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Quantitative Assessment of Pulse Dye Laser Therapy in the Management of Hypertrophic Burn Scars

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Abstract

Background: Several studies have reported the utility of Pulse Dye Laser (PDL) therapy in the management of hypertrophic burn scars. Among the potential benefits including improvement in pruritis, pain, stiffness and surface irregularities, its effect on erythema reduction has been most frequently reported. However, few studies have used quantitative methods to document the degree of erythema reduction in hypertrophic burn scars.

Methods: A retrospective review of patients who received PDL therapy at our burn center was performed. The anatomic area, date, settings and number of treatments were tabulated as were the skin type, and the erythema measurements of the treated areas.

Results: 61 patients received PDL therapy from a period of Mar 2012 to Jul 2013. Among them, 45 patients had enough data for analysis. The average age was 33 (range 18-66) with a 2:1 female to male ratio. The most common mechanism of injury was flame (55%) followed by blast (17.7%). The average TBSA was 16.55% (range 1-65%). The mean fluences used were 7.3 J/cm^2 (range 6-9 J/cm^2) and 5.1 J/cm^2 (range 3.75-6.5 J/cm^2) for the 7 mm and 10 mm spot sizes respectively. An average of 10.7 months elapsed (range 0.75-81 months) prior to treatment initiation. An average of 2.2 treatments were rendered (range 1-5). The average follow up period was 4.6 months with a range of 1 – 14.2 months. Erythema reduction of 5.8% percent (p=0.045) was observed. Subgroup analysis based on Fitzpatrick skin types revealed a 15.3% reduction in type I skin (p=0.047), 7.4% reduction in type II skin (p= 0.036), -5.5% reduction in type III skin (p=0.081) and -2.2% reduction type IV skin (p=0.084).

Conclusion: Pulse dye laser treatment for the management of hypertrophic burn scars resulted in a modest decrease in erythema, with the greatest degree of erythema reduction observed in patients with Fitzpatrick skin types I and II.

Keywords: Pulse dye laser, Hypertrophic burn scars, Colorimeter, Erythema.

Introduction

In the past several years, pulse dye laser (PDL) therapy has been used for the management of hypertrophic burn scars. Other treatment options include surgical excision, pressure therapy, silicone gel, intralesional corticosteroid injection, retinoic acid, radiation, and cryotherapy [1-3].

PDL therapy is based on selective photothermolysis targeting wavelengths of 585-595 nm. This spectrum allows the laser to target the “heme” moiety within hemoglobin and was thus originally used for the treatment of vascular anomalies such as port wine stains, telangiectasia and early hemangiomas [4]. It was only later proposed for scar management with the rationale that increased vascularity is observed both clinically and histologically among hypertrophic scars [5-7]. Many pioneering studies on PDL therapy has been focused on incisional scars [8-16]. While the results have been generally positive, several centers have found less than enthusiastic results [17-21]. As an example, no difference in erythema was found in a prospective randomized controlled study on the effect of PDL on surgical hypertrophic

scars in a cohort of 19 patients with average scar duration of 32 months [18]. As much of the early focus of PDL therapy has been on surgical scars, few studies are limited to hypertrophic burn scars [20-27]. A compilation of studies on hypertrophic incisional scars and hypertrophic burn scars are listed in **Table 1a**. Among the potential benefits of PDL on hypertrophic burn scars including improvement in pruritis, pain, stiffness and surface irregularities, its effect on erythema reduction has been most frequently reported.

One limitation of published studies on PDL and burn scar erythema is the lack of a quantitative, objective assessment tool. Most analyses utilized the Vancouver Scar Scale (VSS) and the Patient and Observer Scar Assessment Scale (POSAS) which are both subjected to inter-observer discrepancies [28,29]. They are also neither quantitative nor easily comparable to one another [28,29]. Meanwhile, colorimetry is a noninvasive, objective and readily available tool to quantify erythema yet it has not been widely adopted clinically for the assessment of hypertrophic burn scars [30]. The aim of this study is to report our center's experience in the use of PDL on hypertrophic burn scars, objectively assessed using a colorimeter.

Materials and Methods

A retrospective analysis was performed of patients who presented to our burn clinic for treatment of hypertrophic burn scars using PDL therapy. Patients were treated based on a clinical diagnosis of a symptomatic hypertrophic burn scar on follow up and their desire for treatment using PDL. The patient demographics (age, gender) as well as the date and mechanism of injury, total body surface area burn (TBSA), Fitzpatrick skin type, colorimeter measurements and the number, date, location and settings of PDL treatments were tabulated and analyzed. Erythema reduction is expressed as a percentage determined by the ratio of the erythema measurement after treatment over the initial measurement before treatment initiation. All data were analyzed using SAS v 9.2 (Cary, NC). For comparison of continuous data, a t-test was used. For comparisons of categorical data, two-tailed Pearson chi-square tests were used. Unless otherwise indicated, significance was defined as $p<0.05$.

Treatment algorithm

Consents, photographs and erythema measurements (DSMII Colorimeter Dermaspectrometer, Cortex Technology, Hadsund, Denmark) were made prior to each treatment. Two colorimeter readings were recorded from each treatment site. Patients were counseled prior to the start of the treatment regimen that generally 4-6 treatments are necessary to appreciate an effect, spaced 4-6 weeks apart. The 7 mm or 10 mm spot sizes were chosen based on the surface area treated. A 595-nm flashlamp-pumped pulsed dye laser with a pulse duration of 450 or 1500 usec Candela V Beam Perfecta pulsed dye laser and Dynamic Cooling

Table 1a Studies of the use of PDL therapy on hypertrophic post-surgical scars

Year/Author	Type	N Pts (Sites)	Results
1994 (Alster et al.) [13]	Retrospective	14	Positive (Flattening, Texture)
1995 (Alster et al.) [14]	Prospective	16	Positive (Erythema, Pliability, Pruritis)
1995 (Dierickx et al.) [12]	Retrospective	26	Positive (Texture, Erythema)
1999 (Wittenberg et al.) [18]	Randomized Control	19	Negative (No difference in scar rating, Erythema, Pliability)
2001 (Manuskiatti et al.) [8]	Randomized Control	10	Positive (Flattening, Pruritis) Negative (Erythema, Pliability)
2003 (Taniguchi et al.) [15]	Prospective	4	Positive (Erythema, Texture)
2003 (Nouri et al.) [16]	Randomized Control	11 (12)	Positive (VSS[a] 54% improvement compared to 10% in control)
2006 (Conologue et al.) [11]	Randomized Control	16	Positive (Vascularity, Pliability) Negative (No differences in height or pigmentation)
2006 (Alam et al.) [17]	Randomized Control	17	Negative (No difference from non treated)
2007 (Manuskiatti et al.) [10]	Randomized Control	19	Positive(Flattening, elasticity) Negative (no change erythema)
2009 (Tierney et al.) [19]	Randomized Control	12 (15)	NAF[b] greater results vs. PDL

[a]VSS (Vancouver Scar Scale); bNAFL (Nonablative Fractional Laser);

Table 1b Studies of the use of PDL therapy on hypertrophic burn scars.

Year/Author	Type	N Pts (Sites)	Results
1996 (Gaston et al.) [22]	Case Report	1	Positive (Erythema, Texture)
1998 (Alster et al.) [36]	Prospective	16(40)	Positive (Pliability, Texture, Erythema)
2002 (Liew et al.) [20]	Retrospective	5 (6)	Negative (initial increased scar resolution, no long term difference)
2003 (Allison et al.) [21]	Randomized Control	38	Negative (No difference in Erythema, Texture or Flattening) Positive (Pruritis)
2003 (Kono et al.) [24]	Retrospective	13 (19)[c]	Positive (Erythema, Flattening, Pruritis, Pain)
2008 (Donelan et al.) [25]	Retrospective	57	Positive (Erythema, Flattening)
2012 (Bailey et al.) [26]	Randomized Control	13(21)	Positive (Erythema, Elasticity, Flattening)
2013 (Hultman et al.) [27]	Prospective Cohort	147	Used with CO2, IPL[d] and Alexandrite (>50% reduction VSS[a] and >1/3 reduction in UNC4P[e] scales)

[c]Only 8 sites from burns; d IPL (Intense Pulsed Light);

Device™ (DCD) setting of 30/20 (Candela, Wayland, MA, U.S.A.) was used. The initial fluences were determined based on titration for the visualization of purpura. Subsequent treatment settings were determined based on the patients' response to the previous treatment. The pulses were delivered with an approximately 30% overlap. Postoperative care consisted of Aquaphor topical ointment and sun avoidance.

Results

Patient demographics

Sixty-one patients received PDL therapy at our burn center between March 2012 and July 2013. Among them, 45 patients have enough data for analysis. The patient demographics are summarized in **Table 2**.

The average age was 33 (range 18-66). There were 30 females and 15 males with a 2:1 ratio. The most common mechanism of injury was flame (55.6%) followed by blast (17.7%), MVA (11.1%), electrical (6.7%), scald (6.7%) and chemical (2.2%). The average TBSA was 16.55% with a range of 1 to 65% TBSA. The distribution of skin color was Fitzpatrick I: 28.9%; Fitzpatrick II: 22.2%; Fitzpatrick III: 28.9%; Fitzpatrick IV: 20%. The anatomic distributions of treatment areas were 39.4% head and neck, 36.3% upper extremities, 18.2% trunk and 6.1% lower extremities.

Table 2 Patient Demographics.

Demographics			
Age	Average	Low	High
	33	18	66
Gender	Sex	Number	Percent
	Female	30	66%
	Male	15	33%
TBSA	Average	Low	High
	16.55%	1%	65%
Months from Injury	Average	Low	High
	10.7	0.75	81
Number of Treatments	Average	Low	High
	2.2	1	5
Length of follow up	Average	Low	High
	4.6	1	14.2
Fitzpatrick	Skin Type	Number	Percent
	I	13	28.9%
	II	10	22.2%
	III	13	28.9
	IV	9	20%
Mechanism	Type	Number	Percent
	Flame	25	55.6%
	Blast	8	17.7%
	MVA	5	11.1%
	Electrical	3	6.7%
	Scald	3	6.7%
	Chemical	1	2.2%
Location	Site	Number	Percent
	Head and Neck	39	39.4%
	Upper Extremity	36	36.3%
	Trunk	18	18.2%
	Lower extremity	6	6.1%

[e]UNC4P (University of North Carolina "4P" Scar Scale)

Treatment characteristics

The mean fluences used were 7.3 J/cm^2 (range 6-9 J/cm^2) and 5.1 J/cm^2 (range 3.75-6.5 J/cm^2) for the 7 mm and 10 mm spot sizes respectively. An average of 10.7 months (range 0.75-81 months) elapsed between the time of injury and the time of treatment initiation. An average of 2.2 treatments (range 1-5 treatments) were rendered. The average follow up with colorimetry readings was 4.6 months (range of 1 – 14.2 months).

Outcome measures

An average decrease in redness of 5.8% (p=0.045) was observed from initial reading to final reading (after 1 to 5 treatments). Patients with Fitzpatrick I skin type had a 15.3% reduction (p=0.047), Fitzpatrick II skin type had 7.4% reduction (p= 0.036), Fitzpatrick III skin type had -5.5% reduction (p=0.081) and Fitzpatrick IV skin type had -2.2% reduction (p=0.084) in erythema from baseline scores (**Figure 1**).

No direct correlation was found between the initial erythema measurement and the duration of scar, Fitzpatrick skin type, patient age, mechanism of injury or the location of treatment.

In analysis of the duration of scar and percentage change in erythema score, it was noted that most changes were observed <20 months from the time of injury. Older scars experienced less changes in their erythema scores (**Figure 2**).

Case Example 1

This is a 25 year old Caucasian female, Fitzpatrick II who sustained superficial burns to her face from a blast injury with a 2.5%. She presented to our burn clinic 3 weeks post injury when initial photographs and colorimetery readings were taken. At this time it was determined that she would benefit from early PDL. She returned 6 weeks after her initial treatment and photographs and colorimetery readings were again recorded and she underwent one additional treatment. Unfortunately no final readings or photographs were recorded after final treatment. Her initial erythema measurement was 21.16 3 weeks after injury with her

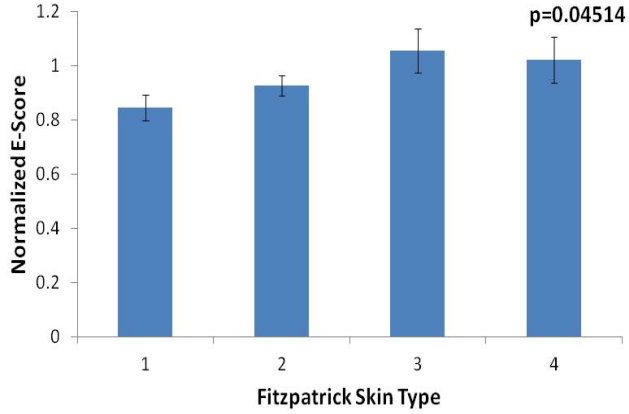

Figure 1 Normalized E-score from final recording broken into Fitzpatrick skin type

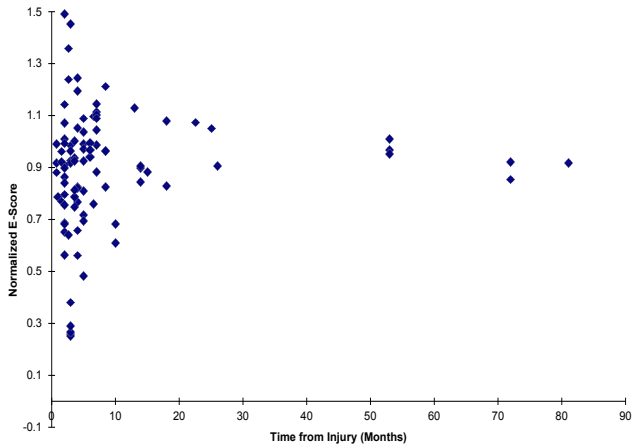

Figure 2 Normalized E-score from final recording broken into Fitzpatrick skin type

final recording, prior to last treatment, was 19.39, with an 8.32% overall reduction (**Figure 3**).

Case Example 2

This 41 year old Hispanic female, Fitzpatrick III who sustained superficial burns to her face from a chemical burn with 3.5% TBSA. It wasn't until 24.5 months post injury that she decided to proceed with PDL therapy at which time first colorimetery readings were obtained and first treatment was performed. She returned to clinic 6 weeks after first laser treatment and additional photographs and readings were made along with PDL treatment. She continued to return for PDL therapy at 6-8 week intervals with the last treatment and recordings at 6 weeks after 5th laser treatment. Her initial erythema measurement was 16.18, taken 24.5 months post injury (photo unavailable), and finally was 16.99, taken 35 months post injury and 6 weeks after 5th laser treatment, with a -4.76% overall reduction (**Figure 4**).

Discussion

While PDL therapy has been increasingly used in the management of hypertrophic burn scars, in particular to decrease redness, few objective studies using quantitative assessment of erythema are available. In this study, we have demonstrated that PDL therapy for the management of hypertrophic burn scars resulted in a modest decrease in erythema, with the greatest degree of reduction in patients with Fitzpatrick skin types I and II. Not surprisingly, most of the changes in scar erythema occurred early after injury with few changes in erythema observed beyond 20 months.

Using quantitative assessment methods, our retrospective analyses support the premise that PDL therapy is associated with a decrease in burn scar erythema. We were however, frankly surprised that the magnitude of reduction was at best modest with only 15% reduction among Fitzpatrick type I skin while no significant changes in erythema were observed among Fitzpatrick types III or IV skin.

Several factors may explain this finding. In this retrospective study, all colorimeter readings were taken prior to a patient's treatment. Consequently, the effect of the last intervention is left undocumented. Furthermore, subjects were not controlled for the number of treatments rendered and patients who had more treatments may have achieved greater reduction in erythema. However, we were not able to demonstrate statistical significance given the number of patients in this study.

Furthermore, even quantitative assessments may suffer from biases. In comparing the percentage of erythema reduction with available photographs, we noted discrepancies in several instances where the degree of photographic improvement far exceeds the quantitative improvement (**Figure 3**). We postulate that this discrepancy may be explained by an unintentional sampling bias. Specifically, the colorimeter probe is only 8 mm in diameter, far smaller than the size of the whole scar (rarely less than 100 cm^2) with a non-uniform color distribution. To eliminate sampling bias, two measurements were taken from two seemingly random areas of the scar. However, we postulate that the operator is likely to choose the more visible or erythematous portion of the scar, thus underestimating the degree of erythema reduction. In future studies utilizing the colorimeter, the randomization should be methodological and the sampling location kept constant throughout the initial and subsequent measurements.

Nevertheless, even accounting for the various biases, the reduction in erythema over the period of laser treatment may still be seen as modest. Some may argue that our follow up period is too short to see much color decrease. While we agree that longer follow up periods will indeed allow for greater erythema reduction, the effect of time on erythema reduction and the natural history of scar maturation may overlook the effect of the PDL therapy itself.

The question of whether an effective dose exists (or fluence measured in Joules per cm^2) for PDL therapy in burn scars is not clear. In our treatment regimen, initial fluences were titrated to the visual appearance of purpura, which we believe to correlate

Figure 3 Treatment example of 25 year old Caucasian female, Fitzpatrick II with a 2.5% TBSA from a blast injury

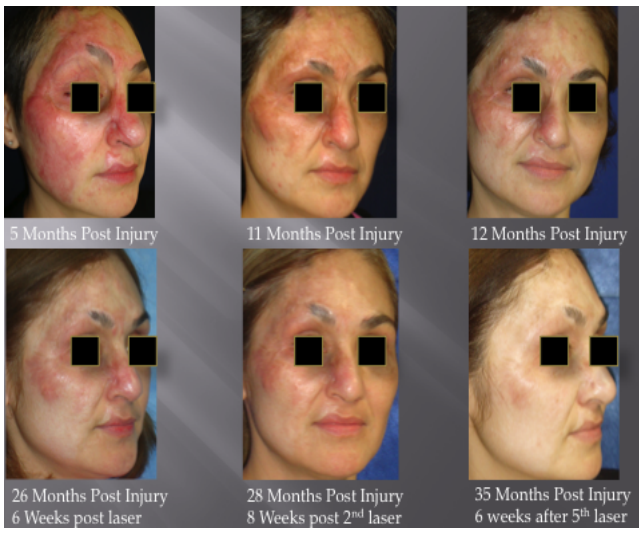

Figure 4 Treatment example of 41 year old Hispanic female, Fitzpatrick III with a 3.5% TBSA from a chemical burn

with the coagulation of the scar's micro-vasculature and accounts for the redness skin within the scar. Some practitioners start therapy at a fixed fluence and then titrate up by 0.5-1 J/cm2 with each subsequent treatment. This has the theoretical advantage of allowing the patient to adjust to the discomfort associated with each laser pulsation. However, this may be under-treating the scar for a significant period of time until a therapeutic dose is reached. However, even if the goal initial fluence is titrated based on the physiology of the scar, about 20% of patients are started with a sub-therapeutic dose simply because of pain intolerance. Half of these patients eventually tolerate a higher dose in time or the addition of a topical anesthetic agent. However, some patients will require general anesthesia to tolerate their PDL therapy.

In our study, we did not observe any quantitative reduction in erythema among patients with higher Fitzpatrick skin types. This is not an uncommon observation and may be explained by melanin acting as a competing chromophore, and decreases the effectiveness of PDL at a given fluence [9]. Indeed, other studies have also found limited changes in erythema scores related to PDL when compared to control in an incisional scar study [18]. Whether the effective and toxic PDL dose range in patients with Fitzpatrick type III and IV skin is simply higher is unclear and deserves further study. Some authors, however, do not believe that greater fluences are better and that higher fluences may result in greater nonspecific thermolytic tissue damages leading to an increase in inflammation and an opposite effect on erythema [18].

Anecdotally, the senior authors have also noted that the effect of PDL therapy on erythema reduction is less noticeable among thicker hypertrophic scars, more commonly seen among patients with higher Fitzpatrick skin types. This is likely a function of the physics of the PDL where the theoretical depth of penetration is only 0.4-1.2 mm, perhaps inadequate for addressing the majority of hypertrophic burn scars whose thicknesses can measure more than a centimeter [31].

The energy delivered by PDL therapy can also be varied by altering the pulse duration. In our practice, pulse duration was chosen based on the initial studies on vascular lesions (1500 usec for 7 mm spot size and 450 usec for 10 mm spot size). This setting reportedly targets vessels of approximately 40-80 um diameter. However, the average hypertrophic scar vessel was smaller (3.3-14.6 um) and further studies may indeed prove that shortening the pulse duration to target these vessels may prove to be more selective [21,32].

Other questions that deserve study include the ideal number of treatment sessions to reach the maximal degree of erythema reduction as well as the optimal time for treatment initiation. While no study in the literature has quantified the natural history of hypertrophic burn scar erythema, we do know that the scar erythema is correlated with the degree of inflammatory activation, which depends both on systemic and local environments. Inflammation is greatest at the time of wound closure and progressively decreases with time. Indeed, hypertrophic burn scars follows a similar temporal sequence. It follows that the best time for PDL therapy may be shortly following injury. As the inflammation subsides, the effectiveness of PDL therapy also decreases. Indeed, we have observed that greatest changes in erythema were seen within 20 months following injury with little change beyond that time. Earlier intervention using the PDL for erythema reduction is likely to be more effective.

Does PDL therapy result in a decrease in erythema independent of the elapsed time from injury? Because hypertrophic burn scars naturally improve with time, this retrospective study is clearly limited in assessing improvement without a control area. This is best answered in the future with a prospective, randomized, blinded, internally controlled study. Though this study did not definitively establish PDL treatment substantially improved the erythema scores of hypertrophic burn scars, we were able to establish shortcomings of our data collection and may help one to design a properly controlled study in the future.

Our study has focused the effect of PDL on its ability to decrease erythema. It is important to note that PDL may have other effects that may better justify its use. Specifically, in a study of post-surgical incisions, Conologue et al. showed no improvement in erythema with PDL therapy, but found significant improvements in both vascularity and pliability of surgical scars [11]. Others have found that pruritis, pain, texture and overall appearance were improved after treatments as described in **Table 1b**. These aspects of PDL therapy may prove to be important, though difficult to objectively quantify, but justification enough to continue treatment in and of itself. We acknowledge the importance of these parameters but were omitted from this study because of a lack of a reliable quantitative assessment. We did attempt to quantify scar stiffness using a durometer but that practice was discontinued shortly because the measurements were highly user dependent and not reliably comparable.

Another aspect of the PDL which deserves additional study is its ability to prevent hypertrophic scar formation. In fact, scar erythema is rarely a significant complaint, but perhaps a surrogate for the future development of hypertrophic scar. After all, the natural history of burn scar is spontaneous decrease in erythema.

In fact, the most dreaded complication of an inflammed burn scar is the progression into a thick and unyieldy hypertrophic scar, which eventually can only be treated using excisional methods. Without knowing the definitive answers to these questions and given the favorable side effect profile of PDL therapy, the potential benefits easily justify the few risks of PDL therapy in the management of hypertrophic burn scars.

Other lasers have shown promise for hypertrophic scars as well but are beyond the scope of this study. Both the Erbium: YAG and CO_2 lasers have been described for the treatment of more mature hypertrophic scars with noted improvement in texture and reduction of hypertrophy [19,33,34]. The Q switched, 532 nm, frequency doubled Nd: YAG laser has also shown potential for treatment of hyperpigmentation [35]. These may offer greater improvement when combined with PDL [36,37]. However, only properly controlled studies can determine the true efficacies of these modalities in treating these late sequalae of burn injuries.

Conclusion

PDL therapy for the management of hypertrophic burn scars resulted in a quantitative, though modest, reduction in erythema, with the greatest degree of change observed in patients with Fitzpatrick skin types I and II.

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