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Second Harmonic Optical Coherence Tomography

Tech ID: 23006 / UC Case 2004-181-0

BRIEF DESCRIPTION

The invention is an apparatus and method for second harmonic optical coherence tomography of a sample comprising a laser coupled to an interferometer which has a reference arm and in a sample arm. A nonlinear crystal in the reference arm generates a second harmonic reference signal. The sample typically backscatters some second harmonic light into the sample arm. A broadband beam splitter optically coupled to the reference arm and sample arm combines the signals from the reference arm and sample arm into interference fringes and a dichroic beam splitter splits the interference fringes into a fundamental and second harmonic interference signal. A detector is optically coupled to the dichroic beam splitter detects interference fringes from which both an OCT and second harmonic OCT image can be constructed using a conventional data processor.

FULL DESCRIPTION

Optical coherence tomography (OCT) is an emerging imaging technology that provides in-vivo high-resolution, cross-sectional images of biological tissues. Using coherence gating technique, OCT is capable of detecting the backscattered light from highly scattering tissues at depths of 2-3 mm. OCT imaging contrast originates from the inhomogeneities of sample scattering properties that are linearly dependent on sample refractive indices. In many instances such as pathological processes in tissue, changes in sample linear scattering properties are small and difficult to measure. For example, many cancers originate in the epithelium that has a thickness suitable for OCT imaging, but in their early stages when these cancers are developing through cell dysplasia, changes in tissue morphology and refractive index between normal and diseased tissues are very small and difficult to detect. Therefore, to meet the challenges found in OCT clinical applications, imaging contrast enhancement is very important.

In recent years, many OCT contrast enhancement methods have been developed. These techniques include Doppler OCT, polarization sensitive OCT, spectroscopic OCT, pump-probe techniques, and using contrast agents for OCT. More recently, applying nonlinear optical effects of second harmonic generation (SHG) and coherent anti-Stokes Raman scattering for OCT contrast enhancement have also been demonstrated.

SHG is a powerful contrast mechanism in nonlinear optical microscopy. SHG signals provide unique information regarding sample structure symmetry because the signals strongly depend on the orientation, polarization and local symmetry properties of chiral molecules. SHG enables direct imaging of anisotropic biological structures, such as membranes, structure proteins, and microtubule ensembles. Besides successfully producing high-resolution and highly contrasting images of tissue morphology, recently SHG microscopy has also been applied to study dynamics in tissue physiology, such as monitoring collagen modification in tumors growing, and optically recording the action potentials change in neuron cells. SHG is emerging as a powerful nonlinear optical imaging modality for cell biology and biophysics.

We have developed a noninvasive optical tomography technique of second harmonic optical coherence tomography and experimentally demonstrated the feasibility of using this technique to image biological samples. Compared with conventional OCT performed at fundamental wavelength, SH-OCT offers enhanced molecular contrast and spatial resolution. It is also an improvement over existing second harmonic scanning microscopy technology as the intrinsic coherence gating mechanism enables the detection and discrimination of second harmonic signals generated at deeper locations. The enhanced molecular contrast of SH-OCT extends conventional OCT's capability for detecting small changes in molecular structure. Second harmonic-OCT is promising for the diagnosis of cancers and other diseases at an early stage when changes in tissue and molecular structure are small.

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PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	7,256,894	08/14/2007	2004-181

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