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Comparing the Effectiveness of 585-nm vs. 595-nm Wavelength Pulsed Dye Laser Treatment of Port Wine Stains in Conjunction With Cryogen Spray Cooling

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Background and Objectives: The objective of this study was to compare the efficacy and safety of cryogen spray cooled laser treatment (CSC-LT) at wavelengths of 585 nm vs. 595 nm for port wine stain (PWS) birthmarks in a large series of patients.
Study Design/Materials and Methods: A retrospective review was conducted of 64 patients with PWS treated with the ScleroPLUS® [Candela (Wayland, MA)] pulsed dye laser ($\lambda = 585$ or 595 nm wavelength; spot size 7 mm, $\tau_p = 1{,}500$ microseconds) over a 3-year period. Subjects' ages ranged between 3 months and 64 years; there were 42 females and 22 males, all of whom were Asian. Number of treatments ranged from 1 to 6. Duration of treatment ranged from 6 months to 2 years 11 months, with a mean of 12 months. Patients (n = 32) received CSC-LT (585 nm) using radiant exposures of 7–10 J/cm^2. A second group of patients (n = 32) received CSC-LT (595 nm) using radiant exposures of 7–10 J/cm^2. The primary efficacy measurement was the quantitative assessment of blanching response scores for CSC-LT (585 nm) versus CSC-LT (595 nm). Patients were monitored for adverse effects.
Results: Based on chi-squared analysis, there were clinical, and statistically significant, differences in blanching response scores favoring PWS receiving CSC-LT (585 nm) as compared to CSC-LT (595 nm) ($P < .001$). Transient hyperpigmentation was noted in 43.7% (n = 14) and 37.5% (n = 12) of patients in the CSC-LT (585 nm) and CSC-LT (595 nm) groups, respectively. In both groups, transient hyperpigmentation resolved in all patients within 1 year. Permanent hypopigmentation or scarring was not observed in either group.
Conclusions: CSC-LT (585 nm) resulted in superior blanching as compared to CSC-LT (595 nm). Further study is required to optimize wavelength selection on an individual patient basis during PWS therapy in order to improve treatment results. Lasers Surg. Med. 31:352–358, 2002.
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Key words: port wine stain; pulsed dye laser; wavelengths

INTRODUCTION

A port wine stain (PWS) is a congenital, progressive vascular malformation of the dermis [1–3]. Since two-thirds of these malformations occur on the face, PWSs are a clinically significant problem. PWSs should not be considered a cosmetic problem per se but a disease with potentially devastating psychological and physical complications. Personality development is adversely influenced in virtually all patients by the negative reaction of others to a "marked" person [4–6]. In childhood, PWSs are faint pink macules, but the lesions tend to darken progressively to red-purple [7]. The subsequent hypertrophy of underlying bone and soft tissue further disfigures the facial features of many patients. Histopathologic studies of PWS show a normal epidermis overlying an abnormal plexus of subsurface blood vessels located in the upper dermis [8].

In the past, PWS treatment has included cosmetic cover-up, skin grafting, ionizing radiation, dermabrasion, cryosurgery, tattooing, and electrotherapy, but none of these modalities provided cosmetically acceptable results [9]. The development of lasers and their ability to selectively damage PWS blood vessels, offered a promising treatment option. A variety of lasers have been utilized for the treatment of PWS birthmarks, but the pulsed dye laser (PDL) has produced the best clinical results with the lowest incidence of adverse effects [10].

PDLs offering wavelengths from 585–600 nm in conjunction with cryogen spray cooling are now available. 585 and 595 nm are the two wavelengths most commonly used for PWS treatment. Many physicians choose 595 nm, believing this wavelength will penetrate deeper into PWS

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blood vessels resulting in more uniform heating. However, the absorption coefficient of blood is a factor of 5 higher at 585 as compared to 595 nm. Moreover, mathematical modeling indicates that 585 nm may result in superior PWS blanching [11–14]. Although, the PDL has become the treatment of choice for PWS birthmarks, only 10–20% of patients obtain 100% fading of their PWS even after many treatments [15]. In order to improve treatment results, laser parameters including wavelength must be optimized.

The purpose of this study was to compare the efficacy and safety of cryogen spray cooled laser treatment (CSC-LT) at wavelengths of 585 nm vs. 595 nm for PWS birthmarks in a large series of patients. The primary efficacy measure was the quantitative assessment of the blanching response scores of CSC-LT (585 nm) as compared, on a blinded basis, to CSC-LT (595 nm). Safety was also evaluated for each treatment group by searching for any adverse effects such as scarring or dyspigmentation.

STUDY DESIGN/MATERIAL AND METHODS

A retrospective review was conducted of 64 patients with head or neck PWS birthmarks treated with the PDL over a 3-year period (January 1998–December 2000). Subjects' ages ranged between 3 months and 64 years; there were 42 females and 22 males, all of whom were Asian. Number of treatments ranged from 1 to 6. Duration of treatment ranged from 6 months to 2 years 11 months, with a mean of 12 months. All patients received multiple laser treatments and were followed for a minimum of 1 year after their last treatment.

Each patient was evaluated by chart review, including pre- and post-treatment photographs. Based on pre-treatment photographs, each patient's PWS was assigned a severity grade using the clinical descriptions summarized in Table 1. Information regarding the following variables was extracted from charts: age, sex, PWS severity grade prior to laser treatment, number of treatments, and improvement following laser therapy. The following adverse effects were defined, tabulated, and reported: scarring (persistent permanent textural changes) and dyspigmentation (transient or permanent, hypo- or hyperpigmentation).

All treatments were performed using the Candela ScleroPLUS® (Wayland, MA) pulsed dye laser ($\lambda = 585$, 595 nm; $\tau_p = 1{,}500$ microseconds). Laser energy was delivered to the skin through an optical fiber and lens, which focused the beam onto a 7-mm spot on the PWS. A 30% overlap of spots was used during treatment to compensate for the Gausian distribution of the beam. Patients ($n = 32$) received CSC-LT (585 nm) using radiant exposures of 7–10 J/cm^2. A second group of patients ($n = 32$) received CSC-LT (595 nm) using radiant exposures of 7–10 J/cm^2. The average radiant exposure for both groups was 9 $\pm$ 1 J/cm^2 for treatment of facial PWS. The energy density was decreased to 7–8 J/cm^2 on the neck. Severity Grade 2 hypertrophic PWS were treated at 10 J/cm^2.

For all patients, the cryogen used was 1,1,1,2-tetrafluoroethane [$C_1F_3CFH_2$ (Rl34a); BP $= -26.2$°C], which is an environmentally compatible, nontoxic, nonflammable, FDA-approved freon substitute [16–18]. Cryogen spurts were sprayed onto the PWS through an electronically controlled nozzle positioned approximately 3 cm from the skin surface. Cryogen spurt duration (50 milliseconds) and delay between cryogen delivery and laser irradiation (10 milliseconds) were controlled with a programmable digital delay generator.

All pre- and post-treatment photographs were taken under standardized conditions for film, light source, and exposure. Based on comparisons between pre- and post-treatment photographs, each patient's PWS was assigned a blanching response score (1–4) of poor, fair, good, or excellent according to the classification system given in Table 2. The pre- and post-treatment blanching assessments were performed by three plastic surgeons knowledgeable and experienced in laser treatment but not previously involved in the study. Each physician was given pre- and post-treatment photographs of each individual patient's PWS lesion to evaluate by paired comparison.

The primary efficacy measure was the quantitative assessment of the blanching response scores of CSC-LT (585 nm) as compared, on a blinded basis to CSC-LT (595 nm). Differences between the mean blanching response scores for both treatment groups were then determined and a chi-squared analysis performed. Safety was evaluated for each treatment group by searching for any adverse effects, such as scarring or dyspigmentation. Scarring was defined as permanent raised hypertrophic, depressed, or atrophic laser-treated PWS sites. Dyspigmentation was defined as a transient (resolving within 1-year post-treatment) or permanent change in skin color on laser-treated PWS sites as compared to adjacent normal skin.

TABLE 1. Classification of Port Wine Stain (PWS)

Severity score	Clinical description
1	Faint, barely discernible borders, plus Well-defined borders with areas of normal skin interspersed within the lesion
2	Well-defined borders, uniform lesion with no areas of normal skin, plus Raised or thickened lesion, plus Nodularity or hypertrophy of involved anatomic structure

TABLE 2. Classification of Blanching Response Scores Following Pulsed Dye Laser (PDL) Treatment

Blanching score	Degree of blanching (%)
1	Poor (<25)
2	Fair (26–50)
3	Good (51–75)
4	Excellent (76–100)

RESULTS

Statistical Analysis of the CSC-LT (585 nm) and CSC-LT (595 nm) Treatment Groups

Information regarding the variables of age, sex, and PWS severity score prior to laser treatment, number of PDL treatments and duration of treatment was obtained for statistical analysis. The mean ages for the CSC-LT (585 nm) and CSC-LT (595 nm) groups were 24.4 and 26.3 years, respectively. The male:female ratios for the corresponding groups were 14:18 and 13:19, respectively. Thirty-three patients had PWS classified as severity Grade 1 and 31 as severity Grade 2. The mean severity grades for the CSC-LT (585 nm) and CSC-LT (595 nm) groups were 1.54 and 1.52, respectively; and the mean number of PDL treatments for the corresponding groups was 3.31 and 3.34, respectively. Based on a multivariate analysis of variance (MANOVA), there were no statistically significant differences between the two groups based on age, sex, PWS severity grade prior to laser treatment, and number of PDL treatments ($P > .05$).

Quantitative Assessment of the Blanching Response Scores for PWS Severity Grades 1 and 2

For combined severity Grades 1 and 2, Table 3 summarizes the quantitative assessment of the blanching response scores of CSC-LT (585 nm) as compared to CSC-LT (595 nm) treated patients. The mean blanching response scores and standard deviations were 2.90 ± 0.96 and 2.34 ± 1.08 for the treatment groups, respectively, indicating an enhanced blanching response in the former group as assessed clinically. Based on chi-squared analysis, this difference was statistically significant favoring PWS receiving CSC-LT (585 nm) as compared to the CSC-LT (595 nm) treated group ($P < .001$) (Figs. 1 and 2).

TABLE 3. Blanching Response Scores of Port Wine Stain (PWS) Severity Grades 1 and 2

	n	CSC-LT (585 nm)	CSC-LT (595 nm)
Poor	12	3	9
Fair	18	7	11
Good	18	12	6
Excellent	16	10	6
Total	64	32	32
Mean blanching response score		2.90 ± 0.96	2.34 ± 1.08

$P < .001$.

A B

Fig. 1. Two-year-old Asian female with port wine stain (PWS) of the left cheek: (**A**) prior to laser therapy; and (**B**) 2 years after five treatments with CSC-LT (585 nm) using an energy density of 9 J/cm^2. Result was evaluated as an excellent blanching response.

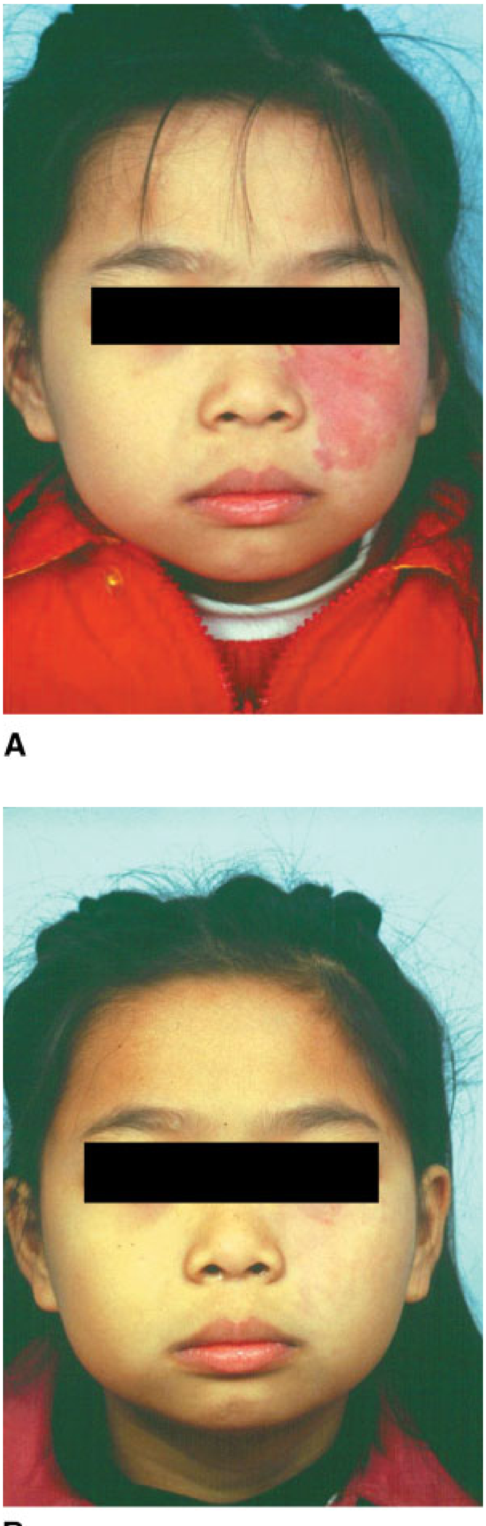

Fig. 2. Six-year-old Asian female with port wine stain (PWS) of the left cheek: (**A**) prior to laser therapy; and (**B**) 3 years after four treatments with CSC-LT (585 nm) using an energy density of 9 J/cm^2. Result was evaluated as an excellent blanching response.

Quantitative Assessment of the Blanching Response Scores for PWS by Severity Grade

For patients with severity Grade 1, Table 4 summarizes the quantitative assessment of the blanching response scores of CSC-LT (585 nm) as compared to CSC-LT (595 nm). The mean blanching response scores and standard deviations were 3.06 ± 0.96 and 2.72 ± 1.02 for the treatment groups, respectively, indicating a somewhat enhanced blanching response in the former group as assessed clinically. Based on chi-squared analysis, this difference was not statistically significant ($P > .05$).

For severity Grade 2, Table 5 summarizes the quantitative assessment of the blanching response scores of CSC-LT (585 nm), as compared to CSC-LT (595 nm). The mean blanching response scores and standard deviations were 2.76 ± 0.97 and 1.71 ± 0.91 for the treatment groups, respectively, indicating an enhanced blanching response in the former group as assessed clinically. Based on chi-squared analysis, this difference was statistically significant favoring PWS receiving CSC-LT (585 nm) as compared to CSC-LT (595nm) group ($P < .001$).

Safety

Safety was evaluated for each group by searching for any adverse effects such as scarring or dyspigmentation following PDL treatment of PWS. Transient hyperpigmentation was noted in 43.7% (n = 14) and 37.5% (n = 12) of patients in the CSC-LT (585 nm) and CSC-LT (595 nm) groups, respectively. In both groups, transient hyperpigmentation resolved without medical intervention in all patients within 1 year. Permanent hypopigmentation or scarring was not observed in either group.

DISCUSSION

Since the clinical objective in PWS laser therapy is to cause selective thermal destruction of a specific chromophore within human skin, a therapeutic laser wavelength should be chosen that will result in greater heat absorption by the targeted molecule relative to other optically absorbing molecules [19]. Choice of wavelength also determines the depth to which the light will penetrate with sufficient energy density to effect tissue change. Many physicians

TABLE 4. Blanching Response Scores of Post Wine Stain (PWS) Severity Grade 1

	n	CSC-LT (585 nm)	CSC-LT (595 nm)
Poor	3	1	2
Fair	9	3	6
Good	10	5	5
Excellent	11	6	5
Total	33	15	18
Mean blanching response score		3.06 ± 0.96	2.72 ± 1.02

$P > .05$.

TABLE 5. Blanching Response Scores of Post Wine Stain (PWS) Severity Grade 2

	n	CSC-LT (585 nm)	CSC-LT (595 nm)
Poor	9	2	7
Fair	9	4	5
Good	8	7	1
Excellent	5	4	1
Total	31	17	14
Mean blanching response score		2.76 ± 0.97	1.71 ± 0.91

$P < .001$.

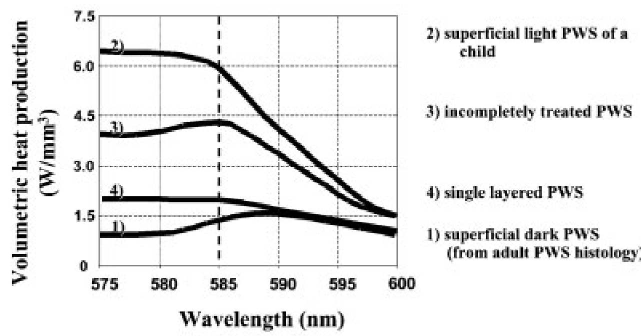

Fig. 3. Volumetric heat production in the targeted port wine stain (PWS) vessel of the four PWS model anatomies (van Gemert et al. PMB 1997;42:41–50). (**1**) A superficial dark PWS consisting of an upper dermal layer of 0.3 mm, 15% blood volume, 50-μm radius PWS vessels; subsequently a 0.6-mm normal perfused dermis of 2% blood volume, 2-μm radius dermal vessels, and the deepest-targeted PWS blood vessel at dermal depth 0.9 mm, 50-μm radius. (**2**) A superficial light PWS of a child, an upper dermal layer of 0.15 mm, 5% blood volume, 12.5-μm radius vessels; a 0.4-mm normal perfused dermis defined as above; and the deepest-targeted PWS vessel at 0.55-mm dermal depth, 12.5-μm radius. (**3**) An incompletely treated PWS consisting of 0.4-mm normal perfused dermis (as defined above) and a 50-μm radius targeted PWS vessel representing the remaining PWS. (**4**) A PWS consisting of 0.75-mm dermal layer of 5% blood volume, 50-μm radius PWS vessels.

choose 595 nm, believing this wavelength will penetrate deeper into PWS blood vessels resulting in more uniform heating.

However, the oxyhemoglobin absorption profile is very "steep" in the 575–600 nm range. The absorption coefficient of blood is a factor of 5 higher at 585 as compared to 595 nm. Mathematical modeling indicates that 585 nm may result in superior PWS blanching. Van Gemert et al. [11] described four PWS models (Fig. 3): (1) a dark PWS with superficial and deep components; (2) a light PWS of a child; (3) an incompletely treated PWS; and (4) a single-layered PWS with vessels evenly distributed in the dermis. For each model, they determined the cross-sectional average volumetric heat production in the deepest-targeted blood vessel as a function of wavelength in an effort to predict optimal heat production. In the first model, the deepest-target blood vessels were most affected by laser light at 590 nm, whereas heat production was approximately equal at 585 and 595 nm. In the other three models, maximum volumetric heat production was achieved at wavelengths between 577 and 587 nm.

In our study, Grade 1 PWS most likely correspond to Model 2 and Grade 2 PWS correspond to Models 1 and 4. As such, the above-described calculations would have predicted the observed result, superior blanching with CSC LT (585 nm) vs. CSC LT (595 nm). It is important to note that this difference was statistically significant for the treated groups with combined severity Grade 1 and 2 and severity Grade 2 PWS. Some clinicians might have expected that patients with severity score 2 PWS might have deeper and larger blood vessels that may benefit from the deeper penetration of the 595-nm light. However, targeted vessel heat production is dependent on a complex array of factors affecting light propagation through the PWS including the size, depth, density, and configuration of vessels within a PWS and even the density of red blood cells within a given vessel.

To further explore the issue of wavelength optimization during PWS treatment, we are currently using a split comparison of blanching on the same PWS using CSC-LT (585 nm) and CSC-LT (595 nm). Some patients clearly respond best to CSC-LT (585 nm) (Fig. 4). However, further study is warranted.

Transient hyperpigmentation was noted in 43.7% (n = 14) and 37.5% (n = 12) of patients in the CSC-LT (585 nm) and CSC-LT (595 nm) groups, respectively. The higher incidence of transient hyperpigmentation in the CSC-LT (585 nm) group is most likely due to the slightly higher absorption by epidermal melanin at this wavelength. In both groups, transient hyperpigmentation resolved without medical intervention in all patients within 1 year. Permanent hypopigmentation or scarring was not observed in either group. We have previously demonstrated [20] and this study further confirms that the millisecond domain cryogen spurts immediately before pulsed laser exposure used in this study permits the safe use of higher laser light doses.

Ideally laser and CSC parameters should be selected from knowledge of the temperature increase in epidermal melanin immediately after pulsed laser exposure as well as PWS blood vessel size and depth. Epidermal melanin concentration and PWS depth vary on an individual patient basis and even from site to site on the same patient. In our laboratories, we are also working on techniques that would allow individual assessment of relevant PWS characteristics prior to PWS therapy in order to optimize laser treatment [21,22].

A B

Fig. 4. Twelve-month-old Asian baby boy with port wine stain (PWS) of the right cheek. Contra lateral comparison of blanching on the same PWS using CSC-LT (585 nm; 9 J/cm^2; left side of photograph) and CSC-LT (595 nm; 9 J/cm^2; right side of photograph): (**A**) prior to laser therapy; (**B**) after two treatments. There was superior blanching on the side of the PWS receiving CSC-LT (585 nm) as compared to the CSC-LT (595 nm).

CONCLUSION

CSC-LT (585 nm) resulted in superior blanching of PWS lesions as compared to CSC-LT (595 nm). The mathematical models of van Gemert et al. and others predicted this result. Further study is required to optimize wavelength selection on an individual patient basis during PWS therapy in order to improve treatment results.

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