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Optical coherence tomography-measured blood vessel characteristics of port-wine birthmarks by depth: A cross-sectional study

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Background: Port-Wine Birthmarks (PWB) are congenital capillary malformations requiring multiple treatments. Optical coherence tomography (OCT), a noninvasive imaging technique, characterizes vessels in cutaneous vascular lesions, including PWBs.

Objective: To assess variability in blood vessel characteristics within and between individual PWBs.

Methods: OCT was used to measure blood vessel density (%) and modal vessel diameter (micrometers) at increments of 0.05 mm from the skin surface to a depth of 0.50 mm at several adjacent spots of single PWBs in this cross-sectional study. Average ratios of vessel density and diameter in affected to control skin were obtained for each PWB by averaging data for all spots within a lesion. Statistical analysis was performed with a linear mixed effects model using SPSS software (IBM Corporation).

Results: There was great variability in vessel density and diameter within and between PWBs. Depths where average ratios of vessel density were consistently greater in affected to control skin were shallow, between 0.15 mm and 0.2 mm deep from the skin surface.

Limitations: Small sample size and device's inability to measure diameters smaller than 20 micrometers.

Conclusion: There is variability in vessel density and diameter within and between PWBs. Individualized treatment planning guided by OCT mapping should be studied further. (J Am Acad Dermatol 2024;91:848-54.)

Key words: blood vessel density; blood vessel diameter; blood vessel; capillary malformation; imaging; nevus flammeus; OCT; optical coherence tomography; port-wine birthmark; port-wine stain; vascular anomaly; vascular characteristics; vascular malformation.

INTRODUCTION

Port-Wine Birthmarks (PWB) are rare, congenital capillary malformations that affect an estimated 0.3% to 0.5% of newborns.[1] Although PWBs most commonly involve the head and neck, they can affect any part of the body.[2] Lesions typically start as flat, pink-to-red patches, which may evolve with age, darkening, and developing tissue hypertrophy and nodules.[2-4] This progression may result in medical complications, such as nodularity, bleeding, and

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facial asymmetry.[2-4] Furthermore, PWBs may be highly disfiguring, giving rise to psychiatric complications; there is evidence that affected patients may experience negative impacts on quality of life.[5]

The gold standard for the treatment of PWBs is pulsed-dye laser (PDL), for which the theory of selective photothermolysis describes the mechanism of action.[2] Hypertrophic and nodular lesions may be treated with 755 nm alexandrite and 1064 nm Nd:YAG laser.[2] Treatment results vary widely among patients, and complete lesion clearance is not common.[2] PDL settings are decided based on clinical response, and patients require multiple treatments.[6] Variability of vessel size and depth between and within PWBs is one factor that makes complete clearance of these lesions difficult.[7]

There have been studies that evaluated PWB vessels by biopsy. Fiskerstrand et al[8] performed biopsies on 51 patients before and after treatment with PDL, assessing the influence of vessel morphology on vessel viability after laser treatment. They found that PWBs that responded well to treatment had significantly more superficially located vessels and moderate-sized vessels than PWBs with poor response to treatment, which had significantly smaller vessels. This study provided important information, but biopsy analysis has limitations, including unavoidable changes to vessels during tissue processing and the inability to monitor a single spot over time or to measure many areas in the same patient.[8]

Optical coherence tomography (OCT) is a noninvasive imaging technique that has been used to obtain information about blood vessel characteristics of cutaneous vascular anomalies, including PWB.[9,10] There are multiple types of OCT. Doppler OCT is a type of OCT that can reveal blood flow and vessels by quantifying the speed of moving particles.[11,12] Dynamic OCT (D-OCT), more sensitive than Doppler OCT, is based on speckle variance and also involves analysis of blood flow in vivo, providing measurements of smaller skin vessels such as capillaries.[11,12] Previous studies of D-OCT-measured vascular characteristics have not defined enough vascular patterns related to the color or body site of lesions to guide the selection of laser parameters.[10,13] There are reports that D-OCT can provide assistance in the treatment of recalcitrant PWBs by providing more information about vascular characteristics.[6] This specific information may ultimately enable individualized selection of laser parameters to optimize treatment.[6]

Given the wide variety of clinical presentations of PWBs and lack of predictable response to standard-of-care, our objective was to study D-OCT-measured blood vessel characteristics within and between PWBs to understand the variability of vascular characteristics with depth and their implications for laser treatment.

CAPSULE SUMMARY

- There was great variability in vessel density and diameter within and between port-wine birthmarks, and the highest blood vessel density in affected skin compared to control, measured by Optical Coherence Tomography, was found at shallow depths (0.15 mm-0.2 mm).
- Individualized treatment planning guided by optical coherence tomography mapping should be studied further.

MATERIALS AND METHODS

This study was conducted with institutional review board approval (#2008-6307). A D-OCT (VivoSight, Michelson Diagnostics Ltd) device was used to measure separate adjacent spots of individual PWBs (Fig 1, *A* and *B*) of patients recruited from the clinic. The D-OCT device measures a 6 × 6 mm region of the skin over a depth of 1 mm in approximately 30 seconds and produces en face and longitudinal cross-sectional images of the measured area. For all measured areas, the D-OCT device's software allows the calculation of vessel density (percent) and modal vessel diameter (μm). Measured blood vessel density is defined as the fraction of the OCT image that consists of vessels. Measured modal blood vessel diameter is defined as that diameter for which 90% of the vessel segments in the image are equal to or less in diameter, where the vessel segment indicates a section of the vessel that is 1 pixel long in the D-OCT image. The primary feature of the D-OCT device used here is the capability to measure vessel density and vessel diameter at 0.05 mm increments of depth from the skin surface accurately over a depth of 0.5 mm. Because the machine cannot accurately measure small blood vessel diameters less than 20 μm in size, small blood vessel diameters where a measurement of "0" micrometers for blood vessel diameters between depths of 0.15 mm to 0.5 mm was indicated by device software were replaced with a measurement of 15 μm to represent small blood vessels in the dermis.

Both individual, adjacent affected spots and an additional control spot were measured with D-OCT for each PWB (Fig 1, *A* and *B*). Control areas

Abbreviations used:

D-OCT: dynamic optical coherence tomography
OCT: optical coherence tomography
PDL: pulsed-dye laser
PWB: port-wine birthmark

consisted of D-OCT measurement of the skin of the same body part on the contralateral anatomic side. Quantitative data for vessel diameter and density were collected from the machine for each of the 5 to 25 spots measured within each PWB at depths between 0.15 mm and 0.5 mm. The quantitative analysis involved a description of the mean and range of vessel density and vessel diameter for each PWB and all lesions overall. Measurement of the mean and range of the vessel density and vessel diameter was performed between depths of 0.15 mm and 0.5 mm, as 0.15 mm indicates the shallow dermis[14] and 0.5 mm is the deepest depth to which measurements were deemed accurate (Table I).[13] The second set of quantitative analyses involved determining a ratio of density or modal diameter at an individual spot for a given depth divided by the density or modal diameter for the control spot at that depth. Then, at each depth between 0.15 mm and 0.50 mm, these ratios were averaged for all spots within a lesion (Figs 2 and 3).

Color coding of Figs 2 and 3 indicates the magnitude of average ratios within a single lesion. Green indicates average ratios <1.2, yellow indicates average ratios 1.2≤ and <1.5, amber indicates average ratios 1.5≤ and <2, and red indicates average ratios ≥2.

Horizontal "en face" images of the skin produced by the device were also collected for each spot measured. These images depicted the network of cutaneous blood vessels and were used to create topical maps overlying clinical images for each spot imaged with OCT (Fig 1, *A* and *B*). History was also collected from patients, including age, color, and type of PWB (Table I).[13]

We used a linear mixed effects model using SPSS software (IBM Corporation) to compare the densities and diameters between affected and non-affected regions. We set the affected status and depth as fixed effects and consider random intercepts by participant identifier. We also considered a linear mixed effects model with the interaction between depth and affected status as a fixed effect. Statistical significance was evaluated at the 0.05 level.

RESULTS

Ten participants were recruited from the clinic (4 women and 6 men; average age 39.8 years, range 8-72 years), and 15 PWB lesion areas were imaged with OCT. Fitzpatrick skin types were I to IV. Between 5 and 25 individual, adjacent PWB 6x6 mm spots were measured with D-OCT for each PWB area (Fig 1, *A* and *B*). One control spot on contralateral uninvolved skin was imaged for comparison for each subject. Total measurement time for subjects ranged from 10 to 60 minutes, depending on the number of spots measured. No subjects reported any discomfort.

For collated blood vessel density data from all OCT-measured spots combined for all lesions, the mean and range vessel density was 11.6% (range, 0.5%-41.3%) in affected skin and 8.7% (range, 0.4%-33.5%) in control skin (Table I).[13] For collated blood vessel diameter data from all OCT-measured spots combined for all lesions, the mean and range vessel diameter was 94.6 μm (range, 12.0 μm-424.5 μm) in affected skin and 69.0 μm (range, 11.3 μm-191.6 μm) in control skin (Table I).[13]

The only depths into the skin where average ratios of vessel density in affected skin were consistently greater than in control skin across all lesions were at shallow dermal depths, between 0.15 mm and 0.20 mm deep into the skin (Fig 2). However, for the vessel diameter, the depths where the diameters were greatest, varied between subjects, with some subjects having larger vessels at deeper dermal depths and some having larger vessels at more shallow dermal depths (Fig 3).

There was a qualitative difference in vessel density and vessel diameter upon assessment of topographical maps of each lesion created using en face scans overlying clinical images (Fig 1).

Comparing 2 PWBs or 2 control areas at the same particular depth in the skin, the data indicated an expected average increase in diameter of 25.7 μm ($P < .05$, 95% CI, 18.3 μm-33.0 μm) for affected lesions. Comparing 2 PWBs or 2 control areas at the same particular depth in the skin, the data indicated an expected additive increase in density of 2.9% ($P < .05$, 95% CI, 1.9%-4.0%) for affected lesions. Comparing 2 PWBs or 2 control areas differing in depth by 0.1 mm, the data indicated an expected increase in diameter of 17.3 μm ($P < .05$, 95% CI, 15.5 μm-19.0 μm). Comparing 2 PWBs or 2 control areas differing in depth by 0.1 mm, the data indicated an expected increase in density of 2.9% units ($P < .05$, 95% CI, 2.7%-3.2%).

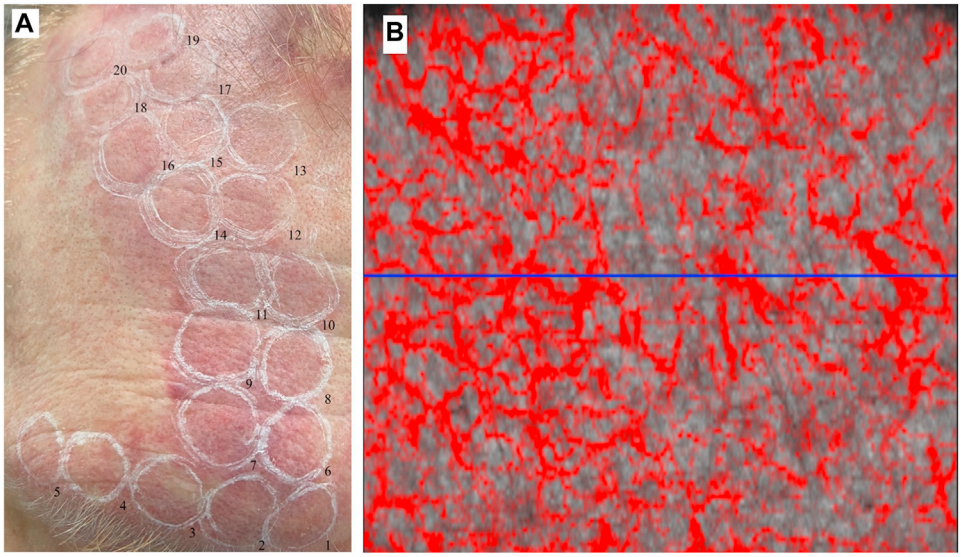

Fig 1. Example of Optical coherence tomography (OCT) mapping of several adjacent spots of a port-wine birthmark (PWB) on the right forehead. **A,** Each white circle delineates a 6x6 mm region measured by OCT. For each white spot, blood vessel density and diameter are quantified accurately up to depths of 0.5 mm, with data provided at increments of depth of 0.05 mm. "En face" horizontal cross-sectional OCT images are also provided. **B,** Depicts an example of an "en face" OCT image in PWB skin. These "en face" scans were mapped overlying clinical images.

We also considered a linear mixed effects model with the interaction between depth and affected status as a fixed effect. However, there was not enough evidence to suggest that this interaction predictor played a role in describing the variability of our outcomes.

DISCUSSION

PWBs can be difficult to treat, partly due to heterogeneity within and between PWBs. This study provides further in vivo evidence of the heterogeneity of these lesions and compares affected lesions to unaffected skin. Using average ratios, we have demonstrated that the only depths where density was consistently greater in affected skin compared to control skin in our subject population were at superficial dermal depths, between 0.15 mm and 0.20 mm. This is clinically relevant because it may help explain why shorter wavelengths (532 nm or 595 nm) may be beneficial for treating many PWBs. Fiskerstrand et al[8] found that PWB with many superficial vessels often responded well. In their study, post-PDL biopsy showed a median depth of 0.15 mm for coagulated vessels, with few coagulated vessels below depths of 0.4 mm.[8] If one were to use longer wavelengths, light from the treating laser would encounter the more superficial blood vessels first. This interaction may shield the deeper vessels, which may be affected less or perhaps even minimally by treatment light. Slightly larger vessels were seen at deeper depths. Of note, all patients included in this study have had treatment and it is possible that this increase in diameter with depth is a result of treatment effect.

As considerable variability in vascular parameters among subjects was noted, individualized information may be needed to guide optimized laser therapy for PWB. Heterogeneity in phenotypes and different treatment responses may be due to the variations in the distribution of mutated endothelial cells, although this needs further study. In a case report by Christman et al,[6] D-OCT-guided subpurpuric settings were used to treat a recalcitrant PWB, which reportedly achieved good clinical response following 3 rounds of treatment. D-OCT measurements were taken before and after treatment.[6] The authors reported visualization of larger diameter vessels reducing in size following treatment.[6] Although specific PDL parameter adjustments based on OCT measurements were not reported, the authors state that having knowledge of the vascular plexus depth can inform the selection of fluence, and knowing the diameter of vessels enables matching of the pulse duration to the thermal relaxation time of these vessels within PWBs.[6] Further formal study of this concept is required.

Of note, it is typical that PWB patients who are treated with PDL standard-of-care may need to be treated with multiple different settings to clear the

Table I. Average and range vessel density and vessel diameter by lesion as measured by optical coherence tomography

				Average and range vessel density (%) and vessel diameter (μm) by lesion							
Lesion number	Anatomic location	Color	Type	Average affected density (%)	Average control density (%)	Range affected density (%)	Range control density (%)	Average affected diameter (μm)	Average control diameter (μm)	Range affected diameter (μm)	Range control diameter (μm)
1	Forehead	Red	Flat	14.8	8.8	1.8-36.0	3.2-12.0	96.1	63.1	21.7-243.2	36.6-86.0
2	Temple/cheek/upper portion of the lip	Red	Flat with scattered nodules	13.1	21.3	2.3-33.5	4.0-33.5	102.2	117.5	41.2-198.7	43.9-191.6
3	Upper portion of the chest	Purple	Flat with many scattered nodules	10.1	8.3	1.2-23.1	1.7-15.0	100.9	84.7	29.7-315.4	27.2-124.2
4	Ventral aspect of the forearm	Purple	Flat with many scattered nodules	6.9	9.4	0.6-21.4	0.8-19.1	62.8	87.2	13.3-121.3	15.0-154.9
5	Cheek/upper portion of the lip	Red/ purple	Hypertrophic with nodules	19.7	7.9	3.6-41.3	2.7-10.4	199.8	73.9	47.3-424.5	32.6-112.7
6	Upper portion of the chest	Red	Hypertrophic	7.0	5.3	0.9-17.1	0.8-12.6	71.0	55.0	15.0-128.4	15.0-88.0
7	Ventral aspect of the forearm	Red	Hypertrophic	5.3	3.8	0.5-18.2	0.7-7.7	51.9	39.5	15.0-120.9	11.3-67.6
8	Cheek/upper portion of the lip	Red	Hypertrophic	14.5	11.6	3.4-31.2	0.9-26.1	96.8	85.6	43.5-183.9	48.9-119.9
9	Cheek	Purple	Flat with few scattered nodules	11.9	6.3	4.5-23.8	2.9-9.1	83.1	50.8	38.5-343.3	15.0-75.1
10	Cheek/upper portion of the lip/ nasal sidewall	Red	Flat	19.5	16.5	4.7-37.8	3.2-25.3	135.7	95.3	66.7-249.9	38.0-143.9
11	Distal upper portion of the arm	Red/ brown	Flat	20.5	3.83	4.5-33.5	0.7-6.5	114.1	35.5	36.9-193.6	15.0-47.7
12	Cheek	Red	Flat	13.4	14.3	3.1-22.3	5.0-17.9	129.3	88.1	43.5-205.2	49.2-114.0
13	Dorsal portion of the forearm	Red	Flat	5.4	3.8	0.6-12.6	0.4-6.2	57.2	62.5	15.0-122.0	42.0-89.0
14	Distal upper portion of the arm	Red	Flat	5.5	4.6	1.2-12.6	0.6-8.1	57.5	58.3	12.0-121.9	27.4-85.7
15	Proximal upper portion of the arm	Red	Flat	6.3	4.4	1.0-15.4	0.8-7.6	60.7	37.5	12.9-118.3	29.4-47.5

Vessel density and modal diameter were measured between dermal depths of 0.15 mm (papillary dermis)[13] and 0.5 mm (the deepest depth to which the machine is able to accurately measure density and diameter). The average density of affected port-wine birthmark (PWB) skin was not consistently greater than that of control, unaffected skin. The range of vessel density in affected PWB skin was typically, but not always, wider than that of control. The average diameter of affected PWB skin was more often greater than that of control, unaffected skin, unlike vessel density. The range of vessel diameter in affected PWB skin was often wider than that of the control.

DENSITY

Average Ratio of Density of Affected to Control per Depth															
	Lesion Number														
Depth (mm)	Lesion 1	Lesion 2	Lesion 3	Lesion 4	Lesion 5	Lesion 6	Lesion 7	Lesion 8	Lesion 9	Lesion 10	Lesion 11	Lesion 12	Lesion 13	Lesion 14	Lesion 15
0.15	1.16	1.43	1.45	1.16	3.25	4.21	3.43	2.88	2.54	3.44	9.94	1.61	2.9	2.37	1.85
0.2	1.26	1.28	1.67	1.16	4.07	3.01	2.7	2	2.29	2.72	9.87	1.31	2.47	1.55	1.99
0.25	1.41	1	1.51	0.81	3.57	2.12	2.58	1.68	2.08	1.96	7.93	1.17	1.78	1.23	1.58
0.3	1.57	0.76	1.34	0.75	3.05	1.77	2.06	1.56	1.79	1.31	6.56	1.1	1.39	1.1	1.35
0.35	1.75	0.61	1.28	0.73	2.45	1.44	1.52	1.47	1.59	1	5.55	0.99	1.33	1.1	1.29
0.4	1.88	0.51	1.14	0.7	2.13	1.17	1.23	1.36	1.58	0.89	4.68	0.82	1.36	1.16	1.4
0.45	1.89	0.44	1.08	0.69	1.83	0.98	1.06	1.26	1.78	0.87	4.26	0.65	1.34	1.21	1.43
0.5	1.77	0.4	1.07	0.7	1.43	0.82	0.8	1.15	2.23	0.85	4	0.55	1.29	1.23	1.49

Fig 2. Average ratios of optical coherence tomography-measured blood vessel density in skin affected by port-wine birthmarks (PWB) compared to control skin (skin unaffected by PWB). Average ratios for each depth for a single lesion were obtained by averaging the ratio of affected density to control density for all measured spots per lesion. *Green* indicates average ratios <1.2, *yellow* indicates average ratios 1.2 ≤ and < 1.5, *amber* indicates average ratios 1.5 ≤ and < 2, and *red* indicates average ratios ≥2. Shallow depths into the skin (between 0.15 mm-0.2 mm) are delineated with a *black border*. These were the only depths where vessel density was consistently greater in affected skin compared to control skin.

DIAMETER

Average Ratio of Diameter of Affected to Control per Depth															
	Lesion Number														
Depth (mm)	Lesion 1	Lesion 2	Lesion 3	Lesion 4	Lesion 5	Lesion 6	Lesion 7	Lesion 8	Lesion 9	Lesion 10	Lesion 11	Lesion 12	Lesion 13	Lesion 14	Lesion 15
0.15	1.1	1.42	1.88	1.58	4.9	2.66	1.75	1.02	3.94	2.74	1.37	2.6	0.54	0.69	0.77
0.2	1.24	1.47	1.45	1	4.67	1.4	2.97	0.93	2.22	2.55	4.67	1.86	0.74	0.76	1.16
0.25	1.52	1.2	1.11	0.96	4.77	1.31	1.29	0.99	2.27	1.92	6.13	1.93	0.71	0.78	1.45
0.3	1.56	1.05	1.13	0.76	3.29	1.47	1.22	1.13	2.27	1.57	3.56	1.87	0.77	0.85	1.72
0.35	1.49	0.92	1.16	0.71	2.82	1.34	1.25	1.26	1.66	1.3	2.7	1.72	1.16	0.9	1.72
0.4	1.59	0.75	1.09	0.61	2.4	1.23	1.33	1.27	1.27	1.19	3.01	1.24	1.45	1	1.86
0.45	1.66	0.66	1.19	0.61	1.63	1.13	1.22	1.22	1.09	1.08	3.3	0.82	0.98	1.18	1.97
0.5	1.66	0.59	1.15	0.68	1.26	0.99	1.12	1.11	0.99	1.04	3.58	0.76	0.89	1.24	2.08

Fig 3. Average ratios of optical coherence tomography-measured blood vessel diameter in skin affected by port-wine birthmarks (PWB) compared to control skin (skin unaffected by PWB). Average ratios for each depth for a single lesion were obtained by averaging the ratio of affected diameter to control diameter for all measured spots per lesion. *Green* indicates average ratios <1.2, *yellow* indicates average ratios 1.2 ≤ and < 1.5, *amber* indicates average ratios 1.5 ≤ and < 2, and *red* indicates average ratios ≥2. There is no consistent association of greatest vessel diameters in affected skin compared to control with a specific range of depth.

heterogenous vessels found in PWBs, and the settings can vary with each treatment session. Sometimes, an experienced laser surgeon may perform 2 passes with different settings during the same session. Moreover, although previous studies have investigated the relationship between OCT-measured blood vessel characteristics, using single variables such as color, location, and age seems to inadequately define these lesions.[10,13] Hence, large-scale mapping of individualized lesions, such as in this study, is necessary to provide information about vessel characteristics at multiple spots at a single time point and then with repetitive measurements over the course of treatment. The ideal scenario would be for measurements of each individual PWB spot to be taken and treatment adjusted (at least pulse duration) for each area. This is not possible with current technology but could be a goal for the future.

A limitation of this study is the small sample size. Another limitation is the lack of a young pediatric population. Additionally, the OCT software cannot accurately measure density and diameter beyond depths of 0.5 mm into the skin. Therefore, the analysis may not capture PWB blood vessels that

lie beyond depths of 0.5 mm. Also, the device cannot measure vessel diameters smaller than 20 μm accurately. Furthermore, the D-OCT device may be limited in its ability to capture measurements of blood vessels in which there is low flow.[12]

CONCLUSIONS

There is variability in vessel density and diameter within and among PWBs. OCT mapping illustrates this variability, and with improved imaging and laser technology, individualized treatment planning guided by OCT could potentially be used and should be studied. With current technology, relatively large areas can be measured within 15 minutes at the bedside. Future directions include large area OCT mapping of blood vessel characteristics in a large cohort spanning the full range of the age spectrum.

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Conflicts of interest

None disclosed.

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