Fiber-optic catheter for cellular resolution imaging

Abstract

This dissertation presents novel developments in micro-optical coherence tomography (µOCT) at cellular resolution towards clinical applications. µOCT has been known as the highest resolution OCT technique available to date. It has an order of magnitude better resolution in both axial and lateral direction than standard OCT. The ability for µOCT to obtain non-invasive, real-time and three dimensional images of biological tissue at unprecedented resolution has brought new opportunities for the advancements of diagnosis of disease pathogenesis and novel therapeutics. Several major developments were included in this dissertation to advance µOCT technique to higher resolution, better image quality and improved clinical usability. Three main topics will be covered:

1. Dual spectrometer for *in vivo* imaging of blood flow.
2. Multifiber µOCT catheter for speckle reduction.
3. µOCT fiber catheter design and prototype toward clinical endoscopic and intravasuclar applications.

The first part presents a dual spectrometer µOCT system for extended spectrum bandwidth detection in order to achieve 1-µm axial resolution. The dual spectrometer utilized two line scan cameras of distinct detection wavelength ranges. One was a Si-based sensor responding at 850 ± 100 nm and the other was an InGaAs-based sensor responding at 1020 ± 80 nm. The two spectral ranges were combined into a supercontinuum with extended full-width-half-maximum of 345 nm and thus the axial resolution in aqueous environment was 0.93 µm (n = 1.37). *In vivo* experiment showed blood flow in zebrafish larvae tail vein. Not only individual red blood cell was observed but also endothelial cells lining along the luminal surface of the blood vessel wall.

Although at 1 µm resolution µOCT has enough resolving power to identity subcellular of biological tissue, some important microstructures was masked behind speckles. With the objective to improve imaging quality at high resolution, a multifiber µOCT catheter was designed to reduce speckle. Simultaneous multichannel spectrometer was employed to detect signals from different channels. The key element in this design was a multi-facet fiber array which actively delivered three light beams onto imaging sample and picked up back-scattered signal at different angles. Speckle reduction was realized by compounding signals from all channels. Rat esophagus imaging using this setup demonstrated an improved signal-to-noise ratio, contrast-to-noise ration and equivalent number of looks. The epithelium was better delineated from the overlying mucus and lamina propria beneath the basement membrane.

Lastly but more importantly, this dissertation presents a novel high-resolution endoscopic µOCT catheter, pushing the clinical usage of µOCT a big step forward. The µOCT catheter discussed here was designed and fabricated to perform longitudinal scanning µOCT imaging *in vivo* in human airways. The 2.4 mm diameter and flexibility allows it to be inserted into the instrument channel of commercially standard bronchoscope. Under the real-time video guidance of the bronchoscope, the endoscopic fiber-optics catheter could reach the regions of interest up to secondary bronchial and conduct high resolution, real time imaging of the functional microanatomy of the airway epithelium, including cilia beat frequency and mucociliary transport rates, etc. The endoscopic µOCT catheter consists of three major segments: inner optics, outer sheath and ergonomics handle. The design, fabrication and test of each segment will be discussed in details. Both *ex vivo* imaging of mouse trachea and *in vivo* imaging of swine trachea and bronchial were performed to show the microanatomy of the airway epithelium.