Effective, Permanent Hair Reduction Using a Pulsed, High-Power Diode Laser

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INTRODUCTION

A solid-state, 800 nm pulsed near-infrared diode laser[1] was studied for permanent hair reduction. The effect of laser fluence (energy per unit area), single vs. multiple treatments, and single vs. multiple pulses were determined in different skin types (Fitzpatrick's type I through VI).

Semiconductor diode lasers are considered the most efficient light sources available and are particularly well suited for clinical applications. The pulsed diode laser used in the study delivers high-power laser pulses, in combination with a proprietary skin cooling system, to target pigmented hair follicles deep within the dermis. Treatment operates on the principle of selective photothermolysis, which combines selective absorption of light energy by the melanin in hair follicles with suitable pulse energies and pulse widths (pulse duration) that are equal to or less than the thermal relaxation time (TRT) of targeted follicles in human skin. There are two important anatomical targets for inactivation of hair follicles: 1) stem cells in a "bulge" of the outer root sheath about 1 mm below the skin surface; and 2) the dermal papilla located at the deepest part of the follicle, which varies with hair growth cycle. Research and extensive clinical use of lasers for hair removal have identified important parameters to optimize the efficacy and safety of laser treatment:

- <u>Wavelength:</u> Most laser hair removal systems are designed to remove unwanted hair through selective photothermolysis. This process involves local selective absorption of an intense light pulse at wavelengths that: 1) are preferentially absorbed by the desired hair follicles but not by the surrounding tissue; and 2) penetrate deeply into the skin to reach the important targets for inactivation of hair follicles. In laser hair removal, the most important and dominant absorber is melanin. In all colors but white hair, there is sufficient melanin in the follicular epithelium and matrix to act as a chromophore for light absorption in the follicle. Laser energy is selectively absorbed by the melanin and causes thermal damage to the hair shaft and follicle. Hair growth is impeded or eliminated with sufficient fluence of the appropriate wavelength, due to selective thermal damage of the hair follicle. The ideal laser wavelength for hair removal is strongly absorbed by melanin but not by surrounding tissue and reaches deeply into the dermis. Wavelengths between about 700 and 1000 nm fit these criteria.

- Pulse Width: Pulse width is a very important parameter for effective laser hair removal without epidermal injury. For hair removal, the optimum pulse duration is approximately equal to the thermal relaxation time (TRT) of the hair follicle. The TRT is defined as the time required for an object to cool to half the temperature achieved immediately following laser exposure. For human terminal hair, TRT varies from about 10 to 100 milliseconds. Laser pulses much shorter than the TRT cause insufficient heating of the target structures (bulb and papilla) surrounding the hair shaft. Pulse widths much longer than the TRT may cause non-selective damage to the surrounding dermis. The first laser hair removal treatment to be cleared by FDA used Nd:YAG laser pulses about a million times shorter than TRT for hair follicles, and failed to produce long-term hair removal. The pulsed diode laser used in this study was specifically designed to produce pulse widths matching the TRT of terminal hair follicles.

- Fluence: Previous studies have shown that stronger laser treatments, or treatments using the highest tolerable fluence, produce better hair reduction results. The risk of side effects also increases with fluence. In the study summarized here, a range of fluences was given without regard to the skin type of the patient.

- Cooling: Even laser light with perfect specificity for melanin can cause damage to the skin surrounding the hair follicles because the epidermis also contains melanin. Therefore, it is imperative to use an epidermal cooling strategy to cool the epidermis while sufficient laser energy is delivered to damage hair follicles. The most effective cooling method available is active cooling. When in contact with a cold object, heat flows from the epidermis. The important targets for hair removal lie at least 1 mm below the skin surface. When the skin is actively cooled for 0.2-1 seconds, these targets remain warm, while the epidermal temperature plummets. Epidermal temperatures less than about –10 °C cause tissue injury from freezing. Clinically, it is valuable to cool the skin before, during and after the laser pulse for maximum epidermal protection and patient comfort. Fast cooling requires good contact with a cold, thermally conductive substance. Sapphire is ideal, as it has excellent thermal characteristics and operates as a heat sink removing heat from the epidermis. In addition, the diode handpiece utilized in the study allowed compression of the area being treated. Compression forms excellent thermal contact, collapses blood vessels (a competing target), and forces hair to lie down, bringing hair follicle roots closer to the surface. Consequently, the laser energy is more effectively targeted to the intended site of action.
- Number of Treatments: Temporary hair removal is easily achieved in a single treatment. The amount of permanent hair reduction per treatment varies between patients, increasing with the fluence used for treatment. Most patients require more than one treatment, typically 2-5, to achieve nearly complete, permanent hair reduction. In this study, 89% of the patients achieved significant permanent hair reduction (defined as greater than 15% hair reduction) after one or two treatments with the pulsed diode laser.

- Number of Pulses (Single versus Multiple Pulsing): Multiple pulses given to a site do not have significantly greater effectiveness than a single pulse. However, the risk of pigmentary side effects is somewhat increased. Intentional multiple pulsing to a single site should be avoided.

STUDY DESIGN

The primary objective was to investigate effectiveness and safety of a pulsed diode laser in permanent reduction of pigmented hair. This large, long-term, prospective, blinded, controlled and quantitative study was designed to study fluence-response relationship, one versus two treatments, and single versus multiple pulses.

Ninety-two (92) patients were treated at two facilities: 46 patients at the Massachusetts General Hospital in Boston and 46 at the Laser and Skin Surgery Center of New York, in New York City. There were 45 males and 47 females with varying hair colors and skin types (Fitzpatrick's skin type I to VI; predominately II to III). All patients were treated and examined at 0, 1, 3, 6 and 9 months, and thirty-five patients were also followed up at 12 months.

TABLE 1. FITZPATRICK CLASSIFICATION OF SKIN TYPES

Skin Type	Characteristic
I	Always burns, never tans
II	Always burns, sometimes tans
III	Sometimes burns, always tans
IV	Rarely burns, always tans
V	Moderately pigmented
VI	Black skin

The device used was a semiconductor diode laser system that delivers pulsed, infrared light at a wavelength of 800 nm, pulse duration from 5-20 ms and fluences from 15-40 J/cm^2. Testing with diode lasers has shown that at 800 nm, the laser light effectively penetrates the dermis, where follicular melanin is the dominant chromophore. Given that the thermal relaxation time for hair follicles ranges from 10-100 ms, the pulse duration of 5-20 ms produced by this device is long enough to allow heat conduction from the pigmented hair shaft during each pulse.

The laser handpiece contains high-power diode arrays, eliminating the need for an articulated arm or fiber-optic beam delivery system. The handpiece integrates a condenser that mixes light to produce a fluence of 15-40 J/cm^2 over a uniform 9x9 mm area. The handpiece contains an actively cooled convex sapphire lens that, when pressed against the patient's skin slightly before and during each laser pulse, provides thermal protection for the epidermis. The cooling lens not only allows higher doses of laser energy to safely and effectively target hair follicles, but also allows compression of the target area placing hair roots closer to the laser energy.

Before each treatment, eight test sites were positioned on a patient's thigh or back with two micro-tattoos or other anatomic landmarks to ensure exact location of the test sites at follow-up visits. Hairs at each site were trimmed to a uniform length using clippers, and the skin was cleaned with isopropanol. Digital images of the treatment sites were taken at the initial visit and at each follow-up visit (1, 3, 6, 9 and 12 months). A charge-coupled-device video camera with a photographic ring flash and frame-grabber was used to provide high-resolution hair imaging. The camera was connected to a computer with image acquisition hardware and image analysis software. The number of hairs was counted blindly in each test area before laser treatment, and at each follow-up visit.

The exposure schedule for the eight treatment sites is shown in Table 2. The fluence range tested was 15-40 J/cm^2 and the pulse duration was 5-20 ms. At those sites receiving two treatments, exposure was repeated one month after the first treatment. At sites receiving multiple pulses, three pulses were applied to the same area, two seconds apart. All patients also had a control site that was unexposed and shaved.

TABLE 2. EXPOSURE SCHEDULE

Site	2 Width (ms) Pulse	Fluence (J/ cm2)	Number of Pulses	Treatments Number of
1	5	15	1	1
2	10	20	1	1
3	15	30	1	1
4	20	40	1	1
5	20	40	1	2
6	20	40	3	2
7	20	40	3	1
8 (Control)	–	–	0	0

Clinical evaluation of results and CCD imaging were conducted at 0, 1, 3, 6, 9, and 12 months after treatment. Approximately 4,000 images were analyzed during this study. Investigators visually assessed skin response, including hypopigmentation, hyperpigmentation, erythema, edema and textural differences, using a response grading scale of 0-3 (none/absent to full/severe). Hair count, hair phase, growth rate, and shaft diameter were quantified using the digital images. Biopsies were also taken at sites with obvious laser-induced hair loss, at different times after exposures, and were processed and examined by light microscopy.

TABLE 3. BIOPSY TIMELINE AND COUNT

Time Biopsy Taken	No. of Biopsies
Before Treatment	5
Immediately After Treatment	3
1 Week After Treatment	1
1 Month After Treatment	1
3 Months After Treatment	1
5 Months After Treatment	2
12-17 Months After Treatment	4

An independent statistician performed data analysis. Hair reduction was defined as the percentage of terminal hairs absent after treatment, compared with the number before treatment. Hair reduction was quantified at each follow-up visit for each site, and the mean hair loss and standard error were calculated.

RESULTS

Treatment demonstrated two different effects on hair growth: hair growth delay and permanent hair reduction. A measurable growth delay was seen in all patients (100%) at all fluence/pulse width configurations tested; this growth delay was sustained for 1-3 months.

Table 4 shows percentage of hair reduction for all sites for all laser configurations. After two treatments at 40 J/cm2 (20 ms pulse duration)[3], the average permanent hair reduction was 46%. Two treatments significantly increased hair reduction as compared to one treatment, with an apparently additive effect. At a fluence of 40 J/cm2, the initial treatment removed approximately 30% of terminal hairs, and the second treatment given one month later removed an additional 25%. Triple-pulsing (3x) did not significantly increase hair reduction over single pulsing, after one or two treatments. However, the incidence of side effects was higher for triple pulsing.

TABLE 4. HAIR REDUCTION RESULTS

Fluence	Number of Treatments	Percentage of Hair Reduction				
		1 mo.	3 mo.	6 mo.	9 mo.	12 mo.
5 ms, 15 J/cm2	1	65.4	21.5	17.9*	15.5*	26.6
10 ms, 20 J/ cm2	1	66.7	21.0	22.2	20.7	25.9
15 ms, 30 J/ cm2	1	70.8	30.2	28.7	30.6	29.4
20 ms, 40 J/ cm2	1	70.2	26.8	29.8	32.5	32.5
20 ms, 40 J/ cm2	2	69.3	51.5	37.1	42.3	46.6
20 ms, 40 J/ cm2 3x	2	71.1	51.9	36.8	41.4	46.2
20 ms, 40 J/ cm2 3x	1	68.9	30.8	32.3	32.4	38.5
Control	0	17.3	10.5	10.8	6.3	5.5

*Percentage is not statistically significant.

Hair regrowth stabilized at 6 months at all fluences; there was no further hair regrowth between 6, 9 and 12 months. This stabilizing of hair regrowth or hair count is consistent with the clinically accepted growth cycle of follicles (Table 5) and the definition of permanent hair reduction, being a significant reduction in the number of terminal hairs after treatment, which is stable for a longer period than the complete growth cycle of follicles at the body site tested.

Statistically significant reduction in average hair regrowth ($p<0.01$) continued at 3, 6, 9, and 12 months for all sites, at all fluence-pulsewidth configurations, after both one and two treatments. Eighty-nine percent of patients exhibited significant permanent hair reduction at all configurations.

TABLE 5. DURATION OF GROWTH CYCLES			
Location	(months) Telogen	(months) Anagen	Total (months)
Back	3-6	3-6	6-12
Thigh	3-6	3-6	6-12
Arm	3-5	1-2	4-7
Calf	3-4	4-5	7-9

In addition to statistically significant hair reduction, treatment with the laser also showed reduction in hair diameter and reduction in color of regrowing hairs. Regrowing mean hair diameter decreased by 19.9%, and optical transmission at 700 nm of hair shafts regrown post-treatment was 1.4 times greater than transmission pretreatment ($p<0.05$). These added benefits of the treatment are cosmetically desirable, since thinner, lighter hairs add to the appearance of hair reduction.

Histological analysis suggested two mechanisms for effective, permanent reduction of terminal hair: miniaturization of coarse hair follicles to vellus-like hair follicles, and destruction of the follicle with granulomatous degeneration with a fibrotic remnant. The histological examination in this study showed that treatments with the pulsed diode laser caused immediate thermal damage in follicles with large, pigmented shafts, while follicles with small vellus shafts showed no effect. Both pigmented and non-pigmented areas of terminal hair follicle epithelium showed thermal coagulation necrosis, with minimal or no damage to the adjacent dermis. Histological analysis also demonstrated that triple pulsing did not produce more follicular damage than single pulsing, although the dermis between closely spaced follicles was occasionally injured by triple-pulsing. Sebaceous glands near the treated follicles showed no or minimal thermal damage, and sweat glands and dermal capillaries appeared normal.

This study was intended to elicit side effects, by covering a wide range of fluences, regardless of skin type. Side effects with pulsed diode laser treatment were fluence and skin type dependent. Hyper- or hypopigmentation was minimal in fair skin, and increased with fluence and with darker skin type. At the highest fluence given of 40 J/cm, the incidence of hyper- or hypopigmentation was greater for patients with skin types III through VI. In addition, clinical experience has shown that these high fluences may elicit somewhat greater side effects in treatments of large areas.

Immediately after treatment, the typical response is perifollicular erythema and edema, which subsides within a few hours. In this dose response study, all fluences were given to most patients, regardless of skin type. (At the New York site, fluences at or above those that showed evidence of epidermal injury were not delivered. This resulted in several patients who did not receive the highest fluences.) Approximately 20% of patients exhibited pigment changes which resolved in 1-3 months. The vast majority of pigment changes were transient, but with darker skin types and higher fluences, some persistent pigment changes were noted. Triple pulsing increased the incidence of hyper- or hypopigmentation as compared to single pulsing, but did not significantly increase hair reduction.

CONCLUSIONS

- The pulsed diode laser utilized in this study[1] provides a safe and effective treatment that achieves both temporary and permanent reduction of unwanted, pigmented hair. Permanent hair reduction occurred in 89% of the patients in this large, long-term, prospective, blinded, controlled and quantitative study.

- On average, about half of the hair had permanent hair reduction after two treatments at a fluence of 40 J/cm[2]. Many patients had nearly complete, permanent hair reduction after two treatments, while a few had little or no permanent hair reduction.

- Regrowing hair is typically thinner and lighter in color, adding to the cosmetic benefit.

- Both the efficacy for hair removal and the risk of side effects increase with increasing treatment fluence. There was an apparent threshold fluence for inducing side effects in each skin type.

- The mechanisms for permanent hair reduction include miniaturization of terminal hairs, and degeneration of follicles damaged by selective photothermolysis.

These study results support the clinical utility of the high-power, pulsed diode laser as a safe and effective device for permanent reduction of pigmented, terminal hair.

In clinical practice, fluence and pulse width should be adjusted for skin type. At one clinical location over 1,000 clinical treatments were performed with this device, in which fluence and skin type were matched to optimize the efficacy and safety of treatment. When this was done, the incidence of side effects was less than 1%, and was limited to transient changes in skin pigmentation.

Footnotes:

[1]Now commercially available
[2]Pulse width setting for the system tested. Current system has a pulse width setting of 7.5 ms for 15 J/cm[2].
[3]A lower fluence is recommended until significant experience is obtained.

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