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Micro-optical coherence tomography (μ OCT) *in vivo*

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Abstract: We have developed a Micro-optical coherence tomography (μ OCT) for *in vivo* use. We extended line width of the light source and have achieved a longitudinal resolution of 1.9 μ m in free space and 1.38 μ m in tissue. *In vivo* imaging was conducted using zebra fish larvae and cellular structures such as red blood cells in tail artery can be observed.

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1. Introduction

Optical coherence tomography was first reported in 1991 as a cross-sectional imaging tool for biological systems [1]. Later in 1993, first *in vivo* retinal imaging was conducted with a longitudinal resolution of 14 μ m [2]. Kerr-lens mode-locked Ti: Sapphire laser technology was used in 1999 to push the longitudinal resolution to $\sim$ 1.5 μ m [3]. Compact sub-10-fs Ti: Sapphire laser later was combined with photonics crystal fiber to improve the longitudinal resolution further to $\sim$ 0.75 μ m [4]. They demonstrated the submicrometer longitudinal resolution OCT *in vitro* on human colorectal adenocarcinoma cells. Maciej Wojtkowski *et al* used broadband, femtosecond KLM Ti: Sapphire laser to achieve a longitudinal resolution of 2.1 μ m in tissue in 2005 with high imaging speed [5]. μ OCT system was proposed recently [6, 7]. However, these high resolution systems used high power pulsed light source and *in vivo* application of such high power systems may be limited due to safety regulations such as those imposed by ANSI.

In this paper, we presented a method to improve the longitudinal resolution of *in vivo* OCT imaging systems using superluminescent diode (SLD) laser sources. Since SLD sources are low noise CW sources, high sensitivity can be achieved at relative low optical power on *in vivo* samples. By extending the line width of the light source we achieved a longitudinal resolution of 1.9 μ m in free space, corresponding to 1.38 μ m in tissue ($n = 1.38$).

2. Setup and Method

In this study, Superlum Broadlighters T-850-HP and Exalos Ultra-Broadband EBS4C32 were used as simultaneous dual balance light sources. They were combined by BS1 to provide extended line width up to 370nm, as shown in figure 1(b). An AViiVA EM4 Line scan camera was used as the detection component with a 3-dB response range of 400nm to 920nm. The incident power was less than 700 μ W, which provided a sensitivity of $\sim$ 95.35dB.

Figure 1: *In vivo* μ OCT schematic. L: lens. M: mirror. BS: beam splitter. SMF: single mode fiber. RM: reference mirror. NDF: neutral density filter. G: grating. CCD: charge-coupled device. PC: personal computer. GS: Galvo scanners.

3. Analysis of longitudinal resolution

Longitudinal resolution was measured using a glass slide and the spectrum is shown in figure 2.

Figure 2: Spectrum of AViiVA EM4 Line scan camera (CCD) with full-width half maximum (FWHM) of 151nm

The FWHM line width of resultant signal was measured to be around 151nm at center wavelength of ~825nm. If a Gaussian power spectrum is assumed, the theoretical longitudinal resolution can be calculated using equation (1).

$$l_c = 0.44 \frac{\lambda_c^2}{\Delta\lambda} = 0.44 \times \frac{825nm^2}{151nm} = 1.98\mu m \quad (1)$$

However, because the actual power spectrum is not Gaussian, the measured FWHM of the axial point-spread function was 1.9 μm in air, which is equal to 1.38 μm in tissue ($n = 1.38$) (Figure 3).

Figure 3: Longitudinal point spread function (LPSF), indicating axial FWHM of 1.9 μm

4. *In vivo* imaging example

In vivo imaging experiment was also conducted using a well-established biological model of zebra fish larvae of 3-day-old and several images of red blood cells in tail artery under notochord were obtained, as shown in figure 4.

Figure 4: Red blood cell flow in tail artery of zebra fish larvae

5. Conclusion

In this paper, we proposed a micro-optical coherence tomography system for *in vivo* applications using extended line width method and achieved a longitudinal resolution of $1.9\mu\text{m}$ in free space and $1.38\mu\text{m}$ in tissue. To demonstrate the merit of our *in vivo* imaging system, we conducted *in vivo* imaging using zebra fish larvae and cellular structures such as red blood cells can be observed clearly in tail artery.

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