the high-energy, long pulse-duration pulsed-dye laser. An elliptical spot and long pulse-duration was used to spot-treat linear telangiectasias, while a circular spot and short pulse-duration was used to treat the entire face. Improvement was determined by blinded evaluation of photographs and by the treating physician's subjective evaluation, before and 8 weeks following the final treatment.

Results: The average rosacea score as estimated by the treating physician decreased from 2.7 ± 1.1 to 1.4 ± 0.7 (mean+SD) on a 0–6 scale with 0 representing no rosacea and 6 representing the most severe rosacea ($P < 0.001$ level). The average rosacea score as rated by blinded physician observers scoring digital photos was 2.3 ± 1.3 before treatment and 1.4 ± 0.9 8 weeks following treatment, using a 0 (mild) to 6 (severe) scale.

Conclusions: The high-energy, long pulse-duration pulsed-dye laser improves rosacea with a very favorable safety profile, and less purpura than resulted from earlier generation pulsed-dye lasers. *Lasers Surg. Med.* 40:233–239, 2008. © 2008 Wiley-Liss, Inc.

Key words: laser; rosacea; dye; pulsed; spider vein; pulse duration

INTRODUCTION

Rosacea is a skin condition characterized by telangiectasia, erythema, flushing, and blushing of facial skin often accompanied by acneiform papules. Rosacea affects sun-exposed sites of facial skin of genetically pre-disposed individuals. Asymmetrical involvement of facial skin often pre-dominantly occurring on the side of the face adjacent to the driver's side car window suggests that ultraviolet A (UVA) radiation plays a significant role in the development of rosacea. Rosacea affects 5% of the American population, although a Gallup survey found that 78% of Americans had

no knowledge of the condition (http://www.rosacea.org/rr/1998/spring/article_1.php). Seventy percent of rosacea patients surveyed said the condition affected their self-esteem, while 30% reported missing work because due to their rosacea (http://www.rosacea.org/rr/1998/spring/article_1.php). Rosacea symptoms of flushing and blushing acutely worsen due to various triggers including: sun-exposure, hot beverages, alcoholic beverages, exercise, hot or cold weather, and various other stimuli. Although these triggers cause the excess blood vessels of the face to fill with blood producing the symptoms of flushing and blushing, the actual cause of the increased vasculature is sun-exposure. The fact that the areas of the face receiving the most sun-exposure are most affected by rosacea, and the asymmetry of involvement of facial skin exposed to UVA through a car window speak to the sun-induced nature of this condition.

Both the 532 nm frequency-doubled, potassium-titanyl-phosphate (KTP), neodymium-doped, yttrium-aluminum-garnet (Nd:YAG) laser, and the 595 nm pulsed-dye laser deliver wavelengths strongly absorbed by hemoglobin resulting in vessel destruction. Longer pulse-durations in the 40–50 milliseconds domain are necessary to remove these linear vessels without vessel rupture and resulting purpura that can last 7–14 days following treatment [1–4]. Until recently, only the KTP laser offered highly-effective, selective, purpura-free removal of these vessels. Previous attempts to produce a PDL that produced results characteristic of a long pulse-duration laser delivered a series of mini-pulses or “pulselets” over the desired pulse-duration. The earlier generation of the laser used in this current study separated four pulselets over 40 milliseconds, failing to deliver the immediate blanching of the vessels seen when using the 532 nm, 50 milliseconds pulse-duration, KTP laser. Instead, vessels treated with the 40 millisecond setting of the older PDL device most often demonstrated purpura when delivering fluences of 15 J/cm^2 or higher using the available elliptical spot, like those treated with the classic

*Correspondence to: Dr. Eric F. Bernstein, MD, Laser Surgery Centers, 931 Haverford Road, 2nd Floor, Gladwyne, PA 19010.

E-mail: dermguy@hotmail.com

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0.45 or 1.5 milliseconds pulse-duration PDL. The new-generation, long pulse-duration PDL utilizes eight pulses spread over the 40 millisecond pulse-duration, affecting immediate blanching of the treated vessels without purpura, as is seen following treatment with the long pulse-duration KTP laser. In the current study we quantify the ability of the variable pulse-duration PDL to improve rosacea using both long and shorter pulse-durations to address linear telangiectasias, and the diffuse erythema and enlarged pores characteristic of rosacea.

MATERIALS AND METHODS

Subjects

Twenty subjects were enrolled in this study, 18 females and 2 males. Seventeen subjects completed four treatments administered at 4-week intervals, and three subjects dropped out of the study due to temporarily moving out of the Philadelphia region, one after two treatments, one after three treatments, and one after four treatments. Seventeen subjects returned for a follow-up visit 8 weeks following the fourth and final treatment. Subjects ranged in age from 29 to 70 years of age, with a mean age of 54.6 ± 12.7 . Two of the subjects had Fitzpatrick skin type I, while 11 had Fitzpatrick type II skin, and 7 had type III skin. The protocol was approved by an independent Institutional Review Board. The severity of rosacea was graded in each subject by the treating physician using the Investigator Global Assessment (IGA) 7-point static scale which grades rosacea severity on a 0–6 scale with a score of 0 representing no rosacea, 1 representing minimal rosacea, 2 representing mild rosacea, 3 representing mild to moderate rosacea, 4 representing moderate rosacea, 5 representing moderate to severe rosacea, and a score of six representing severe rosacea (Table 1) [5]. Three subjects were rated as having grade 1 rosacea, 3 grade 2, 9 grade 3, 4 grade 4, and 1 grade 5 rosacea. Because the study commenced in January in Pennsylvania and ended in June, the potential for acute sun-exposure to be interpreted as rosacea was not a positive factor affecting the outcome of the study. In fact, if sun-exposure was a factor, it biased the current study in favor of artificially reducing the measured effectiveness of laser treatment.

Laser Treatment

The entire face of each subject was treated with the high-energy, long pulse-duration PDL (V-Beam Perfecta laser, Candela Corporation, Wayland, MA). Subjects were treated to all linear telangiectasias visualized using a cross-polarized headlamp (v600, Syris Scientific, Gray, ME) and treated using a 3 mm × 10 mm elliptical spot using a 40 milliseconds pulse-duration and fluences that were found in preliminary studies to eliminate linear vessels with little or no purpura, ranging from 17 to 19 J/cm². The administered fluence averaged 18.4 J/cm² on the first treatment and increased to 19.0, 18.9, and 19.0 J/cm² on the 2nd, 3rd, and 4th treatments, respectively. Immediately following treatment of linear telangiectasias and during the same treatment session, the entire face was treated using a 12 mm-diameter spot using fluences ranging from 6 to 7 J/cm², and a pulse-duration of 3 milliseconds. Fluences averaged 6.25 J/cm² for the first treatment and 6.6, 6.8, and 7.0 for the 2nd, 3rd, and 4th treatment session, respectively. The maximum fluence that can be administered using the 12 mm spot size and a 3 milliseconds pulse-duration is 7 J/cm². For all treatments with the 3 mm × 10 mm and 12 mm spots, dynamic cooling device (DCD) settings of a 40 milliseconds spurt delivered 20 milliseconds prior to the laser pulse were used. Immediately following treatment of linear telangiectasias with the 3 mm × 10 mm hand-piece and treatment of the entire face with the 12 mm spot, subjects deemed to have ephelides or solar lentigos were treated with a compression hand-piece without the DCD. A fluence of 10.5 J/cm² was used for treating ephelides or solar lentigos, using a 7 mm spot.

Subjects were treated at monthly intervals, for a total of four treatments. Subjects returned for a final visit 8 weeks after the last treatment, for a final evaluation of improvement, side-effects, and for digital photographs. Cross- and parallel-polarized digital photographs were taken of all subjects before, and 8 weeks after the final treatment, with the same camera using identical magnification, lighting, and exposure (Visia-CR, Canfield Scientific, Fairfield, NJ).

Subjective Evaluation of Improvement

To assess efficacy, the treating physician determined the rosacea score both pre- and 8 weeks post-treatment

TABLE 1. Rosacea Grading Scale

Rosacea Grade	0	1	2	3	4	5	6
Description	Clear	Minimal	Mild	Mild to Moderate	Moderate	Moderate to Severe	Severe
Inflammatory Lesions	None	Rare	Few	Distinct	Pronounced	Many	Numerous
Erythema	None to Residual	Residual to Mild	Mild	Mild to Moderate	Moderate	Moderate to Severe	Moderate to Severe
Telangiectasia	None to Mild to Moderate	Mild to Moderate	Mild to Moderate	Mild to Moderate	Mild to Moderate	Moderate	Moderate to Severe

(Table 1). In addition, the treating physician counted the number of rosacea papules before treatment, after each treatment, and 2 months following the final treatment. Subjects were also evaluated by the treating physician for improvement in redness, hyper-pigmentation, enlarged pores, and roughness as compared to pre-treatment photographs 8 weeks following the final treatment. Cross-polarized digital photographs were used to evaluate facial veins and hyperpigmentation, while parallel-polarized digital photographs were used to evaluate wrinkles and enlarged pores. The following scale was used by the treating physician: 0 = no improvement, 1 = <25% improvement %, 2 = 26–50%, 3 = 51–75%, and 4 = > 75% improvement.

Blinded Evaluation of Digital Photos

Digital photographs were evaluated in randomized pairs (before/after) by four physicians not otherwise involved in the study, in a blinded fashion. Blinded observers graded subjects pre- and post-treatment for rosacea severity (Table 1). In addition, blinded physician raters used the following scale: 0 = no improvement or clear at baseline, 1 = 1–25% improvement (mild), 2 = 26–50% improvement (moderate), 3 = 51–75% improvement (marked), and 4 = 76–100% improvement (excellent) to rate the degree of improvement in clinical parameters outlined below, from randomized pairs of digital photos. The assessing physician attempted to select the baseline photograph for each treatment, and then rated the degree of overall improvement, as well as improvement in redness, hyper-pigmentation, fine lines, enlarged pores, texture (defined as smoothness), and tone (defined as homogeneity of color). Views of the left, right, and central face were evaluated. Cross-polarized images were used to evaluate overall improvement, linear vessels, diffuse erythema, and pigmentation, while parallel-polarized images were used to assess wrinkling and enlarged pores. If the assessor incorrectly identified the baseline photograph, then the assessor’s score was changed to a negative (i.e., a 2 score was assigned a –2).

Side Effects

Pain was assessed by the subjects, and purpura, edema, and erythema by the treating physician, immediately

after each laser treatment. Pain was evaluated by the subjects using a 0–10 scale, with 0 = no pain, and 10 = severe pain. Purpura, edema, and erythema post-treatment were evaluated by the treating physician using a 0–3 scale with 0 = none, 1 = mild, 2 = moderate, and 3 = severe pain, purpura, edema, or erythema. Potential side-effects of hyper- or hypo-pigmentation or scarring were also evaluated by the treating physician 8 weeks following the final treatment.

RESULTS

Subjective Evaluation of Improvement

Rosacea scores as evaluated by the treating physician decreased significantly 8 weeks following the 4th and final laser treatment. The average rosacea score decreased from 2.7 ± 1.1 to 1.4 ± 0.7 (mean + SD) on a 0–6 scale with 0 representing no rosacea and 6 representing the most severe rosacea. This difference in rosacea score was significant at the *P* < 0.001 level. Breaking down the rosacea scores by severity, subjects with an initial rosacea score of 0–2.0 averaged 1.6 before treatment and 0.8 two months following the final treatment. Those having an initial rosacea score of 3.0 averaged a score of 1.4 two months after the final treatment. Those subjects with the most severe rosacea scores of from 4 to 6 averaged a score of 4.25 before treatment and 2.0 at the final follow-up visit.

The average number of rosacea papules was 6.8 before treatment, 3.0 one month following the first treatment, 2.1 one month following the second treatment, 0.4 one month after the third treatment, and 0.2 two months following the fourth and final treatment. The difference in rosacea papules pre- and post-treatment was significant at the *P* < 0.01 level. The treating physician’s assessment of overall improvement in skin appearance and the amount of improvement of wrinkles, facial veins, enlarged pores, and hyperpigmentation 8 weeks following the final treatment is presented in Table 2. Using a 0–4 scale with 0 representing no improvement and 4 representing maximal improvement, the average improvement in overall appearance, redness, roughness, enlarged pores, and hyperpigmentation were 2.4, 2.6, 1.6, 1.4, and 1.4, respectively. Thus on average, overall appearance as rated by the treating physician improved approximately 36%, while redness improved

TABLE 2. Investigator’s Ratings for Overall Improvement, and Improvement in Redness, Roughness, Enlarged Pores, and Hyper-Pigmentation on a 0 Min to 4 Max Scale; n = 17

Score	Overall improvement	Improvement in redness # (%) assigned	Improvement in roughness # (%) assigned	Improvement of pores # (%) assigned	Improvement of hyperpigmentation # (%) assigned
0	0	0	3 (18)	0	1 (8)
1	0	0	2 (12)	11 (65)	8 (47)
2	9 (53)	6 (35)	10 (59)	6 (35)	8 (41)
3	8 (47)	11 (65)	2 (12)	0	0
4	0	0	0	0	0
Average	2.4	2.6	1.6	1.4	1.4

40%, roughness improved 15%, enlarged pores improved 10%, and hyperpigmentation improved 10% (Table 2).

Blinded Evaluation of Digital Photos

The average rosacea score as rated by blinded physician observers on a scale of 0 (least severe) to 4 (most severe) was 2.3 ± 1.3 before treatment and 1.4 ± 0.9 eight weeks following treatment (Fig. 1). This reduction in rosacea severity score was significant at the $P > 0.001$ level. Improvement was noted by the blinded physician observers in 79% of paired images for overall improvement (Fig. 2), 80% for facial redness, 70% for hyperpigmentation, 62% for fine

lines, 64% for skin texture, 74% for skin tone, and 36% for improvement in enlarged pores (Fig. 3).

Breaking down the rosacea scores by severity, those subjects rated as having a score of from 1 to 2 averaged 1.8 pre-treatment and 1.4 two months post-treatment. Subjects having a score of from 2.5 to 4.0 pre-treatment had a pre-treatment score of 3.0 and a post-treatment score of 1.8.

Side-Effects

Pain was rated on a 0–10 scale with 0 = no pain and 10 = the most severe pain, and averaged 6 for each of the

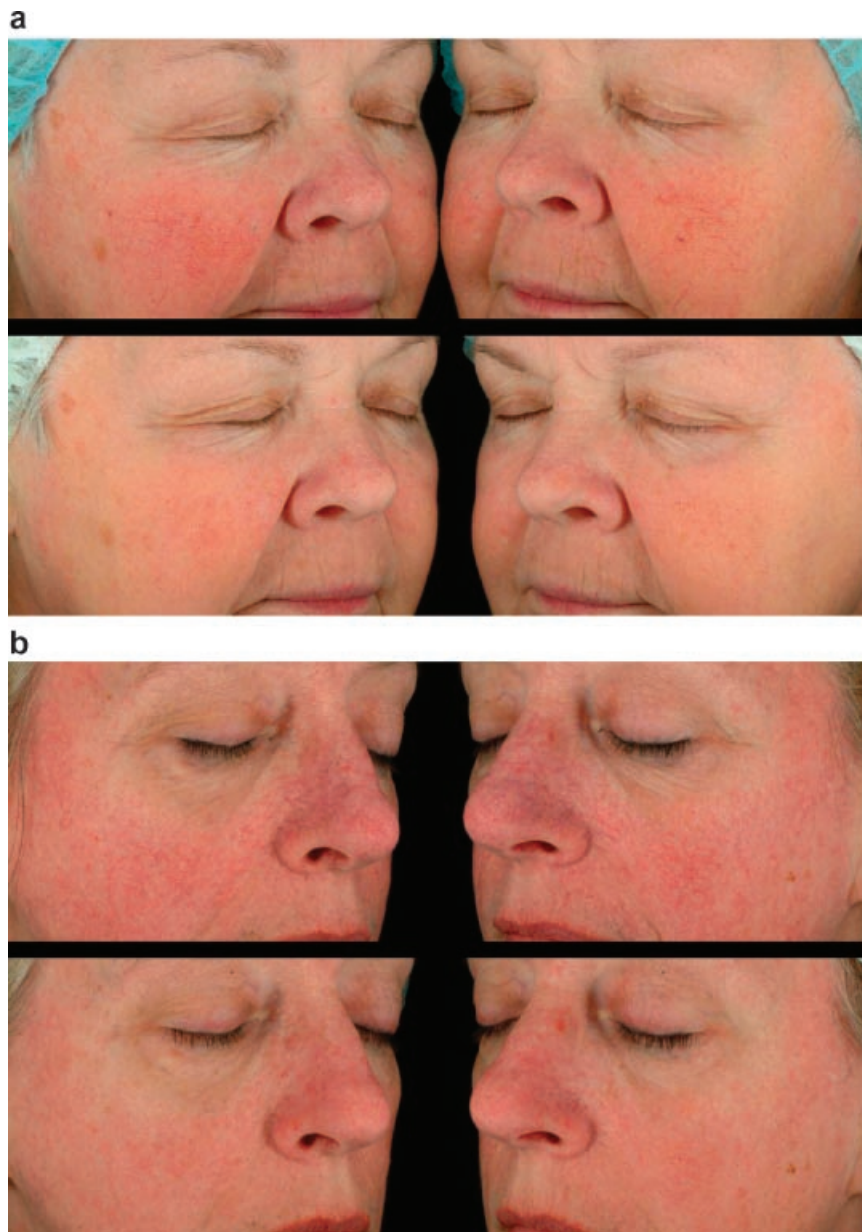


Fig. 1. **a,b:** Cross-polarized images of subjects prior to laser treatment (top image) and 8 weeks after four treatments with the long pulse-duration PDL (bottom image).

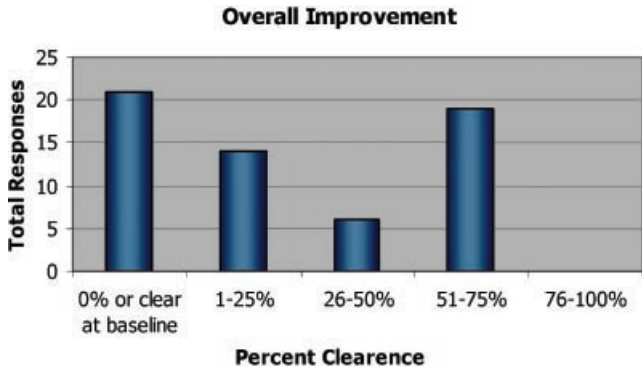


Fig. 2. Overall improvement of skin as assessed by four blinded physician observers evaluating cross-polarized digital photographs.

four treatments. Edema and erythema were noted post-treatment in all subjects and was scored on the 0–3 scale with 0 = no erythema or edema and 3 = severe erythema or edema. Edema ratings averaged 1.2, averaging results from all four treatments, and ranged from 0 to 2. Erythema ratings averaged 1.8, and ranged from 1 to 3. Purpura averaged a score of 1 over all treatments, ranging from 0 to 2. Purpura was noted in 10 of 20 subjects following the 1st treatment, but only 2 of these had purpura from treating linear vessels; while the remaining 8 patients with purpura had it from using the compression handpiece to treat epihelides. Following the 2nd treatment, 17 of 20 subjects had purpura; in 12 subjects it was at the site of the compression handpiece used to treat pigmented lesions, and 5 had purpura at the site of treatment with the 3 mm×10 mm spot for removing linear telangiectasias. After the 3rd treatment, 10 of 19 subjects had purpura, with 8 subjects developing purpura at the sites of the

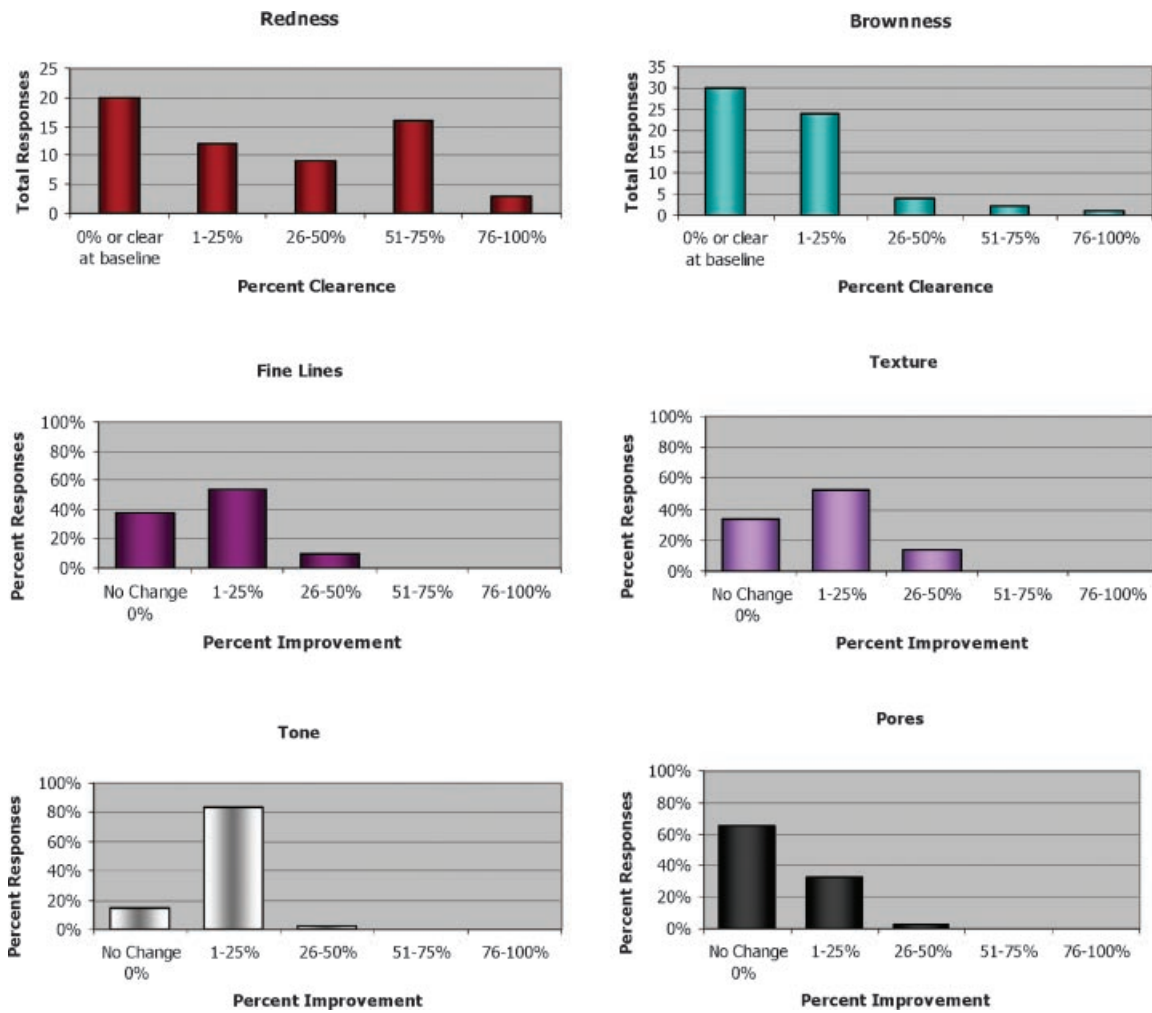


Fig. 3. Evaluation of redness, hyperpigmentation, and skin tone was determined by four blinded physician observers evaluating cross-polarized digital photographs; while improvement in fine lines, texture, and pore reduction were determined evaluating parallel-polarized digital photographs.

compression handpiece and 4 developing it at the site of treatments with the 3 mm×10 mm handpiece. Following the 4th and final treatment, purpura was seen in 13 of 18 subjects, with 6 subjects having purpura at the site where the compression handpiece was used, and 7 having purpura at the site where the 3 mm×10 mm handpiece was used to treat telangiectasias. Thus, 23% of treatments resulted in mild purpura at the sites where the elliptical handpiece was used to treat linear telangiectasias, while 44% had purpura at the sites where the compression handpiece was used to treat ephelides or solar lentigos. No hyperpigmentation, hypopigmentation, or scarring was noted by the treating physician at any follow-up visit, or by the blinded physician observers rating digital photographs taken 8 months following the 4th and final treatment.

DISCUSSION

This study demonstrates that the long pulse-duration, 595 nm, PDL is safe and effective for treating rosacea with minimal side-effects and no long-term complications. Subjective assessment of rosacea scores correlated remarkably well with blinded physician assessment of cross-polarized, digital photographs. The treating physician rated the average rosacea score to be 2.7 pre-treatment, as compared to 2.3 for blinded evaluators; while the final rosacea score was determined by both the treating physician and blinded evaluators to be 1.4. The blinded physician evaluation of photographs rated redness as the parameter most improved of all variables studied. This, of course, is no surprise since subjects were admitted to the study with a diagnosis of rosacea, and the PDL highly targets cutaneous vasculature. The improvement of other signs of photodamage, such as enlarged pores or textural irregularity probably resulted from the subsequent inflammatory response to laser treatment. In addition to a dramatic reduction in facial vessels; wrinkles, enlarged pores, pigmentation, facial tone, and texture also improved but to a lesser degree and in fewer subjects. Changes in the parameters not differing in color from surrounding skin are more difficult to measure from photographs; however, improvement was seen in the current study using cross-polarized digital photos to evaluate changes in pigmentation, tone, and vasculature, while parallel-polarized images were used to compare textural irregularities such as wrinkles, texture, and improvement of enlarged pores.

People with rosacea often have both linear vessels and diffuse redness, and the current study used separate parameters to address these two problems. Thus, the ability to deliver a 40 millisecond pulse-duration enabled optimal treatment of larger vessels, while the 3 millisecond pulse-duration was used to treat diffuse erythema. Using a 1.5 millisecond pulse-duration without the DCD and using compression targeted surface pigment, however purpura resulted after 44% of these treatments. Multiple pulses over the same area and the use of shorter pulse-durations resulted in more purpura than seen in a previous study using this laser but treating patients with a fixed

10 milliseconds pulse-duration [6], although significantly less than results from treatment with previous generation PDLs. The PDL is an ideal device for treating rosacea, since the 595 nm wavelength targets hemoglobin, and unlike intense pulsed-light devices, delivers all of the administered energy in a wavelength that is strongly taken up by the hemoglobin in blood vessels [6,7]. The PDL has an unparalleled safety record and has been used to treat port-wine stains for over two decades [8–12]. Treatment of rosacea with the PDL has been shown to improve not only the telangiectasias and erythema, but also the symptoms associated with rosacea [13–18]. Although purpura-free removal of cutaneous vessels has been documented using pulse-durations of 6 and 10 milliseconds [6,14], the use of two separate settings in the current study enabled optimal treatment of linear vessels and diffuse erythema, while reducing but not eliminating purpura in all subjects. Twenty-three percent of subjects had purpura resulting from treating linear telangiectasias using the 3 mm×10 mm handpiece and a 40 millisecond pulse-duration, during the same treatment session that diffuse erythema was treated with the 12 mm handpiece using a 3 millisecond pulse-duration. Clinical experience has shown that decreasing the pulse-duration to 1.5 milliseconds further increases the risk of purpura post-treatment, and that increasing the pulse-duration to 6 milliseconds reduces that risk. Individual tolerances will determine a patient's threshold for this temporary but embarrassing side-effect. The discomfort noted in our current study averaged 6 out of a maximum of 10, and seems somewhat high for a pulsed-dye laser. However, we believe these ratings to accurately reflect the discomfort felt during treatment. Longer pulse-durations result in less purpura at fluences necessary to remove most vessels as compared to much shorter pulse-durations (0.5–1.5 milliseconds), but added discomfort seems to be the price one pays.

Demonstrating improvement in fine lines, texture, and enlarged pores is more difficult than documenting improvement in redness or pigmentation, since the former are the same color as unaffected skin and demonstrate their presence by creating shadows. However, previous studies have shown improvement in enlarged pores and rhytides following PDL treatment [6,19–24]. Although laser treatment of unwanted vasculature works by targeting unwanted vessels directly, perhaps with the added benefit of an inflammatory response post-treatment; the ability of laser treatment at the 595 nm wavelength to improve fine lines and texture as well as to shrink enlarged pores, probably depends upon a number of intermediate steps involving activation of mast cells and other inflammatory cells, which in turn impart their influence by remodeling sun-damaged extracellular matrix in the dermis. Sixty-two percent of subjects demonstrated improvement in fine lines, with 38% demonstrating no change, as evaluated in pre- and post-treatment photographs by blinded physician observers.

Sixty-six percent of subjects demonstrated improvement in skin texture, with 34% showing no difference. In

addition, 36% of subjects demonstrated photographic evidence of pore reduction, with 64% showing no change. The above improvement in the surface characteristics of treated skin was all noted from blinded physician evaluation of parallel-polarized photographs. Although in the majority of subjects no improvement in pore size was noted, perhaps specific measurements of pore size such as three-dimensional, *in vivo*, optical, topographic imaging might provide better insight into the ability of the PDL to affect pore-size. Improvement in fine lines and texture was noted by blinded, physician assessment of digital photograph as well, but future studies utilizing more sensitive imaging techniques may better quantify this improvement. Although previous-generation PDLs and KTP lasers have been shown to improve rhytides [20–24], the laser used in the current study offers longer pulse-durations and more varied options for treatment including a larger diameter treatment spot that should enable deeper penetration of laser energy. The effect these parameters have on improvement of fine lines and wrinkles, enlarged pores, and sagging skin remain to be fully elucidated. Future studies to further optimize treatment parameters for treating rosacea combined with more extreme strategies to reduce sun-exposure such as daily high-SPF sunscreen use and UVA-blocking window film on car, office, and home windows, should enable even greater and more persistent improvement in rosacea in the future. In addition, longer follow-up should demonstrate how long-lasting the improvement seen in this study can be, when adequate sun-protection is made part of a daily care regimen.

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