Description and Analysis of Treatments for Port-wine Stain Birthmarks

Kristen M. Kelly, MD; Bernard Choi, PhD; Samantha McFarlane, MD; Alison Motosue, MD; Byungjo Jung, PhD; Misbah H. Khan, MD; Julio C. Ramirez-San-Juan, PhD; J. Stuart Nelson, MD, PhD

Port-wine stain (PWS) birthmarks are congenital, low-flow vascular malformations of the skin. Lasers are the modality of choice for the treatment of PWS birthmarks, and for most patients the pulsed-dye laser in conjunction with epidermal cooling offers the greatest efficacy and safety. Other light devices, including the 532-nm frequency-doubled Nd:YAG laser, intense pulsed light, 1064-nm Nd:YAG laser, and combined 1064/532-nm system, may be useful during a treatment course for resistant PWS. Laser treatment results in blanching of most lesions, although complete resolution may not occur and some resistant PWS birthmarks respond minimally, if at all. Factors limiting laser treatment include variable vascular geometry, inadequate damage of some vessels, and lesional posttreatment recurrence as a result of neovascularization. Alternative or adjunct treatment options that address these limitations should be explored, including noninvasive real-time imaging to optimize the selection of treatment settings, photodynamic therapy, and perioperative use of antiangiogenic compounds.

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Port-wine stain (PWS) birthmarks are congenital, low-flow vascular malformations of the skin found in approximately 0.3% of children.[1] Port-wine stain birthmarks are commonly found on the face and neck and, as such, may have serious psychological consequences.[2-4] Port-wine stain birthmarks do not involute over time (unlike hemangiomas) and, in fact, may hypertrophy in adulthood, resulting in increased disfigurement. For these reasons, patients or their families often seek treatment.

Histopathological analysis of PWS reveals a normal epidermis overlying an abnormal plexus of dilated blood vessels located as a layer in the upper dermis. The depth of PWS varies from 100 to 1000 µm, and blood vessel diameter ranges from 10 to 300 µm.[5,6]

Author Affiliations: Beckman Laser Institute, Irvine (Drs Kelly, Choi, Jung, Khan, Ramirez-San-Juan, and Nelson), and Departments of Dermatology (Drs Kelly, McFarlane, and Nelson), Pediatrics (Dr Motosue), and Biomedical Engineering (Dr Nelson), University of California–Irvine; Department of Biomedical Engineering, Yonsei University, Seoul, South Korea (Dr Jung); and Department of Optics, Instituto Nacional de Astrofisica, Optica y Electronica, Puebla, Mexico (Dr Ramirez-San-Juan).

HISTORY OF PWS LASER TREATMENT

Treatment options for PWS have included cosmetic cover-up, skin grafting, radiation, dermabrasion, cryosurgery, tattooing, and electrotherapy, but none of these modalities provide cosmetically acceptable results.[7-9] The development of lasers and their ability to selectively target PWS blood vessels offered an improved treatment option.[7,10]

Argon Laser

The argon laser was one of the first lasers used to treat PWS. Blanching of PWS was achieved; however, hypertrophic scarring occurred in as many as 40% of young infants and children.[11,12] Several factors contributed to argon laser–associated adverse effects. First, significant melanin absorption occurs at the short blue-green wavelengths (488 and 514 nm) used for the argon laser. As light passes through the epidermis to targeted dermal PWS blood

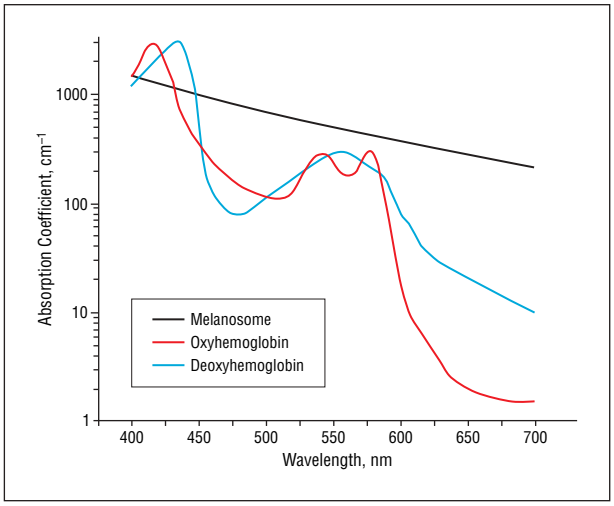

Figure 1. Absorption spectra for melanin (melanosome from Steven Jacques, PhD; available at: http://omlc.ogi.edu/spectra/melanin/index.html; accessed May 10, 2005), oxyhemoglobin, and deoxyhemoglobin (hemoglobin from Scott Prahl, PhD; available at: http://omlc.ogi.edu/spectra/hemoglobin/summary.html; accessed May 10, 2005). The ordinate is on the log scale.

Table 1. Estimated Penetration Depth of Light in Fitzpatrick Type II PWS Skin

Wavelength, nm	Penetration, mm
575	0.50
580	0.53
585	0.65
590	0.80
595	1.00
600	1.10

Abbreviation: PWS, port-wine stain.

vessels, it must pass through melanin in the epidermal basal layer. Absorption of light by melanin can result in excessive epidermal heating and subsequent injury, including scarring and dyspigmentation. Furthermore, early argon laser devices had relatively long pulse durations (0.5 seconds), which resulted in excessive perivascular heating and collagen damage.

Selective Photothermolysis

In 1983, Anderson and Parrish[13] presented the theory of selective photothermolysis, which explained how careful selection of laser treatment settings could result in specific destruction of subsurface targets and minimize adverse effects such as scarring and dyspigmentation. The laser wavelength should approximate an absorption peak of the targeted chromophore in relation to other optically absorbing molecules in the surrounding skin.[13] For PWS vessels, oxyhemoglobin and deoxyhemoglobin serve as the chromophore targets (**Figure 1**), and each has more than 1 absorption peak (418, 542, and 577 nm for oxyhemoglobin). Wavelength also affects depth of treatment, as generally longer wavelengths (≤1200 nm) result in deeper light penetration.[13] As such, for treatment of vascular lesions, lasers with wavelengths approximating but slightly longer than 577 nm (585-595 nm) are most often selected to achieve good light absorption by the target and desired depth of penetration (**Table 1**). Furthermore, as already mentioned, light must pass through the epidermal melanin barrier to reach the targeted vessels. As evidenced by early experience with the argon laser, melanin absorption of light can result in significant epidermal injury. Because melanin absorption decreases with increasing wavelength (Figure 1), the selection of longer wavelengths is deemed advantageous.

The pulse duration (also called the *pulse width*) of laser exposure should approximate the vessel thermal relaxation time, defined as the time required for the temperature rise induced by the absorbed light energy within the target to decrease to 50% of its value immediately after laser exposure.[13] The thermal relaxation time of a vessel is proportional to the square of its diameter. Pulses shorter than the thermal relaxation time of a vessel will not achieve adequate heating of the vessel wall, resulting in insufficient photocoagulation. Excessively long pulse durations result in heat diffusion from the target to the surrounding tissue. This phenomenon can result in adverse effects, including scarring and permanent dyspigmentation, as well as resulting in loss of light energy to the surrounding tissue, which again may cause insufficient photocoagulation of the target. Pulse durations of 1 to 13 milliseconds are thought to be optimal for PWS treatment.[14,15]

Laser energy must be sufficient to coagulate PWS blood vessels, and blood must be heated to approximately 70°C for irreversible vessel destruction.[13] Too much energy, even when delivered at the desired wavelength and pulse duration, may produce residual heat, injuring surrounding structures and potentially resulting in adverse effects.

The application of selective photothermolysis significantly improved treatment outcome; however, maximum allowable radiant exposures (laser energy density incident on the skin surface) were still limited (6-9 J/cm^2) because of epidermal melanin absorption.

Epidermal Cooling

To address epidermal melanin absorption, skin cooling methods were developed. Contact cooling was the first method explored in conjunction with laser therapy. In the early 1980s, Gilchrest et al[12] used ice cubes to chill PWS skin before argon laser treatment. Commonly used forms of contact cooling at present include plates of conductive material (eg, glass or sapphire) continuously cooled by a recirculating refrigerant.[16] Nelson et al[17,18] developed cryogen spray cooling (CSC) as an efficient and effective means of achieving selective epidermal protection. Cryogen (tetrafluoroethane [$C_2H_2F_4$]; boiling point=–26.2°C) spurts, 10 to 50 milliseconds in duration, are delivered to the skin surface immediately before laser exposure. A third method of cooling delivers a continuous flow of air, chilled from –4°C to –32°C, to the treatment site before, during, and after laser exposure.[19] By protecting the epidermis, cooling allows safer use of higher radiant exposures, permits treatment of patients with darker skin types, decreases treatment pain,

and enhances therapeutic outcome. As such, use of cooling is essential during the treatment of PWS birthmarks with most, if not all, currently available laser devices. Although all 3 of these methods offer effective epidermal cooling, CSC is the most spatially selective (ie, it cools the epidermis without affecting the temperature of the targeted blood vessels) and thus may be optimal for use during the treatment of PWS birthmarks.

CURRENT TREATMENT APPROACHES

Pulsed-Dye Laser

The pulsed-dye laser (PDL) in combination with epidermal cooling is the current treatment of choice for PWS birthmarks. Currently available devices use yellow light at a wavelength of 585 to 595 nm, pulse durations from 0.45 to 40 milliseconds (although durations of 0.45-3 milliseconds are most commonly used), and CSC or contact cooling.

Patients, especially those with darker skin types, can be prepared for treatment by using bleaching creams for several weeks before treatment in the PWS area. Faithful application can improve treatment outcome by minimizing the melanin barrier. Immediately before treatment, blood volume and thus the vascular target can be increased by putting the treatment area in a dependent position (Trendelenburg for facial lesions) and/or by applying heat packs to the area. In young children or in those with extensive lesions, we perform treatment with the patient under general anesthesia.

Treatment of infants and young children is initiated at 6 to 8 J/cm^2 (depending on Fitzpatrick skin type) and may be increased by 0.50 to 1.00 J/cm^2 with each treatment if no adverse effects are noted. Lower radiant exposures are used for the eyelid, neck, and upper lip because these areas are more prone to scarring. Pulse duration may be varied, but we most commonly use shorter pulse durations (0.45-3 milliseconds). Spot size is generally 7 or 10 mm. Larger spot sizes offer more uniform energy transmission and rapid treatment, and thus the largest spot size that will permit the desired radiant exposure should be chosen. The CSC settings are in the range of 30- to 50-millisecond spurt durations with a 30- to 50-millisecond delay between the end of the spurt and the onset of the laser pulse.

During treatment, the handpiece is moved across the PWS birthmark in a methodical fashion. The best results are achieved when pulses are overlapped by 10%, which will avoid the checkerboard pattern of treatment seen when spaces are left between pulses. Skip areas can be filled in at the end of the treatment. The clinician wants to observe purpura during PDL treatment because subpurpuric doses have been demonstrated to achieve less effect.[20] Whitening of the skin during treatment indicates that blistering is likely to result and is generally avoided because it increases the risk of scarring.

After treatment, patients experience local swelling, ecchymoses, and postoperative pain that is similar to a sunburn sensation. Ice packs and elevation of the treated area for the first day after treatment will diminish swelling and pain. Cooling soaks, mild analgesics such as acetaminophen, and the application of emollients (aloe vera gel or Aquaphor healing ointment [Beiersdorf Inc, Norwalk, Conn]) can also be used to minimize discomfort. A topical antibiotic ointment should be applied if any scabbing or crusting develops. Patients should be instructed in good sun-protective practices to minimize hyperpigmentation, and bleaching creams can be used once bruising has resolved (approximately 2 weeks after treatment, although it may be longer). Treatments are repeated at 8- to 12-week intervals, and multiple treatments (3 to ≥15) are typically required.

Several studies have demonstrated the safety and efficacy of PDL in combination with epidermal cooling for PWS treatment. Geronemus[21] reported more than 75% clearing after an average of 4 treatments in 63% of 16 infants treated with the PDL in combination with CSC using radiant exposures of 11 to 12 J/cm^2.

Our group examined a series of patients with a wide range of demographics, including ages of 2 months to 55 years (average age, 23 years), Fitzpatrick skin types I to IV, and treated/resistant and untreated PWS.[22] In 20% of subjects, 75% or greater blanching was found after an average of 3.3 treatments. Thirty percent of patients had blanching of 50% to 74%, and 20% had blanching of 25% to 49%. A subset of subjects (30%) demonstrated minimal response (<25% blanching) even after multiple treatments.

Evaluation of Current PDL Treatment

Recent laser device advances and optimization of epidermal cooling allow the use of higher radiant exposures (≤16 J/cm^2) compared with previous evaluations.[21,22] In the past, increased radiant exposures resulted in increased efficacy, and it was hypothesized that safe implementation of fluences of up to 16 J/cm^2 could augment treatment response. We recently evaluated whether the use of current treatment protocols with PDL radiant exposures (≤16 J/cm^2) and CSC would enhance PWS blanching.

Documentation of PWS was obtained by digital photography. A digital color camera (DiMAGE7; Minolta Co, Osaka, Japan) was used to acquire images.[23] A macro ring flash (model 1200; Minolta Co) controlled by a flash controller provided shadowless, uniform illumination. Glare was reduced from the skin surface by using a linear polarizer (model A45-669; Edmund Industrial Optics, Barrington, NJ) placed in front of the macro ring flash; a second cross-polarizer was placed in front of the camera lens. To ensure reproducible subject positioning, a custom device consisting of head and chin rests mounted on a rotary stage was used.

Efforts were made to optimize PDL treatment protocols, including the preoperative use of bleaching creams and implementation of measures to increase the vascular target such as placing the patient in the Trendelenburg position for treatment of facial lesions. The C-Beam, V-Beam, or ScleroPLUS laser (Candela, Wayland, Mass) was used to treat subjects with a 7- or a 10-mm spot size and radiant exposures ranging from 8 to 16 J/cm^2. Treatment was initiated at the lower radiant exposures and increased as tolerated through-

Table 2. Characteristics of PWS Study Subjects, Treatment Settings, and Blanching Response

Patient No./Sex/Age at First Treatment, y	PWS Birthmark Location	Previous Treatment	Fitzpatrick Skin Type	No. of Treatments	Radiant Exposure, J/cm²*	% Blanching
1/M/47	Face	No	III	4	8-16	<25
2/F/46	Face/neck	Yes	IV	3	12-15	<25
3/M/15	Face	Yes	IV	3	8	<25
4/M/55	Face/neck	Yes	IV	3	8	<25
5/F/23	Face	No	III	5	8	50-74
6/F/22	Face	Yes	II	15	8-15	<25
7/F/25	Face	No	IV	9	12-16	25-49
8/M/31	Face	No	III	4	9-15	<25
9/M/22	Face	Yes	I	5	8-15	<25
10/F/11	Face	Yes	III	8	8-15	50-74
11/F/42	Upper lip	No	II	4	8-14	≥75
12/M/30	Face	Yes	I	8	8-16	<25
13/M/32	Face	No	II	4	8-16	<25
14/F/23	Face/neck	No	III	3	8-15	≥75
15/F/17	Face	Yes	II	3	12-16	<25
16/F/27	Face	No	II	6	8-15	<25
17/M/49	Face	No	III	3	8-15	<25
18/F/40	Face	No	IV	8	6-15	25-49
19/M/41	Face	No	II	4	8-15	25-49
20/F/34	Face/neck	No	IV	6	8-12	≥75

Abbreviation: PWS, port-wine stain.
*Lower-level radiant exposures were used for the eyelid and neck.

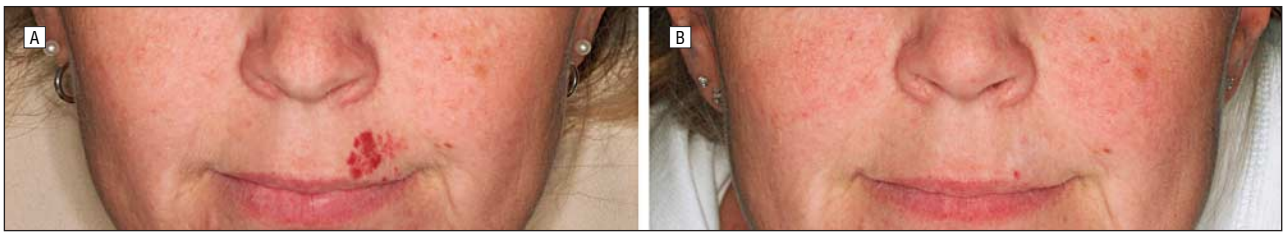

Figure 2. Photographs of a woman aged 42 years with a port-wine stain (PWS) birthmark of the upper lip before (A) and after (B) 4 treaments with the pulsed dye laser in combination with cryogen spray cooling. Blanching of the PWS was graded as 75% or greater by reviewers.

out the treatment course. Lower radiant exposures were used for the eyelid, neck, and upper lip. Cryogen spurt durations of 30 to 50 milliseconds were used with delays of 30 to 50 milliseconds between the coolant spray and the laser pulse. Laser treatments were repeated approximately every 8 to 12 weeks, according to patient availability.

Treatment and evaluation were continued during a 2-year study period or until the subjects no longer desired further treatment. At the completion of the study, pretreatment and posttreatment photographs were evaluated by 4 dermatologists, who were blinded to treatment settings and were not previously involved in the study. They graded PWS blanching in increments of 10% (ie, 10%, 20%, etc), and these scores were averaged and reported as blanching of greater than or equal to 75%, 50% to 74%, 25% to 49%, and less than 25%.

Twenty subjects were enrolled and treated (**Table 2**). Average subject age was 32 years, and the ratio of female-male subjects was 1.2:1. The number of treatments during the study period ranged from 3 to 15, with an average of 5.4 treatments.

Fifteen percent of subjects achieved blanching of 75% or greater after an average of 4.3 treatments (**Figure 2** and **Figure 3**). Ten percent of subjects achieved blanching of 50% to 74%, 15% achieved blanching of 25% to 49% (**Figure 4**), and 60% achieved less than 25% blanching. No subject experienced long-term adverse effects, specifically scarring or permanent dyspigmentation.

We did not find improved blanching results with the high radiant exposures achievable with current technology. In fact, a smaller percentage of our patients (15%) achieved greater than or equal to 75% blanching compared with some previously published work.[21] We do not believe that the use of higher radiant exposures diminished the response, but rather that our results offer a realistic assessment of achievable therapeutic efficacy with current technology for a broad range of patients.

Three aspects of our study population are important to note in regard to assessment of treatment efficacy. First, our patients were older than the populations of some previous studies and included no infants or young children. Many researchers, including us, believe that PWS birthmarks are more amenable to treatment at a younger age[24]; however, this opinion is somewhat controversial.[25] Second, in our study, we included many patients with darker skin types. As described already, the absorption of laser energy by epidermal melanin inhibits light delivery to the targeted PWS vessels and, thus, darker skin types are generally more difficult to treat. Third, and per-

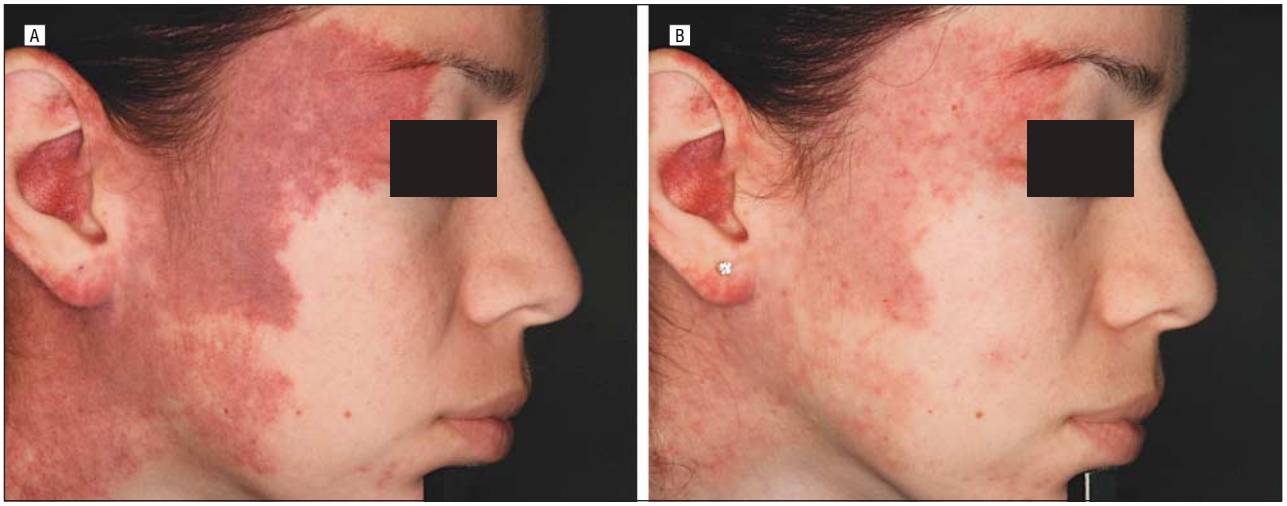

Figure 3. Photographs of a woman aged 23 years with a facial port-wine stain (PWS) birthmark before (A) and after (B) 3 pulsed-dye laser treatments in combination with cryogen spray cooling. Blanching of the PWS was graded as 75% or greater by reviewers.

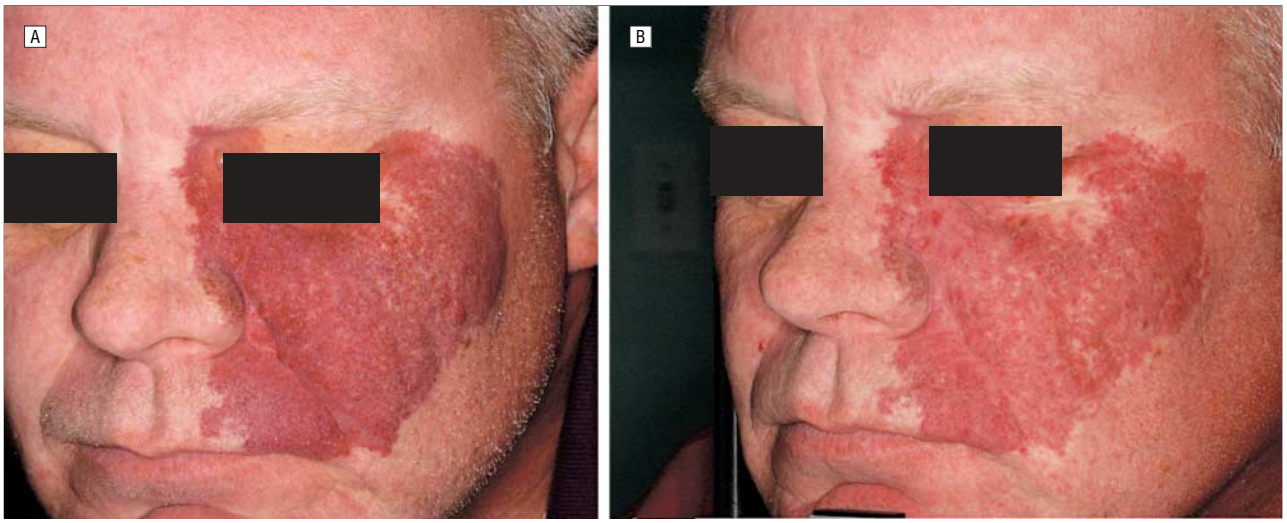

Figure 4. Photographs of a man aged 41 years with a facial port-wine stain (PWS) birthmark before (A) and after (B) 4 treatments with a pulsed-dye laser in combination with cryogen spray cooling. Blanching of the PWS was graded as 25% to 49% by reviewers.

haps most important, 40% of our subjects had resistant PWS birthmarks with a history of limited treatment responses.

Alternative Light Sources for PWS Treatment

In the present study, all subjects were treated with a PDL to standardize treatment for scientific purposes. However, we believe that in an ideal PWS treatment protocol, wavelength and pulse duration should be varied to target vessels of different size and depth throughout the lesion. Some of this variation can be achieved with different PDL devices. At our tertiary PWS referral center, we have 4 different PDLs, each with slightly different wavelengths (585-600 nm) and pulse durations (0.45-40 milliseconds). Additional devices may also be used, and their utility for treatment of resistant PWS is documented.

Chowdhury et al[26] recruited 30 subjects with PDL-resistant PWS birthmarks and treated them 1 to 4 times with a frequency-doubled Nd:YAG laser (532 nm). Sixteen (53%) showed a 25% blanching response and 5 (17%) demonstrated more than a 50% response. They reported the best blanching with radiant exposures from 18 to 24 J/cm^2 and pulse durations of 9 to 14 milliseconds. Scarring and hyperpigmentation were noted in 10% and 7% of subjects, respectively.

Bjerring et al[27] treated 15 patients with PDL-resistant PWS with a second-generation intense pulsed light source (Ellipse Flex; Danish Dermatologic Development A/S, Horsholm, Denmark). The emitted wavelength band was 555 to 950 nm, and a 10×48-mm spot size was used. Fluences were set according to individual purpura thresholds and ranged from 13 to 22 J/cm^2, and pulse durations ranging from 8 to 30 milliseconds were used. After 4 treatments, 47% achieved more than 50% blanching whereas 53% achieved less than 25% clearance. Slight hypopigmentation developed in 3 patients (20%), and 1 (7%) had temporary hyperpigmentation. Slight epidermal atrophy developed in 1 patient (7%), but no hypertrophic scarring was observed.

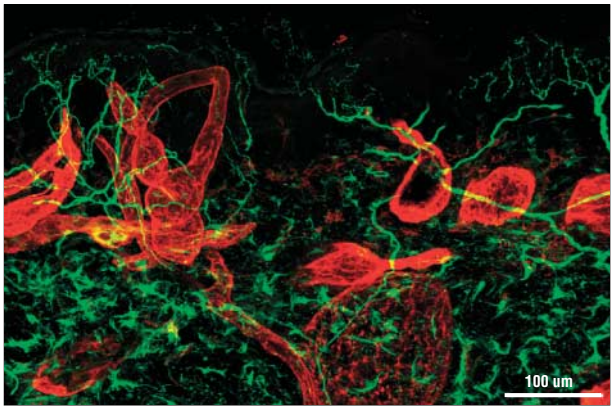

Figure 5. Confocal image from an untreated port-wine stain birthmark. Capillaries are stained with panendothelial marker, CD31 (red), and nerves are stained with panneuronal marker, protein gene product 9.5 (green). Variability is seen in the size and depth of the vessels (courtesy of Mona Selim, MD, William R. Kennedy, MD, and Brian D. Zelickson, MD).

Yang et al[28] treated PWS 3 times with a 1064-nm Nd:YAG laser using a 5- or a 7-mm spot size, radiant exposures of 40 to 130 J/cm^2, and pulse durations of 4 to 10 milliseconds. Performing treatments in conjunction with contact cooling and using nonoverlapping pulses, the authors achieved good blanching results without adverse effects when energies were kept at or below the minimum purpura dose (minimum radiant exposure causing purpura lasting beyond 15 minutes after laser exposure). Scarring was noted in 1 patient who was treated at energies above the minimum purpura dose. Six percent of their subjects had more than 75% clearing, 31% had 51% to 75% clearance, 25% had 26% to 50% clearance, and 38% had clearance of 25% or less. Histological analysis of biopsy specimens confirmed that deeper vessels could be treated with the Nd:YAG laser (≥2 mm) compared with the PDL (1 mm).

A pilot study performed by Ahcan et al[29] looked at the efficacy and safety of a combined Nd:YAG–potassium titanyl phosphate laser system that emits 1064- and 532-nm wavelengths simultaneously and uses CSC for epidermal protection. All 10 subjects achieved blanching (with a range of 26% to >75%) 8 weeks after a single therapeutic session. Atrophic scars were noted in 2 of the 10 patients.

LIMITATIONS OF PWS TREATMENT AND TOPICS FOR RESEARCH

Laser treatment is the current standard of care for PWS because it offers safe and selective vascular destruction that for nearly all patients results in at least some lesion lightening. However, despite technique and device advances and a range of devices in the laser surgeon's armamentarium, there are important limitations of currently available therapy.

Vessel size and depth vary among PWS birthmarks and even from site to site on the same patient (**Figure 5**). Because we currently do not have an established noninvasive method of accurately determining vessel size and depth, laser settings are selected by the clinician on the basis of limited target information. Research is under way to determine noninvasively the depth and size of PWS blood vessels on an individual patient basis and in real time, which should improve selection of laser settings and optimize lesion blanching with currently available devices.

Our group, along with other researchers, has developed optical instruments for noninvasive characterization of PWS skin, including photothermal imaging,[30-32] optical Doppler tomography,[33] and reflectance spectroscopy.[34,35] With these instruments, preoperative knowledge of skin characteristics such as epidermal thickness and melanin content; blood vessel depth, size, flow, and distribution; and skin optical properties can be achieved. van Gemert et al[36] provided a review of these instruments.

Additional optical instruments under development for PWS skin diagnostics and therapy evaluation include videomicroscopy,[37] modulated imaging,[38] cross-polarized diffuse reflectance imaging,[23] and laser speckle imaging.[39] Laser speckle imaging is of particular interest because it can serve as a relatively low-cost, wide-field, vascular imaging instrument to evaluate skin perfusion dynamics intraoperatively. It is analogous to laser Doppler imaging, with the advantage of substantially faster acquisition speeds (on the order of milliseconds). Laser speckle imaging has the potential to provide the clinician with real-time objective feedback regarding PWS responses to laser treatment (**Figure 6**), which may vary throughout a lesion. Areas of persistent flow may be re-treated in the same session, potentially improving the efficacy at each patient visit.

Significant absorption of yellow light by epidermal melanin limits maximum safe radiant exposure, especially in patients with darker skin types. As such, in these patients, additional treatment sessions are often required to achieve desired blanching. Epidermal cooling has diminished the magnitude of this problem, but the issue is not resolved and remains a significant limitation in Fitzpatrick skin types IV through VI.

High radiant exposures can be used safely in lighter-skinned patients; however, even with high energies, some vessels, especially the smallest (<50 μm), are not adequately damaged owing to a number of factors, such as a relatively deep dermal position limiting the achievable effective light dose, the presence of a cluster of vessels that compete for light and shield deeper vessels,[40] and the loss of heat from the vessels due to the choice of a pulse duration longer than the vessel thermal relaxation time.[13,41]

In the future, alternative treatment options may address some of these issues. Our group has demonstrated in animal models that photodynamic therapy (PDT) with benzoporphyrin derivative monoacid ring A and yellow light can be used to achieve selective vascular destruction.[42-44] Unlike PDL, which delivers short pulses at high irradiance, in PDT a laser or filtered noncoherent source provides low-power light at the desired wavelength to drive photochemical reactions that do not generate heat. Milliwatt light exposures used during PDT avoid epidermal thermal injury produced by high-peak-power PDL. Furthermore, because PDT uses continuous low irradiance for long exposures (several minutes), the dose effect accumulates as exposure time is increased. This property contrasts sharply with conventional photothermal

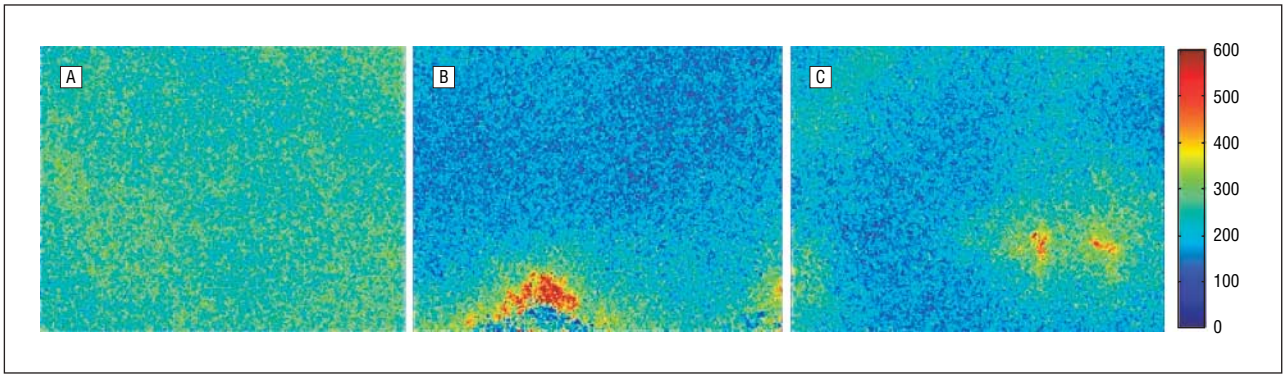

Figure 6. Laser speckle images of an upper extremity port-wine stain birthmark treated with a pulsed-dye laser. Images were acquired immediately before (A) and 10 minutes after (B and C) treatment. A marked reduction in perfusion is apparent after treatment at 2 sites; however, focal regions of perfusion are evident. The color key at right is in arbitrary units.

therapy, which must achieve a sufficient temperature jump with a single PDL exposure (approximately 1 millisecond). Multiple pulses do not increase the depth of treatment or improve PWS blanching response but subject the epidermis to a higher risk of thermal injury. Last, unlike PDL-induced photocoagulation, which spares microvessels (diameter, 10-50 µm),[45] PDT can destroy all vessels containing photosensitizer. This can offer a treatment advantage but also requires careful design of a PDT protocol, because complete destruction of the vascular network will result in necrosis, ulceration, and subsequent scarring. To maximize the benefits of the PDL and PDT approaches, we have designed a treatment protocol whereby we initiate treatment with subtherapeutic PDT exposure, using yellow light ($\lambda = 576$ nm) absorbed by benzoporphyrin derivative monoacid ring A, causing initial vascular damage, and presumably leaving PWS blood vessels more vulnerable to subsequent photothermal damage. The PDL irradiation is then used to selectively heat the pretreated vessels compromised by PDT. In 2 animal models this combined approach has demonstrated an enhanced effect compared with either PDT or PDL alone.[43,44] This protocol is experimental and requires clinical evaluation, which is under way.

Finally, we have demonstrated complete vascular destruction in some cases (**Figure 7**); however, significant lesion blanching was not observed. This may occur as a result of revascularization immediately after treatment or over time. Inflammation initiated by laser treatment may foster a wound-healing response, and/or residual vessels may serve as a source for vascular regrowth. It is possible that very high radiant exposures induce a greater inflammatory response and may adversely affect lesion blanching. The role of wound healing and angiogenesis should be evaluated and perhaps targeted for therapeutic intervention.[46]

CONCLUSIONS

Laser treatment is the current standard of care treatment for PWS because it offers safe and selective vascular destruction. Pulsed-dye laser treatment combined with epidermal cooling results in blanching of most lesions, although complete resolution may not occur and there are resistant lesions. Alternative or adjunct treatments should be explored, including noninvasive real-time imaging to optimize selection of treatment settings, PDT, and perioperative use of antiangiogenic factors.

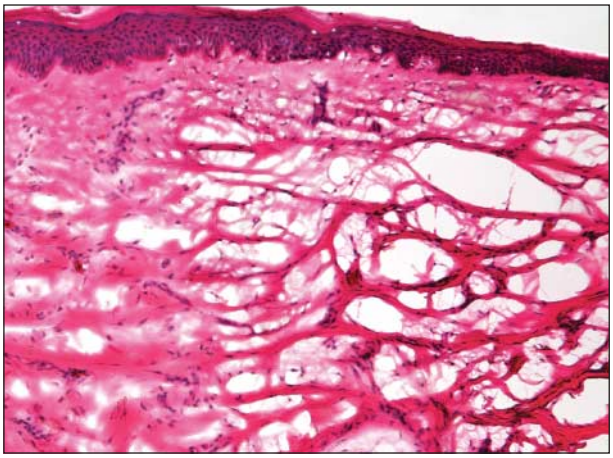

Figure 7. Hematoxylin-eosin–stained biopsy specimen taken from the edge of a treated port-wine stain (PWS) birthmark immediately after pulsed-dye laser exposure (original magnification ×200). Extensive thermal damage and enlarged spaces (destroyed vessels) in the treated area are seen on the right side of the image. Clinically, significant purpura was noted after treatment, but minimal PWS blanching was noted at follow-up.

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Correspondence: Kristen M. Kelly, MD, Beckman Laser Institute, 1002 Health Sciences Rd E, Irvine, CA 92612 (KMKelly@uci.edu).
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