

# Efficacy of Early Treatment of Facial Port Wine Stains in Newborns: A Review of 49 Cases

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**Background:** Port wine stains (PWS) affect 0.3–0.5% of both sexes of newborns, usually occurring on the face.

**Objective:** To document safety and effectiveness of cryogen spray cooled, pulsed-dye laser at higher fluences than previously used to lighten facial PWS in infants  $\leq 6$  months, and establish that frequent treatment early in life yields better clearance than if delayed until later in life.

**Materials and Methods:** Forty-nine infants who had been treated with pulsed-dye laser treatments for facial PWS at  $\leq 6$  months were identified by case review of photographs, age, sex, PWS severity score prior to laser treatment, number of treatments, and improvement following laser therapy.

**Results:** Patients averaged 9.3 (range 2–16) treatments at 4–6 week intervals at 7.75–9.5 J/cm<sup>2</sup>. Average surface area treated was 24.0% with 88.6% average clearance after 1 year. Average clearance was 90.7% for lesions covering  $< 20\%$  surface area and 85.6% for lesions  $\geq 20\%$ . Location (V1, V2, V3, eye, and/or scalp), treated surface area, treatment number, and fluence predicted clearance. Average clearance for sole involvement of V1 was highest (at 93.8%), followed by V2 (at 91.1%), V3 (at 84.3%), V1/V2 (at 83.7%), V1/V2/V3 (at 81.0%), periocular (at 88.6%), and scalp (at 89.9%). All patients tolerated the higher treatment fluences without atrophy or scarring.

**Discussion/Conclusions:** Frequent, high energy pulsed-dye laser treatments are safe and highly effective in improving facial PWS in infants  $\leq 6$  months of age. Patients with PWS should be referred for pulsed-dye laser treatment during early infancy. *Lasers Surg. Med.* 39:563–568, 2007. © 2007 Wiley-Liss, Inc.

**Key words:** birthmarks; children; laser; skin; surgery

## INTRODUCTION

A port wine stain (PWS) or *naevus flammeus* is a vascular birthmark characterized by ectatic vessels within the cutaneous superficial vascular plexus [1,2]. PWS are present at birth and affect 0.3%–0.5% of newborns, with an equal sex distribution [3]. These lesions occur most frequently on the face. Initially a PWS is macular and pink but later in life becomes darker and raised. Port-wine stains persist throughout life. At birth lesions are flat and relatively uniform in color, but evolve with age to become raised, irregularly surfaced, and deeply colored [1]. The majority of these lesions are progressive and can cause

significant physical and psychological morbidity later in life [4–6]. Occasionally, PWSs are associated with other vascular, soft tissue, and neurological findings as part of Sturge-Weber or Klippel-Trenaunay syndrome [4].

In the past, PWS was treated by various methods including excision with skin grafting, cryotherapy, ionizing radiation, dermabrasion, and tattooing. None of these methods were very effective in removing the lesions and often had unacceptable cosmetic results [6,7]. The development of the flash lamp pulsed-dye laser was a tremendous boon to the treatment of PWS [8] since it was the first laser specifically designed for cutaneous vascular lesions using principles of selective photothermolysis. The pulsed-dye laser rarely causes scarring or depigmentation. Moreover there is no anatomical restriction in treating PWS [9].

The pulsed-dye laser has been shown to effectively lighten PWS lesions even in infants and young children [5]. Since PWSs maintain their relative size throughout life, they are consequently smaller during infancy. Repetitive treatment sessions are necessary for maximum benefit and treating a smaller lesion may facilitate the clearing process. Since there is some discomfort associated with the procedure, immobilization of toddlers and school age children becomes a challenge, while compliance has been reportedly greater in very young children.

Importantly, convincing arguments favor treatment early in life, starting in infancy. Two studies one of 83 patients [10] and one of 91 patients [11] demonstrated that the initial size of the PWS impacts outcome. The chances for a successful outcome increase as both age and PWS size decrease [10,11]. When results were grouped by lesion size, the mean improvement was highest for small lesions, 67% for lesions 20 cm<sup>2</sup> and less, larger lesions decreased in size from 45% to 23%. When grouped by age the mean decrease in lesion size was highest, (63%), for children 1-year-old and younger. Decrease in size for children more than 1 year of age ranged from 48% to 54% [11].

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With the addition of dynamic cooling to the pulsed-dye laser, treatment with higher fluences became feasible. The cooling remains localized in the epidermis, leaving the temperature of the deeper PWS blood vessels unchanged. A retrospective analysis of 196 patients demonstrated that early intervention during infancy with longer wavelength, broader pulse width, dynamic cooling spray [12], and high-energy fluences can improve outcomes [13].

Pulsed-dye laser treatment has long been shown to effectively lighten PWS lesions, however, the optimum time for the initiation of treatment and optimal treatment energies have yet to be established. The objective of this study is to document that high fluences are safe and effective in infants 6 months of age and younger. A secondary objective is to document that early, frequent, and high energy pulsed-dye laser treatment may achieve a better chance for significant clearance than delaying treatment until later in life.

## MATERIALS AND METHODS

### Patients

This study was a retrospective review of case records from 2002 to 2005 of infants with PWS who presented to the Laser & Skin Surgery Center of New York. Sixty cases were identified. Cases were eligible for inclusion in the study if patients had begun pulsed-dye laser treatments before 6 months of age for PWS of the face. Cases were excluded if PWS was located other than in the facial area.

Each case was evaluated by chart review, including photographs. Information on age, sex, PWS severity score prior to laser treatment, number of treatments, and improvement following laser therapy was reviewed.

The pre- and post-treatment assessments were performed by three independent dermatologists experienced in laser surgery.

### Laser

All treatments were performed using the 595 nm V-Beam pulsed-dye laser (Candela Corp, Wayland, MA). Fluence settings ranged from 7.75 to 9.5 J/cm<sup>2</sup>, with a 10 mm spot size and 1.5 milliseconds pulse duration, and dynamic cooling (tetrafluoroethane) spray 30 milliseconds prior to each laser pulse followed by a 20 millisecond post-laser pulse delay. Patients underwent a laser treatment every 4–6 weeks until the lesion resolved or until the parents were satisfied. Although patients whose lesions were still visible after 1 year of laser treatment continued treatment, the clearance after 1 year of treatment was evaluated to standardize our study results.

For treatment, patients were immobilized and eyes protected by metal intraocular shields, externally applied aluminum-plated goggles, or multiple layers of gauze. No anesthesia was employed. Multiple non-overlapping pulses were delivered to the entire lesion. Treatment times were generally under 2 minutes. A cool hydrogel dressing was applied immediately post-treatment but further wound care was not required as the epidermis remains intact.

Photographs were taken of all patients prior to each treatment by nurses trained in dermatologic photography using digital cameras under similar lighting conditions.

### Statistical Analysis

Pre-treatment digital photographs were compared to digital photographs taken after 1 year of the initiation of laser treatments. The percentage of lesion clearance was evaluated from 0 to 100% by three dermatologists. A score of 100% represents complete resolution with no detectable difference from normal skin. The following anatomical differences were assessed: (1) percent facial surface area, (2) dermatomal distribution, and (3) scalp or periocular involvement.

All statistical calculations were performed using the Statistical Analysis Systems (SAS Institute Inc., Cary, NC)

## RESULTS

### Demographics and Patient Characteristics

Case record review selected 60 infants who presented to our office between 2002 and 2005 with PWS. These 60 case records were reviewed and 49 infants (22 females, 27 males) were identified who met the eligibility criteria of facial PWS who began pulsed-dye laser treatments prior to 6 months of age. Over the course of a year, patients had undergone treatments every 4–6 weeks for an average of 9.3 (range 2–16) treatments.

Facial locations were subdivided by dermatomal distribution. Of the 49 patients, 35 had PWS in dermatome V1, 18 had PWS in V2, and 18 in V3. Of the 49 patients, 16 had more than one dermatome affected. Periocular involvement was present in 18 of 49 patients and scalp involvement in 7 patients. Table 1 summarizes the patients' lesion characteristics.

### Statistical Analysis and Clearance

The average of three independent evaluators was used to assess clearance. All evaluations were positively correlated (correlations of 0.34, 0.63, and 0.69). The 49 infants had an average surface area of 24.0% (range 5–100%) with an average clearance of 88.6% after 1 year of treatment. Lesions covering less than 20% surface area had an average clearance of 90.7%, whereas lesions equal to or greater than 20% had an average clearance of 85.6%. Table 2 tabulates individual patient data for average clearance, dermatome

**TABLE 1. Patient Lesion Characteristics**

Lesion Location	% Pts (No. of Patients) <sup>a</sup>
V1	71.4 (35/49)
V2	36.7 (18/49)
V3	38.8 (19/49)
> 1 Dermatome	32.7 (16/49)
Periocular involvement	36.7 (18/49)
Scalp	14.4 (7/49)

<sup>a</sup>No. of patients: 49 (22 F/27 M).

**TABLE 2. Patient Surface Area and Clearance—Facial Area and Number of Treatments**

Surface Area (%)	Patient No.	Clearance <sup>a</sup> Average	V1	V2	V3	Eye	Scalp	No. of Treatments	
5	30	97.7	N	N	Y	N	N	3	
10	19	83.3	Y	N	N	N	N	2	
10	24	84	Y	N	N	N	N	4	
10	26	97.7	N	N	Y	N	N	2	
10	31	99.7	Y	N	N	N	N	8	
10	35	97.7	Y	N	Y	Y	N	13	
10	40	99.7	Y	N	N	N	N	2	
10	44	98.7	Y	N	N	N	N	8	
10	51	99.7	Y	N	N	N	N	5	
15	5	99.3	Y	N	N	Y	N	14	
15	9	95	Y	N	N	Y	Y	10	
15	10	95	N	Y	N	N	N	6	
15	11	96.7	Y	N	N	Y	N	9	
15	12	89.3	N	Y	N	N	N	10	
15	14	96	Y	N	N	N	N	8	
15	18	87.7	N	N	Y	N	N	5	
15	21	80	Y	N	N	Y	N	4	
15	23	91.7	Y	Y	N	N	N	4	
15	27	66.7	N	N	Y	N	N	11	
15	29	79.3	N	N	Y	N	N	10	
15	32	73.3	N	N	Y	N	N	10	
15	34	99.7	Y	N	N	N	N	6	
15	37	89	Y	N	N	Y	N	15	
15	38	96	N	Y	N	N	N	7	
15	39	89.3	N	N	Y	N	N	12	
15	43	75	N	N	Y	N	N	14	
15	45	96.3	Y	N	N	Y	Y	10	
15	46	86.7	N	Y	N	N	N	10	
15	49	91	Y	N	N	N	Y	8	
20	1	91.7	Y	Y	N	N	Y	10	
20	4	97	Y	N	N	Y	N	11	
20	13	92.7	Y	N	N	Y	N	10	
20	22	88.3	N	Y	N	N	N	10	
30	2	94	Y	Y	N	Y	N	12	
30	7	80	Y	Y	N	N	N	12	
30	8	92	Y	N	N	Y	N	12	
30	20	92.3	Y	N	Y	N	Y	8	
30	48	80	Y	Y	N	N	N	14	
40	3	91.7	Y	N	N	Y	N	12	
40	6	94.3	N	N	N	N	Y	11	
40	16	89.3	Y	Y	Y	N	N	9	
40	17	87.7	Y	Y	Y	Y	N	15	
40	25	86	Y	N	Y	Y	N	9	
40	33	76	Y	Y	Y	Y	N	16	
40	41	66.7	Y	Y	Y	N	N	9	
50	15	65	Y	Y	Y	Y	N	15	
50	50	89.3	Y	Y	Y	N	N	18	
80	47	88.3	Y	Y	Y	Y	N	7	
100	36	70	Y	Y	Y	Y	Y	6	
Mean = 23.0, range (5–100)	Total no. of patients with affected dermatome Mean = 88.6, range (65–99.7)			35	18	19	18	7	Mean = 9.3, range (2–18)

<sup>a</sup>Average of three raters rounded to nearest decimal point. Arithmetic mean (average) was calculated from the raw data, N = absence of lesion, Y = presence of lesion.

involvement, and number of treatments arranged in order of increasing percent surface area.

Further statistical analysis of these data revealed that the average clearance could be predicted from the extent of the treated regions. These variables were the location of the PWS (V1, V2, V3, eye, and/or scalp), treated surface area, number of treatments, and the fluence ( $\text{J}/\text{cm}^2$  = average energy of the laser). Many patients had V2 as the area to be treated and high surface area. V2 and surface area were highly correlated [ $r = 0.51$ ]. Additionally, V1 and periocular [ $r = 0.48$ ] were highly correlated. On the other hand, a patient seldom had both lesions in dermatomes V1 and V3, but had one or the other. V1 and V3 were negatively correlated,  $r = -0.29$ .

Higher clearance rates were observed for both smaller lesions and V1 dermatome lesions than for either larger lesions or those found in V2 or V3. As shown in Table 3, the highest average clearance, 93.8%, was observed for patients with only V1 involvement. Reduced average clearance was seen for V2 involvement alone, 91.1%, and V3 alone, 83.3%. Involvement of more than one dermatome also was associated with reduced clearance. The average clearance for patients with V1 and V2 involvement was 83.7%, and for patients with all three dermatomes involved was 81.0%. Patients with either periocular or scalp involvement responded very well with average clearance of 88.6% and 89.9%, respectively. Table 3 summarizes these results.

Selected cases of clearance by dermatome and lesion location presented in Table 2 are illustrated in Figures 1 and 2. Patient Nos. 2 and 15 before and after treatment are shown in Figures 1 and 2, respectively. These cases show the better clearance obtained with smaller lesions and those located in V1 and V2 dermatomes in contrast to lesser clearance in hemifacial lesions. Patient No. 2 (Fig. 1) had relatively small lesion and V1 and V2 involvement. Patient No. 15 (Fig. 2) had a hemifacial lesion.

### Predictive Model

A model was developed to predict the average percent clearance after 1 year of treatment based on a forward selection regression model. V3 and surface area were the only predictors which were statistically significant

( $P < 0.05$ ) in the forward selection procedure. The average percent clearance was 94.7%, this was reduced by 1.7% for every 10% of surface area that was treated, with the surface area ranging from 5% to 100% among the 49 patients treated. The average percent clearance was further reduced by 5.3%, if the V3 area was treated. The following equation determined the relationship between clearance and statistical predictors: % Clearance =  $94.7 - (5.3)(V3 \text{ \{where } V3 = 1\}} - (0.17)(\text{surface area})$ . If the child has PWS and any involvement of V3, the predicted percent clearance is decreased by 4.695. If V3 is not involved,  $V3 = 0$ , only the percentage times the surface area is subtracted.

### Safety and Tolerance

All patients tolerated the higher treatment fluences without atrophy or scarring. Topical anesthesia was not applied since the relatively large surface area of application increased the risk of adverse events, such as tachycardia and methemoglobinemia. Since the study was not sufficiently powered, differences in clearance depending on differences between treatments with an average fluence between 7.75 and 9.5  $\text{J}/\text{cm}^2$  could not be determined. Furthermore, the limited power of the study did not enable us to detect statistical differences in clearance with respect to more frequent versus less frequent laser treatments.

### DISCUSSION

This is the first study to show that frequent, high energy pulsed-dye laser treatment is a safe and highly promising approach in treating facial PWS in infants less than 6 months of age.

The results extend our previous observations. The early studies of children 6–30 weeks of age documented that younger children require fewer treatments than older children to achieve the same result [3,9]. In a later study of 16 infants, 63% had 75% or greater clearance after approximately four treatments [13]. Although other studies demonstrated a correlation between lesion size, age, and number of treatments [5] our current study was not sufficiently powered to draw any conclusion on differences in number of treatments. However, high clearance rates correlated with location and size of the lesions.

Most previous studies included infants, but no study to our knowledge included only infants 6 months and younger. Energy densities in studies usually varied according to patient's age and color of the lesion. Early studies [3] of the 585 nm using pulsed-dye lasers used lower fluences, 5.75–6.50  $\text{J}/\text{cm}^2$ , than later studies [10,11] 6–6.5 to maximum of 7.5  $\text{J}/\text{cm}^2$ . However, regardless of patient age or lesion color the highest energy densities used were below 8  $\text{J}/\text{cm}^2$ . When the cryogen spray-cooled laser was used, power levels increased to 8–10  $\text{J}/\text{cm}^2$  at 7 mm spot size. Cryogen spray cooling allows higher incident light to be used, which produces higher intravascular temperature and expedites PWS clearance [12].

New laser technology, using the 595 nm pulsed-dye lasers with cryogen spray cooling, allows physicians to treat at higher fluence levels and greater spot sizes. Our study shows that these higher levels, up to 9.5  $\text{J}/\text{cm}^2$ , are safe and

**TABLE 3. Clearance by Dermatome and Lesion Location**

No. of Patients <i>N</i> = 49	Lesion Location			Clearance (Average %)
	Dermatome			
	V1	V2	V3	
<i>n</i> = 19	+			93.8
<i>n</i> = 5		+		91.1
<i>n</i> = 8			+	83.3
<i>n</i> = 6	+	+		83.7
<i>n</i> = 8	+	+	+	81.0
<i>n</i> = 18		Periocular		88.6
<i>n</i> = 7		Scalp		89.9

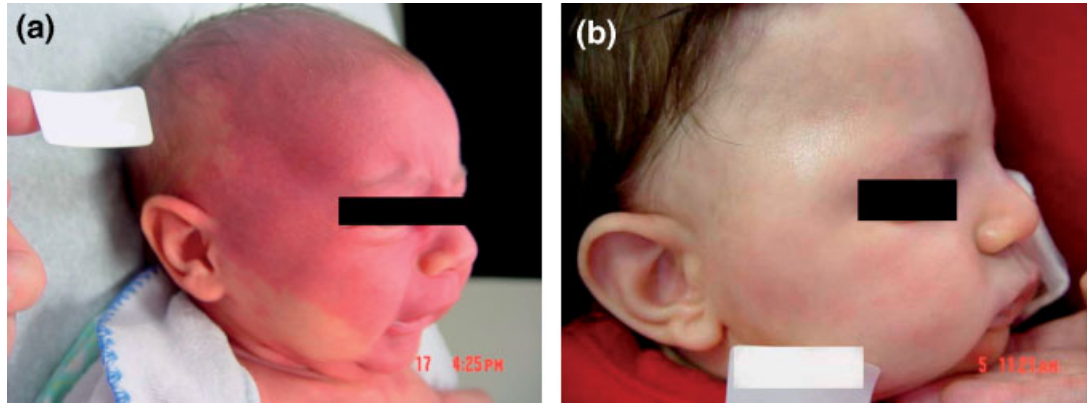


Fig. 1. Patient no. 2: pre- and post-treatment. **a:** Pre-treatment. Age 4 weeks. **b:** After 12 pulsed-dye laser treatments and average fluence of  $8.9 \text{ J/cm}^2$ . Age 13 months.

effective in treating infants less than 6 months of age. Moreover the treatment is well tolerated by infants without need for general anesthesia.

Studies have demonstrated that early treatment is more effective [5,8] One study of 83 patients between ages of 2 weeks and 17 years systematically investigated the effect of laser treatment based on the age of the patient and concluded that outcome improves with early treatment. The study showed that 32% of patients who began treatment before 1 year of age had complete clearance of their PWS, as measured by improvement in lesion size, compared with 18% of older patients achieving complete clearance [10]. In one of our studies even the lowest percent of average clearance, 65%, was significantly higher than a report of 40% average clearance which led to the conclusion that the age of the patient was not a significant factor in the treatment of PWS with the flash-lamp-pumped pulsed-dye laser [14]. However, with improved laser methods this debate apparently has subsided.

Another characteristic favoring early treatment is that the lesions of infants are proportionally smaller and the skin is thinner allowing for better penetration of the laser. This is another argument for early treatment which can be performed when treatment is potentially easier and more effective. Laser light fluence applied to skin surface decreases with increasing penetration depth. A study of 21 children sought to correlate skin thickness, age, and response to pulsed-dye laser. The investigators measured skin thickness at different anatomic sites by ultrasound and found that skin thickness increases with age supporting the fact that better responses are obtained in younger patients who have thinner skin [15].

Clearing lesions before the child is aware of them will likely prevent potential psychological and physical complications later in life. Because most lesions occur on the face, persons with PWS suffer psychologically. Considerable psychological impairment can be avoided if children are



Fig. 2. Patient no. 15: pre- and post-treatment. **a:** Pre-treatment. Age 3 weeks. **b:** After 15 pulsed-dye laser treatments with and average fluence of  $8.80 \text{ J/cm}^2$ . Age 13 months.

treated before school age and before they have to interact with many other children. Psychological morbidity resulting from a feeling of stigmatization among patients may also be avoided [3,16–18].

A limitation of our study was that clearance rates were determined by before and after photographs instead of other more quantitative measures of lesion color. Also, given that this is a retrospective study, we could not control for age of starting treatment or frequency of treatment. Since this was a single center study, future work in our center and with others is necessary to develop optimum treatment strategies for PWS. Our findings have been supported by a recent study showing that high energy pulsed-dye laser treatment of lower extremity PWS in early infancy is highly effective [19].

Future investigations includes studies of long-term follow-up of patients treated at 6 months and younger compared to more than 6 months, since it is likely that earlier clearance also contributes to long-term remission. A recent study reports that approximately 35% of PWS redarken after pulsed-dye laser treatment [20]. However, the majority of patients in this study did not initiate treatment in early infancy. Since redarkening in hypothesized to occur due to lack of complete eradication of vessels and their subsequent progressive ectasia in adulthood, treatment strategies which could more effectively eliminate these vessels, might lessen the chance of PWS redarkening. Our study supports that vessels in PWS can be more effectively cleared by initiating treatment prior to 6 months of life and with higher fluences. Long-term follow-up of our cohort will determine whether this improved vessel clearance contributes to satisfactory long lasting results.

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