

Low-Fluence 585 nm Q-Switched Nd:YAG Laser: A Novel Laser Treatment for Post-Acne Erythema

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Background: Persistent post-acne erythema is one of the most common aesthetic sequelae to arise after active acne resolves. The treatment remains challenging due to lack of effective laser modalities.

Objectives: To evaluate the safety and efficacy of a low-fluence 585 nm Q-switched Nd:YAG laser for the treatment of post-acne erythema.

Materials & Methods: Twenty-five patients with post-acne erythema were treated with a low-fluence Q-switched Nd:YAG laser using the 585 nm Gold Toning™ handpiece (5 mm spot size, 5–10 ns, 0.30–0.55 J/cm², 2–4 passes) for three sessions at 2-week intervals. Erythema lesion (macules) count, inflammatory acne (papules, pustules) count, erythema index, degree of post-acne erythema and overall improvement in post-acne erythema and acne scar were assessed at baseline, every 2 weeks and 6 weeks after the last treatment. Subjective degrees of satisfaction were also evaluated. Adverse events were recorded and pain was scored using a visual analog scale (VAS).

Results: At 6 weeks after 3 sessions of laser treatment, all patients demonstrated clinical improvement. Erythema lesion counts decreased by 20.1% (versus baseline) after the first treatment ($P = 0.004$), by 32.7% after the second treatment, by 46.5% at 2 weeks after the third treatment and by 58.7% at the 6-week follow-up (all $P < 0.001$). Significant improvements were also noted in erythema indices (22.29 ± 2.4 to 17.51 ± 1.8) and mean post-acne erythema scores after the first treatment (both $P < 0.001$). The mean scores of independent physician assessments were 4.04 ± 0.9 in term of the improvement of post-acne erythema and 3.44 ± 0.9 in the improvement of scarring. In addition, we could observe a significant decrease in inflammatory acne lesion counts after two laser treatments with a decrease in mean lesion counts by 67% at the 6-week follow-up. Treatment was well-tolerated and adverse effects were limited to transient erythema and edema at treatment sites.

Conclusions: Low-fluence 585 nm Q-switched Nd:YAG laser treatment is safe and effective for the treatment of post-acne erythema with minimal discomfort and quantifiable improvement in the appearance of early acne scarring and inflammatory acne. *Lasers Surg. Med.*

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Key words: Acne; Post-acne erythema; 585nm Q-Switched Nd:YAG Laser

INTRODUCTION

Acne is a common skin disease that affects individuals of all skin types. Several interrelated pathogenetic factors such as genetic background, abnormal follicular keratinization, sebum production, *Propionibacterium acnes* colonization and inflammation contribute to two main clinical features of acne: non-inflammatory and inflammatory lesions [1,2]. Recently, the concept of acne pathogenesis has focused on inflammatory processes which occur in both early and late stage acne lesions [3]. Therefore, acne is primarily an inflammatory disease from beginning to resolution [3,4]. Thus, the aim of acne treatments should emphasize suppression of inflammation.

Post-acne erythema (PAE), also referred to as Post-inflammatory erythema (PIE), is a common sequela in acne patients. It is defined as lesions consisting of telangiectatic and erythematous macules, which occur as a result of skin inflammation [5]. Some post-acne erythema lesions may improve with time, but persistent post-acne erythema, which is experienced by many patients, is cosmetically unacceptable and is a therapeutic challenge. No particular drugs have shown any efficacy, and some of the acne drugs are known to even exacerbate this problem [6]. In practice, a wide range of laser treatments such as 595-nm pulsed dye lasers (PDL), intense pulsed light and non-ablative (1,550-nm) fractional lasers, have been used to treat this condition. However, results are variable and multiple treatment sessions are generally required for satisfactory results [7–10].

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The purpose of this study was to evaluate the efficacy of a novel laser treatment, a low-fluence, 585-nm Q-switched Nd:YAG laser, for persistent post-acne erythema. Because of the absorption characteristics at this wavelength, we postulate that low-fluence, 585-nm Q-switched Nd:YAG laser treatment may alter the vasculature architecture resulting in the normalization of dilated dermal microcapillaries and decrease to some extent the incidence of post-inflammatory hyperpigmentation (PIH), particularly in PIH-prone darker skin types.

MATERIALS AND METHODS

This prospective study was designed to evaluate the efficacy and safety of a low-fluence Q-switched Nd:YAG laser (SPECTRA™, Lutronic corporation, Goyang, Korea) with the 585-nm Gold Toning™ handpiece for the treatment of post-acne erythema. This study protocol followed the Declaration of Helsinki and was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University.

Subjects

Twenty-five subjects (17 men and 8 women, aged 18–26 years [mean 20.08 years]) with post-acne erythema and Fitzpatrick skin phototypes III–V were enrolled in this study. All subjects had mild to moderate facial acne (acne severity grade 1 or 2 depending on the number of lesions according to modified numerical grading of Plewig and Kligman [11]). In grades 1 and 2, the lesion count of comedones and papulopustular lesions should be fewer than 40 for each. Active acne of these subjects was to some degree adequately controlled with topical agents. Exclusion criteria were pregnancy and breast feeding, skin infection, history of skin cancer and treatment with oral isotretinoin, chemical peeling, any type of laser or intense pulsed light within the previous 3 months and refusal to give informed consent. All subjects were asked to avoid sun exposure, use broad-spectrum sunscreen (SPF \geq 30) and continue only their current topical acne medications throughout the study. After having had all aspects of the study explained to them, subjects gave written informed consent to participate in the study and for the use of their clinical photography.

Laser Treatment

Post-acne erythema lesions were treated using the low fluence Q-switched Nd:YAG laser with the 585-nm Gold Toning™ handpiece. No topical anesthetics were used prior to treatment. Laser treatment was performed over all areas with post-acne erythema, inflammatory acne lesions and acne scars using the following parameters: wavelength 585 nm, spot size 5 mm, pulse duration 5–10 ns, fluence 0.30–0.55 J/cm² and 2–4 passes. Different fluences and treatment passes were applied based on the degree of disease severity, with changes proportional to the amount of erythema, skin types and skin reaction to lasers. For the darker skin types V and VI, the starter fluence was lower compared to others because of the higher concentration of

epidermal melanin. When some improvement in the clinical degree of acne erythema had been achieved, the fluences were increased in subsequent treatment sessions as the epidermal melanocytes adapted to the incident 585 nm energy. The technique used for treatment was to “paint” the laser energy over the target tissue, moving the handpiece smoothly but rapidly, making multiple passes over lesions, until the endpoints were reached, namely mild erythema and edema of the lesions. (Fig. 1A) Ice pack cooling was applied to subjects in whom a moderate to marked reaction was noted. (Figs. 1B, C) Treatments were performed by R.P. at 2-week intervals for a total of 3 sessions.

Clinical Assessments

Therapeutic outcomes were evaluated by post-acne erythema lesion count, inflammatory acne lesion count, erythema index and standardized clinical photography at baseline, prior to each treatment and at the 2-week and 6-week follow-up visits. The primary objective of the study was to demonstrate improvement in facial post-acne erythema as determined by a reduction in post-acne erythema lesion count at 6 weeks after three laser sessions. Post-acne erythema lesions and inflammatory lesions were counted by a trained rater, who did not participate in the laser treatments. The erythema index was measured with a DSM II colorimeter (Cortex Technology, Hadsund, Denmark) on three selected post-acne erythema lesions per subject, averaging the results. We used these same sites at each visit. The color of post-acne erythema lesions was quantified into four severity grades by the primary investigator, R.P., as described in Table 1. The clinical improvements of post-acne erythema and acne scars were determined using a five-point grading scale (1 = 0–10%; 2 = 11–25%; 3 = 26–50%; 4 = 51–75%; and 5 = >75% improvement). Assessment was performed by a blinded evaluation panel consisting of three dermatologists through recorded standardized clinical photographs which were obtained using the VISIA® Complexion Analysis system (Canfield Scientific, Fairfield, NJ, USA).



Fig. 1. Immediately after laser treatment **A**: mild edema and erythema **B**: moderate reaction **C**: marked edema and surrounding erythema. These reactions were transient and quickly improved after application of ice.

TABLE 1. Four-Point Post-Acne Erythema Severity Grading

Grade	Level of disease	Characteristics
0	None	Clear
1	Mild	Faintly detectable erythema, light pink
2	Moderate	Dull red, clearly distinguishable
3	Severe	Deep/dark red

Subjective Assessment

At the end of the study, the subjects' perceptions of overall treatment results were assessed using a questionnaire and the physician grading of the level of improvement in erythema lesions was performed using a five-point scale.

Safety Assessment

Pain scores using the VAS were collected at each treatment visit. Adverse events were recorded following each treatment and at all follow-up visits. Possible side-effects during and after treatment including erythema, edema, pruritus, dryness, tingling sensation, burning sensation, scaling, burns, pain, and pigmentary changes were recorded. Subjects were asked to report any complications during the treatment period.

Statistical Analysis

Data are expressed as means \pm standard deviations. Paired *t*-tests were used to compare mean changes in post-acne erythema lesion counts, erythema indices and inflammatory acne counts at baseline, every 2 weeks and 2 and 6 weeks after the last treatment. The Mann–Whitney U-test was used to compare improvements between groups. Data were analyzed using SPSS software (version 16.0; SPSS Inc., Chicago, IL, USA). *P*-values of less than 0.05 were considered statistically significant.

Results

All twenty-five subjects completed the treatment and follow-up period.

Post-Acne Erythema Lesion Count. At 6 weeks after three sessions of laser treatment, all subjects demonstrated clinical improvement. Photographs of representative cases with comparative response are shown in Figs. Fig. 2 and Fig. 3. Mean post-acne erythema lesion counts decreased significantly from 98.2 ± 59 at baseline to 78.5 ± 37 ($P = 0.004$), after the first treatment and to 66.1 ± 34 , 52.5 ± 34 and 40.6 ± 25 after the second and third treatments, and at the 6-week follow-up, respectively (all $P < 0.001$). This corresponds to a 20.1% reduction after the first treatment, 32.7% after the second treatment, 46.5% at 2 weeks after the third treatment and a total decrease of 58.7% at the 6-week follow-up. (Fig. 4)

In 18 out of 25 subjects, at least one topical agent was used. The topical agents used concurrently were clindamycin phosphate (11 subjects), benzoyl peroxide (10

subjects) and a retinoid (8 subjects). There was no significant difference in terms of clinical response between subjects who used and did not use topical treatments ($P = 0.203$).

Erythema Index

Erythema indices demonstrated a significant decrease after the first laser treatment. Mean erythema indices decreased significantly from a mean baseline value of 22.29 ± 2.4 to 19.84 ± 1.9 after the first treatment ($P < 0.0001$) and to 18.9 ± 1.8 , 18.25 ± 1.9 and 17.51 ± 1.8 after the second, third treatment and at the 6-week follow-up, respectively (all $P < 0.001$). This corresponded to an 11% reduction after the first treatment, 15.2% after the second treatment, 18.12 at 2 weeks after the third treatment and a total decrease of 21.44% at the 6-week follow-up. (Fig. 5)

Physician Assessments

Percent improvement of post-acne erythema determined on a five-point scale. After the three treatment sessions, comparisons between baseline and post-treatment photographs by the independent panel of dermatologists demonstrated that 40% of subjects showed 50–75% improvement in post-acne erythema (Grade 4) and 36% showed more than 50% improvement (Grade 5). The mean investigator assessments score was 4.04 ± 0.9 at 6 weeks after 3 sessions.

Percent improvement of acne scar determined on a five-point scale. At 6 weeks after 3 sessions, improvement of the acne scar appearance was observed in all subjects. Photographs of a representative case are shown in Fig. 6. Evaluators scored 25–50% improvement (Grade 3) in 36% of subjects and more than 50% improvement (Grade 4, 5) in 49%. The mean investigator assessment score was 3.44 ± 0.9 .

Four-Point Post-Acne Erythema Severity Grading

Improvement in the mean post-acne erythema severity scores was also noted after 1 treatment. Mean erythema indices decreased significantly from a mean baseline value of 2.87 ± 0.3 to 2.32 ± 0.5 , 1.65 ± 0.5 , 1.39 ± 0.5 and 1.03 ± 0.6 after the first, second, third treatment and at the 6-week follow-up, respectively (Wilcoxon sign rank test, all $P < 0.001$). The intensity of post-acne erythema decreased with each successive session. The post-acne erythema lesions were rated clear in 16.1% of subjects at 6 weeks after 3 sessions (Fig. 7).



Fig. 2. **A:** Baseline **B:** after one session **C:** after two sessions **D:** 2 weeks after 3 sessions and **E:** 6 weeks after three sessions. Grade 5 or >75% improvement in post-acne erythema and grade 4 or 51–75% improvement in acne scars were achieved as determined by independent clinician assessment of the clinical photography.

Inflammatory acne count. The number of inflammatory acnes significantly decreased after only 2 laser sessions. Mean inflammatory acne lesion counts decreased significantly from a baseline value of 22.72 ± 14.2 to 18.04 ± 9.4 after the first treatment ($P = 0.072$) and to 16.28 ± 9.2 ($P = 0.016$) after the second treatment and 12.04 ± 7.4 and 7.48 ± 4.3 at 2 weeks and 6 weeks' follow-up visit, respectively (all $P < 0.001$). This corresponds to a 20.6% reduction after the first treatment, 28.35% after the second treatment, 47% at 2 weeks after the third treatment and a total decrease of 67% at the 6-week follow-up. (Fig. 8) Subgroup analysis of the reduction in inflammatory acne count showed no significant difference between subjects who used and did not use topical treatments ($P = 0.739$).

Patient Subjective Assessment

At the 6-week follow-up visit, subjects were asked to assess their treatment results while referring to baseline photos comparing how they looked in the mirror with their pre-treatment photos on a five-point scale (excellent, good, fair, some, little/no improvement). Eighty-nine percent of subjects assessed their overall improvement as good or excellent (Grade 4, 5). All subjects felt that their post-acne erythema had improved after treatment in terms of fading in color and reduction in the number of lesions. Reduction in inflammatory acne and smoother skin texture/acne scar depression were also reported in 56% and 48% of patients, respectively. In addition, all patients would like to recommend this treatment to their friends and family members.

Safety Assessment

Treatment-related pain was well-tolerated by all subjects without the need of topical anesthetic use. The mean

VAS for pain was 3.0 [0–7]. The side effects were limited to temporary accentuated erythema and edema at the treatment sites, which resolved within 10–60 minutes.

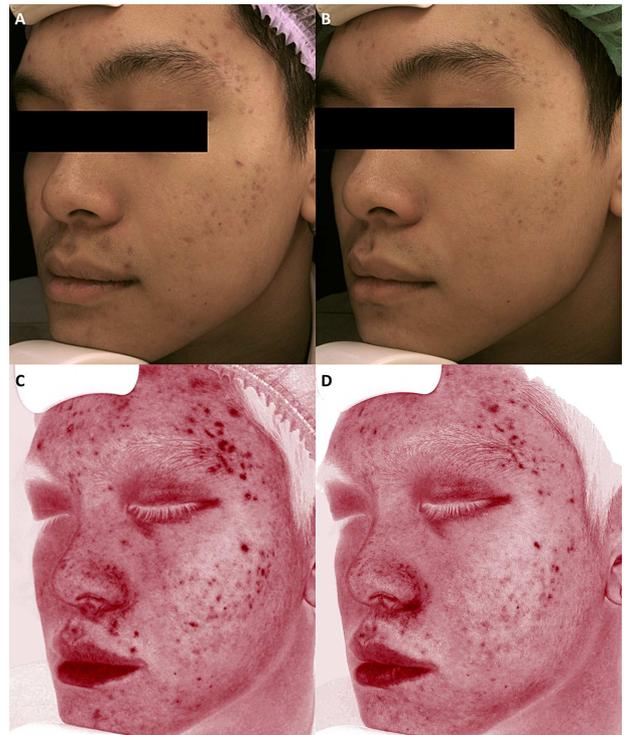


Fig. 3. **A** and **C:** Baseline **B** and **D:** 6 weeks after three sessions. The improvement of acne erythema is better visualized with red enhanced images (**C** and **D**). Grade 5 or >75% improvement in post-acne erythema and grade 3 or 26–50% improvement in acne scars were achieved as determined by independent clinician assessment of the clinical photography.

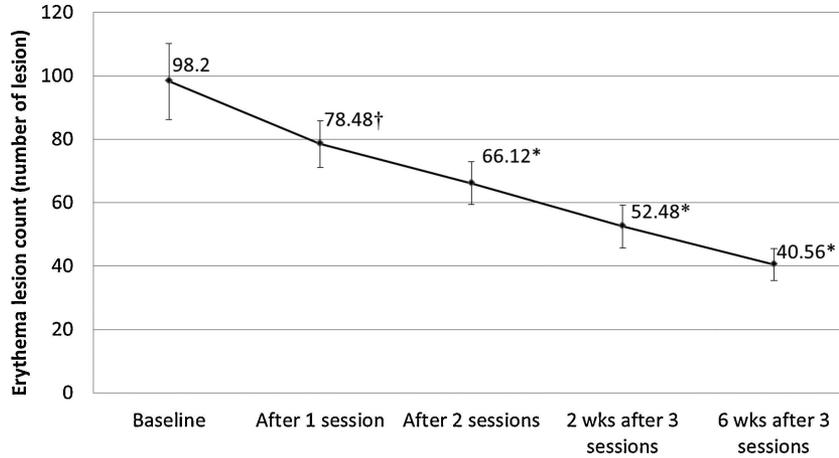


Fig. 4. Post-acne erythema lesion count at different time points. The data represent mean scores with error bars corresponding to the standard error of the mean. (paired *t*-test, †*P* < 0.05, **P* < 0.001 compared with baseline) The number of erythema lesion significantly reduced after 1 treatment.

Purpura was not observed in any subjects, and adverse effects related to laser treatment, such as pigmentary changes, burns, and scarring were not seen.

DISCUSSION

Acne vulgaris affects almost 80 percent of adolescents and young adults [11]. It can result in many consequences including post-acne erythema, post-inflammatory hyperpigmentation (PIH), and scarring, causing huge psychological and social burdens to affected individuals even after the active disease has waned [12]. Psychological deficits do not necessarily correlate with disease severity, as mild to moderate disease can often negatively impact on self-esteem and can be associated with significant depression, body dysmorphic and suicidal ideation [13]. The aims of therapy should therefore not be limited only to achieving clearance of acne, but also to preventing the sequelae.

Post-acne erythema is one of the most problematic cosmetic concerns in acne patients. This is postulated as being due to wound healing-related dilatory changes in

microvascular structures such as the microcapillary plexus in the very superficial dermis which are not detectable by the naked eye as visible telangiectasia but as general redness. In addition, the epidermis is still in the process of maturation after repair and is therefore thinner, allowing more incident light to be reflected off the dilated microvasculature, also part of the wound healing process, which adds to the perceived “redness”. Some believe that this condition is also caused by exogenous stimuli, such as the application of certain anti-acne topicals. These lesions may resolve over time, but the persistent post-acne erythema is quite common, sometimes lasting for 2–6 months (authors’ observation). However, the mechanism for this long-lasting phenomenon after successful treatment of acne has not been elucidated [12].

A variety of therapeutic options has been described with variable clinical outcomes and side effects [7,10,14–16]. Unfortunately, there is no standard treatment and the number of published clinical studies is limited. PDL

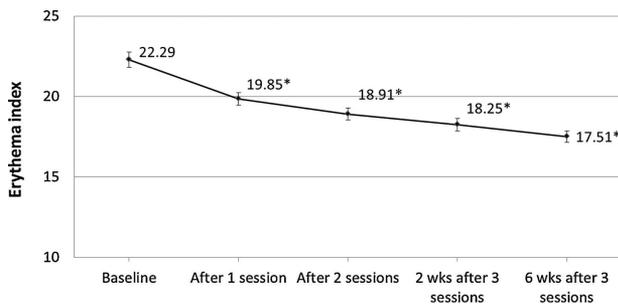


Fig. 5. Erythema index at different time points. The data represent mean scores with error bars corresponding to the standard error of the mean. (paired *t*-test, **P* < 0.001)

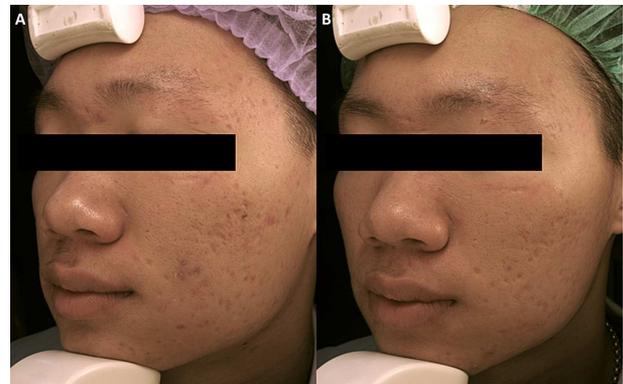


Fig. 6. **A:** Before treatment **B:** 6 weeks after 3 sessions. The improvement in = acne scar texture is especially notable on the temple region.

treatment, arguably the most studied intervention for vascular lesions, was also investigated in the treatment of inflammatory acne itself, however the results were inconsistent [17–23]. In 2008, Yoon *et al.* studied the efficacy of a long-pulsed, 595-nm PDL for the treatment of post-acne erythema. The study showed significant reduction in post-acne erythema lesion counts and the erythema index as well as improvement in skin elasticity after two laser treatment sessions with minimal downtime [8]. Regrettably, in our practice satisfactory outcomes of treating post-acne erythema with PDL have been slowly achieved, have not always been successful, and multiple sessions have usually been required for optimal clearing. This is perhaps because of the higher density of the competitive chromophore melanin in the darker skin type associated with the general population in Thailand compared with other lighter skin types in other countries. Purpura is a potential side effect associated with PDL treatment of any vascular-related lesion, especially at shorter pulsewidths, and the induction of purpura can increase the possibility of PIH formation. Additionally, cryogen cooled devices are not without risks in darker skin types [24].

Recently, Park *et al.* reported a split-face study comparing the effect of non-ablative, 1,550 nm fractional laser and a 595 nm PDL for the treatment of post-acne erythema. Three laser sessions were performed at 4-week intervals in 12 subjects. Results showed both lasers were effective and safe for post-acne erythema: however, the 1,550-nm, erbium-glass fractional laser yielded slightly better outcomes. Some limitations of Park's study included the small sample size and lack of adequate quantitative assessments [14].

Our study has a major limitation, in that the follow-up period was only 6 weeks. However, from our experience, the shortest reasonable period to assess the improvement in post-acne erythema, active acne and acne scars is six weeks. Naturally a longer-term follow-up of 12 weeks to 6 months would be ideal, and such a study is being planned. In the present study, we observed marked improvement in post-acne erythema after treatment with low-fluence 585-nm Q-switched Nd:YAG which significantly reduced post-acne erythema lesion counts and the degree of redness

without any downtime. Quantitatively, colorimeter readings showed a significant decrease in the degree of erythema after the first treatment. However, complete clearing of post-acne erythema in all cases would likely need multiple treatment sessions. In addition, the inflammatory acne count significantly decreased after two laser sessions. Because we targeted post-acne erythema lesions, not inflammatory acne per se, concurrent topical acne medications were allowed to prevent the exacerbation of the inflammatory acne. These medications, however, had little or no effect on the telangiectatic properties of post-acne erythema, and no significant difference was noted between subjects who used or did not use topical medications. Hence, this laser modality could also be helpful in controlling inflammatory acne.

Post-acne erythema can occur alone or in combination with immature or mature atrophic scars or other scar types. Laser treatment was also performed all over areas of acne scarring with and without erythema. Some improvement in acne scar texture was clearly observed in all subjects. The appearance of these depressed scars can also be improved when the base turns less red. Therefore, our results suggest that the low-fluence 585-nm Q-switched Nd:YAG laser could be utilized as a non-ablative dermal remodeling therapy for depressed acne scars.

Adverse events of this laser modality were limited to temporary accentuated erythema and edema. Purpura was not seen in this technique, compared with the PDL which has a high likelihood of inducing purpura at pulse durations below 3 ms. This technique is thus safer, especially in darker skin (skin types IV–V), in which purpura is, in turn, related to an increased risk of PIH.

The use of the 532-nm frequency-doubled Q-switched Nd:YAG laser in the treatment of small cutaneous vascular lesions such as telangiectasia and angioma has been documented in 1996. The incidental clinical purpura following treatment of epidermal lesions with 532-nm Q-switched Nd:YAG laser, even though it is also highly absorbed in melanin as well as by oxyhemoglobin, led to the hypothesis that this laser modality might be effective in treating small vascular lesions as well [25,26]. In our study,

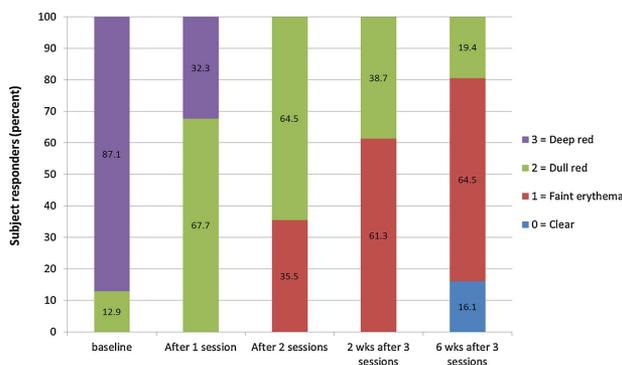


Fig. 7. Changes in degree of acne erythema at different time points. Decrease in the intensity of post-acne erythema lesions is confirmed by the subsequent decrease in erythema indices at each visit.

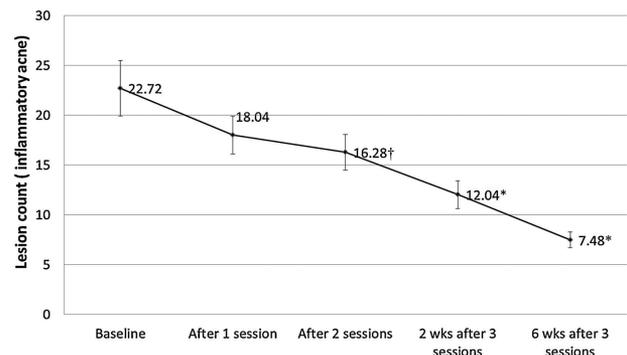


Fig. 8. Inflammatory acne lesion counts at different time points (paired *t*-test, † $P < 0.05$, * $P < 0.001$)

we used an ultrashort Q-switched laser (in the nanosecond domain) at the 585 nm wavelength. This wavelength is generated by wavelength conversion from the 532-nm frequency-doubled KTP/Nd:YAG into 585 nm using a solid dye gel rod in a handpiece, and as such, is actually slightly better absorbed in oxyhemoglobin than 532-nm but less well-absorbed in melanin, thus removing that as a competing chromophore. The nanosecond-domain pulse duration used in this study was significantly shorter than the thermal relaxation time of the microvasculature (arterioles and venules). Nevertheless, the Q-switched Nd:YAG laser can produce a high peak power which, together with the ultra-short pulse duration, induces both a photoacoustic and photothermal effect at higher fluences, quite distinct from the selective photothermolytic effect associated with other laser systems with longer pulsewidths [27]. The 585-nm laser in the present study was, however, applied with low fluences and multiple passes in a sub-purpuric fashion. Clinical purpura due to vascular rupture and hemorrhage did not occur in our study. As to the underlying mechanisms, we suggest the following considerations: the 585 nm Q-switched Nd:YAG laser applied at the low fluences used in the present study could possibly have had some photo-inhibitory effect on the endothelial structure and physiology secondary to the primary reaction, such as endothelium-dependent relaxing factors; highly selective photocoagulative destruction, as in the extended theory of selective photothermolysis [28–33], targeted the sub-visible microvasculature in which the diameter of the microvessels is small enough to allow full coagulation of vessels and contents, even with nanosecond-domain pulses; or a combination of both mechanisms. Moreover, this technology had some effect on dermal structural proteins as evidenced in the clinical improvement of the acne scars, especially boxcar-type scars, because these scars are usually lined with very thin epidermis and have vascular accentuation. However, the underlying mechanism of the laser-tissue interaction behind these optimistic findings is not fully understood, as is seen in the use of low-fluence, multi-pass 1,064-nm Q-switched laser energy for the treatment of melasma, achieving its effect through the theory of subcellular selective photothermolysis [15,34,35]. Further studies on the dysfunctional and disorganized nature of the microvasculature associated with post-acne erythema will enable more targeted and customized treatments for patients. The low-fluence 585-nm Q-switched Nd:YAG could be useful in various clinical conditions with abnormal microvascular structure including post-acne redness, post-traumatic erythema, hypertrophic and keloid scar, facial flushing, the telangiectatic type of rosacea, post-inflammatory hyperpigmentation and melasma with underlying vascular prominence.

In conclusion, low-fluence 585-nm Q-switched Nd:YAG laser treatment is safe and effective for the treatment of post-acne erythema as well as early acne scarring and inflammatory acne. The advantages of this new laser treatment compared to others are less pain, greater patient comfort and almost no downtime. Therefore the low-fluence 585-nm Q-switched Nd:YAG should be considered as an

adjuvant or alternative treatment options in patients with persistent post-acne erythema and early erythematous atrophic scar. In addition, this treatment modality may be useful to control the exacerbation of acne. However, further research into the mechanisms that underlie the actions of this laser is suggested. The follow-up of 6 weeks in the present study is arguably short, however the optimistic results of the present study merit verification through further studies with a longer follow-up.

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