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Phase-resolved optical coherence tomography and optical Doppler tomography for imaging blood flow in human skin with fast scanning speed and high velocity sensitivity

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We have developed a novel phase-resolved optical coherence tomography (OCT) and optical Doppler tomography (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. Using the phase change between sequential scans to construct flow-velocity imaging, this technique decouples spatial resolution and velocity sensitivity in flow images and increases imaging speed by more than 2 orders of magnitude without compromising spatial resolution or velocity sensitivity. The minimum flow velocity that can be detected with an axial-line scanning speed of 400 Hz and an average phase change over eight sequential scans is as low as 10 $\mu\text{m/s}$, while a spatial resolution of 10 μm is maintained. Using this technique, we present what are to our knowledge the first phase-resolved OCT/ODT images of blood flow in human skin. © 2000 Optical Society of America

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Optical Doppler tomography (ODT),¹⁻⁴ also termed Doppler optical coherence tomography, is a recently developed optical technique for imaging both the tissue structure and the flow velocity of moving particles in highly scattering media. The noninvasive nature and exceptionally high spatial resolution of ODT have many potential applications in the clinical management of patients in whom imaging tissue structure and monitoring blood-flow dynamics are essential. Examples include burn-depth determination, evaluation of the efficiency of laser treatment of port wine stains, photodynamic therapy monitoring, and brain injury evaluation. We have described an *in vivo* ODT imaging system with high spatial resolution and accurate blood-flow velocity measurements in vessels in rodent skin.^{1,2} However, previously developed ODT systems were unable to achieve simultaneously both high imaging speed and high velocity sensitivity, which are essential for measuring blood flow in human skin.¹⁻⁴ We describe a novel fast-scanning ODT system that uses phase information derived from a Hilbert transformation to increase the sensitivity of flow-velocity measurements while maintaining high spatial resolution. The significant increases in scanning speed and velocity sensitivity made it possible for us to image *in vivo* blood flow in human skin.

ODT combines the Doppler principle with OCT⁵ to yield high-resolution tomographic images of static and moving constituents simultaneously in highly scattering biological tissues. The flow velocity of moving particles in the sample can be determined by measurement of the Doppler shift of the fringe frequency with a short-time Fourier transform. Since detection of the Doppler shift requires sampling the interference fringe intensity over at least one oscillation cycle, the minimum detectable Doppler frequency shift (Δf_D) varies inversely with the short-time Fourier transform window size (Δt_p) at each pixel (i.e., $\Delta f_D \approx 1/\Delta t_p$). For a

given time-window size at each pixel, the velocity sensitivity (ν_{\min}) is given by

$$\nu_{\min} = \frac{\lambda_0}{2n \cos(\theta) \Delta t_p}, \quad (1)$$

where λ_0 is the light-source center wavelength, n is the sample's refractive index, and θ is the angle between the probing beam and the direction of flow. Therefore, the higher the value of Δt_p , the higher the velocity sensitivity. However, spatial resolution, Δx_p , is proportional to the short-time Fourier transform window size and is given by

$$\Delta x_p = V \Delta t_p, \quad (2)$$

where V is the one-dimensional scanning speed of the ODT system. Consequently, velocity sensitivity and spatial resolution are coupled. A large pixel time-window size increases velocity sensitivity while decreasing spatial resolution. Increasing the image frame rate also decreases velocity sensitivity. For example, for a rate of one frame per second for an image with 100×100 pixels, the maximum data-acquisition time for each pixel (Δt_p) is 1/10,000 s. Accordingly, the minimum resolvable Doppler frequency shift is 10 kHz, which corresponds to a velocity sensitivity of approximately 25 mm/s for $\lambda_0 = 1300$ nm and $\theta = 80^\circ$. To measure blood flow in small vessels in which red blood cells are moving at low velocity, one must reduce the imaging frame rate if the spectrogram method is used. When ODT goes to real-time imaging, the time for each axial scan (A scan) is very short. As a result, the velocity sensitivity decreases dramatically, because the window time for each pixel is so short that a fast Fourier transform algorithm can detect any large Doppler frequency shift.

To overcome these limitations we developed a method that uses the phase change between sequential

line scans for velocity image reconstruction. The ODT signal phase can be determined from the complex function, $\Gamma_{\text{ODT}}(t)$, which is determined through analytic continuation of the measured interference fringes function, $\Gamma_{\text{ODT}}(t)$, by use of a Hilbert transformation⁶:

$$\begin{aligned} \tilde{\Gamma}_{\text{ODT}}(t) &= \Gamma_{\text{ODT}}(t) + \frac{i}{\pi} P \int_{-\infty}^{\infty} \frac{\Gamma_{\text{ODT}}(\tau)}{\tau - t} d\tau \\ &= A(t) \exp[i\phi(t)], \end{aligned} \quad (3)$$

where P denotes the Cauchy principle value and $A(t)$ and $\phi(t)$ are the amplitude and the phase of $\tilde{\Gamma}_{\text{ODT}}(t)$, respectively. The phase change in each pixel between sequential A-line scans is then used to calculate the Doppler frequency shift:

$$\omega = \Delta\phi/T, \quad (4)$$

where T is the time interval between successive A scans. Because T is much longer than the pixel time window, very small Doppler shifts can be detected with this technique. For example, in an OCT/ODT image with 100×100 pixels, if the data-acquisition time at each pixel is $100 \mu\text{s}$, using the phase difference between sequential A-line scans increases the time window from $100 \mu\text{s}$ to $100 \times 100 \mu\text{s} = 10 \text{ ms}$. Therefore, the frequency resolution improves from 10 kHz to 100 Hz, and the velocity sensitivity improves from 3 mm/s to $30 \mu\text{m/s}$. In addition, spatial resolution and velocity sensitivity are decoupled. Furthermore, because two sequential A-line scans are compared at the same location, speckle modulations in the fringe signal cancel each other and, therefore, will not affect the phase-difference calculation. Consequently, the phase-resolved method reduces speckle noise in the velocity image. Finally, if the phase difference between sequential frames is used, then the velocity sensitivity can be increased further.

A schematic of the optical device and signal-processing algorithm is shown in Fig. 1. The light source for the interferometer is a broadband $1.3\text{-}\mu\text{m}$ superluminescent diode from AFC, Inc. (Quebec, Canada). The polarized output power is 5 mW, with a bandwidth of 65 nm. In the reference arm a rapid-scanning optical delay line is used that employs a grating to control the phase and the group delays separately⁷ so that no phase modulation is generated when the group delay is scanned. The phase modulation is generated through an electro-optic phase modulator that produces a stable carrier frequency. A digital delay generator from Stanford Research Systems (Stanford, California) is used to synchronize the electro-optic phase modulator, an analog-digital converter, and an A-scan controller. We then process the digitized fringe signal with a computer to generate both structural and Doppler images from complex analytic continuation of the interference fringes.

The optical probe in the sampling arm consists of a gradient-index lens (N.A., 0.2) that is placed so that light from the end of the fiber is focused into the sample with a beam size of approximately $10 \mu\text{m}$. The prob-

ing beam is aligned at a small angle ($5^\circ\text{--}10^\circ$) with respect to the tissue surface normal so that blood flow parallel to the surface can produce a Doppler frequency shift. Mounting the probe upon a voice-coil translation stage (PI, Inc., Waldbronn, Germany) generates a stepped lateral scan for tomographic imaging. At each step in the lateral scan, we record eight A-line scans at a speed of 400 Hz to increase the signal/noise ratio in the velocity image. The time for acquiring an image with 100×100 pixels is 2 s. The Doppler frequency shift is determined by calculation of the average phase shift between sequential A-line scans.

To demonstrate the ability of phase-resolved ODT to image *in vivo* blood flow we imaged subsurface microcirculation in human skin. Figure 2 shows images obtained from the ring finger of a human volunteer. Cross-sectional structural (Fig. 2A) and velocity (Fig. 2B) images are obtained simultaneously. The image size is 200 (lateral) by 200 (axial) pixels, with a size of $10 \mu\text{m}/\text{pixel}$. The rapid-scanning optical delay scanning rate is 400 Hz, and the electro-optic phase modulator's modulation frequency is 800 kHz. The sampling rate of the analog-digital converter is 5 MHz, and the number of data points for each A scan is 4069, for convenient Hilbert transformation. To prevent surface movement we place the image area in tight contact with a glass window. We insert index-matching oil between the glass and the skin to decrease the light reflection from the skin surface. The velocity image is color coded, where red represents blood flow moving toward the probe (positive Doppler shift) and blue represents flow in the opposite direction. Pixel intensity represents the absolute velocity. No blood vessels are observed in the structural OCT image (Fig. 2A). One large vein (diameter $60 \mu\text{m}$) with positive blood-flow velocity (red coded) is indicated by arrow 1 in Fig. 2B. Several smaller vessels (diameter $10\text{--}30 \mu\text{m}$) can be detected at a depth of

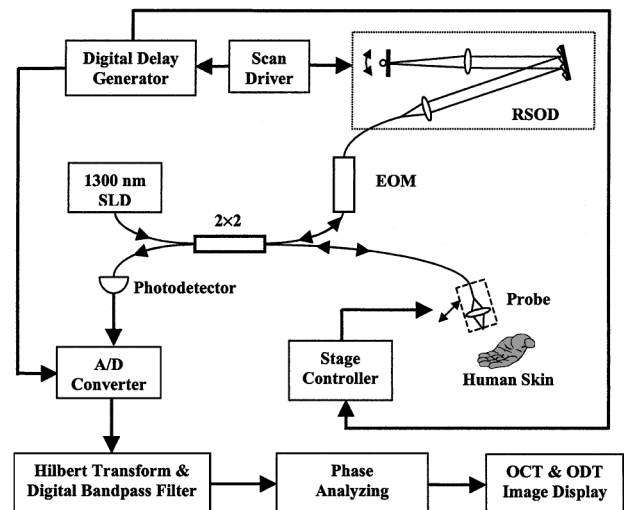


Fig. 1. Schematic of the optical device and signal-processing algorithm for ODT imaging. RSOD, rapid-scanning optical delay line; EOM, fiber-pigtailed electro-optic modulator; SLD, superluminescent diode; A/D, analog-digital. The probe is mounted upon a stage for lateral scanning.

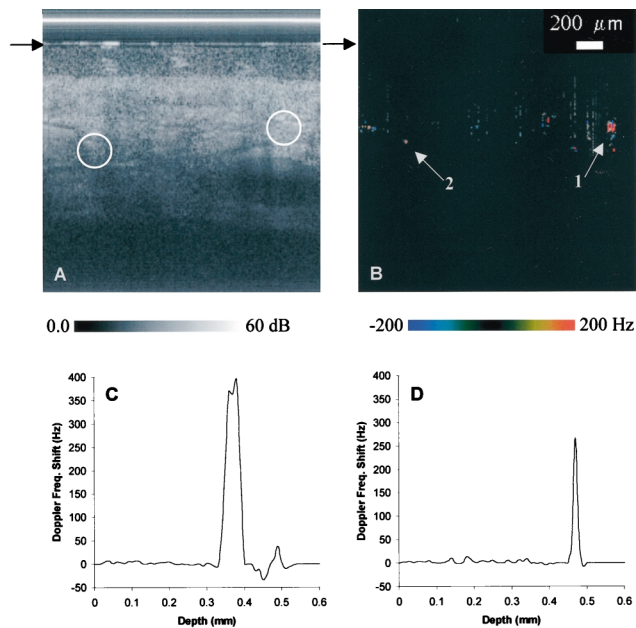


Fig. 2. ODT blood-flow images and velocity profile from human skin (finger). A, gray-scale structural image; B, color-coded velocity image of blood flow; C, Doppler frequency shifts (velocity profile) along a vertical cross section passing through the largest vein in the velocity image (indicated by arrow 1 in B); D, Doppler frequency shifts of a 20- μm capillary (indicated by arrow 2 in B).

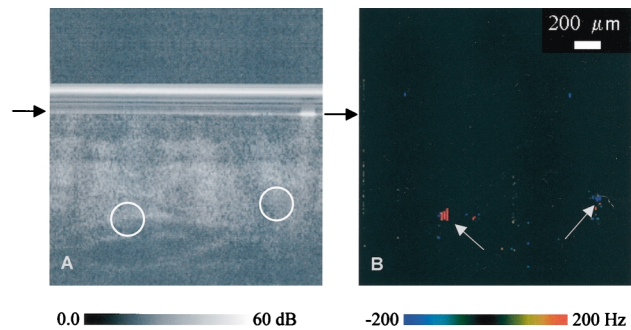


Fig. 3. OCT/ODT images of blood flow in human skin (hand palm). A, gray-scale structural image; B, color-coded velocity image of blood flow.

300 to 600 μm . The velocity profile in the axial direction in the center of the vein indicated by arrow 1 in Fig. 2B, is shown in Fig. 2C. The measured Doppler frequency shift in the center of the vein is 400 Hz, which corresponds to a blood-flow velocity of approximately 3.0 mm/s and is in close agreement with known values,⁸ assuming that the angle between the direction of blood flow and the optical probe is 85°. The background noise in the velocity image is very small, and velocity sensitivity of the order of 10 $\mu\text{m/s}$ was achieved in previous experiments with an *in vitro* tube model. It is important to note that the background noise in some pixels under the large vein is much higher than normal, because when light passes through a vessel containing moving particles (red blood cells), some forward scattering will also introduce a Doppler frequency shift. Since forward scattering does not change the optical path length and the

Doppler shift is unpredictable, this effect appears as shadowing in the velocity image. We believe the small red and blue dots in the velocity image (Fig. 2B) to be capillaries, because similar structures are observed at exactly the same position in repetitive scans. The velocity profile (Fig. 2D) from one capillary, indicated by arrow 2 in Fig. 2B, shows that the vessel diameter is approximately 20 μm , which we believe is the smallest vessel ever imaged by ODT.

OCT and ODT images of blood flow taken from the palm of the hand of a human volunteer are shown in Fig. 3. Two large vessels with blood flow in opposite directions (red and blue) can be seen approximately 1.0 mm below the surface, indicating that phase-resolved OCT/ODT can image blood flow from relatively deep vessels in highly scattering human skin.

In summary, we have demonstrated a novel fast-scanning phase-resolved OCT/ODT system that can measure blood flow in human skin with high velocity sensitivity. The phase-resolved technique decouples spatial resolution and velocity sensitivity in flow images and increases imaging speed by more than 2 orders of magnitude without compromising either spatial resolution or velocity sensitivity. The minimum flow velocity that can be detected with an A-line scanning speed of 400 Hz is as low as 10 $\mu\text{m/s}$, while a spatial resolution of 10 μm is maintained. Finally, we have presented what we believe to be the first phase-resolved OCT/ODT images of blood flow in human skin.

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