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Effect of Dynamic Cooling on 585-nm Pulsed Dye Laser Treatment of Port-Wine Stain Birthmarks

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BACKGROUND AND OBJECTIVE. *The objective of this study was to determine the effectiveness of a dynamic cooling device (DCD), spraying the skin with a brief spurt of cryogen prior to the laser pulse, in reducing transient pain associated with 585-nm pulsed dye laser (PDL) treatment of port-wine stains (PWS), and reducing epidermal damage (hypo/hyperpigmentation) caused by this laser during PWS treatment.*

MATERIALS AND METHODS. *Matched treatment sites were compared with and without the use of the cryogen spray in 47 patients at two investigational sites. Pain ratings, clearance of the PWS, and pigmentation changes were assessed. The results were analyzed by skin type and patient age.*

RESULTS. *A statistically significant reduction in pain ratings was found in all patient groups using the DCD without changing the efficacy of PWS clearance. Pain reduction was most remarkable in patients with darker skin types. Dynamic cooling prevented the occurrence of epidermal damage or pigmentation change in most cases.*

CONCLUSIONS. *This study suggests that dynamic cooling can dramatically diminish pain during PWS treatment with the 585-nm PDL without reducing treatment efficacy. The absence of epidermal damage in most patients suggests that precooling with the DCD may allow the use of higher laser fluences to expedite clearance without inducing epidermal change. Dynamic cooling has potential use with other lasers and different lesions where discomfort and epidermal effects limit therapy.* © *1997 by the American Society for Dermatologic Surgery, Inc. Dermatol Surg 1997;23:657–662.*

Extensive clinical research has demonstrated that the 585-nm pulsed dye laser (PDL) is effective in eradicating port-wine stains (PWS) with an extremely low incidence of scarring.[1–3] However, undesirable aspects remain. Each laser pulse causes a pinprick pain sensation that is difficult or impossible for many pediatric patients and some adult patients to tolerate. Since clearance of PWS typically requires several laser treatments, each with multiple laser pulses, many patients require topical, local, or general anesthetics with the incumbent risks and side effects.

A second problem is that the melanin in darker-skinned patients (skin types IV–V) interferes with absorption of the incident laser light by the deeper PWS vessels.[4] When melanin absorbs laser light, the resultant temperature increase can induce epidermal blistering. In these patients, the laser treatment dosages must be kept very low, often subtherapeutic, to avoid damage to the epidermis and prevent the possibility of scarring.[5]

Recent research has suggested a method that may both reduce pain associated with the PDL treatment and protect the melanin-absorbing epidermis. Nelson et al have developed a dynamic cooling technique for PDL treatment of PWS.[6] The skin is sprayed with a brief spurt of liquid cryogen prior to the laser pulse. Earlier attempts at precooling the skin employed ice cubes or chilled water and produced a steady-state cooling effect on the skin, so that both the epidermis and underlying PWS vasculature were chilled.[7] The cooled PWS vessels required higher laser dosages for their eradication, negating the benefit of cooling of the epidermis. In the Nelson et al model, the cryogen spurt is so short, it can rapidly cool the epidermis without affecting the temperature of the deeper PWS blood vessels.

Cooling the epidermis protects this layer of skin because, while the absorption of laser light by melanin still causes an epidermal temperature jump, both the initial and final temperatures are much lower. The first

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Dr. Waldorf was a Mohs, laser, and dermatologic surgery fellow at the time the work leading to this manuscript was done.

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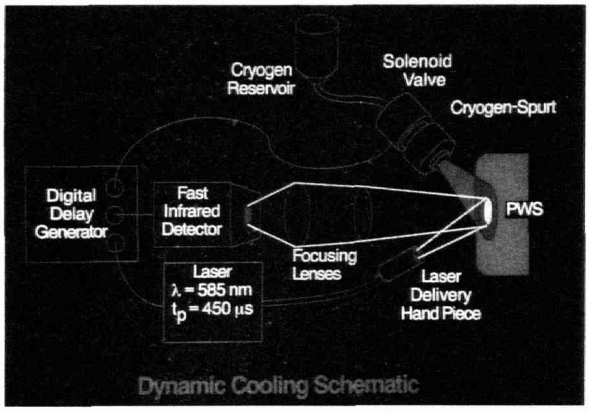


Figure 1. *PWS = port wine stain, λ = wavelength, tp = pulse duration. Reproduced with permission from reference 6.*

clinical tests of a dynamic cooling device (DCD) did not result in epidermal damage even at high fluences.

The purpose of this study was to determine the effectiveness of the DCD, spraying the skin with a brief spurt of cryogen prior to the laser pulse, in reducing transient pain associated with 585-nm PDL treatment of PWS, and reducing epidermal damage (hypo/hyperpigmentation) caused by this laser during PWS treatment.

Materials and Methods

Patients

Forty-seven patients were enrolled in the study at two investigational sites: 30 patients at the Laser and Skin Surgery Center, New York, NY, and 17 patients at the Washington Institute of Dermatologic Laser Surgery, Washington, DC. Patients enrolled in the study were 5 years of age or older (range, 7–54) with skin types I–IV and a PWS birthmark. Patients who were pregnant or nursing or those with a history of anticoagulation, thromboembolic condition, photosensitivity, or hypersensitivity to dichlorodifluoromethane (cryogen) were excluded from the study. Permission to conduct an experimental protocol was sought and obtained from the Essex Institutional Review Board, Inc. (Lebanon, NJ).

Laser and Dynamic Cooling Device

An SPTL-1b pulsed dye laser (Candela Laser Corp., Wayland, MA), with wavelength 585 nm and pulse duration 450 microsec was used. A prototype DCD was attached to the standard 5-mm-diameter spotsize handpiece of the laser (Figure 1). This device produced a 7-mm-diameter sprayed spot on the skin centered on the site to be irradiated by the laser. The cooling device was controlled electronically to produce a spray with a duration of approximately 40 millisec immediately preceding the laser pulse. The exact spurt duration could not be controlled by the treating physician in this prototype. The cryogen utilized was dichlorodifluoromethane, which is nonflammable and has a well-established history of safe use in the pharmaceutical and medical industries.

Protocol

During the first treatment visit, an area of PWS was selected having two areas with similar clinical appearance for PDL treatment with and without cooling. The test consisted of a PDL treatment of one site with the PDL plus cooling and one with the PDL alone. The therapeutic fluence selected for the PDL alone was based on the patient's skin type and PWS location. The fluence was increased by 10–20% for the PDL plus cooling due to optical scattering of irradiant light by the liquid cryogen droplets. A second test of the same areas was scheduled 6–8 weeks after the first. Each patient had a follow-up visit 6–8 weeks after the final laser treatment to assess efficacy.

Immediately after PDL treatment, patients were asked to rate the pain experienced with the PDL with and without cooling on a scale of: 0 (none), 1 (slight), 2 (moderate), or 3 (severe). Investigators made observations of differences in the purpura produced at each site.

One investigator at each site (HAW and TSA) evaluated the treatment areas objectively before each PDL test utilizing a hand-held spectrometer (Derma Spectrometer; Cortex Technology, Hadsund, Denmark). This reflectance instrument obtains an "erythema index" related to blood content of the superficial dermis.[8] Spectral differences in pigmentation between adjacent areas of skin are used to measure a "melanin index."[9] These values provided a quantitative assessment of the percent clearance of the PWS and of hypo- or hyperpigmentation, respectively. In addition, photographs were taken before each session and at follow-up. One investigator at each site (HAW and TSA) also noted any observed pigmentation or skin textural change.

Results

Effectiveness of Dynamic Cooling in Reducing Pain during PWS Treatment with PDL

During the first treatment session, none of the 47 patients reported a pain rating of 0 in the absence of dynamic cooling, however, 15 patients reported 0 pain during treatment with dynamic cooling (Figure 2). Without cooling, most patients described the pain as moderate (2) or severe (3); with cooling most described it as slight (1) or none (0). Only two patients reported an increase in pain with cooling during the first treatment.

Effect of Patient Skin Type on Effectiveness of Dynamic Cooling in Reducing Pain

Skin type was recorded for 44 of the 47 patients in the study. Of the 13 patients with skin types III and IV, none reported severe pain with cooling and none reported an absence of pain without cooling (Figure 3). Most of these patients reported severe pain without cooling. In comparison, most of the 31 patients with skin types I and II reported moderate pain without cooling and slight pain with cooling (Figure 4). While patients in both groups had a reduction in pain rating with cooling, the improvement was most pronounced for darker skin types (Figure 5).

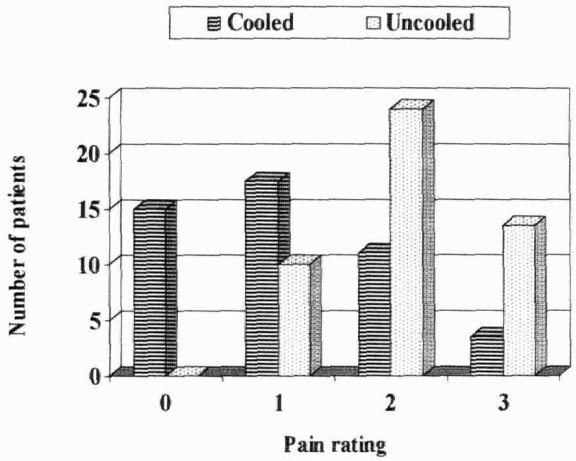
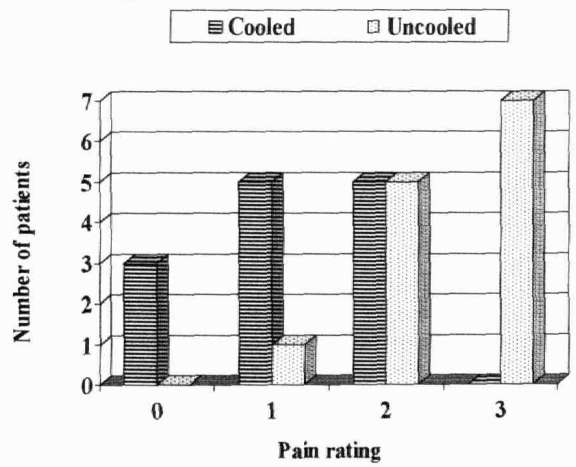


Figure 2. Effectiveness of cooling in reducing pain during PWS treatment with PDL. Number of patients reporting pain ratings of 0 (none), 1 (slight), 2 (moderate), and 3 (severe) during the first treatment, with and without dynamic cooling. None of the patients reported a pain rating of 0 without cooling. Fifteen patients report 0 pain with cooling. Most patients described the pain as 2–3 without cooling and 0–1 with cooling. Two patients had an increase in pain with cooling.

Effect of Patient Age on Effectiveness of Dynamic Cooling in Reducing Pain

To determine whether children benefit more or less than adults from dynamic cooling to reduce pain, the patients at the two sites were divided into two arbitrary groups: those 12 years of age and younger, and those over age 12. At the first treatment session the younger group had lower pain ratings with cooling than without cooling, however, the benefit was less pronounced than for the older group (Figure 6).

Figure 3. Effect of patient skin type on effectiveness of dynamic cooling in reducing pain. Number of patients with skin types III–IV reporting pain ratings of 0 (none), 1 (slight), 2 (moderate), and 3 (severe) during the first treatment sessions, with and without dynamic cooling. Total number of patients = 13. Most reported severe pain and none reported an absence of pain without cooling. None reported severe pain with cooling.



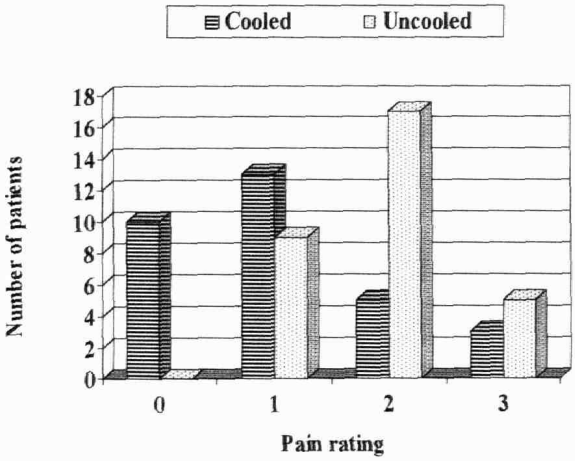
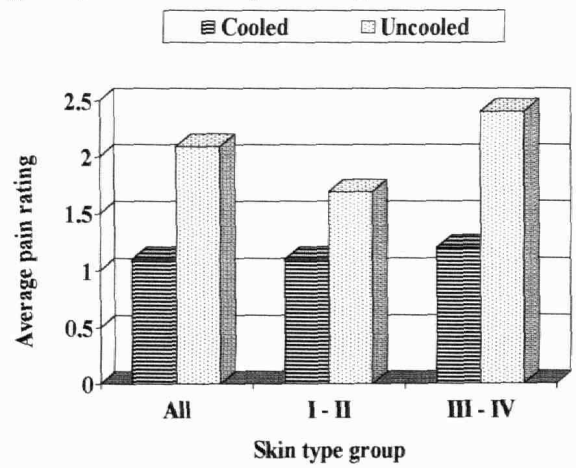


Figure 4. Effect of patient skin type of effectiveness of dynamic cooling in reducing pain. Number of patients with skin types I–II reporting pain ratings of 0 (none), 1 (slight), 2 (moderate), and 3 (severe) during the first treatment session, with and without dynamic cooling. Total number of patients = 31. Most patients reported moderate pain without cooling and slight pain with cooling.

Statistical Significance of Pain Reduction Ratings with Cooling

The pain reduction data were analyzed in terms of paired differences (Figure 7). The means of the changes

Figure 5. Effect of patient skin type on effectiveness of dynamic cooling in reducing pain. Average pain ratings reported by patients grouped by skin type, during first treatment session, with and without dynamic cooling. A greater reduction in pain is apparent for darker versus lighter skin types.



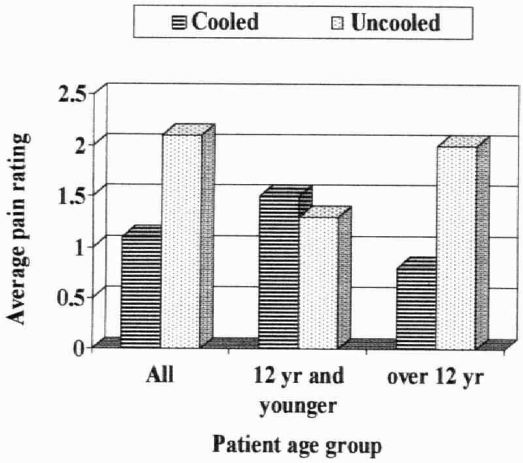


Figure 6. Effect of patient age on effectiveness of dynamic cooling in reducing pain. Average pain ratings reported by patients grouped by age. Number of patients aged 12 years of age or younger = 12. Number of patients over 12 years old = 35. The younger group had lower pain ratings with cooling than without cooling, however, the benefit was less pronounced than for the older group.

in pain rating for all 47 patients at the first treatment session, and the subgroups consisting of: 1) 31 patients with skin types I–II; 2) 13 patients with skin types III–IV; 3) 35 patients over 12 years of age; and 4) 12 patients 12 years of age and younger were compared. *P* values were calculated to test the statistical significance of pain reduction in each group (Table 1). From these results, it is apparent that the reduction in pain is statistically significant even for the group consisting of patients 12 years old and younger, which shows the least benefit from cooling on pain.

Longer-Term Consistency of Pain Reduction with Cooling

In order to test the assumption that significant pain reduction with cooling occurs in subsequent treatment sessions, the pain reduction data from the second treatment session were analyzed. For all 40 patients undergoing the second treatment, the mean change in pain rating was −0.93 (SD = 0.73). This can be compared to the corresponding results from the first session. The *P* value is calculated as 0.61, so clearly the hypothesis that there is no difference in the mean pain reduction at the two treatment sessions can be accepted.

Figure 7. Statistical significance of pain reduction with cooling. Mean reduction in pain rating for patients at first treatment sessions. The pain reduction data were analyzed in terms of paired differences. The reduction in pain was shown to be statistically significant in all groups (P <<0.05).

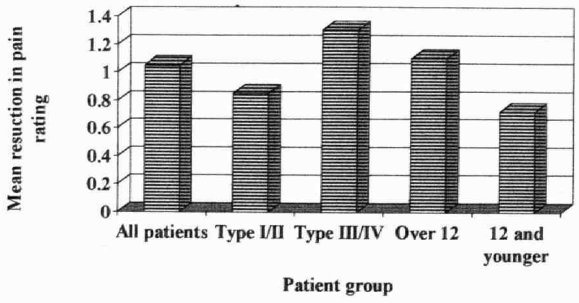


Table 1. Statistical Significance of Pain Reduction Ratings with Cooling

	n	Δ *pain*	*SD*	*SE*	*z*	*P*
All patients	47	−1.02	0.92	0.13	−7.6	<<0.05
Skin types I–II	31	−0.84	0.86	0.16	−5.4	<<0.05
Skin types III–IV	13	−1.13	0.85	0.24	−5.6	<<0.05
Age >12 years	35	−1.11	0.90	0.15	−7.3	<<0.05
Age ≤12 years	12	−0.75	0.97	0.28	−2.67	0.0076

n = number patients; Δ pain = mean change in pain rating; SD = standard deviation; SE = standard error.

Efficacy of PWS Clearance with and without Cooling

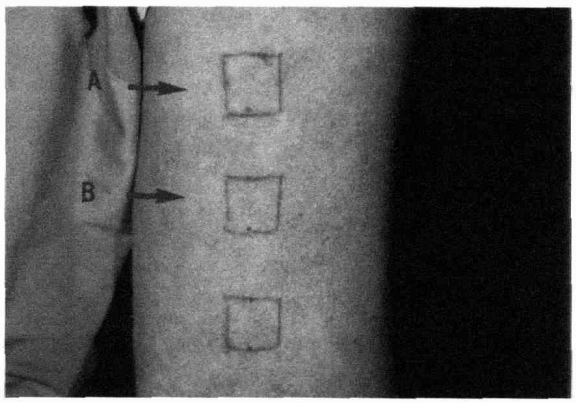
The difference in the percent change in erythema rating taken with the spectrometer pretreatment and at the third (evaluation) visit was taken as the measurement of treatment efficacy. Statistically, there was no effect of cooling on treatment efficacy ($P = 0.98$). Clinically, both sites had equal clearing (Figure 8). Posttreatment purpura was equal for both sites in the majority of patients.

Reduction in Epidermal Damage with and without Cooling

Spectrometer measurements were complicated by the appearance of both hypo- and hyperpigmentation, and analysis could not indicate whether pigmentation changes were more or less likely with cooling. From observational data, four patients showed textural or pigmentation changes at the third visit at both areas treated. One of these patients had greater hyperpigmentation at the cooled site. The patients who had epidermal changes were not limited to any particular skin type nor were they treated with particularly high fluences.

Discussion

Utilizing the theory of selective photothermolysis, the PDL has revolutionized the treatment of PWS by allowing lightening or clearance of these lesions without scarring.[1–3,10–12] The challenge that remains to improve this therapy is twofold: 1) decreasing the pain associated with individual laser pulses would allow many pediatric and some adult patients to tolerate larger areas to be treated without anesthesia at each session; and 2) treatment of darker-skinned patients has been limited by the



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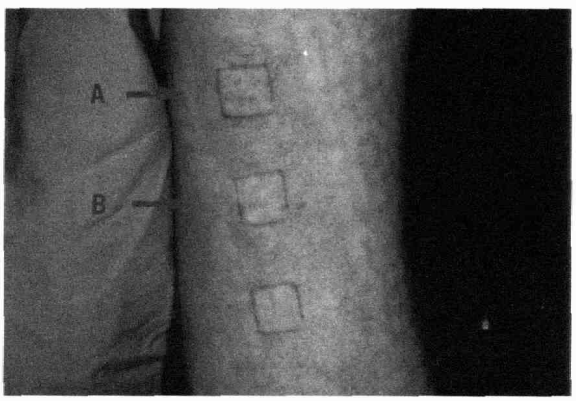

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Figure 8. PWS test sites a) pretreatment and b) at final evaluation, A) 1 month after second PDL test treatment with cooling at 8.25 J/cm², and B) without cooling at 7.5 J/cm². Clearance of the PWS and the absence of epidermal change are notable at both sites.

use of subtherapeutic fluences in an attempt to avoid the scarring and pigmentation changes that may result from epidermal melanin absorption of laser pulses. In this study, the DCD, a system for precooling the skin with a cryogen, was used in an attempt both to decrease pain and protect the epidermis.

The majority of patients treated noted a significant reduction in pain associated with use of the DCD during their two laser treatments. This benefit may be explained by the effect of the rapid drop in skin temperature provided by the cryogen spray. The anesthetic effect of cold temperatures is well recognized: physicians treating pediatric patients have traditionally used ice cubes to "numb" the site of an injection and cold packs are often used to relieve discomfort postoperatively. It is interesting that the improvement in pain with cooling, though still statistically significant, was less pronounced for the younger patients enrolled in this study. One possible explanation is the increased anticipatory fear that many of the younger patients routinely exhibit prior to PDL treatment. Also, some children are frightened by the "hissing" sound associated with the cryogen spurt.

It is recognized that patients with darker skin types generally experience more discomfort during PDL treatment than those with lighter skin types. This effect may be due to greater heating of the epidermal layer when the concentration of melanin is higher. Precooling of the epidermis should offset the greater temperature increase in darker skin and reduce pain during treatment. Indeed, in this study darker-skinned patients (skin types III and IV) had a particular improvement in pain ratings when cooling was used compared with the PDL alone.

Unlike other methods of precooling the skin, the dynamic cooling reduced pain without reducing treatment efficacy. PDL treatments with cooling produced equivalent lightening to the PDL alone. This confirms the anticipated results, because the epidermis is cooled by the cryogen but the dermal blood vessels remain unaffected. Ten to 20% higher fluences were used with the DCD in an attempt to achieve the same threshold vascular temperature as with the PDL alone. Clinically, the immediate purpuric response at these fluences was identical for the cooled and uncooled sites, which suggests that the dosages received were equivalent.

This study could not confirm epidermal protection with the DCD. Pigmentation changes and textural changes were uncommon and variable. They occurred with or without cooling and in any skin type. The inability of the DCD to completely protect the epidermis may reflect some limitations in the original prototype device used in this study. Because of the need to minimize modifications to the lasers at the investigational sites, the timing of the cryogen spurt relative to the laser pulse may have been off by as much as 10–15 millisec. Spurt-to-spurt variation in the amount of cryogen fluid sprayed on the skin was noted at both sites, perhaps due to bubbles created in the hose near the nozzle during repetitive pulsing. Because the liquid cryogen in the hose is at a higher temperature than in its receptacle, it may have converted into a gas phase between uses. This gas is not an effective coolant and must be purged from the system before treating with the DCD. Furthermore, the orientation of cryogen delivery onto the target laser spot may not have been optimal.

Dynamic cooling is a valuable adjunct to standard therapy of PWS with the PDL. Further study is needed to assess its role to optimize PDL therapy of PWS. It remains to be seen whether an improvement in the DCD timing and/or spurt-to-spurt reproducibility will enhance its ability to protect the epidermis. Regardless, the absence of epidermal damage in most patients suggests that precooling with the DCD may allow the use

of higher laser fluences to expedite clearance, without inducing epidermal change. This system has potential for use with other lasers and for different lesions where discomfort and epidermal effects limit therapy.

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