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# Monitoring laser treatment of port wine stains using phase-resolved optical Doppler tomography

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## ABSTRACT

We used a novel phase-resolved optical Doppler tomographic (ODT) technique, with very high flow velocity sensitivity (10  $\mu\text{m/s}$ ) and high spatial resolution (10  $\mu\text{m}$ ), to image blood flow in port wine stain (PWS) birthmarks in human skin. The variance of blood flow velocity is used to locate the PWS vessels in addition to the regular ODT images. Our device combines an ODT system and laser so that PWS blood flow can be monitored *in situ* before and after treatment. To our knowledge, this is the first clinical application of ODT to provide a fast semi-quantitative evaluation of the efficacy of PWS laser therapy *in situ* and in real-time.

**Keywords:** ODT, OCT, Hilbert transform, Phase-resolved ODT, PWS, Laser therapy

## 1. INTRODUCTION

Numerous methodologies have been investigated in search of the ideal blood flow imaging technique for human skin, including fluorescein injection, isotopic clearance, angiography and angiography, electromagnetic flowmetry, interstitial fluid pressure, transcutaneous  $\text{pO}_2$ , reflective photoplethysmography, dermofluorometry, magnetic resonance imaging, and temperature probes. Inasmuch as all of these methods have shown but limited utility for imaging human skin, more recent approaches have incorporated the Doppler effect.

Optical Doppler Tomography (ODT) [1-3] combines Doppler velocimetry with optical coherence tomography (OCT) to measure blood flow velocity at discrete user-specified locations in highly scattering biological tissues. The exceptionally high spatial resolution of ODT allows noninvasive imaging of both *in vivo* blood microcirculation and tissue structures surrounding the vessels. We have recently developed a novel phase-resolved OCT/ODT system that uses phase information derived from a Hilbert transformation to image blood flow in human skin with fast-scanning speed and high velocity sensitivity [4]. Our phase-resolved system decouples spatial resolution and velocity sensitivity in flow images and increases imaging speed by more than two orders of magnitude without compromising spatial resolution and velocity sensitivity. The minimum blood flow velocity that can be detected in human skin is as low as 10  $\mu\text{m/s}$  while maintaining a spatial resolution of 10  $\mu\text{m}$ . The noninvasive nature and high spatial resolution of ODT should have many applications in the clinical management of patients in whom imaging blood flow in human skin is required.

Port wine stain (PWS) is a congenital, progressive vascular malformation of capillaries in the dermis of human skin [5]. Histopathological studies of PWS show an abnormal plexus of layers of dilated blood vessels located 150-750  $\mu\text{m}$  below the skin surface in the upper dermis, having diameters varying on an individual patient basis, and even from site to site on the same patient, over a range of 10-150  $\mu\text{m}$ . The pulsed dye laser can coagulate selectively PWS by inducing microthrombus formation within the targeted blood vessels [6]. In preliminary studies conducted on PWS patients, the feasibility and potential

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application of ODT to characterize and image blood flow with high spatial resolution at discrete user-specified locations in highly scattering human skin has been demonstrated.

## 2. ODT SYSTEM FOR IMAGING PWS

The optical device is based on the phase-resolved ODT system that is shown in Fig. 1. Low-coherence light generated by amplified spontaneous emission (ASE) of a 1300 nm diode is coupled into the source arm of a fiber-based Michelson interferometer. The output power of the light source is 5 mW with a bandwidth of 65 nm after polarization. In the reference arm, a rapid-scanning optical delay line (RSOD) is used for axis scanning. The RSOD [7] employs a grating to control the phase- and group-delays separately and is aligned such that no phase modulation is generated when the group-delay is scanned. Alternatively, a fiber-based electro-optic phase modulator (EOM) is inserted in the reference arm to produce a stable carrier frequency. The interferometric fringes in the detector arm are received by a fast photodiode with a preamplifier and then digitized by an A/D converter in a computer. A digital delay generator (DDG) is used to synchronize the EOM, A/D converter and A-scan controller. There are several modules inside the computer to process the signal. First, the digitized fringe  $F_{i,j}$ , where  $i$  and  $j$  denote discrete axial and lateral coordinates, respectively, is passed through the digital bandpass filter to increase the signal to noise ratio (SNR). Second,  $F_{i,j}$  is transformed to a complex function  $Z_{i,j}$  by adding the imaginary part  $\tilde{F}_{i,j}$ , which is the Hilbert transform of  $F_{i,j}$ . Third, the phase difference between  $Z_{i,j}$  and  $Z_{i,j-1}$ , caused by the Doppler effect, is calculated in a complex plane. Finally, the two-dimensional structural and velocity images are shown on a computer monitor.

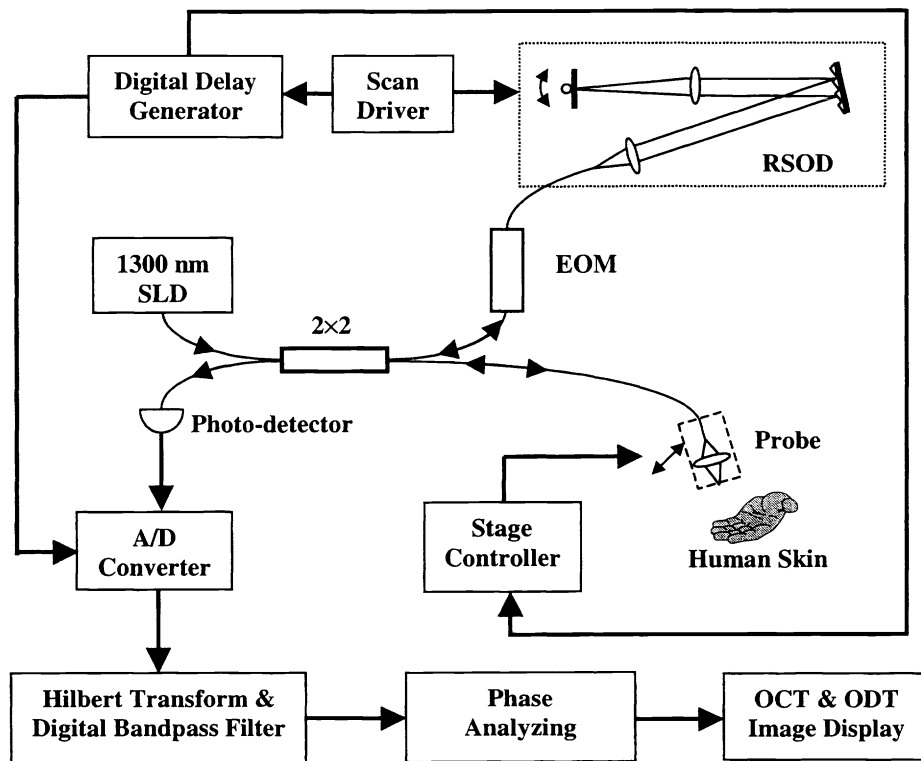


Fig. 1 Schematic of phase-resolved ODT system.

To obtain two-dimensional structural and blood flow velocity images of PWS, an optical fiber focuser is mounted on a voice-coil translation stage in the sampling arm of the interferometer for lateral scanning. The probing beam has a diameter of approximately 10  $\mu\text{m}$  and is oriented at a small angle (5-10 degrees) with respect to the skin surface normal. We chose such an angle so that the system is sensitive enough to detect the Doppler frequency shift produced by blood flow parallel to the skin surface. Furthermore, a small angle helps to increase the optical penetration depth of the ODT system. The RSOD (for A-scan) is operated at 1000 Hz and the voice-coil stage (for L-scan) is driven linearly such that  $n$  A-scans are completed along a line of 10  $\mu\text{m}$ . The phase shift ( $\Delta\phi$ ) between subsequent A-scans can be precisely calculated after averaging 20 A-scans using the following equation:

$$\Delta\phi = \tan^{-1} \left( \frac{\text{Im} \left( \sum_{j=1}^n Z_{i,j} \cdot Z_{i,j+1}^* \right)}{\text{Re} \left( \sum_{j=1}^n Z_{i,j} \cdot Z_{i,j+1}^* \right)} \right) \quad (1)$$

When  $n > 4$ , the sensitivity and SNR in the ODT images is improved dramatically. Moreover, speckle noise in the ODT image, which is characteristic of turbid tissues, is significantly reduced.

Cross-sectional structural and velocity images of a PWS located on the left upper extremity of a human volunteer, obtained by our system are shown in Figure 2. The scanning range is 2 mm (lateral) by 2 mm (axial) but only the linear part (1.25 mm) of the axial scan is shown in the images. The image size is 800 (lateral) by 500 (axial) pixels with a size of 2.5  $\mu\text{m}/\text{pixel}$ , which keeps the image resolution consistent with the coherence length of light source (10  $\mu\text{m}$ ). To prevent surface movement, the area imaged was in tight contact with a glass window and index-matching oil was inserted between the glass and PWS to decrease light reflection from the skin surface. The index-matching oil also helped to flatten the skin surface so that the wavefront distortion of the probing beam at the skin surface is minimized. Figures 2A (structural image), 2B (velocity image) and 2C (variance image) are taken from the palmar surface of the ring finger. In addition to an organized network of collagen fibers in the dermis, the epidermal-dermal boundary is clearly noted in the structural images (Figures 2A). Many PWS vessels in the dermis 400  $\mu\text{m}$  to 1 mm below the skin surface are imaged in Figures 2B.

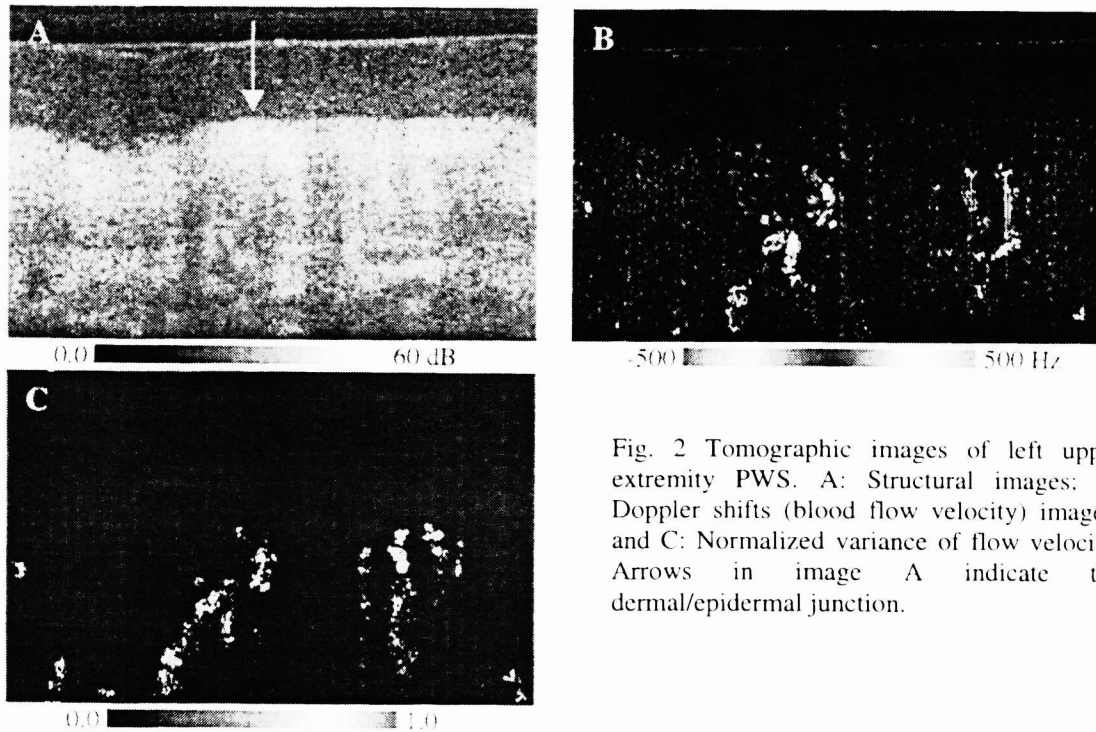


Fig. 2 Tomographic images of left upper extremity PWS. A: Structural images; B: Doppler shifts (blood flow velocity) images; and C: Normalized variance of flow velocity. Arrows in image A indicate the dermal/epidermal junction.

In addition to direction and mean velocity, flow turbulence, which is represented by the variance of the velocity distribution, is shown as a two-dimensional images in Figures 2C. Denoting the standard deviation of the Doppler frequency shift with  $\sigma$ , the variance  $\sigma^2$  can be obtained by the following:

$$\sigma^2 = \frac{1}{T^2} \left( 1 - \frac{\sum_{j=1}^n Z_{i,j} \cdot Z_{i,j+1}^*}{\sum_{j=1}^n Z_{i,j} \cdot Z_{i,j}^*} \right) \quad (2)$$

where  $T$  is the time interval between sequential A-scans (0.001 second). As noted in Figures 2C, it is much easier to identify the PWS blood vessels in the variance images as opposed to the velocity images (Figures 2B). We believe this can be attributed to the pulsative nature of blood flow. Given the fact that blood flow turbulence is only determined by the physical characteristics of blood and vessel structure, determining the variance provides a much more accurate representation of total blood flow within human skin.

### 3. COMBINATION OF ODT AND LASER THERAPY SYSTEM

In order to monitor the efficacy of PWS laser treatment *in situ*, we constructed another lateral scanning system in the sampling arm of the interferometer, which is shown in Figure 3. Since the optical biopsy area is only 2 mm (width) by 1 mm (depth) with a thickness of 10  $\mu\text{m}$ , it would be very difficult to scan and image the identical site before and after laser treatment using the probe described above. Light coming from the end of the fiber is collimated with an aspheric lens L1 ( $f = 11\text{mm}$ ), and then scanned by a galvanometer which is located at the focusing point of a doublet lens L2 ( $f = 70\text{ mm}$ ) and in telescope configuration with another doublet lens L3 ( $f = 50\text{ mm}$ ). In this configuration, the beam is still collimated and can be angle-scanned by the galvanometer. An aspheric lens L4 ( $f = 8\text{ mm}$ ) is then used to focus the beam into the skin with a spot diameter of 10  $\mu\text{m}$ . Different scanning-angles of the galvanometer produce different focus positions in the lateral direction. A dichromatic 45-degree reflecting mirror M1, which is highly reflective at 1300 nm and highly transmissive at 595 nm, is inserted between lenses L2 and L3. The therapeutic laser beam is passed through mirror M1, lenses L3 and L4, and then irradiated the PWS skin. Because lenses L3 and L4 are also in telescope configuration, the therapeutic laser beam is not focused into the skin but has a constant spot size of 3.5 mm. This is important because the laser energy density must be controlled such that only the targeted PWS blood vessels are destroyed while sparing adjacent skin structures. The laser used for PWS treatment is a ScleroPlus<sup>®</sup> pulsed dye laser (Candela Laser Corp, Wayland, MA) with a wavelength of 595 nm and pulsed width of 1.5 ms.

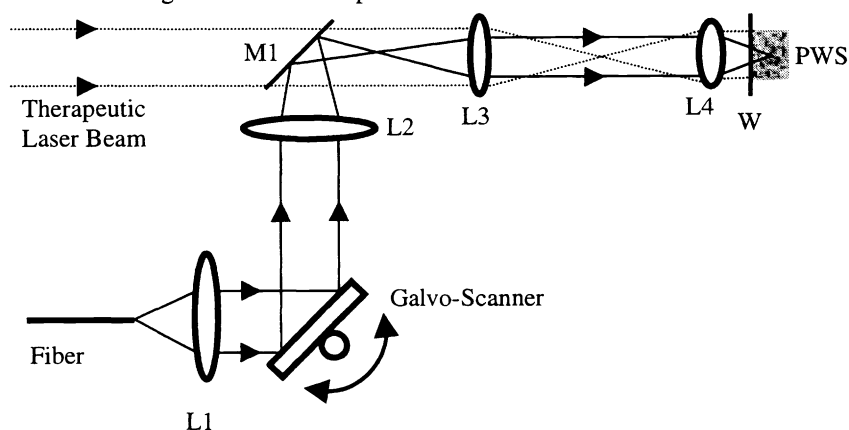


Fig. 3 Optical scanning probe for monitoring PWS laser treatment. L1, L2, L3, L4: lenses; M1: dichromatic mirror; W: glass window; PWS: PWS skin.

The treatment results shown in Figure 4 are in response to a  $12 \text{ J/cm}^2$  therapeutic laser pulse. In the structural images (Figures 4A and 4D), there is no visible difference before and after laser exposure, which implies the adjacent skin structures were not affected by the treatment. In the velocity (Figures 4B and 4E) and variance (Figures 4C and 4F) images, however, no blood flow is noted after laser exposure indicative of irreversible microthrombus formation in the PWS blood vessels. Blood flow did not return to pre-treatment values as determined up to 24 hrs. after laser exposure.

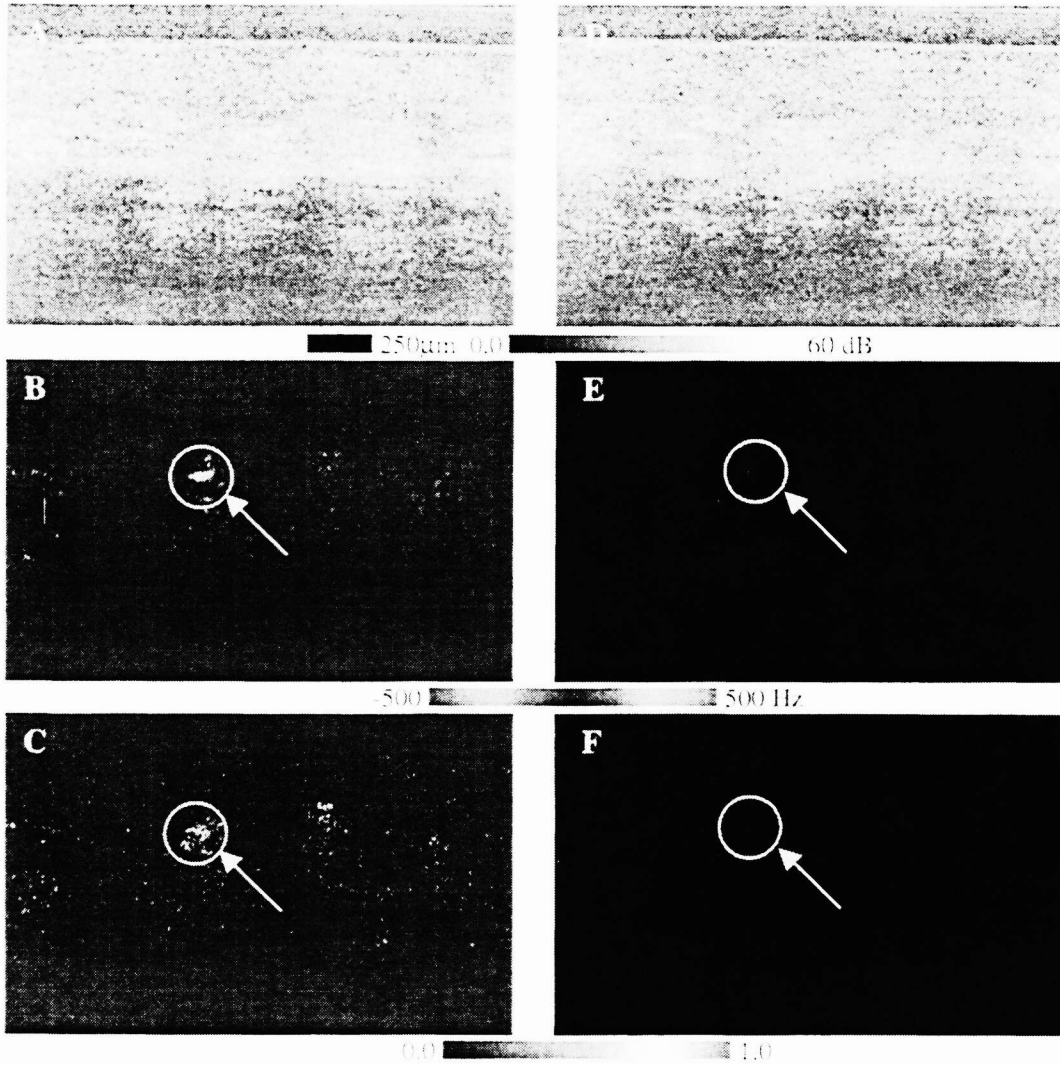


Fig.4 Tomographic images of identical PWS sites before laser (A, B, C) and after (D, E, F) laser treatment. A and D: Structural images; B and E: Doppler shifts (blood flow velocity) images; and C and F: Normalized variance of flow velocity. The vessels area is indicated by circle and arrow in velocity and variance images.

The rationale for using ODT in the clinical management of PWS is that the technique offers a means of providing a fast semi-quantitative evaluation of the efficacy of laser therapy in real-time. If partial restoration of flow occurs immediately or shortly after pulsed laser exposure, indicative of reperfusion due to inadequate blood vessel injury, the PWS can be retreated using higher light dosages. Retreatment is continued until the measured Doppler shift is zero due to a permanent reduction in blood flow, indicative of irreversible microthrombus formation in the PWS vessels.

#### 4. CONCLUSIONS

In summary, we have shown that ODT can be used to image blood flow in human skin and monitor the efficacy of PWS laser treatment *in situ*. ODT will allow laser therapy to be optimized on an individual patient basis by providing a fast semi-quantitative evaluation of the efficacy of PWS laser therapy in real-time. We have also developed a new imaging method, which uses velocity variance to determine the location and shape of blood vessels below the skin surface.

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