Non-invasive efficacy assessment of pulsed dye laser and photodynamic therapy for port-wine stain

Rongqian Tian, Qin Wang, Sijin Li, Xiang Nong

Department of Dermatology, First Affiliated Hospital of Kunming Medical University, Kunming, China

Abstract

Port wine stain (PWS) is a congenital vascular malformation that commonly occurs on the face and neck. Currently, the main treatments for port wine stain are pulsed dye laser (PDL) and photodynamic therapy (PDT). However, the efficacy evaluation of PWS mostly relies on the subjective judgement of clinicians, and it is difficult to accurately respond to many small changes after treatment. Therefore, some non-invasive and efficient efficacy assessment methods are also needed. With the continuous development of technology, there are currently many visualisation instruments to evaluate PWS, including dermoscopy, VISIA-CR™ system, reflectance confocal microscopy (RCM), high-frequency ultrasound (HFUS), optical coherence tomography (OCT), Photoacoustic imaging (PAI), laser speckle imaging (LSI) and laser Doppler imaging (LDI). Among them, there are simple and low-cost technologies such as dermoscopy and the VISIA-CR™ system, but they may not be able to observe the deeper structures of PWS. At this time, combining techniques such as HFUS and OCT to increase penetration depth is crucial to evaluate PWS. In the future, the combination of these different technologies could help overcome the limitations of a single technology. This article provides a systematic overview of non-invasive methods for evaluating treatment efficacy in port wine stains and summarises their advantages and disadvantages.

Key words: Efficacy assessment methods, port-wine stain, non-invasive diagnostic techniques

Introduction

Port-wine stain (PWS) is a low-flow congenital vascular malformation manifesting in the skin and mucous membranes, usually found in 0.3% to 0.5% of newborns and typically occurring on the face and neck.[1–3] At birth, PWS presents as pink, well-defined patches which may also be localised or segmental and within which capillary malformations, venous malformations, and arteriovenous malformations are seen.[4] As age progresses, the vessels of PWS become larger in diameter, their walls become thicker and they appear to be deeper and generally do not fade on their own. In addition, the type of vessels in PWS changes, with a gradual increase in venous malformations and the development of arteriovenous malformations and tissue hyperplasia which also makes treatment more difficult.[5,6] Currently, the main treatments for PWS are pulsed dye laser (PDL) and photodynamic therapy (PDT). Clinicians often rely on subjective judgement to assess PWS treatment's efficacy, making it difficult to accurately reflect many small changes. Therefore, efficient, accurate, safe, and non-invasive methods are necessary for evaluating efficacy.[7] This systematic review comprehensively looks at the main methods utilised for evaluating the efficacy of PWS treatments in recent years.

Efficacy assessment methods

The complex and irregular subcutaneous blood vessel deformities that characterise PWSs make it challenging to accurately identify and extract lesions from clinical images.

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Corresponding author: Ms. Rongqian Tian, Department of Dermatology, First Affiliated Hospital of Kunming Medical University, Kunming, China. rongqian.tian@outlook.com

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Jinrong Mu *et al*. have introduced a multi-colour space adaptive fusion network (M-CSAFN) in their recent study which integrates diverse colour models.[8] Concurrently, the authors fabricated the most extensive segmentation dataset for PWS to date. The study aimed to facilitate clinical segmentation of PWS lesions in images, enabling clinicians to evaluate treatment progress and efficacy accurately and optimise treatment planning.[8] This approach has not been widely used to assess PWS lesions.

In recent years, non-invasive diagnostic techniques such as dermoscopy, VISIA-CR™ system, reflectance confocal microscopy (RCM), high-frequency ultrasound (HFUS), optical coherence tomography (OCT), photoacoustic imaging (PAI), laser scatter imaging (LSI) and laser Doppler imaging (LDI) have been attempted in the examination of PWS.

Dermoscopy

Dermoscopy, also known as surface microscopy, is a non-invasive technique that allows for rapid and magnified observation of morphological features of the skin that are difficult to perceive with the naked eye. PWSs are flat red patches consisting of dilated capillaries located in the papillary and reticular dermis.[9] Dermoscopy can be used to assess the depth of PWS vessels.[10] The dermoscopic pattern consists of two main forms, type I, superficial or papillary, consisting of rounded red structures representing the vascular system in the superficial dermis, and type II, deeper or reticular, represented by prominent red linear structures forming an irregular network in the horizontal subepidermal plexus, representing the vascular system in the deep dermis. An off-white veil, streaks of white linear structures against a white or blue background, and pale circular areas surrounding a central brown dot are also observed. [9,11] A study retrospectively analysed 212 patients with facial PWS who underwent haematoporphyrin monomethyl ether photodynamic therapy (HMME-PDT) and after two PDT sessions, punctate or bulbous vessels demonstrated the highest response rate (60.0%), whereas reticular and linear vessels demonstrated lower response rates (5.3% and 14.5%, respectively). Following multivariate logistic regression analysis, the results revealed a significant association between suboptimal efficacy and the presence of linear and reticular vessels.[12] In another retrospective study, an efficacy analysis by dermoscopy of a total of 216 patients with PWS who underwent HMME-PDT showed that punctate and bulbous vessels were highly associated with excellent outcomes (41.82%); linear vessels were mainly associated with good outcomes (54.55%); reticular vessels were mainly associated with normal outcomes (55.07%) and mixed vessels were mainly associated with no improvement (26.66%). This shows that punctate and bulbous vessels as well as linear vessels showed better efficacy.[5] However, this technology is limited in its ability to assess the depth of PWS blood vessels and focuses more on vascular morphological characteristics.

VISIA-CR™ system

The VISIA-CR™ Skin Tone Analysis System is an image acquisition software that uses ultraviolet light and cross-polarised light to generate enhanced red/brown (RBX) images of human skin. Information on PWS vascular features and facial erythema has been reported to be recorded through VISIA's red images to visualise the discolouration of lesions before and after treatment.[7,13] One study confirmed that the response was higher than visual assessment and also more sensitive to colour bleaching at the baseline of the treated area.[14,15] However, quantitative assessment of lesion response in retrospective studies and multicentre clinical trials remains a challenge for PWS efficacy assessment which may be influenced by a variety of conditions from image acquisition to efficacy assessment. Therefore, some studies have combined ImageJ with VISIA to calculate the erythema index (EI) to analyse PWS.[16] ImageJ software, a Java-based image processing software package developed by the National Institutes of Health (NIH), serves as a public domain tool utilised for quantifying image area and tissue volume measurements.[17,18] In a study, Li *et al*. collected VISIA red images of 30 patients with PWS and calculated the lesion reduction before and after treatment using ImageJ which showed a cure in 5 cases (16.67 %), good efficacy in 10 cases (33.33 %), 8 cases (26.67 %) and was ineffective in 7 cases (23.33 %). The total effective rate was 76.67 % which was in general agreement with the photograph (76.67 % vs. 77.42 %). The results show that combining VISIA and ImageJ to assess clearance rates is more objective.[19] However, this technique can only assess the extent of fading and cannot observe the deeper structures of PWS.

Reflectance confocal microscopy (RCM)

RCM is a novel imaging technique that offers non-invasive, high-resolution, and high-contrast capabilities. This technique allows for in vivo assessment of skin lesions with a resolution similar to histology. Specifically, it enables the evaluation of skin vascular structure, blood flow, and velocity.[20–22] The vascular anomalies present in PWS lesions are characterised by dilated vessels of varying sizes and depths.[23] RCM is capable of distinguishing small vessel diameters present in benign telangiectasias from the large dilated venules observed in PWS.[21] The expansive field of view provided by RCM allows for the evaluation of a greater number of lesions compared to standard histopathological analysis.[24] In the study, the authors proposed that PDL demonstrated enhanced clearance with diminishing pulse duration.[23] Concurrently, within the same pulse duration group post-treatment, significant reductions were noted in vessel diameter and density. The investigators utilised RCM to observe vascular changes in PWS lesions before and after PDL treatment. This examination aimed to evaluate the clinical effectiveness of PDL across various pulse durations, contributing to the refinement of therapeutic parameter settings.[23] Studies have shown that RCM is a valuable tool for assessing vascular changes in PWS lesions before and after PDL treatment. By assessing the clinical

effectiveness of PDL with various pulse durations, RCM can aid in optimising treatment parameter settings.[23] Furthermore, certain experts posit that RCM may have prognostic value in assessing laser-resistant PWS lesions before treatment, thereby enhancing the therapeutic outcomes of PDL.[25] It is important to note that RCM has some limitations. Its main limitation is the depth of imaging. The study indicates that the reach of RCM examination is confined to the upper dermis, rendering it incapable of evaluating the deepest vascular aspects. The maximal penetration depth of RCM into the human skin is established at 250–300 µm. Notably, the imaging quality of PWS is markedly diminished when the penetration depth exceeds 150 µm during examination [20,25]. The emphasis lies in the refinement of treatment parameters through the mitigation of motion artefacts during imaging. This is particularly pertinent in the diagnostic application of PWS in paediatric patients, where the challenge of sustaining body stillness is compounded. In addition, prolonged image capture times present an additional drawback in this context.[21,26]

High-frequency ultrasound (HFUS)

HFUS is an affordable, simple, and objective imaging technique with high resolution that allows visualisation of the skin and its attachments, subcutaneous tissue, and deep structures.[14,27] In contrast, the lesions of PWS are mainly located in the papillary and reticular layers of the dermis.[7] The use of HFUS allows for the visualisation and accurate measurement of the thickness and depth of deep lesions in PWS, as well as the assessment of haemodynamics which helps clinicians adjust treatment plans and evaluate prognosis.[28,29] Tang *et al*. quantitatively evaluated 195 patients with PWS (238 skin lesions) by high-frequency ultrasound of the skin with shear wave elastography (SWE) and classified the lesions into four types: pink, purple, thickened and nodular. The results showed that the skin thickening and skin energy Doppler (PD) signal levels were significantly higher in the nodular and thickened groups than in the pink and purple groups, respectively. The PD signal level was significantly higher in the purple-type group than in the pink-type group and the results suggest that skin HF ultrasound can be used as a potential quantitative assessment tool for classifying erythema skin loss.[30] In another study, high-frequency ultrasound of the skin was performed on 45 PWS patients before and after HMME-HDT treatment to assess efficacy, skin thickness, and density. Ultimately, a significant reduction in the number of twisted and dilated PWS vessels was observed under high-frequency ultrasound. The differences in skin thickness and skin density before and after treatment were statistically significant ($F = 14.528, 5.428, P < 0.001$).[31] It indicates that the clinical efficacy of HMME photodynamic therapy can be objectively evaluated by using high-frequency ultrasound as a method to monitor the changes in skin thickness and lesion tissue density and also provides a basis for the formulation of individualised photodynamic therapy.[31] Nevertheless, owing to suboptimal imaging contrast, the efficacy of the technique in discerning intricate structures beneath the skin surface is compromised, particularly when utilising ultrasound frequencies below 20 MHz.[32] An additional constraint pertains to the precision and skill of the ultrasound operator. The operator must ensure the adequate application of coupling gel between the probe and the patient's skin to prevent the formation of bubbles, thereby enhancing the quality of tissue images.[33,34]

Optical coherence tomography (OCT)

OCT is an advanced technique that captures subtle changes in tissue structure quickly and accurately without trauma to the skin. OCT uses a low-coherence laser to localise backscatter events within the sample, similar to ultrasound.[35] OCT holds promise for the real-time in vivo and in situ monitoring of skin vascular lesions. This capability allows for the non-invasive detection of skin diseases.[36] Previous studies have also successfully used OCT to examine vascular structures in the skin.[37] PWS is characterised by marked vascular hyperplasia, vasodilation and superficial lesion distribution, whereas OCT images can distinguish dilated capillaries from normal tissue and the thickness of the epidermal and papillary layers; therefore, OCT provides a suitable imaging modality for PWS.[38,39] In a previous study, OCT images of PWS lesions and contralateral normal skin were compared in 41 patients and showed that dilated dermal vessels could be clearly distinguished from normal tissue. It also demonstrated that OCT may be a useful tool for non-invasive imaging of PWS.[39] Current studies have demonstrated that OCT can accurately measure the vascular diameter and depth of PWS which helps clinicians to objectively diagnose the pathological type of PWS and select the optimal clinical treatment dose, as well as make accurate predictions about the effectiveness of treatment.[40] Nonetheless, inherent limitations arise due to biological light scattering, impacting the technique's penetration depth to approximately 2 mm.[41]

1. Dynamic Optical Coherence Tomography (D-OCT)
   D-OCT is a diagnostic device that utilises speckle analysis of variance to measure the features of skin vasculature, including the depth and diameter of the superficial plexus and the density of surface vessels. It offers a depth measurement capability of around 1.5– 2.0 mm.[42-44] In a cross-sectional observational study, experts utilsed D-OCT to measure the diameter and density of blood vessels and depth of the superficial nerve plexus in various regions of the body among patients presenting with PWS. The research aimed to explore whether these blood vessel features varied across body locations. The findings indicated that lesions of the superficial plexus of PWS were deepest in the extremities, whereas vessels were largest in the neck, followed by the face and torso. In comparison to OCT, D-OCT can also evaluate the vascular characteristics of PWS, providing valuable

information for clinicians regarding PWS parameters.[26] Joseph N Mehrabi *et al.* conducted a study using D-OCT to measure the affected blood vessels of 108 patients diagnosed with PWS. The research observed the blood vessel characteristics such as depth of superficial nerve plexus, density, and diameter among various colour types of PWS. The results indicated that PWS of the purple type usually had larger vessels, while pink PWS exhibited substantial variation in the superficial plexus depth and smaller vessels.[43] This method provides measurements of deeper blood vessels and allows for more precise analysis by clinicians. Nevertheless, the signal in D-OCT emanates from blood flow. During examinations, heightened attention must be directed toward the instability of contact between the handheld OCT probe and the skin, as this instability could potentially compromise result accuracy.[44]

2. Optical Coherence Tomography Angiography (OCTA)
   OCTA is a functional modality of OCT that utilises a non-invasive approach to image vessels based on their flow properties. This technique enables the visualisation of functional vascular networks in microcirculatory tissue beds.[45,46] In an observational clinical study, researchers employed OCTA to examine the vascular morphology and structure of various types of PWS patients. By comparing the PWS lesions with the contralateral normal skin, the findings indicated that the vessels with PWS lesions had higher density and larger diameters and the thicker type showed a higher probability of larger diameter and higher density than the purple type. These results signify the remarkable capability of OCTA to precisely assess PWS lesions in a comprehensive manner.[47] Recent research has demonstrated that a novel optically clear agent (OCA) can significantly enhance the imaging quality of contrast-enhanced OCTA in healthy human skin. This improvement results in better imaging depth and contrast for OCTA and facilitates a more accurate evaluation of the blood vessels in patients with PWS.[48] OCTA is based on intrinsic motion contrast to distinguish functional vessels from static tissue background. However, visualising the static structure of skin tissue in the basal layer of PWS may be impeded by the absence of flowing red blood cells within the blood vessels in this region.[49] Moreover, artefacts may be present in OCTA technology, manifesting as elongated tail shadows of blood vessels. These artefacts can pose challenges in the accurate assessment of vessel morphology.[50] Recently, certain researchers have introduced inverse signal-to-noise ratio (iSNR)-decorrelation (D) optical coherence tomography angiography (ID-OCTA) technology. This approach employs mean subtraction for decorrelation, mitigating artefacts to a certain extent and enhancing overall image quality. However, a notable limitation is its inability to determine the direction of blood flow.[51] But, in the future, we can still use this technology to evaluate deep vessel morphology.[14,52] The subsequent course of action entails investigating the amalgamation of diverse technologies to surmount the limitations inherent in individual technological approaches.

3. Doppler Optical Coherence Tomography (Doppler-OCT)
   Doppler-OCT is a morphological imaging modality that integrates laser Doppler flowmetry with OCT.[53] Although OCT images are crucial in evaluating PWS lesions, they may not always accurately differentiate PWS vessels from cavities or other adjacent structures, such as sebaceous glands. However, Doppler-OCT can leverage the Doppler effect to capture the motion of particles within the blood flow, facilitating the differentiation of vessels from adjacent structures.[54] Current studies suggest that Doppler-OCT is distinct from laser Doppler velocimetry due to its ability to measure deeper blood flow velocity and locate vessel walls. These findings highlight the potential of this non-invasive method for analysing vessel structure. In addition, Doppler-OCT has the potential to enable rapid and semi-quantitative evaluation of in situ and real-time efficacy of PWS treatment on an individual patient basis, offering promising avenues for optimising the treatment of PWS.[41,53] The diminished resolution and sensitivity observed in Doppler optical coherence tomography can undoubtedly lead to an inability to detect smaller as well as deeper vessels.[54]

Photoacoustic imaging (PAI)

PAI is a novel hybrid medical imaging technique that capitalises on the inherent optical absorption of human tissue chromophores, including haemoglobin, melanin, lipids, and water, to evaluate subcutaneous blood perfusion levels.[55,56] PAI demonstrates a good depth of penetration and high contrast, making it a viable option for visualising blood vessels in PWS lesions.[57,58] Chloe J Chua and colleagues have put forth a novel photoacoustic-guided ultrasound focusing technique for treating PWS. This method combines the optical contrast selectivity of photoacoustics and the ultrasound penetration capability, enabling ultrasound energy to be focused on deeper PWS vessels. Preliminary results revealed that the ultrasound was successfully focused on the vasculature, indicating the feasibility of this approach for PWS treatment. However, additional experimental and clinical evaluations are necessary to establish the effectiveness of this innovative technique.[59] As an application mode of PAI, photoacoustic microscopy is capable of providing high-resolution images and capturing information on tissue morphology, function, and molecular characteristics.[60] This promising technology is a novel assay to visualise microvascular structures without invasive manipulation.[49,56] Nevertheless, the utilisation of a narrow-band ultrasound transducer in this technology imposes constraints on the axial resolution and overall imaging capabilities of the system.[61] Furthermore, photoacoustic dermoscopy (PAD) represents an additional application

mode of PAI. This emerging approach offers high-resolution full-thickness imaging, facilitating non-invasive observation of deep skin structures.[56,62] It can delineate intricate anatomical structures spanning from the epidermis to the subcutaneous tissue.[62] This compensates for the limitation of high-frequency skin ultrasound which is unable to interrogate the finer structures beneath the epidermis. Exploring the combination of photoacoustic imaging and high-frequency skin ultrasound for the assessment of PWS holds promise for future investigations and warrants exploration. The potential clinical utility of these imaging techniques lies in their ability to detect skin blood vessels in PWS and accurately display their parameters.[57]

Laser speckle imaging (LSI)

LSI is a technique exhibiting sensitivity towards the motion extent of light scatterers, including red blood cells.[36] It typically utilises a low-intensity near-infrared laser with a low-power and long-wavelength light source to irradiate the skin.[63] Scattering transpires when coherent light, dispersed back from biological tissue, diffracts through the confined aperture of the focusing optics.[64] Moving scatterers cause this scattering pattern to blur and a model is constructed by inversely correlating the degree of blurring, also known as scattering contrast with scatter velocity to detect areas of dynamic perfusion or vascular flow.[64] During PDL treatment, LSI is a straightforward and instantaneous intraoperative monitoring tool that offers a singular value for blood flow. This value has been found to have a strong correlation with the extent of bleaching achieved through laser treatment which can aid clinicians in determining whether immediate additional treatment is necessary for regions displaying sustained perfusion.[65,66] Certain researchers have employed LSI to assess alterations in blood perfusion pre- and post-PDL treatment for PWS. Their findings indicated a decrease in blood perfusion within PWS lesions following the treatment.[67] The LSI system has demonstrated high precision in imaging PWS perfusion and has yielded outstanding outcomes in evaluating changes in tissue perfusion following vascular-targeted photodynamic therapy. This technique offers objective and quantitative data, real-time imaging, and reduced detection times, thereby presenting an efficient assessment approach for PWS treatment.[68] Nevertheless, this methodology presents certain constraints, notably susceptibility to considerable motion artefacts. These limitations could curtail the efficacy of imaging modalities when assessing paediatric patients with PWS.[63,69] Furthermore, there exists a constraint on the maximum depth at which this technology can generate laser speckle contrast information.[70] This may require evaluation of the disease in conjunction with other imaging modalities, such as instruments like high-frequency ultrasound of the skin.

Laser doppler imaging (LDI)

LDI is a widely accepted technique for real-time measurement of microvascular perfusion in biological tissues. This method allows for wide-field imaging of skin perfusion and has been commonly used to evaluate tissue microvascular function.[67,71] Studies have confirmed the utility of LDI in evaluating skin perfusion in PDL-treated PWS patients. LDI has been shown to measure perfusion values of PWS vessels and assess changes in PWS perfusion following continuous laser treatment.[72] A study utilised LDI to track blood perfusion dynamics in PWS during vascular-targeted photodynamic therapy (V-PDT). Initial findings revealed significant changes in blood perfusion during treatment, possibly due to the V-PDT effect and local temperature increase from laser irradiation. However, the authors suggest that further research is needed to clarify the relationship between changes in blood perfusion and the therapeutic response of V-PDT in PWS treatment.[73] Studies utilising both LDI and LSI techniques have compared skin perfusion values in PWS patients undergoing V-PDT, revealing a linear relationship between the values.[74] In a study, researchers substantiated the conventional clinical approach of employing LDI in the context of PDL treatment for PWS. Findings indicated partial reconstitution of blood flow within the capillary malformation of PWS during the interim period between successive treatments. However, it was observed that this restoration was not complete. Moreover, a reduction in the interval between laser sessions demonstrated an enhancement in treatment outcomes.[72] The specific laser treatment interval requires us to design more research and hypotheses to explore. LDI is a well-established clinical technique that utilises the interaction of light and the fluidity of red blood cells to visualise perfusion in the microcirculatory system, providing valuable insights into microcirculation. It is frequently used in clinical practice.[75-77] Undoubtedly, the spatial resolution and reproducibility of this technology are suboptimal. Consequently, there is a compelling need to investigate the utilisation of higher-quality instruments in clinical practice.

Conclusion

Currently, in the evaluation of PWS, the use of dermoscopy can be simple and easy to use to assess the type of vascularisation objectively. The VISIA-CR™ systems are important when identifying erythematous changes with the naked eye is challenging. However, they are unable to detect deep vessels. The RCM, conversely, is characterised by high resolution and high contrast and can assess cutaneous vascular outcomes, blood flow, and flow velocity. However, its capabilities are limited to the upper dermis, limiting the assessment of deep vessels. In contrast, HFUS is an effective tool for measuring the thickness and depth of deep lesions in PWS.

OCT is a fast and accurate way to capture subtle tissue structural changes. Different, more refined examination methods are available to more accurately evaluate the various types of PWS, such as Doppler OCT, D-OCT, and OCTA. These methods provide a better assessment of the vascular information of PWS, help to diagnostically determine the pathological type of PWS, and assist in the selection of the

Table 1: Comparison of the advantages and disadvantages of different non-invasive examination methods for PWS

Methods	Advantage	Disadvantage
Dermoscopy	Easy to operate	Penetration depth is limited
	Assess vessel morphology	
	Predict efficacy	
VISIA-CR™ system	Objectively assess the fading of lesions before and after treatment	Unable to assess deeper structures
	More accurate than naked-eye observation	
	Calculable erythema index to objectively evaluate efficacy	
Reflectance Confocal Microscopy (RCM)	With high resolution and high contrast	When the penetration depth is greater than 150 μm, the imaging quality of port wine stain (PWS) decreases
	Applied in the assessment of skin vascular structure, blood flow, and velocity	Penetration is limited to the upper dermis and cannot assess the deepest vessels
	Wide field of view	Image capture takes long
	Reduce motion artefacts during imaging to optimise treatment parameters	
	The maximum depth that can penetrate human skin is 250–300 μm	
High-Frequency Ultrasound (HFUS)	High resolution	Poor imaging contrast
	The skin and its appendages, subcutaneous tissue, and deep structures can be observed	When ultrasound is below 20 MHz, it has poor ability to identify fine structures below the skin surface
	Measuring the thickness and depth of deep lesions in PWS	Unable to assess fading
	Assess haemodynamics	Ultrasound operators require high levels of precision and proficiency
Optical Coherence Tomography (OCT)	Monitoring cutaneous vasculopathy in situ, in vivo, and in real-time	Penetration depth is poor, about 2 mm
	Accurately measure vessel diameter and depth in PWS	Inability to distinguish PWS vessels from other structures such as cavities or sebaceous glands
Dynamic Optical Coherence Tomography (D-OCT)	Calculation of superficial plexus depth and diameter, as well as density characteristics of surface vessels	Handheld OCT probes are unstable when in contact with skin
	Assessing vascular characteristics of PWS	
Optical Coherence Tomography Angiography (OCTA)	Visualising functional vascular networks within microcirculatory tissue beds	Artefacts may exist
	Imaging blood vessels based on flow properties	Unable to determine the direction of blood flow
Doppler Optical Coherence Tomography (Doppler-OCT)	Show blood flow and differentiate between blood vessels and other structures	Low resolution and sensitivity
	Measure deeper blood flow velocities and locate vessel walls	Small blood vessels as well as deeper vessels cannot be detected
Photoacoustic Imaging (PAI)	Good depth of penetration	Poor axial resolution and imaging capability
	High contrast ratio	
	Fine anatomy from the epidermis to the subcutaneous tissue can be depicted	
Laser Speckle Imaging (LSI)	Assessing changes in perfusion before and after pulsed dye laser (PDL) treatment	Produces significant motion artefacts
	Intraoperative monitoring tools	Maximum depth to generate laser scatter contrast information is limited
	With objective and quantitative data	
	Short detection time	
Laser Doppler Imaging (LDI)	Real-time measurement of microvascular perfusion in biological tissues	Lower spatial resolution and repeatability
	Evaluating changes in PWS Perfusion after sequential laser therapy	
	Visualising perfusion in the microcirculatory system	

optimal clinical treatment plan. In addition, photoacoustic imaging is characterised by high penetration depth and high contrast. These include photoacoustic microscopy and photoacoustic dermoscopy. The former facilitates non-invasive examination of microvascular structures, while the latter can depict fine structures from the epidermis to the subcutaneous layers, thus compensating for the inherent limitations of high-frequency skin ultrasound. PDL treatment

for PWS, LSI, and LDI has proven valuable in monitoring blood perfusion. This review systematically describes the advantages and disadvantages of non-invasive methods for assessing the efficacy of PDL and PDT in port wine stain. These methods can help clinicians assess treatment parameters and endpoints [Table 1].

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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