

1450 nm Diode Laser with Dynamic Cooling: A Novel Approach for Acne Treatment

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Introduction

Acne vulgaris is the most common skin disease in the United States, and accounts for 25 percent of all visits to dermatologists.¹ It is a disease of the pilosebaceous unit of the skin wherein there is an inflammatory reaction in the oil-producing follicle.² While the highest incidence of acne occurs between the ages of 15 and 18 years in both males and females, acne can begin at virtually any age and occasionally persist into adulthood. Because it most commonly affects the face and can lead to permanent scarring, acne can have profound and long-lasting psychological effects. Pustules and scarring occur at an age when the potential impact on the patient is greatest. Acne appears to have the potential to damage, perhaps even in the long term, the emotional well being of patients.³

The basic lesion of acne is the comedo, a distension of the sebaceous follicle. The formation of the comedo begins with defective keratinization of the follicular duct, resulting in abnormally adherent epithelial cells and plugging of the duct with sebum and keratinous debris. When the lipid egress is blocked and the plug pushes up to the surface, it causes a blackhead (or open comedo). When the opening is very tightly closed, the material behind it causes a whitehead (or closed comedo). Some comedones evolve into inflammatory papules, pustules, nodules, or chronic granulomatous lesions. Proliferation of *Propionibacterium acnes* (*P.acnes*) results in the production of inflammatory compounds resulting in neutrophilchemotaxis.² Acne occurs where the

sebaceous glands are most concentrated such as the face and back. Within skin, the sebaceous glands are located at depths from about 200 to 1000 microns below the stratum corneum.⁴ The entire skin itself can be divided into three layers: epidermis (up to a depth of 60-100 microns), the dermis (up to a depth of about 2-5 mm), and subcutaneous fat, just below the dermis.

Acne patients routinely receive years of topical or systemic therapies. Current treatment options include topical anti-inflammatory, topical peeling agents, topical and oral antibiotics, topical and oral retinoids, and hormonal agonists and antagonists. These treatments must be used over long periods of time and are associated with several potential side effects. Pervasive use of antibiotics can lead to emergence of resistance in *P.acnes*.⁵ Systemic isotretinoin has been successfully used to treat acne. However, it has extraordinary teratogenicity and its side effects include dry mouth and skin, itching, dermatitis, eye irritation, and hepatotoxicity.⁶ Most of these therapies are expensive and associated with at least mild systemic or localized side effects.¹ With the exception of systemic isotretinoin, traditional acne remedies do not alter the sebaceous glands and they remain non-curative. The results include years of therapy, potential scarring, and high treatment costs for patients. On the other hand, acne does tend to spontaneously involute after adolescence. This phenomenon is not well understood.⁷ Also, interventions such as isotretinoin, which are associated with a remarkable decrease in sebum output during treatment, are usually associated with a restoration of pre-treatment sebum output levels after one year. Despite this return to the pretreatment sebum levels, many patients remain clear.



A New Laser for the Treatment of Acne and its Mechanism of Action

The Smoothbeam laser employs a combination of laser light at 1450 nm and cryogen spray cooling. The laser light heats the dermis, sebaceous glands, and associated structures within the dermis. The cryogen cooling allows preservation of the epidermis, thus minimizing treatment side effects. The mechanism of action in the treatment of acne is the thermal alteration of the sebaceous glands, which is the cause of pathogenesis of acne lesions

Clinical Study

The objective of this study was to evaluate the effectiveness of the 1450 nm laser for the treatment of acne on the back. Twenty-seven subjects were enrolled in the study conducted at the Naval Medical Center in San Diego after receiving an IRB approval. Volunteers with acne on bilateral areas of the upper back were recruited. At baseline, the acne severity was similar on the control and treated areas of the back.

The treatment area received laser and cryogen, while the control area received only cryogen spray. Randomization of treatment and control side selection was performed to eliminate side-by-side variations that could influence the results. The area of treatment and control sites on the back was up to approximately 36 cm². Four treatments separated by a period of three weeks were administered. Lesion counts and locations were tracked and counted at all time points.

After the first treatment, subjects were seen for a one-day and a one-week follow-up. For subsequent treatments, the subjects were seen every three weeks for treatments and follow-ups for a total of four treatments. After the fourth treatment, subjects were seen for follow-up visits at six weeks, 12 weeks, and 24 weeks. Photographs of the treatment and control sides were taken before the initial treatment and during every visit for treatment visit or follow-up visit. Fluence values ranged between 14-22 J/cm²; the average fluence was 18 J/cm².

During all treatments and follow-up visits, the physicians and staff involved recorded and maintained records of all subjects describing clinical observations including lesion counts, acne severity, as well as before and after photographs. Lesion counts include all non-inflammatory and inflammatory lesions. In some cases, biopsies of representative treatment sites were obtained immediately after treatment. Biopsies were performed for histological analyses of the laser treatment effects on both the skin and the sebaceous glands.

Clinical observations of the treatment and control sides were graded and recorded. Clinical observations included acne severity, erythema, edema, blistering, abnormal pigmentation (hyper- or hypo-), and scarring. The assessment of the clinical observations were performed at all time points on scale of 0 to 3 as follows: 0: absent, 1: mild, 2: moderate, and 3: severe.

Safety and Side Effects

There were no unusual side effects or adverse reactions. All data describing the clinical and physical observations, improvement indices, and pain associated with treatment were tabulated. In brief, the most common clinical change seen in subjects as a response to the treatments was erythema that was expected. Three out of 27 subjects showed hyperpigmentation during the treatment regimen. Hyperpigmentation was graded 'severe' for one subject at one time point; the other two were classified as 'mild'. Hyperpigmentation had uniformly resolved for all the subjects at the six-week and later follow-ups after the fourth treatment. No purpura or scarring was noted in any subject at any time point.

Acne Improvement

Student's t-test (paired samples) was performed comparing the difference in acne lesion count at each follow-up time point from the count at baseline on the treatment side with that on the control side.

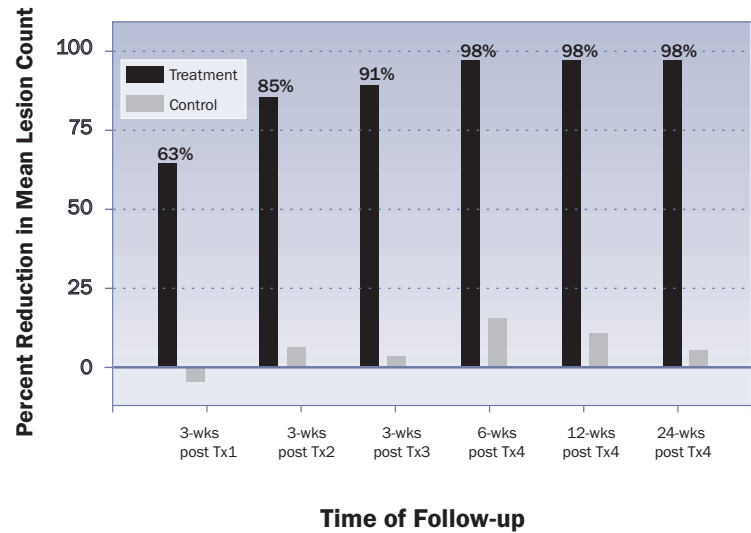
At each of the follow-up time points, a statistically and clinically significant reduction in lesion count is seen on the treatment side compared to the control side with $p < 0.001$.

Figure 1 illustrates the percent reduction in mean lesion count on the treatment and control sides. As illustrated in the figure, a continuous reduction in acne lesions was observed on the treatment side, while only small changes occurred on the control side. At the 6-week follow-up, there was a 98% reduction in mean lesion count on the treatment side as opposed to 12% reduction on the control side. Similarly, at the 12-week follow-up, there was a 98% reduction in the mean lesion count on the treatment side as opposed to 8% reduction on the control side. Furthermore, 98% reduction in mean lesion count on the treatment side while 3% reduction on the control side was observed for the 17 subjects who had their 24-week follow-up. At the 24-week follow-up, 16 of the 17 subjects had zero lesions on the treated side.

Figure 2 (back page) shows a photograph of the treated area on a subject's back three weeks after the second treatment in which lesion clearance is seen. Figure 3 (back page) shows a photograph of the control area on the same subject's back at the same time point in which several lesions are seen. The box in each of the photographs delineates the treated and control areas.

Conclusions

A human clinical study for the treatment of acne vulgaris was conducted on backs of males with a 1450 nm laser combined with cryogen spray cooling. The results have shown that this modality is helpful in the reduction of acne lesions on the back. A statistically and clinically significant reduction in lesion counts upon treatment up to the 24-week follow-up after the fourth treatment was demonstrated. No significant changes on the control side were noted. Side effects included transitory erythema and edema. Histological analysis of biopsies done immediately after treatment indicated an alteration in sebaceous gland structure.



MEAN LESION COUNT

Follow-up	Treated Site			Control (untreated) Site		
	Baseline	Follow-up	Reduction	Baseline	Follow-up	Reduction
3 Wks Post Tx1	7.22	2.67	63%	5.81	5.93	-2%
3 Wks Post Tx2	7.13	1.04	85%	5.70	5.48	4%
3 Wks Post Tx3	7.18	0.68	91%	5.77	5.68	2%
6 Wks Post Tx4	6.80	0.15	98%	5.65	4.95	12%
12 Wks Post Tx4	6.94	0.12	98%	5.53	5.06	8%
24 Wks Post Tx4	5.88	0.12	98%	5.29	5.12	3%

Figure 1—Percent reduction in mean lesion count compared to baseline for Treated and Control (untreated) sites.

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Figure 2—Three weeks after the second treatment. Clearance of lesions is seen.

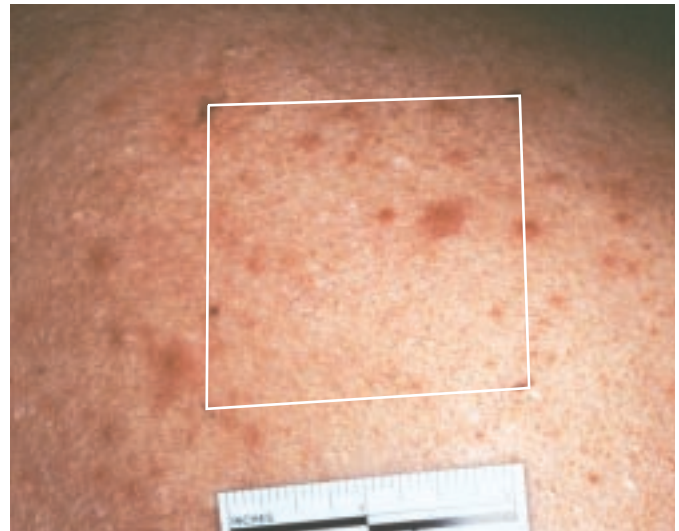


Figure 3—Control area at three weeks after the second treatment. Lesions are still present.

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