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CLINICAL REPORT

Analysis of port-wine birthmark vascular characteristics by location: Utility of optical coherence tomography mapping

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Abstract

Introduction: Port-wine birthmarks (PWBs) are congenital capillary malformations that can be located on any area of the body. Vascular features include vessel size, depth, and density, which can greatly differ between patients, individual lesions, and even sites within the same lesion. Previous studies have determined that the location of PWB lesions has impacted their clinical response to laser treatment.

Objective: We utilized dynamic optical coherence tomography (D-OCT) to measure in vivo vessel diameter, density, and superficial plexus depth in patients of all ages with PWB on various sites of the body. We hypothesized that these vascular characteristics would differ according to body location.

Materials and Methods: Patients who had a PWB and presented to clinic at three sites for treatment with the pulsed dye laser (PDL) were enrolled into the study. A D-OCT scanner was utilized for noninvasive, in vivo imaging of PWB lesions. The depth of the top portion of the superficial vascular plexus was estimated as the depth at which the vessel density reaches 50% of the maximum. Vessel diameter and density were calculated by incorporated software algorithm.

Results: A total of 108 patients were enrolled into the study. There was a total of 204 measurements of PWB lesions. Of all patients, 56.5% ($n = 61$) reported having a previous treatment with PDL. Of all D-OCT scans, 62.3% ($n = 127$) were located on the head, 14.2% ($n = 29$) the upper extremities, 8.3% ($n = 17$) the lower extremities, 7.8% ($n = 16$) the trunk, and 7.8% ($n = 15$) the neck. All locations were compared for each vascular characteristic. For superficial plexus depth, lesions on the head were significantly shallower than those on the upper extremities (217 vs. 284 μm; $p < 0.001$) and lower extremities (217 vs. 309 μm; $p < 0.001$). For vessel diameter, lesions on the head had significantly larger vessels than those on the upper extremities (100 vs. 72 μm; $p = 0.001$). For vessel density, lesions on the head had significantly denser vessels than those on the trunk (19% vs. 9.6%; $p = 0.039$) and upper extremities (19% vs. 9.3%; $p < 0.001$)

Conclusions: PWB lesions have distinct vascular characteristics, which can be associated with their body location. This includes superficial vascular plexus depth as well as vessel diameter and density.

KEYWORDS

cutaneous optical imaging, optical coherence tomography, port-wine birthmark, port-wine stain, vascular skin lesion

INTRODUCTION

Port-wine birthmarks (PWBs) are congenital capillary malformations that can be located on any area of the body.[1] They can vary in size, shape, color, depth, nodularity, duration, and vascular characteristics.[2,3] Vascular features include vessel size, depth, and density, which can greatly differ between patients, individual lesions, and even sites within the same lesion. This likely contributes to the clinical variability in treatment outcomes.[4,5]

Selective photothermolysis posits that laser treatment of PWB should be guided by the characteristics of the targeted vessels, including diameter and density of vessels as well as depth of the superficial vascular plexus.[6] Since PWB lesions can be easily classified by their location upon clinical inspection, knowledge about their vessel characteristics as determined by body location can be useful for optimizing laser treatments and maximizing clinical outcomes.

Previous studies have determined that the location of PWB lesions has impacted their clinical response to laser treatment.[7–14] Biopsies of PWB lesions at various sites, such as the face, neck, trunk, and extremities, have also revealed differences in the diameter and depth of vessels.[9] Even PWB lesions in different locations on the face have demonstrated variable vascular characteristics.[13]

Optical imaging has been used to study the vascular characteristics of PWB lesions in a limited number of patients.[12,15–17] Since 1997, optical coherence tomography (OCT) has been adapted for use in dermatology. OCT is a noninvasive imaging technology that has been used to examine several skin lesions and disorders, including cutaneous carcinomas, actinic keratoses, psoriasis, dermatitis, and various vascular lesions.[18,19] Dynamic OCT (D-OCT), which is based on speckle variance analysis,[20] can additionally assess certain vascular characteristics of skin lesions, such as the diameter, density, and depth of superficial blood vessels.

In this cross-sectional observational study, we utilized D-OCT to measure in vivo vessel diameter and density as well as superficial plexus depth in patients of all ages with PWB on various sites of the body. We hypothesized that these vascular characteristics would differ according to body location. The location of lesions on the body can be easily determined in clinical practice, and the corresponding information about its vascular characteristics may help to inform treatment parameters for laser procedures.

MATERIALS AND METHODS

Patients who had a PWB and presented to clinic for treatment with the pulsed dye laser (PDL) were enrolled into the study. Three sites participated in recruiting patients, which included Laser & Skin Surgery Center of New York, New York, NY; Department of Dermatology at the University of California-Irvine, Irvine, CA; and Miami Dermatology and Laser Institute, Miami, FL. This study was approved by an independent IRB for each location. Informed consent was obtained.

Patient demographics were gathered, including age, sex, and Fitzpatrick skin type. Previous treatment of the PWB was determined. Some patients had multiple PWB lesions. Various areas of patients' birthmarks were scanned with OCT. Larger lesions, especially those with different clinical morphologies within, had multiple portions examined to capture a more accurate picture of the lesion's characteristics. Digital photographs and OCT images were taken of PWB lesions.

An OCT scanner (VivoSight; Michelson Diagnostics) was utilized for noninvasive, in vivo imaging of PWB lesions. This OCT scanner uses a low-power 1300 nm laser with multi-beam swept-source frequency domain processing. The imaging device provides <7.5 μm resolution within a 6x6mm field of view. The penetration of the OCT scanner can reach up to 1–2 mm of depth. However, the sensitivity and granularity of OCT does begin to decrease at depths greater than 500 μm. The OCT images were captured with multi-slice scans consisting of up to 500 frames per scan, since it provided sufficient granularity and suitable images for data acquisition.

The depth of the top portion of the superficial vascular plexus was estimated as the depth at which the vessel density reaches 50% of the maximum. This device finds the density of D-OCT as a fraction of the total scanned area at 50 μm depth intervals to a depth of 1000 μm. It finds the maximum density and calculates 50% of this. It then finds the depth that corresponds to that density value and outputs it. Vessel diameter and density were calculated as the averages of the top 100 μm of the vascular plexus by incorporated software algorithm. A surface fitter program was used to measure the distance from the skin surface to the particular depth of interest.

Patient demographics and PWB characteristics were analyzed by descriptive statistics. Not all outcomes were normally distributed in each group using the Shapiro–Wilk test, and the homogeneity of variance assumption did not hold in all comparisons using Levene's test. Therefore, non-parametric Kruskal–Wallis rank-sum test was used to compare the distributions of each outcome between groups. All analyses were conducted using R v4.0.3 (R Core Team).

RESULTS

A total of 108 patients who had a PWB and presented to clinic for PDL treatment were enrolled into the study. There was a total of 204 measurements of PWB lesions. Mean patient age was 32.3 years (*R*: 0–74 years), and

63.0% of patients ($n = 68$) were female. Fitzpatrick skin types I–IV were represented. Of all patients, 56.5% ($n = 61$) reported having a previous treatment with the PDL.

Of all OCT scans, 62.3% ($n = 127$) were located on the head, 14.2% ($n = 29$) the upper extremities, 8.3% ($n = 17$) the lower extremities, 7.8% ($n = 16$) the trunk, and 7.8% ($n = 15$) the neck. For vascular plexus characteristics, each of these locations were associated with various vessel depths, densities, and diameters (Table 1).

All locations were compared for each vascular characteristic. For superficial vascular plexus depth, lesions on the head were significantly shallower than those on the upper extremities (217 vs. 284 μm; $p < 0.001$) and lower extremities (217 vs. 309 μm; $p < 0.001$). For vessel diameter, lesions on the head had significantly larger vessels than those on the upper extremities (100 vs. 72 μm; $p = 0.001$). For vessel density, lesions on the head had significantly denser vessels than those on the trunk (19% vs. 9.6%; $p = 0.039$) and upper extremities (19% vs. 9.3%; $p < 0.001$) (Figure 1).

Representative clinical photographs with their associated en-face (at 250 μm) and cross-sectional OCT images are demonstrated in Figure 2. Figure 2D demonstrates relatively larger vessels on the head, Figure 2E demonstrates a relatively low density of vessels on the upper extremity, and Figure 2F demonstrates a relatively high density of vessels on the lower extremity.

In sub-group analysis of the extremities, PWB lesions in the proximal and distal locations were compared (Figure 3). There were no differences in vessel diameter (85.5 vs. 80.5 μm; $p = 0.982$) and density (9% vs. 15%; $p = 0.603$) of the proximal and distal lesions. However, depth of the superficial vascular plexus trended deeper for the distal lesions compared to those that were proximal (320 vs. 286 μm; $p = 0.068$).

DISCUSSION

This is the first study to use in-vivo D-OCT to characterize the vessels of PWB in over 100 patients and classify them by location on the body. A previous study looking at biopsies of PWB lesions from 22 patients concluded that vessel diameter and depth can be predicted—to some extent—by the location and color of the lesion.[9] In general, lesions on the neck had the largest vessels (47 μm) followed by those on the face, proximal

TABLE 1 Superficial vascular plexus characteristics of PWB lesions sorted by location

Location	# Scans (# Patients)	Depth (μm)	Diameter (μm)	Density (%)
Head	127 (71)	217 (174, 255)	100 (77, 136.5)	19 (10.5, 29)
Neck	15 (12)	233 (197.5, 298.5)	83 (62, 103)	11 (6.1, 23)
Trunk	16 (14)	235.5 (203.75, 341.75)	102.5 (75.75, 118)	9.6 (6.38, 18.3)‡
Upper extremities	29 (15)	284 (232, 359)*	72 (58, 105)†	9.3 (3.9, 20)‡
Lower extremities	17 (12)	309 (287, 326)*	118 (47, 174)	14 (4.9, 32)

Note: Values for depth, diameter, and density are median (IQR). *, †, and ‡ denote significant relationships ($p < 0.05$) compared to location on the head within each measure.

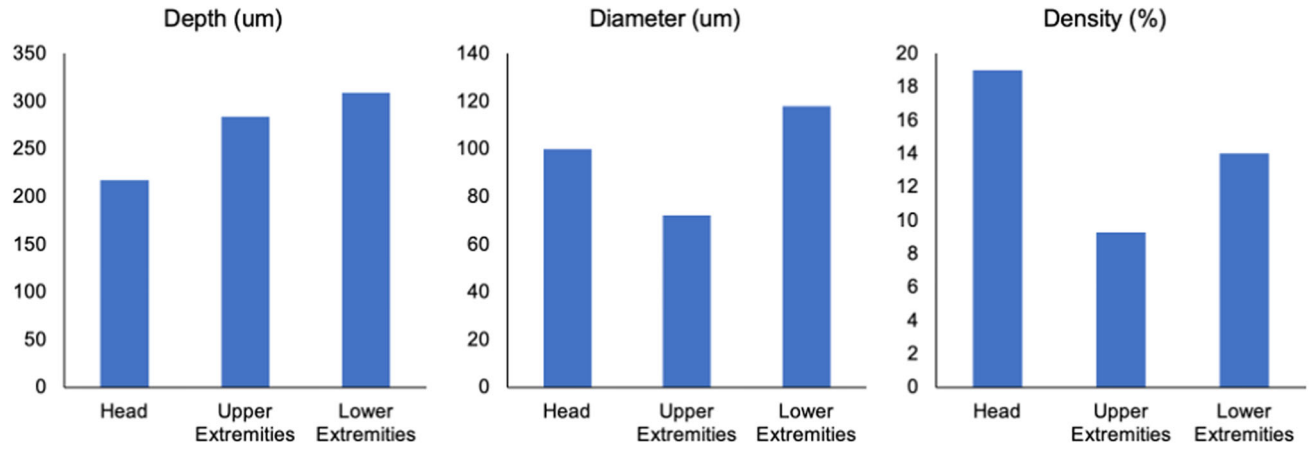

FIGURE 1 Superficial vascular plexus characteristics of PWB lesions by location, including depth, diameter, and density. Values are median. PWB, port-wine birthmarks

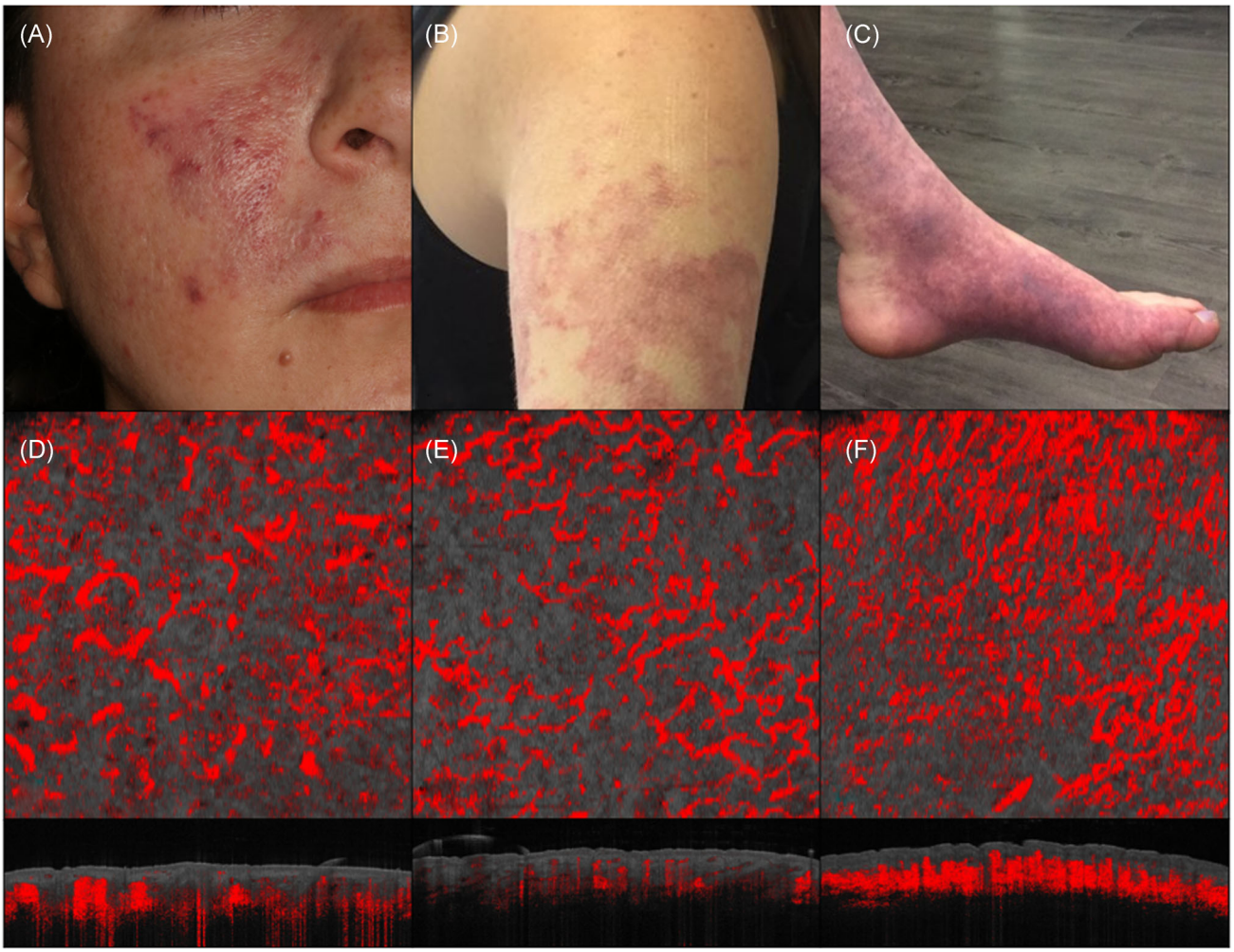

FIGURE 2 Representative clinical photographs of PWB lesions with their associated en-face and cross-sectional OCT images on the (A, D) head, (B, E) upper extremity, and (C, F) lower extremity. OCT, optical coherence tomography

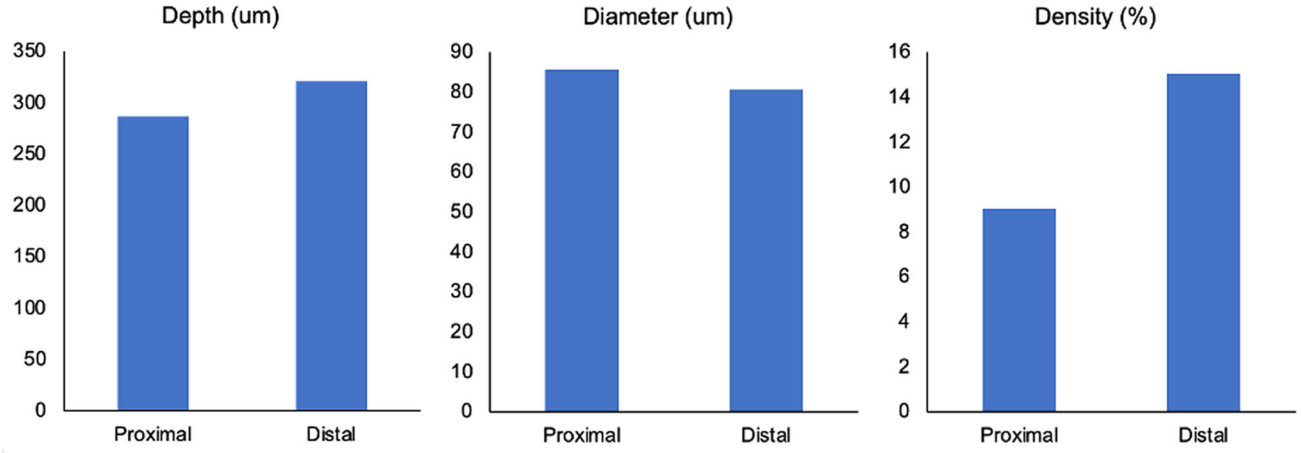

FIGURE 3 Superficial vascular plexus characteristics of PWB lesions sorted by proximal versus distal location on extremities. Values are median. PWB, port-wine birthmarks

extremities, and then trunk (25 μm). Lesions on the face were the deepest (352 μm) compared to other locations, which had similar depths in the range of 224–230 μm. Another study performed histologic analysis on 13 patients and found that centrofacial PWB lesions had greater vascular depth (510 vs. 289 μm) and larger vessels (46 vs. 32 μm) compared to those in lateral facial regions.[13] However, vessel diameter in these studies were likely underestimated, since biopsy specimens are fixed and without real-time blood flow, which would contribute to vessel collapse. Biopsies are also only able to capture cross-sectional snapshots of a small sample of the lesion, which may not be representative of its entirety.

Reflectance confocal microscopy (RCM) is an alternative skin imaging modality that can provide images of higher resolution and contrast at the cost of limited depth of penetration, smaller field of view, and lengthy image-capturing time.[12,21] Using RCM, vessels of PWB lesions on the extremities were observed to be larger and deeper compared to facial lesions.[12] However, it must be noted that the maximum depth of image acquisition with RCM is only 100–200 μm below the skin surface.[21] Therefore, only the most superficial portions of lesions were measured. High-frequency ultrasound has also been used to measure PWB, which can offer greater depth of viewing, but with less resolution and contrast.[22,23]

In contrast, this cross-sectional observational study evaluated the vascular characteristics of PWB lesions, including vessel density and diameter and superficial plexus depth, using D-OCT. D-OCT has much greater depth of penetration than RCM (1–2 mm vs. 100–200 μm), which can allow for more accurate examination of lesions. PWB lesions were located on various parts of the body, including the head, neck, trunk, and upper and lower extremities. Compared to the head, the superficial plexus vessels of lesions on the upper extremities were smaller, deeper, and less dense, while those on the lower extremities were deeper. The extremities had the deepest superficial plexus of PWB lesions of all body sites. It is important to note that the algorithm in this OCT scanner is based on speckle variance and detects vessels by the presence of flow. Therefore, if flow is very slow, then it will not detect a vessel or may do so quite poorly. This may have affected the measurements of lesions on the lower extremities, which may have slower flow and be impacted by the effects of dependency and gravity. Improving the sensitivity to slow flow vessels comes with a trade-off, including increasing the sensitivity to small bulk movements of the probe or subject, which would cause undesirable image artefacts.[24]

Vascular characteristics can impact the selection of PDL treatment parameters and clinical outcomes. PDL treatment of vascular lesions relies on hemoglobin in the blood to serve as the chromophore that absorbs energy from the laser. Heat is then transferred to the vessel walls to cause irreversible damage and destruction. Lesions that have more superficial and larger cutaneous vessels with increased density may theoretically be more easily targeted with PDL and can have greater absorption of energy. Caveats are that superficial vessels can become too large and have too high of a density, which could potentially shield the vessels beneath from being fully treated initially. D-OCT may also provide helpful insights for treatment-resistant PWB lesions. For example, D-OCT may reveal unique findings about the depth of the lesion, which may subsequently lead to changes in the selection and parameters of the laser, including its wavelength and spot size.

Given the findings in this study, it could be suggested that lesions on the extremities may be more difficult to treat. In clinical practice, we have noticed this to be true in several cases. Lesions on the face generally respond better to PDL than those on the upper extremities, while those on the lower extremities fare even worse. Our data demonstrate that lesions on the face have shallower superficial plexus depths with vessels that are larger and denser, which may contribute to treatment success. It is likely that increased epidermal and papillary dermal thickness contributes to the deeper vascular plexus noted on the extremities. This thickness can vary according to many factors, including age, sex, and location. The depth of the superficial vascular plexus may affect how much of the PDL can reach the target, which could in turn affect the efficacy of treatment. Anecdotally, lesions on the distal extremities can also be more resistant to treatment than more proximal lesions, which trended deeper in our study. However, this was not statistically supported, which was likely limited by the small number of lesions on the proximal and distal extremities. There are other lesion characteristics that we did not evaluate, which may affect clinical outcomes and contribute to what we are experiencing in clinical practice, such as blood flow, inflammatory reaction and healing, gravity and dependence, rate of growth and progression, thickness and nodularity, and color as it relates to vessel characteristics.

Previous studies have examined clinical outcomes following PDL treatment of PWB lesions on different parts on the body. However, this was mostly for lesions located on the head and neck.[4,9–14] Renfro and Geronemus observed that the number of treatments required per PWB varied based on their anatomic location.[10] Centrofacial lesions had mean lightening of 70.7%, which corresponded to a good response, while those in the remaining regions had mean lightening of 82.3%, which corresponded to an excellent response. Lesions in dermatomes V1, V3, C2, and C3 had greater clinical response than those in V2. This was supported by a more recent study that observed greater improvements using a chromameter in lateral facial PWB compared to those located on the central face (average blanching rate of 34.01% vs. 8.68%).[13] By measuring mean decrease in size following the first five and the second five PDL

treatments, another study demonstrated improved response in lesions on the forehead (100%, 0%, respectively) and peripheral face (58%, 28%, respectively) compared to centrofacial lesions (48%, 14%, respectively).[14] Although our study did not analyze various facial locations due to limited sample sizes, facial PWBs have already been examined as described.

Limitations of this study included certain characteristics of the patient population. Many patients had previous laser treatment, which may have influenced the vascular characteristics of PWB lesions. However, we included these lesions to offer a representative sample of cases seen in everyday clinical practice. The majority of lesions were located on the head, and there were less located on other body sites, which limited sub-group analysis. Although D-OCT has a penetration depth of 1–2 mm, some lesions likely have vessels that are much deeper. This OCT scanner measures the depth of the superficial vascular plexus, which may underrepresent the depth of the entire lesion. Additionally, measurements of vessel diameter and density are calculated at this superficial depth, which may not be fully representative of the lesion. However, OCT remains helpful in that it provides real-time images in a noninvasive, in-vivo setting. It should also be noted that certain confounding factors, such as age, gender, comorbidities, room temperature, and patient positioning, were not assessed in this study, which may play a role in OCT measurements.[25] Many infants and young children were not included in this study due to the difficulty in obtaining D-OCT scans of sufficient quality in this population.

This study offers insights into the vascular characteristics of PWB lesions by body location. D-OCT has utility in assessing vascular lesions at the bedside, which may aid in the selection of treatment parameters for laser procedures. The information from this study can be incorporated by physicians into their practice. However, additional studies should look into how PWB characteristics can influence the selection of PDL treatment parameters and clinical outcomes. Based on the information in this study, it would also be worthwhile to examine which vascular characteristics are the most impactful determinants of treatment response.

CONCLUSION

PWB lesions have distinct vascular characteristics, which can be associated with their body location. This includes superficial vascular plexus depth as well as vessel diameter and density. Compared to the head, the superficial plexus of lesions on the upper extremities were smaller, deeper, and less dense, while those on the lower extremities were deeper. The extremities had the deepest superficial plexus of all sites. PWB can be easily classified by their location upon clinical examination, so this data can be readily incorporated into clinical practice.

CONFLICT OF INTERESTS

Roy Geronemus, Kristen Kelly, and Jill Waibel have received investigative equipment from Michelson Diagnostics Ltd. Jon Holmes is an employee of Michelson Diagnostics Ltd. Kristen Kelly has received equipment and honoraria from and serves as a consultant to Sciton Inc. Christopher Zachary serves on the advisory board of Allergan, Soliton, and Sofway.

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