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Phase Resolved Optical Coherence Tomography And Optical Doppler Tomography: Technology And Applications

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Abstract — A novel phase resolved optical coherence tomographic (OCT) and optical Doppler tomographic (ODT) system is developed for simultaneous imaging of tissue structure and physiology with high imaging speed and high spatial resolution.

Index Terms — Optical coherence tomography, optical Doppler tomography, biomedical imaging

I. INTRODUCTION

Direct visualization of tissue anatomy and physiology provides important information to the physician for diagnosis and management of disease. High spatial resolution noninvasive techniques for imaging *in vivo* tissue structure and blood flow dynamics are currently not available as a diagnostic tool in clinical medicine. Such techniques could have a significant impact on biomedical research and clinical medicine.

Optical coherence tomography and optical Doppler tomography is a newly developed tomographic imaging modality that combines Doppler velocimetry with coherent gating of the partial coherence source to imaging *in vivo* tissue structure and blood flow velocity with high spatial resolution (2-10 μm) and high velocity sensitivity (10 $\mu\text{m/s}$) [1-6]. The technology is similar to ultrasound and Doppler ultrasound. However, it uses near infrared optical waves instead of sound waves and it has the advantage of non-contact and high spatial resolution. The exceptionally high spatial resolution of phase resolved OCT/ODT allows *in vivo* "optical biopsy" of tissue structure and physiology for tumor diagnosis. The noninvasive nature of this technique has many applications in the clinical management of patients in whom imaging tissue structure and monitoring blood flow dynamics is essential. Applications of this technique to imaging changes in tissue structure and hemodynamics following pharmacological intervention and photodynamic therapy, screening vasoactive drug, evaluating efficacy of laser treatment of port wine stain patient, and mapping cortical hemodynamics for brain research has been demonstrated. However, previously developed OCT/ODT systems were unable to achieve simultaneously both high imaging speed and high velocity sensitivity, which are essential for measuring blood flow in clinical applications [2, 3, 6].

In this report, we describe a novel phase resolved OCT/ODT system that uses phase information derived from a Hilbert transformation to image tissue structure and blood flow with fast-scanning speed and high velocity sensitivity.

Using 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 two orders of magnitude without compromising spatial resolution and velocity sensitivity. The minimum flow velocity that can be detected using an A-line scanning speed of 1 kHz is as low as 10 $\mu\text{m/s}$ while maintaining a spatial resolution of 10 μm . The significant increases in scanning speed and velocity sensitivity made it possible for us to image *in vivo* blood flow in both normal and port wine stain human skin.

In addition to the regular structure and flow velocity images, the variance of blood flow velocity is used to map location and size of the microvasculature. This method has the advantage that it is less sensitive to the pulsatile nature of blood flow and does not depend on the flow direction. It provides better mapping of vessel size and location that are important for many clinical conditions. Furthermore, this method can also be used to study turbulence and separate Doppler shift due to biological flow from the background motion of the tissue under study.

II. METHODS

The schematic diagram of the phase resolved OCT/ODT system is shown in Figure 1. A broadband 1.3 μm SLD from AFC, Inc. (Quebec, Canada) is used as the light source. Polarization control devices are inserted into the fibers to control the polarization states of the light. A rapid-scanning optical delay (RSOD) line is used for group phase delay or depth scanning. RSOD is based on the principle that a linear phase ramp in the frequency domain produces a delay in the time domain [7]. A grating in the delay line is used to spread the spectrum of the source across a galvanometer-mounted mirror. Tilting the mirror introduces an optical path delay that varies linearly with wavelength. Scanning speeds of a few kHz with a depth range of several mm have been achieved with the RSOD. Because RSOD can uncouple the group delay from the phase delay [7], an electro-optical phase modulator is introduced to produce a stable carrier frequency to improve the accuracy of the velocity measurements.

Fig. 1: Schematic diagram of high resolution, high speed, phase resolved OCT/ODT

Light reflected from the sample is recombined with that from the reference beam in the 2x2 beam coupler to form interference fringes. The fringe signal is detected by photodiode and digitized with A/D converters for image reconstruction.

In conventional OCT, the fringe signal from each A-line scan is used to calculate the Doppler shift of the power spectrum using a short-time Fourier transformation (STFT) algorithm. Because the time window used in STFT is inversely proportional to the A-line scanning speed, the velocity sensitivity is limited by A-line scanning speed. In our phase resolved OCT/ODT, phase change of interference fringe between sequential A-line scans is used to calculate the Doppler frequency shift. Consequently, the 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 digitized fringe signal $\Gamma_j(t)$ is first passed through a digital bandpass filter to increase the signal to noise ratio (SNR). The complex function $\tilde{\Gamma}_j(t)$ is then determined through an analytic continuation using the Hilbert transformation:

$$\tilde{\Gamma}_j(t) = \Gamma_j(t) + \frac{i}{\pi} P \int_{-\infty}^{\infty} \frac{\Gamma_j(\tau)}{\tau - t} d\tau \quad (1)$$

where j denotes j th A-line scan and P denotes the Cauchy principle value. The Doppler frequency shift is determined from the average phase shift between sequential A-scans using the following equation:

$$\Delta f = \frac{1}{2\pi T} \tan^{-1} \left(\frac{\text{Im} \left(\sum_{j=1}^n \tilde{\Gamma}_j \cdot \tilde{\Gamma}_{j+1}^* \right)}{\text{Re} \left(\sum_{j=1}^n \tilde{\Gamma}_j \cdot \tilde{\Gamma}_{j+1}^* \right)} \right) \quad (2)$$

where T is the time interval between sequential scans, and n is the number of sequential scans averaged. To increase the SNR in ODT images, 8 sequential A-line scans are averaged. The standard deviation of the Doppler frequency spectrum, σ , is calculated by the following:

$$\sigma^2 = \frac{\int_{-\infty}^{\infty} (\omega - \bar{\omega})^2 P(\omega) d\omega}{\int_{-\infty}^{\infty} P(\omega) d\omega} = \frac{1}{T^2} \left(1 - \frac{\left| \sum_{j=1}^n \tilde{\Gamma}_j \cdot \tilde{\Gamma}_{j+1}^* \right|^2}{\sum_{j=1}^n \tilde{\Gamma}_j \cdot \tilde{\Gamma}_j^*} \right) \quad (3)$$

where $P(\omega)$ is the Doppler power spectrum and $\bar{\omega}$ is the centroid value of the Doppler frequency shift. σ value depends on the flow velocity distribution. Variations in flow velocity will broaden the Doppler frequency spectrum and result in a larger σ value. Value of σ as a function of spatial location can be used to construct a standard deviation of Doppler frequency spectrum image (σ image), which provide additional information on the characteristics of flow.

Because the time interval (T) between each A-scan is much longer than the pixel time window, very small Doppler shifts can be detected using 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, 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 is 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.

III. RESULTS AND DISCUSSIONS

To demonstrate the ability of phase resolved ODT to image *in vivo* blood flow, we imaged the subsurface microcirculation in human skin. Figure 2 shows the images obtained from the ring finger of a human volunteer. Cross-sectional structural (Fig. 2A), velocity (Fig. 2B), and standard deviation of Doppler frequency spectrum (Fig. 2C) images are obtained simultaneously. In this experiment, the RSOD scanning rate is 400 Hz and the EOM modulation frequency is 800 kHz . The velocity image is color-coded where red represents blood flow moving towards the probe (positive Doppler shift) and blue represents flow in the opposite direction. In the OCT structure image (Fig. 2A), one can clearly see the boundary between the stratum corneum and the epidermis. In the OCT velocity (Fig. 2B) and standard deviation (Fig. 2C) images, many vessels are detected in the dermis between $400 \mu\text{m}$ and 1 mm below the skin surface. As can be seen, it is much easier to identify the blood vessel dimension and location in the σ image (Fig. 2C) as opposed

to the velocity images (Fig. 2B). In many clinical applications, where the dimension and location of the microvasculature is more important than the absolute value of the flow velocity, σ image has the advantage that it is less sensitive to the orientation of the flow direction and pulsatile nature of the blood flow. Vessels as small as $10\ \mu\text{m}$ diameter can be detected.

A typical velocity profile from a small vein in human skin is shown in Fig. 3. 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 assuming that the angle between the direction of blood flow and the optical probe is 85 degrees. The background noise in the velocity image is very small and velocity sensitivity on the order of $10\ \mu\text{m/s}$ can be achieved.

Fig. 3: Doppler frequency shift (Velocity Profile) along a vertical cross section passing through the center of a vein of human skin.

Fig. 2: Phase resolved *in vivo* OCT/ODT images from human skin. A: tomographic structural image; B: velocity image of blood flow; and C: standard deviation of the Doppler frequency spectrum image (σ image).

IV. SUMMARY

In summary, we have demonstrated a novel fast-scanning phase resolved 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 two orders of magnitude without compromising either spatial resolution or velocity sensitivity. The noninvasive nature of phase resolved OCT/ODT has many applications in the clinical management of patients in whom imaging tissue structure and monitoring blood flow dynamics is essential. The exceptionally high velocity sensitivity and high spatial resolution of phase resolved OCT/ODT may allow, for example, imaging and mapping of three-dimensional tumor microvasculature for tumor diagnosis and angiogenesis studies.

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