

Fiber-optics based Optical Coherence Tomography for Biomedical Application

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Abstract

Optical coherence tomography (OCT) is a fast evolving noninvasive imaging technology for biomedicine in recent years. Its fundamental principle is to use a low coherent light on biological sample and collect the backscattering light with an interferometer configuration. It can achieve high spatial resolution of several micrometers and reconstruct two or three-dimensional images with various scanning mechanisms. Based on a fiber-optics based OCT, we implemented an optical delay-line on the reference arm for fast scanning speed and a handheld probe on sampling arm for surface scanning applications. We also reported a simple image compensation scheme, which is based on the distortion profile of scan depth, to enhance the image quality.

Keywords: Optical coherence tomography, Optical phase delay line, Handheld probe, Imaging distortion compensation.

Introduction

Biomedical imaging technology can provide important information to the physician for diagnosis and management of diseases. Although several imaging modalities, such as x-ray computed tomography, magnetic resonance imaging, ultrasound, and radioisotope imaging all have found apparent applications in clinical medicine, they often have limited imaging resolution, especially for cellular level. Thus, there are demands for an imaging modality with higher spatial resolution, noninvasive, safe, inexpensive, compact, and capable of monitoring in real time. It provides the impetus for the intense research activities in biomedical optical imaging.

Optical coherence tomography (OCT) is a fast evolving optical technology that can perform micron-meter scale spatial resolution, cross-sectional imaging of the internal microstructure in materials and biologic tissues [1]. The probing depth can exceed 2 cm in transparent tissues [2], [3]. For nontransparent tissues, e.g. skin and other highly scattering tissues, OCT is limited by reaching depth of few millimeters beneath the surface. However, a number of interesting clinical imaging applications do exist in this range [4]–[10]. Since OCT was first demonstrated in 1991 by Fujimoto [1], it has found many applications in diagnosing diseases in various biological tissues. Studies of ophthalmic OCT have

successfully demonstrated significant potential for routine clinical examinations of the anterior eye, the lens, retina, retinal nerve fiber layer, retinal pigment epithelium, and choroids [11]–[13]. Commercial ophthalmic OCT scanner is also becoming available for the clinical applications. Other applications, such as human skin [4], teeth [5], blood vessels [6], gastrointestinal tracts [7], respiratory tracts [8], genitourinary tracts [9] and cardiovascular [10] are also under development. OCT can be readily adaptable to minimally invasive diagnostic modalities, such as catheterization and endoscope with fiber optic implementation [14]–[16]. OCT image provides sufficient resolution of morphological information relevant to pathological diagnosis without the need for biopsy [16].

Functional images of biological tissue can also be obtained with modification OCT method. Optical Doppler Tomography (ODT) can obtain high-resolution tomography images of static and moving constituents simultaneously in highly scattering biological tissues [6], [17]. Using a Michelson interferometer with a low coherent light source, ODT measures the amplitude and frequency of the interference signal generated by reference and sample arms to reconstruct structural and velocity images of object [17]. Polarization sensitive OCT (PS OCT) has permitted additional information on the polarization properties of tissue carried by the reflected light to be obtained. Many biological tissues have linear or fibrous structure such as tendon, muscle, nerve, bone, cartilage, and teeth, which have birefringence phenomenon. The

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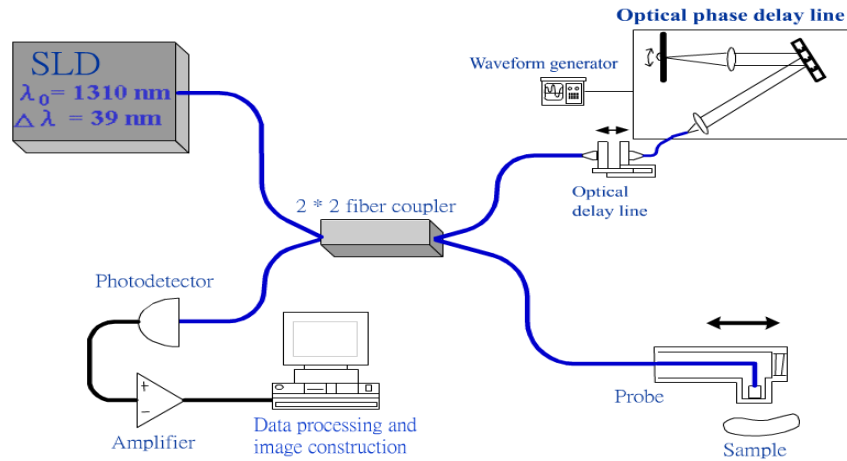


Figure 1. Schematic diagram of the fiber optics based OCT system.

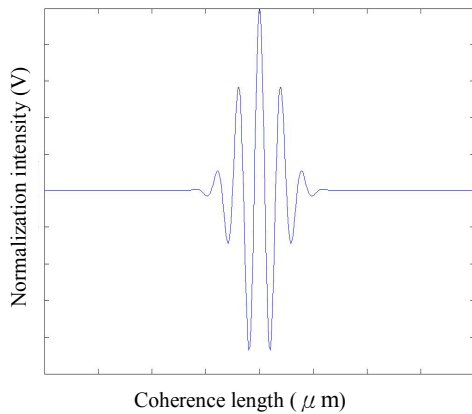


Figure 2. A typical low coherence length interference signal.

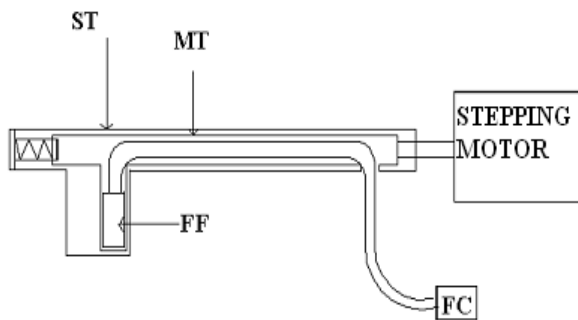


Figure 3. Schematic diagram of the handheld probe setup. ST is stationary case; MT is moving tube; FF is fiber focuser; FC is Fiber connector.

advantages of PS OCT are enhanced contrast and specificity in identifying structures in OCT images by detection of changes induced in the polarization state of light that reflected from the sample [18]. Spectroscopic OCT combines spectroscopic analysis with OCT to yield depth-resolved tissue absorption spectra that can enhance image contrast and provide additional information on tissue inhomogeneity [19].

Materials and Methods

OCT System overview

The setup of fiber-optics based OCT system is shown in Figure 1. Using a Michelson interferometer with superluminescent diode (SLD) light source with center frequency, λ_0 , of the light source is $1300 \mu\text{m}$ and bandwidth of the light source is 39 nm , OCT performs coherent gating that the two returned beams interfere only when both arm's path lengths match within the source coherence length. It thus be able to enhance axial resolution and to discriminate against scattered light. Figure 2 shows a typical interferogram signal of the low coherence length light source. A variable optical delay between the reference and sample arms is used to produce an interference signal and simultaneously, an axial scan through the sample. The detected signal is proportional to the reflectivity of the sample in the detection volume. Two-dimensional sample image is obtained by performing repeated axial measurements at different transverse positions as the optical beam is scanned across the tissue. The resultant data constitute a two-dimensional mapping image mapping of reflectance from internal architecture and cellular morphology in the tissue.

Spatial resolution

In OCT system, the transversal and axial spatial resolutions are determined by different physical mechanisms. Center frequency and bandwidth of light source decide axial spatial resolution [20].

$$l_c = \frac{2c \ln 2}{\pi \cdot \Delta \nu} = \frac{2 \ln 2}{\pi} \cdot \frac{\lambda_0^2}{\Delta \lambda} \quad (1)$$

where $\Delta \nu$ is the bandwidth of the light source. where c is the speed of light, $\Delta \lambda$ is full-width half-maximum (FWHM) of the light source and l_c is the coherence length, which is inversely proportional to the FWHM of the spectral bandwidth. From (1), we can say that the axial spatial resolution or coherence length l_c in free space is governed by the center wavelength λ_0 and the spectral bandwidth $\Delta \lambda$ of the source. In

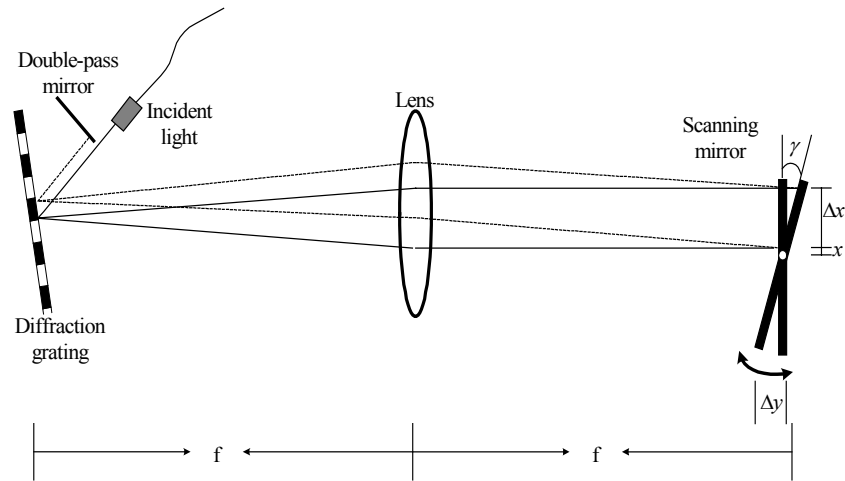


Figure 4. Schematic diagram of the optical phase delay line. (Above view)

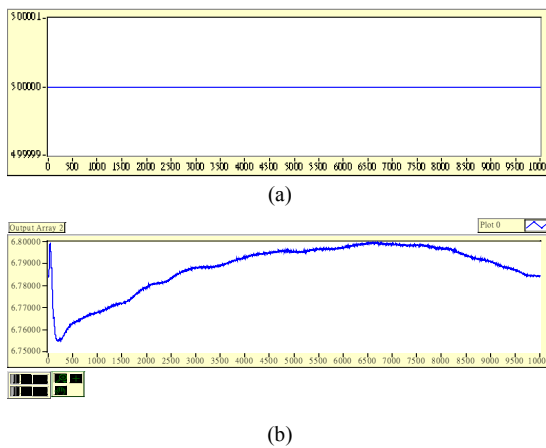


Figure 5. (a) An ideal intensity of reference arm; (b) real intensity of reference arm in OCT constitute by phase delay line; (c) light propagation in sample arm.

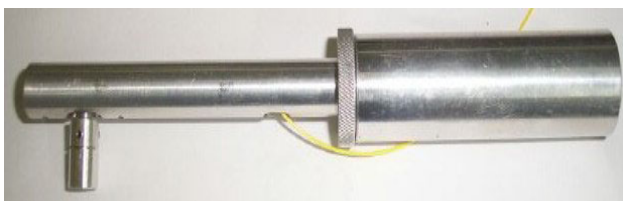


Figure 6. Photograph of the probe setup.

the system the axial spatial resolution of the system is thus determined to be $19.4 \mu\text{m}$.

The transversal spatial resolution of OCT is determined by the focusing properties of an optical beam.

$$\Delta x = 4 \frac{\lambda_0 f}{\pi d} \quad (2)$$

Note that the spot size of the focused beam Δx is the minimum spot size that proportional to the focal length f of the focusing lens and inversely proportional to the diameter d of the beam.

Probe design

A variety of clinical applications of OCT have been made possible by designing OCT probes. L-shaped probe used a single mode fiber focuser (FF) that inserts into a moving tube (MT) has been constructed. The moving tube was inserted into a stationary one (ST) and then coupled to a stepping motor for lateral translation scanning. Figure 3 is the complete setup of the probe. Fiber focusers with low back reflection, designed to focus light exiting a fiber to a desired beam spot size. The transversal spatial resolution of $20 \mu\text{m}$ can be achieved [21]. The size of the probe is designed to be used surface of open area especially for oral tissue.

Phase delay line

OCT based on high speed Fourier-domain variable-phase optical delay line provides imaging speed up to video rate [22]. Phase delay line is an effective and popular method for high speed OCT system. Figure 4 shows configuration of Fourier-domain variable-phase optical delay line. It consists of a grating and a lens in folded geometry. Scanning mirror is placed at the focal plane, and then driven by a galvanometer.

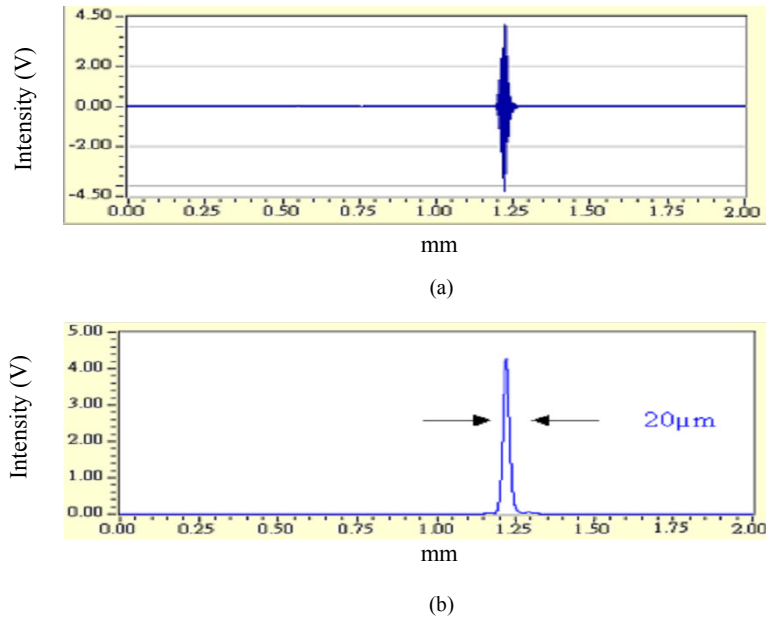


Figure 7. Measured signals obtained from a mirror plate as the sample: (a) interferogram; (b) envelope.

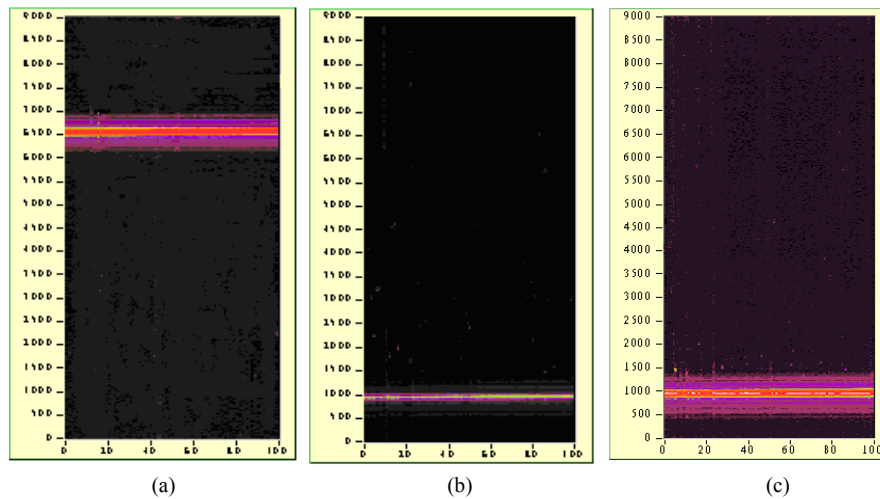


Figure 8. Mirror plane OCT image: (a) the first position in sample arm; (b) the image from second position before correction; (c) after correction the.

In our system, the diffraction grating is 400-lines/mm and the focus length of lens is 10cm. The grating spreads the spectrum of the incident light; first order diffracted light is transformed to frequency domain by lens and incident on the galvanometer-scanning mirror. The scanning mirror produces a wavelength dependent phase shift. The reflected light is inverted Fourier transforms by the lens and re-coupled into the reference arm. The wavelength dependent phase shift in frequency domain corresponds to a group delay in time domain. So, if the mirror is rapidly scanned, a time dependent optical group delay is produced and achieved axial scanning. The mirror scans at 100Hz can achieve 0.9 m per second in our system.

Image Compensation

There are two issues that can influence the returned real sample arm information. The first is in reference arm

constituted by phase delay line. The ideal intensity of reference arm in OCT is shown in figure 5(a). However, the real intensity comes out from reference arm in OCT constitute by phase delay line is shown in figure 5(b), which shows the difference intensity of varied optical delay length in phase delay line. The other issue is depth of focus in sample arm. The light propagation in sample arm is shown in Fig 5(c). The reflective intensity and resolution will degrade when out of focus. The two issues cause the same object at difference sample position arm has different intensity in reconstructed image. To compensate this problem, we propose an algorithm that will restore the issue.

Results and Discussions

The handheld probe is shown in Fig. 6, which is suitable

in skin or oral application. Figure 7(a) shows the interferogram and figure 7(b) shows the envelope of inference signal after demodulated. The FWHM of the envelope is the spatial resolution of OCT system. Fig. 8 shows the reconstructed image of reflective mirror. Two different position of mirror in sample arm is shown in Figure 8(a) and 8(b). The discrepancy of intensity between two images is obvious. Figure 8(c) shows the result of reconstructed reflective mirror image after processing by compensation algorithm. Due to lower signal intensity and thus greatly affected by noise, it might thus need a filter or other noise reduction algorithm in the future. The details of reflective layers can be clearly restored as compared to figure 8(a).

Conclusions

A fiber optics based OCT imaging system designed for biomedical application has been build for *in vivo* scanning skin and oral mucosa applications. The major components of the system include a phase control optical delay line for fast scanning rate, a 2×2 fiber coupler, and a L-shaped handheld probe with a stepping motor for lateral scanning and fiber focuser for beam focusing. The optical components are integrated into a computer system that containing detection electronics and data processing.

References

- [1] D. Huang, E. A. Swanson, C. P. Lin, J. S. Schuman, W. G. Stinson, W. Chang, M. R. Hee, T. Flotte, K. Gregory, C. A. Pualiafito, and J. G. Fujimoto, "Optical coherence tomography," *Science* 254: 1178-1181, 1991.
- [2] M. R. Hee, J. A. Izatt, E. A. Swanson, D. Huang, C. P. Lin, J. S. Schuman, C. A. Pualiafito, and J. G. Fujimoto, "Optical coherence tomography of the human retina," *Arch. Ophthalmol.*, 113: 326-332, 1995.
- [3] S. A. Boppart, M. E. Brezinski, B. E. Boump, G. J. Tearney, and J. G. Fujimoto, "Investigation of developing embryonic morphology using optical coherence tomography," *Dev. Biol.*, 177: 54-64, 1996.
- [4] J. Welzel, E. Lankenau, R. Bringruber, and R. Engelhardt "Optical coherence tomography of human skin," *J. Am. Acad. Derm.* 37: 958-963, 1997.
- [5] B. W. Colston, U. S. Sathyam, L. B. DaSilva, M. J. Everett, P. Stroeve, and L. L. Otis, "Dental OCT," *Opt. Express*, 3: 230-238, 1998.
- [6] Y. H. Zhao, Z. P. Chen, C. Saxer, Q. Shen, S. H. Xiang, J. F. de Boer and J.S. Nelson, "Doppler standard deviation imaging for clinical monitoring of *in vivo* human skin blood flow," *Opt. Lett.* 25: 1358-1360, 2000.
- [7] J. A. Izatt, M. D. Kulkarni, Hsing-Wen Wang; K. Kobayashi and M. V. Sivak, Jr., "Optical coherence tomography and microscopy in gastrointestinal tissues," *IEEE Journal of Selected Topics in Quantum Electronic*, 2: 1017-1028, 1996
- [8] A. M. Sergeev, V. M. Gelikonov, G. V. Gelikonov, F. I. Feldchtein, R. V. Kuranov, N. D. Gladkova, N. M. Shakhova, L. B. Snopova, A. V. Shakhov, I. A. Kuznetzova, A. N. Denisenko, V. V. Pochinko, Y. P. Chumakov, and O. S. Streltzova, "In vivo endoscopic OCT imaging of precancer and cancer states of human mucosa," *Opt. Express* 1: 432-440, 1997.
- [9] T. Q. Xie, M. L. Zeidel and Y. T. Pan, "Detection of tumorigenesis in urinary bladder with optical coherence tomography: optical characterizaion of morphological changes," *Opt. Express*, 10: 1431-1439, 2002.
- [10] M. Gupta, A. M. Rollins, J. A. Izatt and I.R. Efimov, "Imaging of the Atrioventricular Node Using Optical Coherence Tomography," *Journal of Cardiovascular Electrophysiology*, 13: 95, 2002.
- [11] S. Radhakrishnan, A. M. Rollins, J. E. Roth, S. Yazdanfar, V. Westphal, D. S. Bardenstein and J. A. Izatt, "Real-Time Optical Coherence Tomography of the Anterior Segment at 1310 nm," *Arch Ophthalmol.* 119:1179-1185, 2001.
- [12] A. Gh. Podoleanu, J. A. Rogers, D. A. Jackson and S. Dunne, "Three dimensional OCT images from retina and skin," *Opt. Express*, 7: 292-298, 2000.
- [13] J. A. Rogers, A. Gh. Podoleanu, G. M. Dobre, D. A. Jackson and F. W. Fitzke, "Topography and volume measurements of the optic nerve using *en-face* optical coherence tomography," *Opt. Express*, 9: 533-545, 2001.
- [14] X. Li, C. Chudoba, T. Ko, C. Pitris, and J. G. Fujimoto, "Imaging needle for optical coherence tomography," *Opt. Lett.* 25: 1520-1522, 2000.
- [15] A. M. Sergeev, V. M. Gelikonov, G. V. Gelikonov, F. I. Feldchtein, R. V. Kuranov and N. D. Gladkova, "In vivo endoscopic OCT imaging of precancer and cancer states of human mucosa," *Optics Express* 1: 432-440, 1997.
- [16] G. J. Tearney, M. E. Brezinski, B. E. Bouma, S. A. Boppart, C. Pitris, J. F. Southern, and J. G. Fujimoto, "In Vivo Endoscopic Optical Biopsy with Optical Coherence Tomography," *Science*, 276: 2037-2039, 1997.
- [17] Z. Chen, Y. Zhao, S. M. Srinivas, J. S. Nelson, N. Prakash, and R. D. Frostig, "Optical Doppler Tomography," *IEEE J. of Quantum Elec.* 5: 1134-1142, 1999.
- [18] C.E. Saxer, J. F. de Boer, B. H. Park, Y. Zhao, Z.Chen and J. S. Nelson, "High-speed fiber-based polarization-sensitive optical coherence tomography of *in vivo* human skin," *Opt. Lett.* 25: 1355-1357, 2000.
- [19] U. Morgner, W. Drexler, X. D. Kartner, C. Piltris, E. P. Ippen, and J. G. Fujimoto, "Spectroscopic optical coherence tomography," *Opt. Lett.* 25: 111-113, 2000.
- [20] J. M. Schmitt, "Optical Coherence Tomography (OCT): A Review," *IEEE Journal of Selected Topics in Quantum Electronic* 5: 1205-1215, 1999.
- [21] T. C. Luo, "Fiber-Optics based Optical Coherence Tomography for *In Vivo* Oral Tissue," Master thesis, Graduate Institute of Biomedical Engineering, National Taiwan University, Taipei, Taiwan, 2002.
- [22] A. M. Rollins, M. D. Kulkarni, S. Yazdanfar, R. Ung-arunyawee and J. A. Izatt, "In vivo video rate optical coherence tomography," *Opt. Express*, 3: 219-229, 1998.

生醫應用之光纖式光學同調斷層掃描

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摘 要

光學同調斷層掃描，為近年來快速進步的非侵入式醫學造影系統，其基本原理為使用低同調之光源，照射於生物組織，並以反射式干涉術量測背向散射光，可藉由不同機制之掃描方式，重建出二維或三維之生物組織影像，並具有達微米級之高空間解析度。我們完成一套光纖式光學同調斷層掃描系統，為了增加系統之臨床實用性，故以光學相位延遲器做為參考端之快速掃描，配合手持式造影探頭為樣本端之掃描，亦針對掃描深度之強度失真問題，進行最佳化補償，以增進影像之品質。

關鍵詞：光學同調斷層掃描、光學相位延遲器、手持式造影探頭、影像失真補償

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