Effects of Hypobaric Pressure on Human Skin: Feasibility Study for Port Wine Stain Laser Therapy (Part I)

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Background and Objectives: Since the development of laser-induced photothermolysis for the therapy of port wine stain (PWS) birthmarks, clinical results have shown that dark purple lesions usually respond well to the first three to five treatments. However, for most PWS, complete blanching is never achieved, and the lesion stabilizes at a red–pink color. The aim of this feasibility study is to demonstrate that with the aid of a local vacuum applied to the lesion site prior to laser exposure, photocoagulation of the smaller PWS blood vessels may be successfully achieved.
Study Design/Materials and Methods: Suction cups were designed to fit onto the hand pieces of commercial laser devices used for PWS laser therapy. One subject with normal skin and another with PWS skin were recruited for this study. Laser pulses of various fluences were applied at atmospheric pressure or shortly after (5–15 seconds) hypobaric pressures (17–51 kPa) were placed as test sites on the forearm of both subjects. The laser-induced purpura at the test sites was documented over the course of 1 week on both subjects and the resulting PWS blanching was optically quantified by visible reflectance spectrometry 7 months after therapy.
Results: For the subject with normal skin, the laser fluence needed with hypobaric pressure (51 kPa) to induce similar purpura intensity to that observed with atmospheric pressure was approximately 35% lower. For PWS skin, all suction application times (5–15 seconds) and hypobaric pressures (17–51 kPa) resulted in more intense purpura and the PWS blanching 7 months after treatment was clinically significant for test sites treated with hypobaric pressures ranging from 17 to 34 kPa.
Conclusions: The temporary and controlled dilation of the targeted blood vessels achieved with a local vacuum can significantly reduce the "small-vessel-limitation" in the treatment of PWS without increasing the risk of epidermal damage. Lasers Surg. Med. 36:124–129, 2005.
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Key words: laser surgery; selective photothermolysis; skin vacuum

INTRODUCTION

The clinical objective in laser therapy of selected hypervascular dermatoses, such as port wine stain (PWS) birthmarks is to maximize thermal damage to the targeted blood vessels, while preventing injury to the overlying epidermis [1]. However, despite the widespread use of this therapeutic modality, clinical studies have demonstrated that the treatment success rate for the vast majority of PWS patients is very low ($<10\%$), when the ultimate standard required is complete blanching of the lesion [2,3]. In particular, clinical results show that dark purple PWS usually respond well to the first three to five laser treatments, with progressive lesion blanching noted after each successive treatment. However, complete blanching is rarely achieved in most cases, and the PWS lesion color stabilizes at a red–pink color [2–5]. Furthermore, PWS that are initially a faint red–pink color, such as those seen in infants and young children, generally respond poorly to laser therapy [5].

A possible reason for poor clinical results or treatment failure of faint red–pink PWS may be the difficulty in destroying smaller (10–30 μm diameter vessels), because the blood volume therein is too small a fraction of the entire heated volume, which is composed of blood, vessel wall, and perivascular tissues [6]. As a result, the thermal confinement required to reach the threshold for permanent PWS vessel photocoagulation is insufficient. Multiple treatments using the highest possible laser fluences will not achieve and sustain the critical temperature necessary to destroy these small PWS blood vessels irreversibly, regardless of the number of treatments performed. This hypothesis seems plausible since faint, red–pink stains are likely due to a lower blood volume fraction (BVF) associated with smaller capillaries [4] although larger but deeper capillaries may lead to a similar appearance. However, the following specifics lead us to believe smaller capillaries are the predominant ones in faint, red–pink PWS: (a) normal skin physiology encompasses smaller capillaries closer to the skin surface [7] and even PWS skin maintains this relationship [8]; (b) PWS blood vessels of children after biopsy and histological evaluation are smaller, on average, than those of adults [8,9]; and (c) initial treatments are usually successful in removing the most superficial PWS blood vessels [5], especially those within the size range that

is optimal for required thermal confinement (30–50 μm in diameter) [6]. Therefore, the faint appearance that red–pink PWS present after several treatments is likely due to the remaining vessels that were either "shielded" initially [10] by more superficial vessels, or those that have always been out of the optimal size range [11].

On the basis of this hypothesis, it is expected that improved clinical outcome for PWS patients receiving laser therapy might be achieved by inducing an intentional, controlled, and temporary alteration in skin physiology, whereby smaller blood vessels are dilated and thus the BVF is increased immediately before laser exposure. A recent study [11] demonstrated that it was possible to increase the dermal BVF in normal skin on the distal upper extremity by obstructing venous return in the proximal arm with a pressure cuff (13.3 kPa = 100 mm Hg). Under such conditions, 40% less radiant exposure was required to induce the same amount of purpura after a single laser pulse as compared to that observed without the pressure cuff.

Due to obvious shortcomings of the aforementioned procedure, including patient discomfort that venous blood flow obstruction causes and, most importantly, the impracticality of using this procedure for therapy of head/neck and trunk PWS lesions, we have developed a new method where the intended vessel dilation can still be attained locally, faster, and more reliably using a small suction device to create a local vacuum on the skin surface. This physiological skin alteration may achieve sufficient thermal confinement in the smaller (10–30 μm) by temporarily dilating the smaller PWS blood vessels. In this feasibility study (Part I), we present the first clinical results that demonstrate proof of principle of using a local vacuum on the skin surface to improve laser-induced PWS blanching. The implications for cryogen spray cooling (CSC) are discussed in Part II.

EXPERIMENTAL METHODS AND PROCEDURES

Technical Systems

Short round Plexiglas® tubes, 25.4 mm (1 in) inner diameter were used to build two skin suction cups that fit tightly around the laser coupling and handpieces of laser medical devices that produce 0.45 millisecond laser pulses at a 585 nm wavelength (Fig. 1a). The tight seal is ensured by a rubber band that holds the suction cup to the laser coupling. The suction cups are designed to be pressed gently against the skin and create a tight seal when a vacuum hand pump (9963K21, McMaster-Carr, Los Angeles, CA) is operated to remove the air within the cups. With moderate hypobaric pressures (17–51 kPa) significant bulging of the skin and temporary increase in the BVF can be obtained (Fig. 1b). A built-in manometer indicates the hypobaric pressure reached during operation and a small valve releases the cup from the skin after laser exposure.

Patient Study Protocol

After signing informed consent, two subjects with Fitzpatrick skin type II were enrolled in the study. One subject had normal skin and one subject had an untreated dark purple–red color PWS covering the left upper extremity and anterior/posterior trunk.

A rectangular frame of 178×51 mm (7×2 in) was drawn on the right forearm of the subject with normal skin. The frame was subdivided into 25×25 mm (1 in^2) subsections as shown in Figure 2. The top row was designated for procedures without vacuum (N), while the bottom row was for identical laser fluences using 34 kPa (10 in Hg) hypobaric pressure (V), applied for 10 seconds prior to laser exposure. The following laser fluences were selected: 3.00, 3.25, 3.50, 3.75, 4.00, 4.50, and 5.00 J/cm^2 and were applied along each of the seven frame columns. Each test site received a single laser exposure. All laser spots were 10 mm diameter and delivered without CSC.

For the PWS patient, a 76.2×76.2 mm ($3'' \times 3''$) grid was drawn on the posterior left upper arm (Fig. 3). Three different hypobaric pressures were applied across each row: 17, 34, and 51 kPa (5, 10, and 15 in Hg, respectively) and maintained for three different time periods (5, 10, and 15 seconds, respectively), as indicated on top of each column. For comparison, three laser spots under atmospheric pressure were placed in a fourth column to the right of the grid. Although hypobaric pressures in kilopascal (kPa) are an appropriate scale, we will refer hereafter to these pressures in inches of mercury (in Hg) to simplify
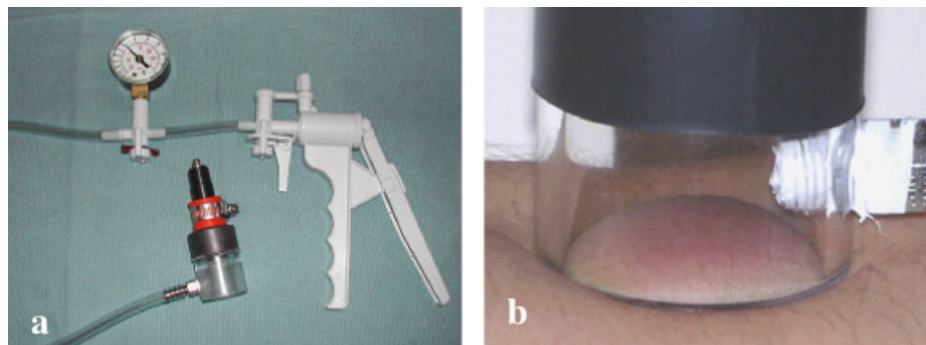

Fig. 1. (**a**) Suction cup and vacuum pump for commercial medical laser. (**b**) Skin bulging and increase in BVF upon application of local vacuum. [Figure can be viewed in color online via www.interscience.wiley.com.]
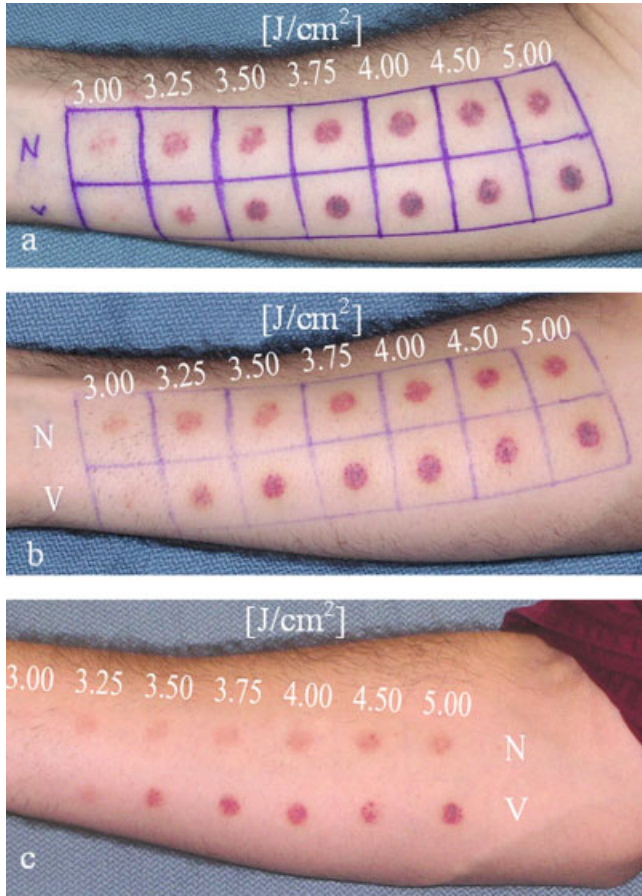
Fig. 2. Images of purpura induced on normal skin (**a**) 6 hours, (**b**) 3 and (**c**) 8 days after laser irradiation. **Top row** (N): normal or atmospheric pressure; **bottom row** (V): vacuum or hypobaric pressure (34 kPa = 10 in Hg) applied for 10 seconds prior to laser irradiation. [Figure can be viewed in color online via www.interscience.wiley.com.]

using round numbers equivalent to application times (i.e., 5, 10, and 15 seconds). Each test site received a single laser pulse with a fluence of 6 J/cm^2 delivered on a 10 mm spot diameter without CSC.

Imaging System and Visible Reflectance Spectroscopy (VRS)

A standard digital camera (Nikon Coolpix3100, with a 38–115 mm optical zoom lens and 3.2 Megapixels) was used to photograph the laser-induced purpura on both subjects, up to 8 days after laser exposure.

Additionally, a spectrophotometer (SD2000, Ocean Optics, Dunedin FL) coupled with a 10 mm-aperture integrating sphere (ISP-REF, Ocean Optics) was used to quantify the visible reflectance spectra (VRS) on the test sites of the PWS subject 7 months after laser exposure.

These measurements were made on normal skin of the PWS patient, untreated PWS and all test sites. Reflectance spectra measured over the 450–800 nm wavelength range were used as a means to compare the effect of hypobaric pressures on the overall blanching of the treated
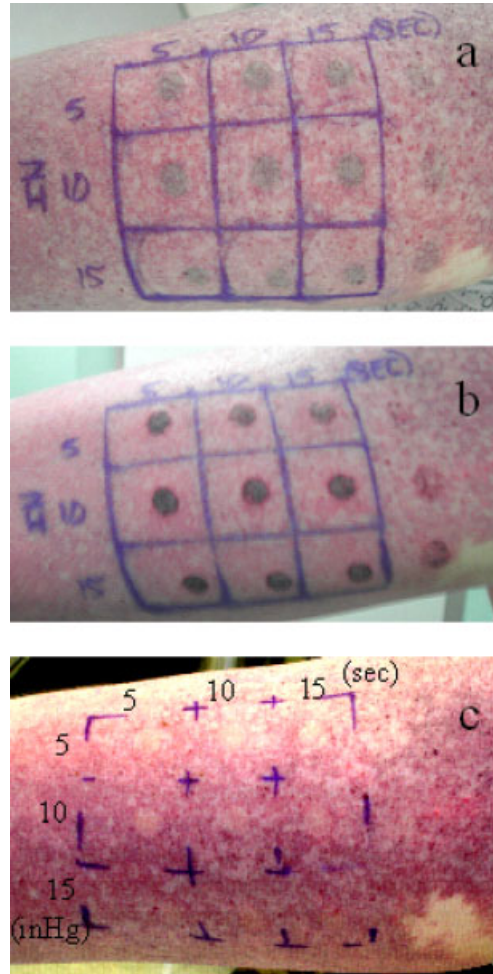
Fig. 3. Laser-induced purpura (**a**) acutely (**b**) 1 day, and (**c**) 7 months after laser irradiation on PWS skin. Rows show the hypobaric pressures applied prior to laser irradiation in [in Hg] and columns the time it was applied in [seconds]. The column right of the grid shows the induced purpura without vacuum for the same fluence. Note the obvious clearing on the upper two rows after a single laser pulse. [Figure can be viewed in color online via www.interscience.wiley.com.]

PWS spots. The percentage of blanching was computed as follows:

$$\% \, \text{Blanching} = \frac{(\text{VRS}_{\text{PWS,treated}} - \text{VRS}_{\text{PWS,untreated}})}{(\text{VRS}_{\text{normal}} - \text{VRS}_{\text{PWS,untreated}})} \times 100,$$

(1)

where $\text{VRS}_{\text{PWS, treated}}$, $\text{VRS}_{\text{PWS, untreated}}$, and $\text{VRS}_{\text{normal}}$ are the reflectance spectra of the treated PWS spots, untreated PWS region and normal skin of the PWS patient, respectively.

RESULTS AND DISCUSSION

Figures 2a–c show photographs of laser-induced purpura on the normal skin subject taken 6 hours, 3 and 8 days after laser exposure without and with local vacuum. There

appears to be an insignificant difference between atmospheric and hypobaric (vacuum) pressure for fluences ≤ 3.25 J/cm^2. In fact, the lowest fluence used (3 J/cm^2) was barely sufficient to induce mild purpura without and with local vacuum. The difference in the purpura intensity becomes noticeable for fluences >3.25 J/cm^2 at all times, although more noticeable by days 3 and 8. In fact, note that by day 8, the laser test sites without vacuum have almost vanished, while all but the two lowest fluence test sites under local vacuum still show intense purpura. Assuming the difference in purpura intensity always took about 3–8 days to become noticeable for PWS skin as it does for normal skin, this would be a drawback for the determination of the threshold fluence needed for PWS laser therapy. However, this procedure could be omitted during the clinical management of PWS patients once systematic studies are carried out to determine what is the average reduction of laser fluence that leads to the same purpura intensity and ultimately to lesion blanching. It is notable to observe (Fig. 2b) that the test site with fluence of 3.25 J/cm^2 under local vacuum results in purpura similar to that induced by the highest fluence (5 J/cm^2) at atmospheric pressure. This suggests that the threshold for purpura is reduced under hypobaric pressure by approximately 35%.

Figures 3a–c show photographs of the PWS subject taken acutely, 1 day and 7 months, respectively, after laser exposure. Figures 3a–b show much more intense purpura on all test sites performed under vacuum as compared to those where no vacuum was applied. Most importantly, 7 months after laser exposure (Fig. 3c), the blanching at the test sites irradiated with 5 and 10 in Hg for all times (top two rows) is quite remarkable, especially considering that only a single laser pulse was delivered to the PWS test site. Interestingly, the row with the highest hypobaric pressure (lowest absolute pressure), 15 in Hg, shows the least PWS blanching.

Figure 4 shows VRS measurements obtained from (a) normal skin on the PWS subject, (b) untreated PWS skin, (c) the average of the blanched spots corresponding to the following time/pressure combinations: 5/5, 10/5, 15/5, 5/10, 10/10 and 15/10 seconds/in Hg, that is, spots in the top two rows of the 3×3 grid (Fig. 3), and (d) the average of the blanched spots corresponding to the remaining time/pressure combinations: 5/15, 10/15 and 15/15 seconds/in Hg, that is, spots in the bottom row of the 3×3 grid (Fig. 3). It is seen from the region of high hemoglobin absorption (530–600 nm) that more PWS blanching was obtained using all the studied combinations of time with hypobaric pressures of 5 and 10 in Hg, while for all times and 15 in Hg less blanching was achieved. Although the reason for this disparity is unknown, it may be explained by the following three reasons:

(1) Excessive dilation of vessels within the papillary dermis may shield the smaller, deeper vessels;
(2) Excessive hypobaric pressure may enlarge vessels beyond the optimum size and, thus, make them less susceptible for damage. According to a light diffusion approximation model [6], current PWS laser surgery
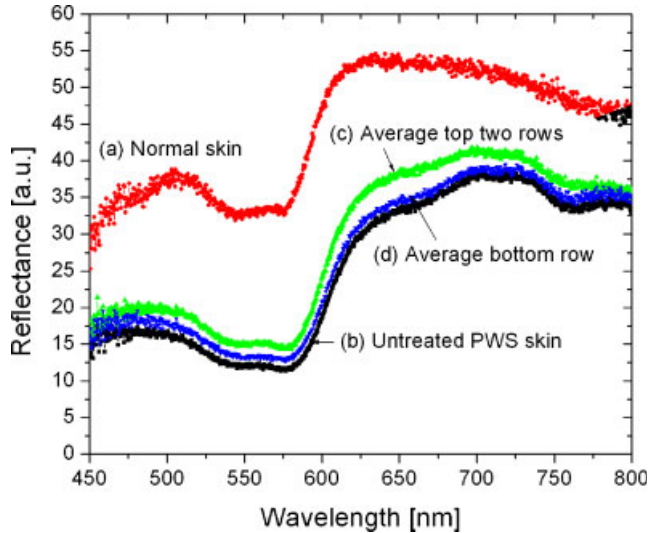

Fig. 4. Visible reflectance spectra for (**a**) normal skin on the PWS subject, (**b**) untreated PWS and average of laser spots 7 months after laser irradiation for: (**c**) 5/5, 10/5, 15/5, 5/10, 10/10, and 15/10 (seconds/in Hg)—**top two rows** and (**d**) 5/15, 10/15, and 15/15 (seconds/in Hg)—**bottom row**. [Figure can be viewed in color online via www.interscience.wiley.com.]

performed at normal atmospheric pressure effectively photocoagulates PWS vessels sizes ranging from 30 to 50 μm in diameter but up to 40% higher fluences are needed to target smaller vessels. Figure 5 illustrates the theoretical computations of the light diffusion approximation which show how the threshold fluence for damage (F_T—in this case defined as the fluence
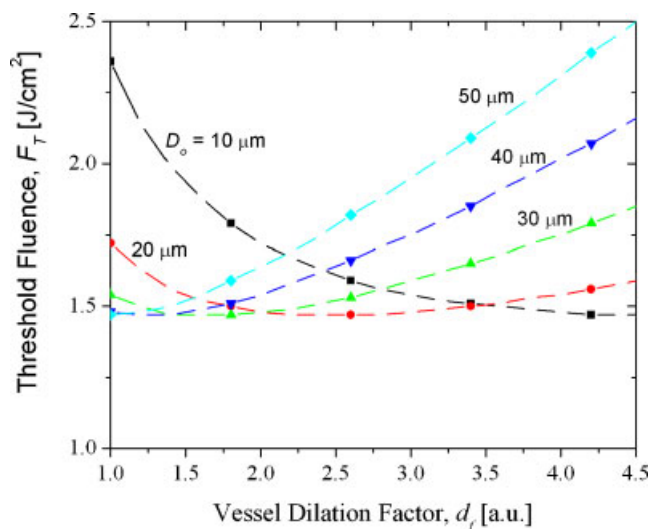

Fig. 5. Threshold fluence (F_T) required to elevate the vessels' average temperature to 70°C as a function of vessel dilation factor (d_f). Note that as smaller vessels are dilated, lower fluences are required to reach F_T, while as larger vessels dilate, higher fluences are required. [Figure can be viewed in color online via www.interscience.wiley.com.]

needed to elevate the vessel's average temperature to $70°C$) is normally about 1.5 J/cm^2 for vessel of normal diameters (D_o) larger than 30 μm, while it is up to 2.4 J/cm^2 for vessels of $D_o = 10$ μm in diameter (see vessel dilation factor, $d_f = 1$). However, as the smaller vessels are dilated, much lower fluences are required to reach F_T. Note too, that F_T for vessels larger than $D_o = 30$ μm increases with d_f. It follows that external hypobaric pressure may optimize the size of a certain range of blood vessel diameters ($D_o = <30$ μm), while it would deteriorate the other ($D_o = >30$ μm), and;

(3) Excessive hypobaric pressure may also induce erythrocyte leakage through the capillary walls before laser irradiation, reducing the heat generated and subsequent blood temperature increase necessary to destroy the capillary walls. This would still lead to the intense purpura observed acutely and 1 day after therapy, but lesser or no blanching would take place after several weeks.

Figure 6 shows the percentage blanching computed using Eq. 1 for curves (c) and (d) throughout the whole spectrum. For curve (c), the increase in the reflectance spectra at the isosbestic point (586 nm) in the blood absorption spectrum (vertical dotted line) is of 14% relative to the difference between the normal and untreated PWS sites. Considering that only a single laser pulse was necessary to achieve this level of blanching, the result is very promising. Conversely, for curve (d), blanching is only 6%.

While the suction cups used in the preliminary studies described herein were adequate to study the feasibility of using hypobaric pressure during PWS laser therapy, more professionally engineered devices are under construction whereby hypobaric pressure, application and suction release will be electronically controlled.

These studies suggest that an intentional, controlled, and temporary dilation of the smaller PWS vessels induced

by application of a low local vacuum to the skin immediately before laser exposure is a feasible procedure to increase locally the BVF and, therefore, provide sufficient thermal confinement for successful laser therapy of faint red–pink color or poorly-responding PWS.

CONCLUSION

The use of low hypobaric pressures (17–51 kPa or 5–15 in Hg) prior to laser exposure during PWS laser therapy results in more intense purpura at the same fluence. It was estimated that approximately 35% less fluence is required to induce the same degree of purpura 3 days after laser exposure on a normal subject with Fitzpatrick skin type II. Excellent average blanching of about 14% was quantified by VRS on a PWS subject 7 months after laser exposure to single laser pulses entailing 5–15 seconds of 5–10 in Hg of local vacuum (17–34 kPa hypobaric pressure).

The implementation of this procedure is straight-forward and should be pursued for PWS that are initially a red–pink color and for poorly-responding PWS, which are believed to be composed primarily of small capillaries (10–30 μm in diameter) that must be dilated for proper thermal confinement during laser exposure. Further studies are underway to optimize the relevant parameters, such as application time, magnitude of hypobaric pressure required and proper timing of laser exposure.

Fig. 6. Percentage blanching for curves (**c**) and (**d**) shown in Figure 4.

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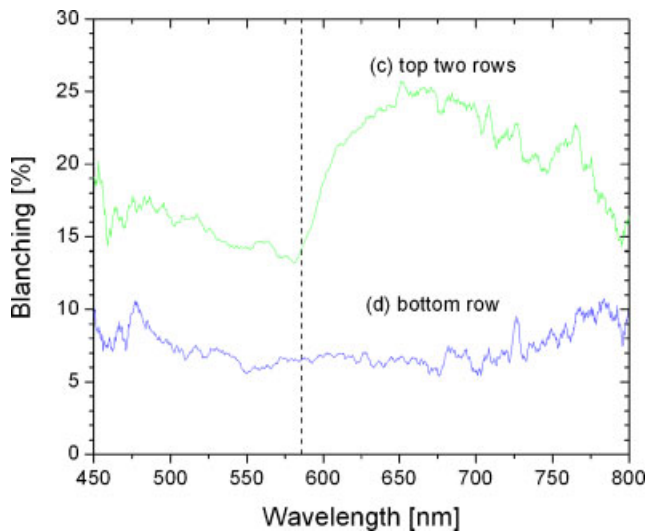
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