Received: 18 October 2022 | Revised: 28 November 2022 | Accepted: 13 December 2022

DOI: 10.1111/jocd.15602

JCD Journal of Cosmetic Dermatology WILEY

ORIGINAL ARTICLE

Selective photothermolysis with a novel 1726 nm laser beam: A safe and effective solution for acne vulgaris

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Abstract

Background: Selective photothermolysis on sebaceous glands is an effective method for treating acne vulgaris (AV); however, safety, efficacy, and discomfort hinder its utilization in clinical settings.

Aims: The primary objective is to evaluate the safety and efficacy of a novel 1726 nm laser with contact cooling to treat AV.

Methods: Seventeen patients aged 18 to 36 were enrolled and treated in this IRB-approved, single-center, open-label study. Patients received up to three facial laser sessions up to seven weeks apart. Follow-up visits happened ten days post-session and at the 4 and 12 weeks following the final session. The investigator assessed the severity of device-related adverse events (AEs). Investigator Global Assessment (IGA) and inflammatory lesion counts (ILC) were used as metrics to evaluate acne resolution and skin condition enhancement. Patients' perspectives on satisfaction and comfort using this technology were assessed using Subject Experience Questionnaires (SEQ).

Results: Safety assessment showed mild and transient AEs. All subjects tolerated anesthetics-free treatments well, with a mean treatment discomfort score of 4.9 ± 1.5. Compared to baseline, a statistically significant reduction in ILC ($p = 0.003$) of 52% to 56% is achieved four to twelve weeks following treatment. Long-term follow-ups showed progressive improvement 24 months post-treatment with a 97% reduction in ILC. SEQs revealed high subject satisfaction (71%) with psychosocial improvement three months post-treatment.

Conclusion: The novel 1726 nm laser appears safe and effective for treating mild-to-severe acne. Acne resolution is apparent within the first month and progresses beyond the study duration.

KEYWORDS
acne vulgaris, Diode laser, Photothermolysis, dermatology, Sebaceous glands

1 | INTRODUCTION

Acne vulgaris impacts up to 50 million Americans annually and is the most common skin condition in the United States. Acne occurs at any life stage and is not limited to adolescence. Peak incidence is between the ages of 12 to 24, with up to 85% of individuals in this age group experiencing at least minor acne. Acne vulgaris substantially affects a person's quality of life, affecting self-esteem and psychosocial development.[1]

Acne is an inflammatory condition that affects the skin's pilosebaceous units, resulting in follicle obstruction, increased bacterial load, and inflammation. Different acne treatments target various steps in the pathogenesis of acne, from neutralizing androgens, lowering sebum production, controlling follicular occlusion, and reducing *Cutibacterium Acnes* (*C. acnes*) proliferation and inflammation. Topical medications include retinoids, benzoyl peroxides, and topical antibiotics, including clindamycin, erythromycin, or tetracycline.[2,3]

Systemic medications also manage more severe acne and include oral antibiotics to reduce inflammation. The current oral antibiotics used to manage acne include azithromycin, doxycycline, erythromycin, minocycline, tetracycline, and trimethoprim.[4]

Current acne therapy has proven to be successful, but there is a growing concern for antibiotic resistance with the use of topical and oral antibiotics. The *C. acnes*' resistance to antibiotics, such as erythromycin, is increasing by more than 50%[5,6]; moreover, there is a concern for patient compliance with topical therapy that requires daily applications, especially in younger age groups.[7] The most effective systemic medication for moderate-to severe acne remains oral isotretinoin.[8] However, it runs the risk of serious side effects such as teratogenicity.[8,9]

Consequently, new yet safe and effective acne treatments are needed for acne vulgaris. Such alternatives include light therapy. The first well-known effect of light therapy is ultraviolet (UV) exposure from natural sunlight to treat acne—however, although natural, it runs the risk of increased skin aging and premalignant and malignant skin lesions with *excessive* UV exposure.[10] This phenomenon is a natural photodynamic therapy (PDT) response. Photosensitive porphyrins produced within *C. acnes* react to select intervals of the light spectrum, creating reactive oxygen species that destroy *C. acnes* immediately.[11] For example, blue-light treatment in the 407- to 420-nm wavelength range has a bactericidal effect on *C. acnes*, with reports of a 40%–80% reduction in lesion counts among studies.[8,9] Similarly, green-light, yellow-light lasers, and intense pulsed light (IPL) devices kill *C. acnes* directly.[11] Alternatively, radiofrequency (RF) devices and short-wave infrared (SWIR) lasers downregulate the collective sebaceous glands' activity, limiting the sebum secreted and inflammation. In the 1320–1450 nm ranges, SWIR devices target water, the main component of bodily tissues. These devices have shown efficacy in treating acne, reducing lesion counts by up to 80%–90% after four treatments. However, the non-selectivity of SWIR devices at this range comes with the caveat of undesirable side effects such as intense pain during irradiation, long-lasting erythema, oozing, and crusting from epidermal damage, often requiring the use of topical anesthetics.[11]

Although photons with the previously mentioned wavelengths improve acne clearance, none are preferentially absorbed directly by the sebaceous glands. Exogenous chromophores introduced into the sebaceous gland complex, for example, light-absorbing gold microparticles,[12] promote sebaceous gland selective photothermolysis with infrared light, and the treatment is well-tolerated.

Sebum, which has an absorption coefficient slightly higher than water at 1726 nm (1.8:1),[13,14] looks to be a viable endogenous alternative to exogenous chromophores for sebaceous gland selective photothermolysis.[15] Early evaluations showed histologic changes of 1726 nm laser selective destruction of sebocytes and clinical improvement that can last two years after treatment (Figures 1 and 3).

In this study, we evaluated the 1726 nm laser technology for safety and efficacy for acne by selectively targeting the sebum in the sebaceous glands. The study's primary endpoint was to assess the safety of the high-power 1726 nm laser by the adverse events (AE) reported or seen and the subject's discomfort scores during treatment. The exploratory endpoint was to evaluate this technology's short-term and long-term efficacy in reducing the severity of acne vulgaris. Finally, we assessed the patients' satisfaction, willingness to continue treatment, and overall improved psychosocial effects of acne.

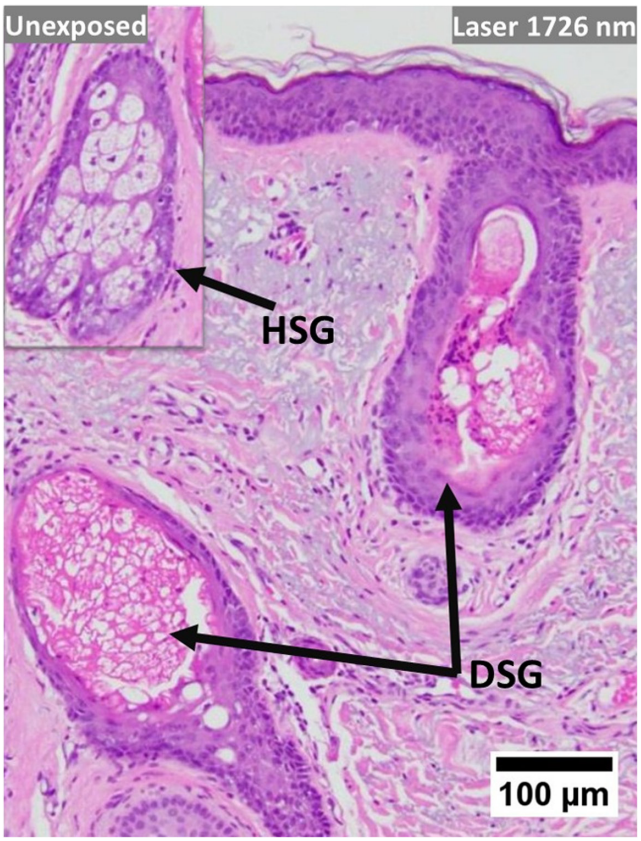


FIGURE 1 Histology image of human skin exposed to 1726 nm. Laser exposure shows selective targeting of sebocytes resulting in damaged sebaceous glands (DSG) preserving the dermis and the epidermis; the inset shows the unexposed skin, preserving healthy sebaceous glands (HSG).

2 | MATERIALS AND METHODS

2.1 | Study design and subjects

The study was single-center, open-label, and Institutional Review Board (IRB)-approved in which seventeen (n = 17) subjects consented and enrolled for treatment of facial acne vulgaris. Female and male subjects, 18 to 36 years of age, with Fitzpatrick Skin Types II-IV and acne severity levels grade 2–4, were enrolled in the study. Subjects received up to three laser treatments up to seven weeks apart and follow-up visits at 4 and 12 weeks post-final treatment with an optional 2-year follow-up visit.

The main inclusion criterion for this study was subjects diagnosed with acne vulgaris of severity grade 2, 3, or 4 on the Investigator Global Assessment (IGA) scale. In addition, subjects consented to adhere to instructions regarding the treatment, precautions, and follow-up visits. Subjects were instructed to use a daily facial sunscreen of SPF-30 or higher as approved or provided by the investigator and practice strict, diligent prevention of sun exposure.

The investigator evaluated and documented all AEs, including transient and mild side effects. Immediately following each treatment, subjects were asked to rate the pain associated with the laser treatment by indicating a number that best represents the highest average pain level experienced during treatment using the 0–10 visual analog Mosby Pain Rating Scale.

Standardized photographs were taken using a Cannon EOS 5D Mark III set in Manual Capture mode, shutter speed 1/125, aperture f/13, and ISO 100. Before photography, the subject's face was cleansed, jewelry removed, and hair pulled back. The same photographer took photographs for the study duration within the same room and same room lighting. Before images, subjects were instructed to maintain a neutral facial expression during photo capture. Subject body posture and facial angles were standardized using angle-specific wall markers, flat feet placement, sitting upright, and keeping the neck upright. Photographs were taken of full frontal facing, right and left 90-degree angles, and right and left 45-degree oblique angles.

2.2 | Treatment and study device

Before treatment, the investigator assessed the baseline acne severity using the Investigator's Global Assessment Scale for Acne Vulgaris. The patients cleaned their faces with an investigator approved mild cleanser to remove all make-up, cosmetics, and lotions. Immediately before the start of treatment, the study staff degreased the subject's face with an acetone swab.

During treatment, subjects and study staff wore appropriate laser-protective eyewear with an optical density sufficient to protect the eyes from accidental exposure to the 1726 nm. Subjects were lying flat, with the investigator having easy access to the subject's facial treatment area. The 1726 nm laser energy was delivered in an array of 3 ×3 laser beams with a total area = 68 mm^2. Laser specifications for the study were the following: A 1726 nm Diode laser (AviClear™, Cutera, Inc., Brisbane, CA) with a fluence and a pulse duration ranging between 10–60 J/cm^2 and 10–60 ms, respectively, whereas laser power, spot size (3.1 mm), and the cooling temperature (5°C) remained fixed. During treatment sessions, the treating investigator adjusted the fluence based on the facial region being treated and the clinical endpoint observed.

Immediately post-treatment, subjects rated the level of discomfort felt during the treatment. The investigator assessed for post-treatment adverse events (AEs). Throughout the treatment, there was no overlap of treated areas. All treatments were single-pass for the entire face.

Follow-up visits occurred 10 ± 3 days post each treatment and 4 to 12 weeks post-final treatment visit (±2 weeks). An optional 2-year follow-up visit was also offered to the willing subjects. In all follow-up visits, the investigator assessed post-treatment AEs, and trained study staff took follow-up digital photographs of the subject's treated area. The investigator assessed the follow-up visit acne severity using the IGA scale for Acne Vulgaris. The investigator counted the inflammatory acne lesions. Finally, the subjects completed and returned the Subject Experience Questionnaire (SEQ).

2.3 | Endpoint reporting and statistical analysis

2.3.1 | Primary | Assessment of safety

The primary endpoint of this study was to evaluate the safety of the high-power 1726 nm laser device for treating acne vulgaris by reporting the incidence and severity of adverse events and patients' discomfort during laser treatment.

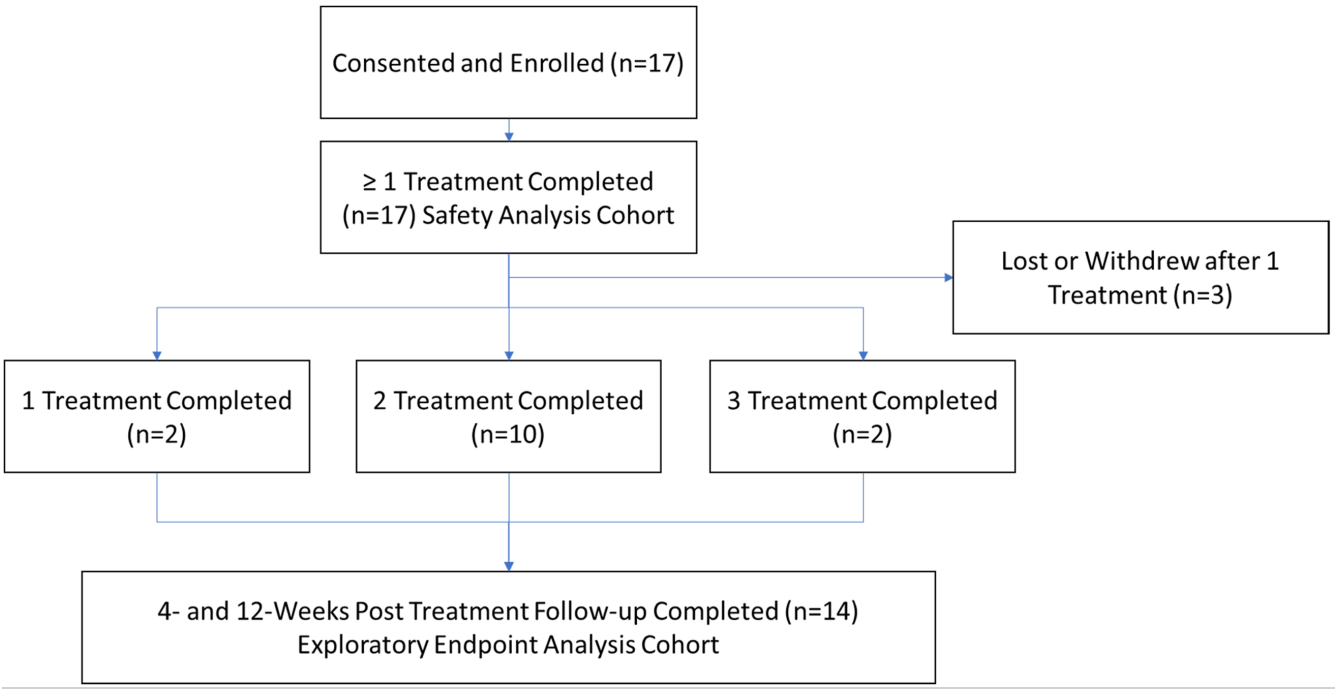
All AEs observed or reported were listed, documenting course, outcome, severity, and device-relatedness. For a given AE term (e.g., dryness), counting was done by subject and treatment session. Patients report pain levels from 0 to 10, with 0 being no pain and 10 being the worst possible pain.

All adverse events were recorded regardless of severity or the cause/effect relation. The severity of the AEs is graded as mild, moderate, or severe. We define a mild event as requiring minimal or no treatment and not interfering with the subject's daily activities; a moderate event, which may cause some interference with functioning; and a severe event as interrupting the subject's usual daily activity and may require treatment. The relationship of an adverse event to the study device was determined as unrelated, possible, probable, or definite.

2.3.2 | Secondary | Assessment of efficacy

Exploratory efficacy of the high-power 1726 nm laser for treating acne vulgaris was assessed by comparing the baseline *IGA scores* and *inflammatory lesion count* (*ILC*) for each subject with the IGA scores and ILC at the 4- and 12-week post-final treatment.

TABLE 1 Consolidated standard of reporting trials (CONSORT) subject flow diagram



2.4 | Analysis of subject questionnaire

All subjects had to complete a baseline questionnaire before their first treatment and a follow-up questionnaire during the follow-up visits. The baseline questionnaire asked the subjects to grade their acne severity according to the Subject Global Assessment (SGA) scale and how embarrassed or self-conscious they were due to acne.

The follow-up questionnaire included all questions from the baseline questionnaire. Moreover, we asked the subjects to rate their satisfaction with the results they achieved from the laser treatments according to the scale. Finally, we assessed their willingness to restart the study, knowing in advance the treatment discomfort, outcome, and side effects they would personally experience.

2.5 | Statistical analysis

All descriptive and inferential statistical analyses were performed using Microsoft excel and OriginPro 2022b. Descriptive statistics for continuous variables consisted of the mean, standard deviation, median, quartile, minimum, and maximum values. For categorical variables, the number and percent of each category were displayed. A two-sided statistical test with a 5% significance level was used.

The primary endpoint/safety analysis set includes all subjects enrolled in the study who completed at least one laser treatment session. The exploratory efficacy analysis set includes all subjects who completed baseline, received at least one laser treatment session, and completed at least one follow-up visit. Missing data were not imputed for safety or exploratory endpoints.

Changes from baseline in the exploratory efficacy variables (i.e., IGA scores, inflammatory lesion counts, and SGA scores) were analyzed using a two-tailed, paired-data Student's *t* test.

3 | RESULTS

3.1 | Subject demographics and baseline characteristics

As shown in the subject flow diagram of Table 1, a total of $n = 17$ subjects consented and enrolled in the study. Three subjects were lost to follow-up or withdrew from the study after one treatment. Of the remaining $n = 14$ subjects, $n = 2$ completed one treatment, $n = 10$ completed two treatments, and $n = 2$ completed three treatments. All 17 subjects were included in the safety analysis cohort, and the 14 remaining subjects who completed the 4- and 12-week post-treatment follow-up were included in the exploratory endpoint analysis.

The subjects' demographics, baseline IGA scores, and baseline characteristics are summarized in Tables 2, 3, and 4. The mean age of subjects was 25.2 ± 6.2 years [range: 18 to 38 years]. The majority of subjects were females (82%), Caucasians (53%), and not Hispanic/Latino (65%); all subjects had Fitzpatrick Skin Types II-IV. Recruiting methods allowed subjects with mild-to-severe acne (2–4 IGA scores) to be enrolled. Most subjects, 88% or 82%, had non-severe baseline acne, according to IGA or SGA scores, respectively. Moreover, all subjects (100%) reported feeling embarrassed regarding their acne condition.

TABLE 2 Subject demographics

Variable	(*n* = 17)
Age (years)	
Mean ± SD	25.2 ± 6.2
Median (P25, P75)	25 (19,29)
Min, Max	18, 38
Gender	
Female	14 (82%)
Male	7 (18%)
Race	
Caucasian	9 (53%)
Black/African American	0 (0%)
Asian	6 (35%)
American Indian/Alaskan Native	1 (6%)
Other	1 (6%)
Ethnicity	
Hispanic/Latino	6 (35%)
Non-Hispanic/Latino	11 (65%)
Fitzpatrick skin type	
II	1 (6%)
III	13 (76%)
IV	3 (18%)

Abbreviation: SD, standard deviation.

TABLE 3 Investigator IGA score (baseline)

IGA description	IGA Score	(*n* = 17)
Clear	0	0 (0%)
Almost Clear	1	0 (0%)
Mild	2	5 (29%)
Moderate	3	10 (59%)
Severe	4	2 (12%)

3.2 | Safety variable analysis

3.2.1 | Subjects' discomfort

The seventeen subjects enrolled received 31 laser treatment sessions in total. Facial regions treated included the forehead, cheeks, chin, and perioral regions. All subjects tolerated all treatments well. Topical or local anesthetics were not used for treatments, and no sessions ended prematurely due to excessive discomfort. The mean treatment discomfort score is 4.9 ± 1.5.

3.2.2 | Adverse events assessments

During the study, there was no reporting of serious nor unanticipated adverse device effects during 52 weeks post-final treatment.

TABLE 4 Subject baseline questionnaires (baseline)

SGA description	SGA score	(*n* = 17)
Clear	0	0 (0%)
Almost clear	1	0 (0%)
Mild	2	7 (41%)
Moderate	3	7 (41%)
Severe	4	3 (18%)
Embarrassment level	**Score**	**(*n* = 17)**
Not at all	0	0 (0%)
A little	1	7 (41%)
A lot	2	5 (29%)
Very much	3	5 (29%)

We recorded seventy post-treatment events belonging to nine categories during or following the thirty-one treatment sessions. Table 5 reports all categories and events post-treatment, documenting severity and resolution time. All subjects (*n* = 17, 100%) experienced *mild erythema*, the desired treatment endpoint during all 31 treatments (100%). Five subjects (29%) developed *mild edema* (swelling) during or immediately following 11 treatment sessions (35%). *Erythema* and *edema* are expected and typical of laser therapy; consequently, these effects are labeled with "*Definite*" relatedness with the device use. All occurrences of *erythema* and *edema* were *transient* and resolved within hours to several days of ending treatment. Both device effects accounted for 60% of the total post-treatment events reported, where the resolving duration is less than three days (75th percentile).

The remaining adverse events include blistering, scabbing, hyperpigmentation, scarring, worsening of acne, sensitivity/ tingling, and dryness. All reported AEs were rated as mild and resolving.

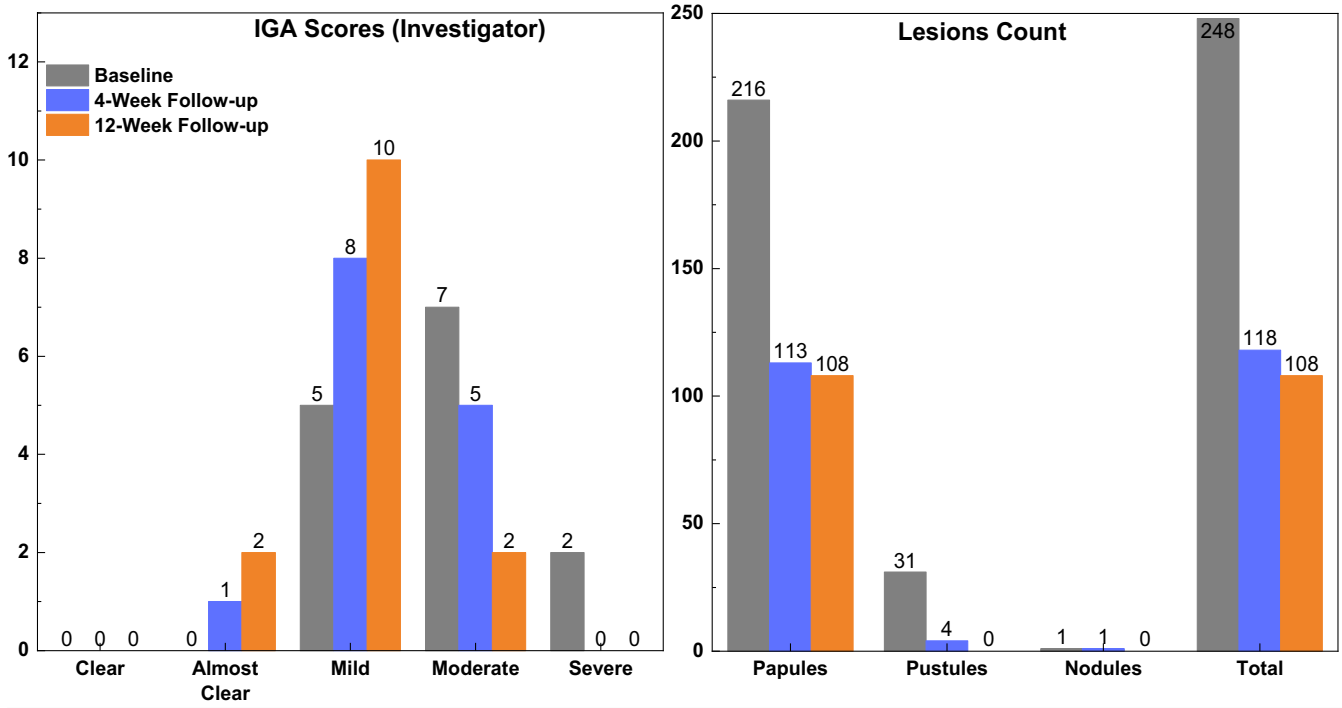
Five subjects (29%) reported developing mild severity blistering in small areas of the treatment field, which self-resolved into small areas of minor severity scabbing in less than six days (75th percentile) until naturally sloughing in less than ten days (75th percentile) later. As blistering and scabbing are known effects of laser therapy, they were labeled as "*Definitely*" related to the device use. These subjects observed *transient* hyperpigmentation and scarring of *mild* severity. These events are common during skin healing following *blistering* and *scabbing*. Four *mild hyperpigmentation* events were self-resolved by the third month; two occurrences had improved significantly and, according to the subjects, were continuing to lighten without intervention. Of the five occurrences of *mild* severity *scarring*, all had improved significantly without intervention. Some patients had pre-existing *hyperpigmentation* and *scarring* at baseline. Consequently, the device-relatedness is 50% "*Probable*" for patients with pre-existing and 50% "*Definite*" for patients without baseline *hyperpigmentation*; *similarly*, 40% is "*Probable*," and 60% is "*Definite*" for scarring events.

Three subjects (18%) reported transient *acne flaring* of pustules and papules in the treatment field 2–4 days following three sessions, which resolved without intervention in 2 days, 21 days, and 49 days, respectively; flaring of acne was rated as *probably* related to the device treatment. One subject reported a mild *tingling* sensation in a

TABLE 5 All post-treatment events, including AEs by occurrence by severity and the resolution time (median, min, and max)

Post-treatment events	Subjects experiencing ≥ 1 occurrence (%)	Occurrence by Severity			Duration
		Mild	Moderate	Severe	
		n (%)	*n* (%)	*n* (%)	Median (P25, P75)
Erythema	17 (100%)	31 (100%)	–	–	2 days (1 day, 3 days)
Edema	5 (29%)	11 (100%)	–	–	2 days (2 days, 3 days)
Blistering	5 (29%)	6 (100%)	–	–	4 days (3 days, six days)
Scabbing	5 (29%)	6 (100%)	–	–	Six days (3 days, 10 days)
Hyperpigmentation	5 (29%)	6 (100%)	–	–	101 days (91 days, n/a)
Scarring	5 (29%)	5 (100%)	–	–	79 days (63 days, n/a)
Worsening of acne	3 (18%)	3 (100%)	–	–	21 days
Sensitivity/Tingling	1 (6%)	1 (100%)	–	–	2 days
Dryness	1 (6%)	1 (100%)	–	–	21 days

TABLE 6 (Left) IGA acne severity reported and (Right) Count of inflamed papules, pustules, nodules, and total lesions for all subjects at the baseline, 4-week, and 12-week follow-up visits



treatment area only while showering up to a day following one of the treatment sessions. Another subject reported *mild* skin *dryness* four days after their second treatment session. Both events were resolved without intervention and rated as *possibly* related to device use.

3.2.3 | Efficacy variable analysis

All subjects completed one or more treatment sessions, and the 4- and 12-week follow-up visits were included in the exploratory efficacy variable analysis cohort ($n = 14$). The acne vulgaris severity scores assigned by the investigator (IGA) or by the subjects (SGA) during baseline, 4- and 12-week follow-up visits are shown in Table 6 for each subject. Significant improvement ($p < 0.05$) persists at all time points for IGA scores. Significant improvement is also found from baseline to 4-week and 12-week post-final treatment sessions for SGA scores.

The baseline and 4- and 12-week follow-up visits for inflammatory lesion counts are summarized in Table 6. In total, 248 inflammatory lesions (216 papules, 31 pustules, and 1 nodule) were counted at baseline. The number of inflammatory lesions per patient ranged from 8 to 43 (mean: 17.7 ± 9.5). Four and twelve weeks after an average of two treatment sessions, a substantial and statistically significant reduction in inflammatory lesions was observed (Reduction > 52%, $p = 0.003$). Only one nodule was counted at baseline. Hence,

significant data are not viable for this category. Between the 4- and 12-week follow-up visits, the total inflammatory lesion count and individual papules, pustules, and nodule counts all showed further reductions from baseline levels.

3.2.4 | Subject experience questionnaire

Subjects completed a questionnaire at baseline and during their 4- and 12-week follow-up visits that asked, among other questions, "*How embarrassed or self-conscious are you because of your acne?*" The subjects' responses at each time point are shown in Table 7.

At baseline, subjects reported they were "Extremely" (n = 2; 14%), "A lot" (n = 5; 26%), or "A little" (n = 7; 50%) embarrassed or self-conscious because of their acne; no subjects reported they were "Not at all" embarrassed or self-conscious because of acne. Four weeks after an average of two treatment sessions, the embarrassment/self-consciousness scores had improved significantly (p = 0.02), with subjects reporting they were "Not at all" (n = 4; 29%), "A little" (n = 7; 50%), and "A lot" (n = 3; 21%) embarrassed/self-conscious because of acne. By the 12-week follow-up visit, embarrassment/self-consciousness scores had further improved from baseline scores (p = 0.001) with subjects now reporting they were "Not at all" (n = 5; 36%), "A little" (n = 7; 50%), and "A lot" (n = 2; 14%)

TABLE 7 Subject Experience Questionnaire (SEQ) at baseline, 4-week, and 12-week follow-up visit—"How embarrassed or self-conscious are you because of your acne?"

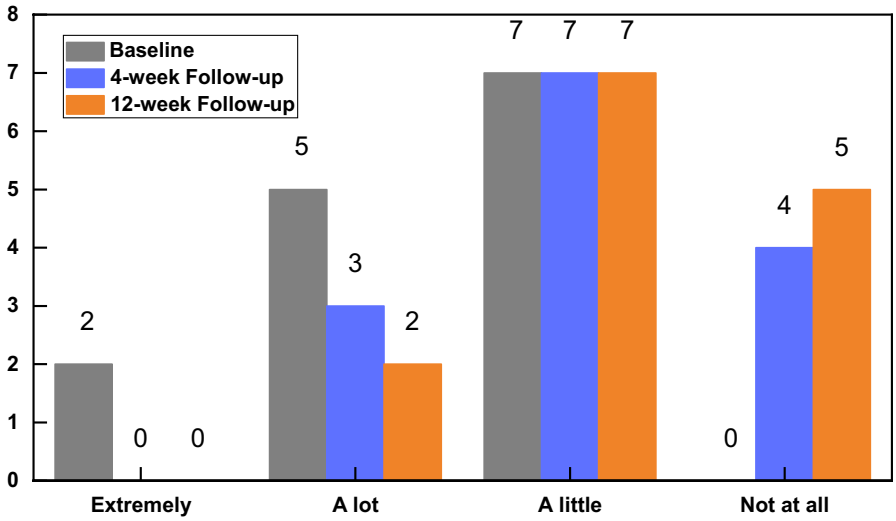
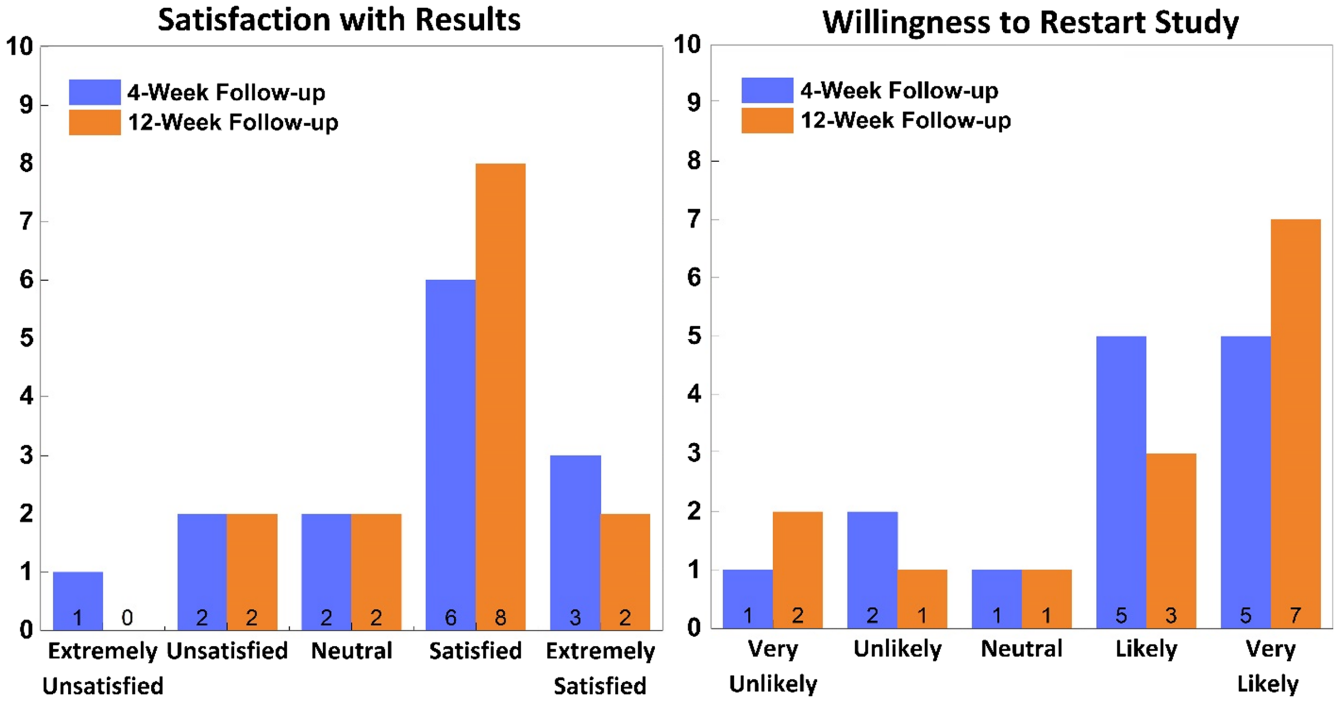


TABLE 8 Subject Experience Questionnaire (SEQ) at baseline, 4-week, and 12-week follow-up visit—(Left) Survey asking the subjects about their satisfaction and (Right) willingness to restart the treatment at the follow-up visits



embarrassed or self-conscious because of acne. With all subjects suffering psychosocial consequences of acne, subject assessment questionnaires showed a 36% decrease ($n = 5$) in the number of patients experiencing embarrassment from acne by the third month after treatment.

Follow-up visit questionnaires also asked subjects to rate their satisfaction with the results achieved; and their willingness to restart the study, knowing in advance the treatment discomfort, the outcome they would achieve, and the side effects they would personally experience. Subject responses to these questions are shown in Table 8.

Subject satisfaction with the treatment results was high, with nine subjects (64%) satisfied or extremely satisfied at the 4-week follow-up visit, which improved to 10 subjects (71%) satisfied or extremely satisfied by the 12-week follow-up visit. At the 4-week follow-up visit, two subjects (14%) were neutral, two subjects (14%) were unsatisfied, and one subject (7%) was extremely unsatisfied. At the 12-week follow-up visit, no subjects were extremely unsatisfied, and two subjects (14%) were unsatisfied and neutral, respectively.

At the 4-week follow-up visit, 5 (36%) and 5 (36%) subjects responded that they would be likely and very likely, respectively, to restart the study, which improved to 3 (21%) and 7 (50%) subjects responding they would be likely or very likely, respectively, to restart the study by the 12-week follow-up visit. At both time points, one subject (7%) was neutral, and 3 (21%) subjects responded that they would be unlikely or very unlikely to restart the study again if able to.

Patients were also photographed at each stage of the clinical treatment. Before and after pictures of two patients who were highly satisfied with the laser treatment are shown in Figure 2. At three months post-treatment, these subjects showed a significant improvement in their skin condition and continued to see improvement in their inflammatory lesions beyond the 12-week follow-up period. Particularly, SEQs show statements such as "It has helped a lot with clearing acne on my face." or "there is no price on the confidence I have been given."; these statements give a personal essence to the enhanced quality of life experienced by satisfied patients.

Other patients followed up two years after their treatment.

Figure 3 shows the before and after photographs of a subject, out of three subjects in total, who followed up two years after ending the treatment. The subject was 25 years old at the beginning of the treatment with moderate acne severity (IGA score = 3). At baseline, the subject started with $n = 43$ inflamed lesions (38 papules and 5 pustules). The pustules cleared entirely by the first-month post-treatment. The total number of inflamed lesions (papules) was reduced to $n = 14$, $n = 8$, and $n = 1$ at the 4-week, 26-week, and 52-week post-treatment visits, respectively. The subject's overall acne condition was rated as almost clear (IGA acne grade score = 1), with no more than one inflamed lesion at a time until the second year post-treatment. Similarly, in the other patients' 2-year follow-up visits, the latest acne condition of both subjects shows significant and comparable improvements, indicating a durable and consistent efficacy of the novel 1726 nm laser.

Notably, the subjects' strict adherence to positively contributing habits[16,17]—for example, washing the face, eating clean, or avoiding excessive sunlight—fades with time, which might explain rare reoccurrences of some inflammatory lesions on the treated area seen after two years. Nonetheless, once improvement is achieved,

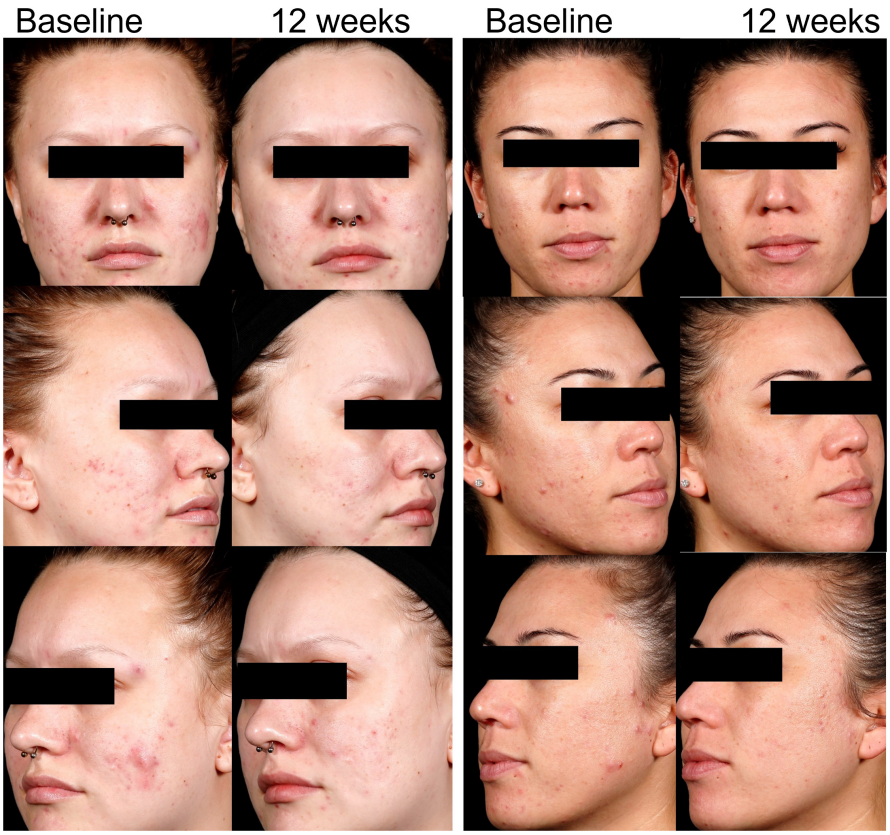


FIGURE 2 Before and after photography at baseline and 12 weeks after the last treatment session of two female patients showing improvement in skin condition and acne healing twelve weeks after three treatment sessions with 1726 nm laser.

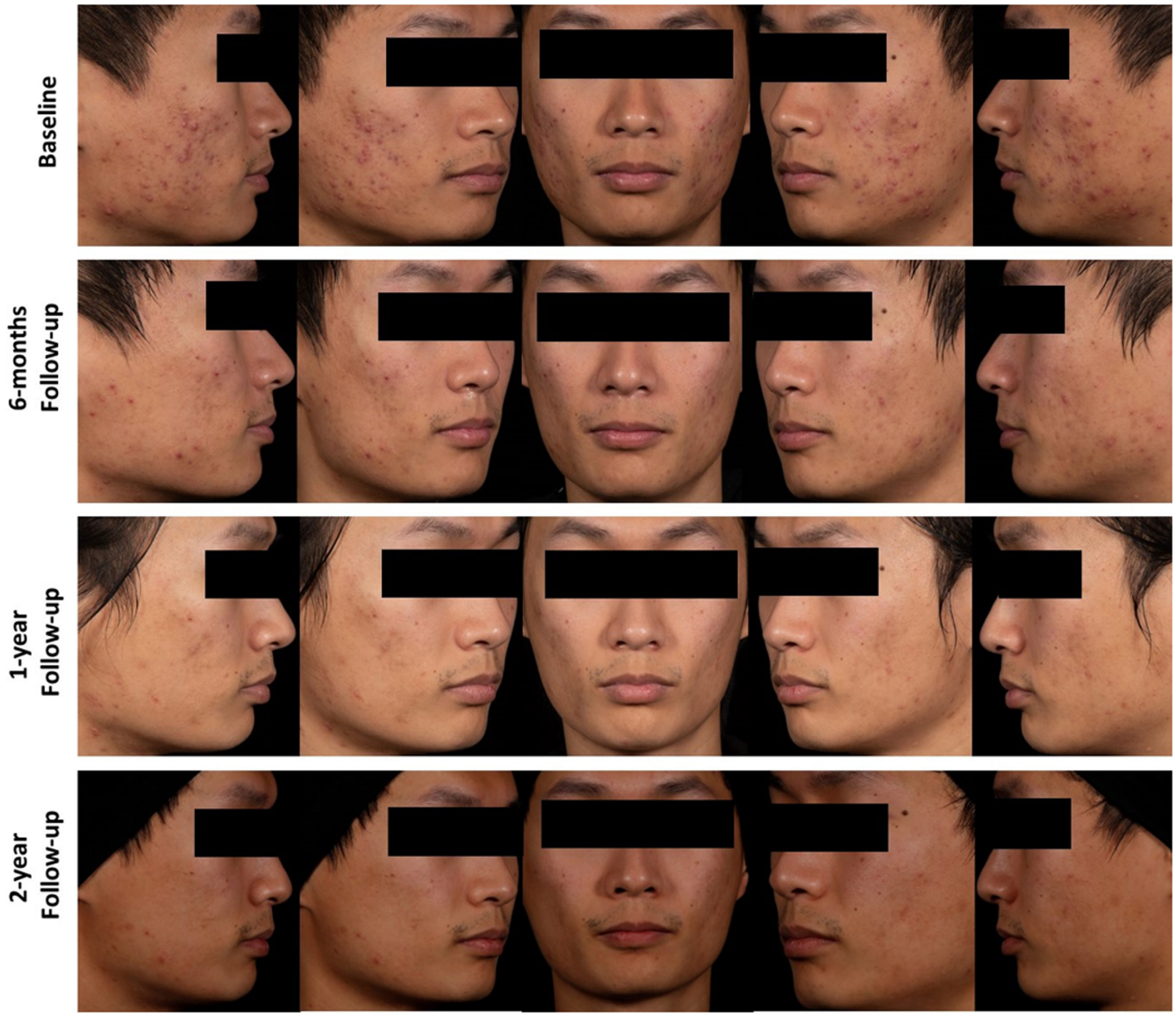


FIGURE 3 Progress of acne condition at six months, one year, and two years after three-session 1726 nm laser treatment of a male subject, Asian, age 25, at the baseline visit, with a Fitzpatrick skin type III and moderate acne severity (IGA score = 3).

it lingers beyond the duration of the study to at least two years post-treatment.

4 | DISCUSSION

A recent study by Scopelliti et al.[18] used Monte Carlo and Finite Element models to simulate the thermal damage on sebaceous glands and surrounding skin and found that selective photothermolysis is achieved with a 1726 nm laser energy and contact cooling while preventing collateral damage to the dermis and epidermis. Our clinical study corroborates the previous findings in human subjects, and we found that selective photothermolysis with a 1726 nm laser device is safe and effective for treating acne vulgaris in patients with mild-to-severe acne. We demonstrated that post-treatment side effects were all mild and anticipated. All subjects reported mild erythema, a desired and typical outcome of laser treatments. Adverse device effects occurred mildly and were resolved entirely by the end of the study. Notably, there was no incidence of any serious adverse events or unanticipated device effects. Compared to topical and systemic medications, this high-power 1726 nm laser is a safer alternative where side effects are mild, superficial, and quickly resolving.

Moreover, statistically significant findings showed that this novel laser technology effectively enhanced the skin's inflammation by directly controlling sebaceous glands. In this study, the high-power 1726 nm laser treatment reduced the total number of inflammatory lesions by more than 52% within one month of treatment and improved further to 56% by the third-month post-final-treatment session. IGA acne scores improved by up to three points—a comparable efficacy with mainstream acne treatments. Also, this technology is a minimalist attempt compared to other selective photothermolysis

laser devices that require exogenous chromophores for activation. Besides, it is worth noting that the two subjects, rated with severe acne, improved their acne condition within the first month and continued to improve by the 12-week post-final-treatment session.

Moreover, the high treatment satisfaction and willingness to restart the treatment (71%) provided a positive subjective perspective on the efficacy and viability of this therapy. The SEQ showed psychosocial improvement in subjects during and after treatment with no adverse neuropsychiatric events; this, in addition to the topical, non-invasive nature of the 1726 nm laser technology, suggests a neuropsychiatric-safe alternative to isotretinoin which has been linked to depression.[19]

The main limitation of this study is the small number of patients enrolled and sustained the duration of this clinical evaluation. Out of the 17 subjects, two lost to follow due to non-responsiveness, and one patient stated he could not commute to the treatment site. Besides, the simultaneous outbreak of COVID-19 and the launch of this study (December 2019) limited the in-person follow-up to 12 weeks. Although a more extensive study exploring the longevity of the treatment and the psychosocial benefits associated with it is necessary, the post-treatment follow-up with eligible subjects showed a sustained acne improvement even after two years with a remarkably enhanced quality of life. The three patients in this study who continued to follow-up for two years witnessed long-lasting results. Short-term durability may be due to transient stunting of the sebaceous glands, which is sufficient to stop the proliferation of *C. acnes* at the host sebaceous glands and heal inflammatory acne lesions. Biopsies taken after treatment showed miniaturization of sebaceous glands and pilosebaceous follicles without morphologic damage to epidermal and dermal structures. We hypothesize that the long-term durability of this laser is isotretinoin-like. In the long term, sebaceous glands' function gets re-normalized to levels enough to sustain sebum production but not enough for bacterial proliferation. Consequently, the first two steps in acne's pathogenesis: hyperkeratinisation (the follicular epidermal hyperproliferation with subsequent plugging of the follicle) and excess sebum production, are normalized to homeostatic levels for optimal SG functioning—hence long-term acne clearance.[8,20] These results should motivate studies on the long-term effect of the 1726 nm laser energy on skin histology and treatment efficacy in a large number of patients to understand the exact mechanism of long-standing positive results.

Our study concludes that selective photothermolysis with the novel laser technology at 1726 nm is a safe and effective treatment for acne with all severities. This technology can be a safer alternative than mainstream approaches—topical or systemic medications, for example, isotretinoin and antibiotics. Due to the small number and relatively narrow demographics of subjects enrolled in this study, additional studies with an extensive database can upscale these findings.

AUTHOR CONTRIBUTIONS

A.K. and M.D. were involved in the conceptualization and design of the study. SR and MD were responsible for study execution and completion. A.K. and A.H-S. were responsible for data analysis. D.G., S.R., Ar.K., and A.H-S. were involved in writing the original draft, reviewing, and editing. D.G., S.R., A. H-S., A.K., M.D., Ar.K, and J.F. were involved in the final review and approval of the manuscript.

ACKNOWLEDGMENTS

We thank the Cutera Clinic personnel and the participating evaluators for their time and contributions throughout the study. We also thank Dr. Stephen J. Ronan (Black Hawk Plastic Surgery & Medspa) and his staff for consenting and enrolling subjects for this study.

CONFLICT OF INTEREST

Dr. Stephan Ronan is the Medical Director of Cutera, and he has received no additional funding for the study or preparation of this manuscript. Dr. David Goldberg received funding to conduct the clinical trial. Dr. Jeffery Fromowitz did not receive funding for his contribution. Amogh Kothare, Margot Doucette, Arshdeep Kaur, and Dr. Amer Hamidi-Sakr are employees of Cutera Inc.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This study's protocol number: C-19-AC01, the informed consent, and any other relevant documents were reviewed and approved by an IntegReview Institutional Review Board (IRB) before the beginning of the study on September 20, 2019. The study was conducted in accordance with IRB and federal regulations as well as ICH-GCP requirements. The collection and evaluation of all protected patient health information were performed in a HIPAA-compliant manner. General study informed consent and photo informed consent were obtained before performing study procedures and taking photographs. Permission for publication was also ascertained during the informed consent process.

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How to cite this article: Goldberg D, Kothare A, Doucette M, et al. Selective photothermolysis with a novel 1726 nm laser beam: A safe and effective solution for acne vulgaris. *J Cosmet Dermatol*. 2023;22:486-496. doi:10.1111/jocd.15602