Chinese Medical Journal®

# Non-invasive detection technology in port-wine stain treatment

**Xue Wang[1], Yangxue Fu[2,3], Yan Liu[2,3], Wenjia Nie[2,3], Xingyu Su[2,3], Xianbiao Zou[4], Rusong Meng[5], Yan Li[2,3], Juan Tao[2,3]**

[1]Department of Dermatology, The First Affiliated Hospital, Medical College of Shihezi University, Shihezi, Xinjiang 832008, China;
[2]Department of Dermatology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (HUST), Wuhan, Hubei 430022, China;
[3]Hubei Engineering Research Center for Skin Repair and Theranostics, Wuhan, Hubei 430022, China;
[4]Department of Dermatology of the Fourth Medical Center of People's Liberation Army General Hospital, Beijing 100048, China;
[5]Department of Dermatology, Specialty Medical Center of the Air Force, People's Liberation Army, Beijing 100142, China.

Port-wine stain (PWS) is a type of disfiguring disease and its molecular pathogenesis remains ambiguous. The current gold standard treatment for PWS is pulsed dye laser (PDL);[1] meanwhile hematoporphyrin monomethyl ether-photodynamic therapy (HMME-PDT) has also been utilized for clinical use for 5 years.[2] Due to the vascular heterogeneity, it is difficult to predict and evaluate its efficacy with naked eyes. Therefore, a technology that is consistent, repeatable, and non-invasive will be required to provide accurate images and quantitative evaluation indicators. In this study, we have reviewed dermoscopy, reflectance confocal microscopy (RCM), high-frequency ultrasound (HFUS), optical coherence tomography (OCT), and laser speckle imaging (LSI), etc. in predicting efficacy, intra-operative monitoring, and objective evaluation of effectiveness of PWS treatment [Figure 1].

PWS can be divided into 3 types under dermoscopy: superficial, deep, and mixed type. Dermoscopy can predict the therapeutic effect of PWS through the detection and distribution of vascular depth. Superficial PWS lesions in dermal papillary layer respond well to PDL and PDT; while deep PWS lesions in deep dermis respond poorly [Supplementary Table 1, http://links.lww.com/CM9/B23].[3,4] Different and single features of blood vessels that are observed under dermoscopy can also predict the therapeutic effect: dotted and globular vessels, short clubbed vessels, and curved vessels correspond with excellent curative effects to HMME-PDT, pale halos surrounding brown dots and arborizing vessels correspond with moderate efficacy, and mixed vessels, a grayish-white veil and reticular patterns correspond with poor curative effect.[5] Red dotted and globular vessels have greater responses compared to curved vessels and grayish-white veil when they respond to laser treatment.[6]

There are various dermoscopic features of patients with PWS that may correlate with age, sub-type, location, previous treatment history, and PDL resistance.[7]

RCM can predict and evaluate the lesions of PDL laser-resistant before treatment. PWS lesions with higher blood flow, larger diameters, and deeper location tend to have poorer responses in PDL treatment.[8]

Moreover, HFUS can indicate the effectiveness of PDT through detecting skin thickness and blood flow signals of different types of PWS. The nodular PWS with thicker lesion (3.98 ± 2.20 mm) and lower dermal echo have poorer response to PDT.[9]

LSI can perform intra-operative monitoring through detecting blood perfusion values. The blood perfusion value reached the maximum threshold (1537 ± 982 PU) within 10 minutes during PDT and dropped to 780 ± 591 PU at the end of the treatment. If persistent blood perfusions persist after treatment, PWS lesions are required to be re-treated immediately.[10] LSI can be used as a simple intra-operative monitoring tool in laser treatment and PDT operation, however, a stable and controlled ambient temperature is required.

Apart from this, OCT can show the overall organizational structure and the changes of blood flow velocity in order to create PWS vascular structure images and provide guidance for PDT.[11] The dynamic monitoring of blood flow changes with high sensitivity and fast semiquantitative real-time feedback can potentially optimize personalized laser treatment for each PWS patient.[12]

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000002124

Xue Wang and Yangxue Fu contributed equally to this work.

**Correspondence to:** Yan Li, Department of Dermatology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (HUST), Wuhan, Hubei 430022, China
E-Mail: littleagong@163.com



Chinese Medical Journal 2022;135(21)

**Received:** 25-10-2021; **Online:** 20-10-2022 **Edited by:** Lishao Guo

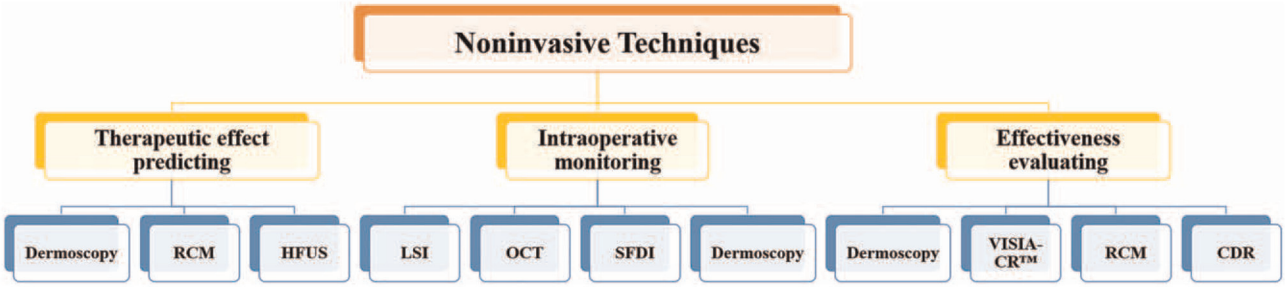


**Figure 1:** A summary of the full text. CDR: Cross-polarized diffuse reflectance imaging system; HFUS: High-frequency ultrasound; LSI: Laser speckle imaging; OCT: optical coherence tomography; RCM: Reflectance confocal microscopy; SFDI: Spatial frequency domain imaging.

Furthermore, spatial frequency domain imaging can capture the tiny damaged blood vessels that cause acute hypoxia. It can analyze the changes of biochemical composition from each skin lesion, which may provide the basis for individualized treatment.

PWS lesions that are observed under dermoscopy have shown white areas (vessel wall structure disappeared) and purpura reaction immediately after PDL treatment, which indicated a good therapeutic endpoint, efficacy, and also avoided the occurrence of adverse reactions that are caused by higher laser energy.[13]

Dermoscopy can evaluate the efficacy of different types of PWS after PDL treatment. For the pink type, there was a decrease in vascular density after treatment (1 and 4 weeks), and the red spot gradually disappeared while a light brown spot has formed after 8 weeks. For the purple type, the globular and dotted vessels decreased first (1 week and 4 weeks), and the remaining light brown patches were observed after 8 weeks. For the thickened PWS type, only gradual changes in colors could be observed (8 weeks).[14]

VISIA-CR$^{TM}$ system can capture standard images, which objectively reflect the degree of erythema regression. The declined erythema index value was related to the efficacy score. It is suitable for facial lesions but has certain limitations for limbs and trunk.

RCM can assess the average blood vessel density and diameter of blood vessels by PDL before and after PWS treatment, which also corresponds to the degree of erythema bleaching.[15]

Cross-polarized diffuse reflectance imaging system included L*a*b* color spaces where a* represents color saturation, which is a determinant of erythema in PWS. A higher a* value indicates profound erythema, and reduction in the a$^{*}$ value post-treatment is an indicator of treatment efficacy.[16]

In summary, the non-invasive skin examination techniques can be widely used in the prediction of therapeutic effects, assessment of effectiveness, and intra-operative monitoring. By means of detecting vascular depth, single features, blood perfusion, and other characters, these non-invasive techniques can reflect the efficacy of PDL and PDT on PWS lesions. This further assists dermatologists with the development of further reasonable strategies and parameters. These techniques will also become excellent methods for achieving greater outcomes for personalized treatment. However, each technique has its own limitations [Supplementary Table 2, http://links.lww.com/CM9/B23] and will need to be utilized in combination with specific clinical outcomes.

## Funding

This work was supported by grants from the National Natural Science Foundation of China (No. 82071844) and PhD Fund (No. BS202111) of the First Affiliated Hospital, Medical College of Shihezi University.

## Conflicts of interest

None.

## References

1. Huikeshoven M, Koster PH, de Borgie CAJM, Beek JF, van Gemert MJC, van der Horst CMAM. Redarkening of port-wine stains 10 years after pulsed-dye-laser treatment. N Engl J Med 2007;356:1235–1240. doi: 10.1056/NEJMoa064329.
2. Zhao Y, Zhou Z, Zhou G, Tu P, Zheng Q, Tao J, *et al*. Efficacy and safety of hemoporfin in photodynamic therapy for port-wine stain: a multicenter and open-labeled phase IIa study. Photodermatol Photoimmunol Photomed 2011;27:17–23. doi: 10.1111/j.1600-0781.2010.00555.x.
3. Li Y, Wang X, Liu Y, Tao J. Dermoscopy predicts outcome in hemoporfin mediated photodynamic therapy of port wine stains: a prospective observational study. J Am Acad Dermatol 2020;83:1765–1767. doi: 10.1016/j.jaad.2020.03.063.
4. Vazquez-Lopez F, Coto-Segura P, Fueyo-Casado A, Perez-Oliva N. Dermoscopy of port-wine stains. Arch Dermatol 2007;143:962. doi: 10.1001/archderm.143.7.962.
5. Wang X, Suo H, Gao Y, Du H, Fu Y, Sha S, *et al*. Correlation between the hemoporfin-mediated photodynamic treatment response and the dermoscopy vascular pattern in patients with a port-wine stain: a prospective study. J Eur Acad Dermatol Venereol 2020;34:2795–2801. doi: 10.1111/jdv.16596.
6. Kwiek B, Rozalski M, Sieczych J, Paluch L, Kowalewski C, Ambroziak M. Predictive value of dermoscopy for the treatment of port-wine stains with large spot 532 nm laser. Lasers Surg Med 2019;51:569–583. doi: 10.1002/lsm.23083.
7. Huang Y, Yang J, Li Z, Zhang L, Sun L, Bi M, *et al*. Dermoscopic features of port-wine stains: a study of 264 cases. Australas J Dermatol 2021;62:e201–e206. doi: 10.1111/ajd.13470.

8. Fu Z, Huang J, Xiang Y, Huang J, Tang Z, Chen J, *et al*. Characterization of laser-resistant port wine stain blood vessels using in vivo reflectance confocal microscopy. Lasers Surg Med 2019;51:841–849. doi: 10.1002/lsm.23134.
9. Tang Y, Cheng S, Tang X, Guo R, Zhang L, Qiu L. Quantification of skin lesions using high-frequency ultrasound and shear wave elastography in port-wine stain patients: a clinical study. Ann Transl Med 2019;7:803. doi: 10.21037/atm.2019.12.57.
10. Qiu H, Zhou Y, Gu Y, Ang Q, Zhao S, Wang Y, *et al*. Monitoring microcirculation changes in port wine stains during vascular targeted photodynamic therapy by laser speckle imaging. Photochem Photobiol 2012;88:978–984. doi: 10.1111/j.1751-1097.2012.01153.x.
11. Zhao Y, Chen Z, Saxer C, Shen Q, Xiang S, de Boer JF, *et al*. Doppler standard deviation imaging for clinical monitoring of in vivo human skin blood flow. Opt Lett 2000;25:1358–1360. doi: 10.1364/ol.25.001358.
12. Waibel JS, Holmes J, Rudnick A, Woods D, Kelly KM. Angiographic optical coherence tomography imaging of hemangiomas and port wine birthmarks. Lasers Surg Med 2018;50:718–726. doi: 10.1002/lsm.22816.
13. Latif AAA, Abdel-Hameed AKS, Salama OAAM. Immediate postirradiation dermoscopic vascular changes versus purpura as a therapeutic endpoint in pulsed-dye laser treatment of port wine stains. Dermatol Ther 2019;32:e13094. doi: 10.1111/dth.13094.
14. Li DC, Nong X, Hu ZY, Fang TW, Zhao TT, Sun SH, *et al*. Efficacy and related factors analysis in HMME-PDT in the treatment of port wine stains. Photodiagnosis Photodyn Ther 2020;29:101649. doi: 10.1016/j.pdpdt.2020.101649.
15. Ren J, Qian H, Xiang L, Pan Z, Zhong L, Yan S, *et al*. The assessment of pulsed dye laser treatment of port-wine stains with reflectance confocal microscopy. J Cosmet Laser Ther 2014;16:21–25. doi: 10.3109/14764172.2013.862552.
16. Jung B, Choi B, Durkin AJ, Kelly KM, Nelson JS. Characterization of port wine stain skin erythema and melanin content using cross-polarized diffuse reflectance imaging. Lasers Surg Med 2004;34:174–181. doi: 10.1002/lsm.10242.

**How to cite this article:** Wang X, Fu Y, Liu Y, Nie W, Su X, Zou X, Meng R, Li Y, Tao J. Non-invasive detection technology in port-wine stain treatment. Chin Med J 2022;135:2535–2537. doi: 10.1097/CM9.0000000000002124