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Ultrahigh resolution optical coherence tomography with femtosecond Ti:sapphire laser and photonic crystal fiber

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Abstract

Optical coherence tomography (OCT) with ultrahigh axial resolution was achieved by the super-continuum generated by coupling femtosecond pulses from a commercial Ti:sapphire laser into an air-silica microstructure fiber. The visible spectrum of the super-continuum from 450 to 700 nm centered at 540 nm can be generated. A free-space axial OCT resolution of 0.64 μm was achieved. The sensitivity of OCT system was 108 dB with incident light power 3 mW at sample, only 7dB below the theoretical limit. Subcellular OCT imaging was also demonstrated, showing great potential for biomedical application.

Keywords

optical coherence tomography; femtosecond laser; continuum generation; photonic crystal fiber

Optical coherence tomography (OCT) is an emerging technology for micron-scale cross-sectional imaging of biological tissue and materials. OCT is analogous to ultrasound imaging except that it uses low coherence light instead of sound waves[1]. High-resolution detection of reflected or backscattering light is performed using low coherence interferometer. Compared with the conventional X-ray computed tomography, magnetic resonance imaging and ultrasound imaging, OCT is noninvasive, safe, portable and of high resolution.

In fact, current time domain OCT systems are mainly based on an amplitude division interferometer like a Michelson interferometer or a Mach-Zehnder interferometer. In the amplitude division interferometer a 50/50 beam-splitter divides a source beam into two parts/beams, whose wave fronts are the same as the source beam but with half amplitude. In a conventional OCT system, the two beams serve as a sample arm and a reference arm light, respectively. Interference will occur at the detector when the light reflected by the sample and that by the reference mirror rejoin in the detection arm, provided that the optical path difference of the two beams is less than the coherence length of the light source. The interference signal is then demodulated and digitized by an A/D converter to form one line of the sample image. With scanning along the sample, a 2-D image can be obtained.

Recently, OCT technology has experienced a rapid development. By combining with the Doppler principle, rapid-scanning optical delay line, and catheter-endoscope technology[2-4], the application of OCT has been expanded. Spectral optical coherence tomography or Fourier domain optical coherence tomography (FDOCT) has drawn significant attention, for it can implement very fast axial scan speed and high sensitivity[5].

In recent years there are increasing applications of optical imaging for biomedical study. Two requirements for the techniques are crucial: one is safety for fast imaging and long time observation, and the other is high resolution for acquisition of detail information. Due to the development of ultrafast laser technology and high nonlinearity of photonic crystal fibers, air-silica microstructure fibers[6] and tapered fibers[7] can generate an extremely broadband continuum extending from 390 to 1600 nm using low energy femtosecond pulses. This bandwidth enables ultrahigh resolution OCT because of the $\lambda^2/\Delta\lambda$ dependence of the axial OCT resolution.

Here we demonstrate that the broad bandwidth of the continuum from 450 to 700 nm centered at 540 nm in the visible spectral region can be generated by femtosecond pulses from a commercial Ti:sapphire laser coupled into an air-silica microstructure fiber. The spectrum is limited on the side of shorter wavelength by the transmission properties of the microscope objective and on the side of long wavelength by the free spectral range of the spectrum analyzer. Because of the $\lambda^2/\Delta\lambda$ dependence of the axial OCT resolution the current bandwidth is probably the best to achieve high resolution, as shorter the wavelength and broader the bandwidth, higher the resolution. We show that longitudinal OCT resolution below 0.64 μm is feasible using the visible part of the continuum. Because of the high dispersion of the typical optical materials in this wavelength range and the lack of broadband fiberoptic couplers, we used a free space optical setup to demonstrate ultrahigh resolution OCT in the visible spectral range as shown in Figure 1. Dual balance detection is employed to reduce the noise from the light source, the half-wave plate to optimize the coupling of laser beam and the crystal fiber, apertures before detectors to block the scattering background light and Faraday isolator to remove the retro-reflection of the laser from fiber coupling for stable running of the laser system.

The feasibility of OCT imaging with submicron longitudinal resolutions in air using the supercontinuum light source was shown by an isolated reflection from a silver mirror. The spectrum of the collimated continuum (Figure 2(a)) was measured by an optical spectrum analyzer and had a bandwidth (FWHM) of 26 nm centered at 540 nm. The detected optical spectrum (Figure 2(c)) is calculated by Fourier transform of the interferometric signal, which is shown together with its envelope in Figure 2(b). The free-space axial OCT resolution of 0.64 μm was obtained by measuring the full width at half maximum of the envelope. This is, to our knowledge, the highest longitudinal OCT resolution demonstrated to date in this wavelength range[8,9].

The detected optical spectrum (Figure 2(c)) was calculated by Fourier transforming the interferometric signal. The detected spectral bandwidth is 170 nm. This broadening of the bandwidth occurs possibly due to an attenuation of the short wavelength part of the light source and also the spectral responsibility of the detector. This is because that the optics in experimental setup and also the window of the detector have lower transmission at the short wavelength. Furthermore the electronic response of the detector at sharp spectral variation may lead to some smoothing effect as it is not so spectral sensitive or resolvable. Therefore to some extent the Fourier transform of the electronic signal of the interference can remove the two undesirable peaks on the spectrum. Pronounced spectral features of the light source are still visible after spectral shaping and are marked with dashed vertical lines between Figure 2(a) and (c). The group delay dispersion mismatch between the two interferometer

arms is obtained from the phase of the Fourier transformed interferometric signal and is shown in Figure 2(d) and is relatively low in the visible spectral range from 480 to 700 nm due to the symmetrical setup. Pinholes of 15 μm in diameter are placed before the two detectors respectively to eliminate the background caused by multiscattering of tissue samples. To reduce the noise level, dual balance detection is further utilized. The light intensity on the photodiode is balanced by adjustment the diameter of aperture A before the detector D2 and MO.

We place a 3.5 O.D. neutral filter at the sample arm and use a reflective mirror as the sample. With incident light power 3 mW at sample the interferometric signal still gives 38 dB signal to noise ratio. Therefore in total the system sensitivity is 108 dB, only 7dB below the theoretical limit by the formula of signal to noise ratio or sensitivity in the shot-noise limit: $\text{SNR} = 10 \ln[(\theta P / (\hbar \omega B))]$, where θ is quantum efficiency of the detector, $\hbar \omega$ the energy per photon, P the power of the light scattered from the sample to the detector, and B the noise-equivalent bandwidth. The bandwidth of the detection electronics must be specified commensurate with the source optical bandwidth, indicating that for fixed SNR higher optical power is required for higher-resolution optical sources. The measured sensitivity is very good to provide high quality images of biological samples.

For most of current OCT systems, a superluminescent diode (SLD) is often used as the light source. But the bandwidth and power of SLD is limited, and the resolution and sensitivity of OCT system are relatively low[10]. Femtosecond laser and the air-silica microstructure fiber supply the so-called “super-continuum”, a new light source with extremely broad bandwidth and sufficient power for OCT application. The new light source greatly enhances the performance of OCT imaging. To show the dramatic improvement, OCT imaging with SLD and super continuum is demonstrated respectively in Figure 3. The sample is onion. OCT imaging with SLD as light source, as shown in the left, can only give the scalariform information, as the resolution is only about 15 μm , while using super continuum it can give subcellular structure of tissue with ultrahigh resolution, which is $0.64 \mu\text{m}/1.35=0.47 \mu\text{m}$ in sample (index ≈ 1.35), more than 20 times enhancement in resolution. More details such as the size and membrane thickness of the cell are thus measurable. These informations are very helpful for biological study and clinical application like early diagnosis of cancer, as the appearance of a normal cell is quite different from that of a tumor cell.

In summary, we have demonstrated ultrahigh resolution optical coherence tomography, which utilizes the visible spectral range of super continuum generated by femtosecond pulses from ultrafast Ti:sapphire laser coupled into an air-silica microstructure fiber. Ultrahigh resolution OCT can permit micrometer-scale, subcellular and cross-sectional imaging of tissue, providing a powerful tool for biomedical application.

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Figure 1. Ultrahigh resolution OCT system using continuum generation in an air-silica microstructure fiber as the light source. MO, microscopic objective lens; BS, beam splitter; D1, D2, detector; $\lambda/2$, half-wave plate; A, aperture.

Figure 2.

(a) Typical spectrum of the light source before spectral filtering; (b) Interference fringes recorded by an isolated reflection. The full width at half maximum was measured to be $0.64 \mu\text{m}$. Detected optical spectrum (c) and group delay dispersion mismatch of the interferometer arms (d) obtained from the Fourier transform of the interferometric signal (b). The vertical dashed lines mark pronounced spectral features.

Figure 3.

Comparison of the OCT imaging of onion sample with SLD light source and super continuum from femtosecond laser pulses coupled into an air-silica microstructure fiber. (a) is the OCT image with SLD source (approximately $15\ \mu\text{m} \times 25\ \mu\text{m}$ longitudinal $\times$ transverse resolution, size $10\ \text{mm} \times 4\ \text{mm}$) and the appearance of a cell is only like a dot and can be hardly distinguished. (b) is the subcellular image (approximately $0.64\ \mu\text{m} \times 4\ \mu\text{m}$ longitudinal $\times$ transverse resolution, objective $20\times$, bar $10\ \mu\text{m}$, size $0.27\ \text{mm} \times 0.125\ \text{mm}$) of a small part of the sample imaged by OCT system using super continuum. The cellular structure is clearly shown with such high resolution. More details such as the size and wall thickness of the cell are thus measurable.