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Office-based laryngeal imaging in awake patients with swept-source optical coherence tomography

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Abstract
Optical coherence tomography (OCT) is an evolving noninvasive imaging modality and has been used to image the human larynx during surgical endoscopy. The design of a long GRIN lens based probe capable of capturing images of the human larynx by use of a swept-source OCT during a typical office-based laryngoscopy examination is presented. An optical-ballast-based 4F optical relay system is proposed to realize variable working distance with a constant optical delay. In vivo OCT imaging of the human larynx is demonstrated with 40 frame/second. Office-based OCT is a promising imaging modality to study the larynx.

Key words: optical coherence tomography, larynx, biomedical imaging, early diagnosis, laryngeal cancer

Introduction
Laryngeal carcinoma is one of the commonest primary head and neck malignancy. Despite significant advances in cancer treatment, early detection of malignant lesion and its curable precursors is paramount to ensure successful treatment and patient survival. Flexible fiber-optic or rigid endoscopes are normally used for conventional physical examinations, but difficult to differentiate benign, pre-malignant and malignant lesions, which are characterized by identical symptoms such as throat pain, coughing, or hoarseness. Both conventional examination and endoscopy lack the ability to visualize the depth of penetration of disease into the deeper layers of the tissue. Therefore, conventional laryngeal diagnosis has to rely on biopsies, which requires a general anesthesia and surgical endoscopy. This invasive procedure may have a detrimental effect on the patient’s voice. Risks of a biopsy with surgical endoscopy may be considerable since it is often difficult to obtain a representative biopsy from a suspicious malignant lesion, which sometimes may be missed due to sampling errors. Repeated biopsies are common in order to ascertain a definite diagnosis, and will bring even higher risks.

Hence, there is a huge need to develop a fast, mobile and noninvasive diagnostic technology for early detection and monitoring of laryngeal malignant lesions. Optical coherence tomography (OCT) is an evolving technology for performing high-resolution cross-sectional micron scale imaging [1]. OCT performs imaging in biological tissues by directing an optical beam of infrared light onto the tissue and measuring the intensity and phase of the backscattered light from microstructures of the tissue at different depths. OCT can function as a powerful imaging technology for optical biopsy and has been used to image the larynx during surgical endoscopy [2-4]. OCT imaging of the larynx in
awake patients in an office setting has been limited because several challenges exist including patient and physician movements and the position of the larynx deep within the neck. Recently we reported an office based laryngeal time-domain OCT imaging device [5]. A rigid laryngoscope serves as a platform to which a second device can be attached to perform simultaneous OCT imaging. However, the scanning mechanism was slow, thus it was very difficult to obtain OCT images due to movements of both the physician’s hand and patient’s larynx.

The majority of OCT probes developed for endoscopic applications have fixed optical arrangements, and thus a fixed working distance. In laryngeal endoscopy, the depth of the larynx in the throat and the path length light must travel from the incisors to the vocal cords vary markedly from patient to patient. Hence, a mechanism is required to allow active adjustment of the working distance for tracking the larynx. Here we report our recent developments of office-based laryngeal OCT imaging device to address difficulties we met in our previous studies [5]. We use a novel GRIN lens based probe capable of capturing images of the human larynx by use of swept-source OCT. An optical relay system based on the principle of optical ballast [6] is designed to fulfill constant-optical-delay dynamic focusing. In vivo noninvasive and cross-sectional imaging is possible during awake office-based laryngoscopy examination.

System setup and results
The schematic diagram of the fiber-based swept source OCT system is shown in Fig. 1. The output light from a swept light source at 1310 nm with a FWHM bandwidth of 100 nm and output power of 5 mW was split into reference and sample arms by a 1 × 2 coupler. The light source was operated at a sweeping rate of 20,000 Hz. The reference power was attenuated by an adjustable neutral density attenuator for maximum sensitivity. The GRIN lens based endoscope was connected to the sample arm with 80% power from the source. Two circulators were used in both reference and sample arms to redirect the back-reflected light to a 2x2 fiber coupler (50/50 split ratio) for balanced detection. The measured axial resolution of 8 μm was close to the theoretical axial resolution of 7.5 μm since the spectrum of the swept light source is nearly Gaussian shaped. The lateral resolution, which is determined by the endoscope’s focus spot, was measured to be 15 μm.
The probe design should address a variable working distance with a constant optical delay. A one-pitch long GRIN (gradient index) lens (22 cm, Gradient Lens Corporation, Rochester, NY) used in this design can be considered as an optical relay for visible wavelength [6]. The focal length of a long GRIN lens is given as 

\[ f_{\text{GRIN}} = \left[ n_0 \sqrt{A} \sin L \sqrt{A} \right]^{-1}, \]

where \( A \) is a constant for a particular lens for particular wavelength, \( L \) is the length of the GRIN lens. For an ideal one pitch, \( L \) is given as \( 2\pi/\sqrt{A} \) and the focal length \( f_{\text{GRIN}} \) becomes infinite. Any light beam entering the GRIN lens rod will come out from the distal end of the lens with the same direction and same height (relative to the axis of the rod), thus, an ideal one pitch GRIN lens can be considered as an optical relay. However, for 1310 nm wavelength, which is the center wavelength of the OCT light source, the GRIN lens is closed to one pitch but cannot be considered as an ideal optical relay any more, especially when the average working distance of the probe (or the beam coming out of the probe tip) reaches about 65 mm for laryngeal imaging. However, the long GRIN lens (less than an ideal one pitch for 1310 nm wavelength) can be considered as a composite of an ideal one-pitch GRIN lens which will be an ideal optical relay for IR light of 1310 nm, and a negative short GRIN (NS-GRIN) lens, of which the focal length is the same as that of the original long GRIN lens as 

\[ f_{\text{GRIN}} = \left[ n_0 \sqrt{A_{\text{IR}}} \sin L \sqrt{A_{\text{IR}}} \right]^{-1}, \]

where \( A_{\text{IR}} \) is now the lens constant for 1310 nm light.

In order to achieve an ideal optical relay, the GRIN lens is used with a group of lenses \( L_1, L_2 \) to form a so-called optical-ballast [6] within a 4f optical system. Assume the focal lengths of the above three lengths are labeled as \( f_{\text{GRIN}}, f_1, \) and \( f_2 \) (with \( f_1 = f_2 = f_0 \)), respectively. Figure 1 shows the sketch diagram of the probe design. If the distance between the two principal planes of the lens \( L_2 \) and NS-GRIN lens is equal to \( f_0 \), i.e., the NS-GRIN lens is located at the rear focus of lens \( L_2 \), the composite focal length of \( L_2 \) and the NS-GRIN lens will be

\[ \frac{f_0 f_{\text{GRIN}}}{f_0 + f_{\text{GRIN}}} = f_0, \]  

which shows a same focal power of the lens \( L_2 \). Hereby the lens \( L_2 \) is named as optical ballast. If the distance between the two principal planes of \( L_1 \) and the composite lens (of the NS-GRIN lens and \( L_2 \)) is adjusted to be \( 2f_0 \), they will make up a 4f optical system with magnification of one and can be considered as an optical relay.

The sample beam from the OCT system is collimated, passes through a focusing lens \( L_3 \), and reflects 90° to the fixed lens group by a scanning galvo (Fig. 2a). The fiber and collimating and focusing lenses are fixed together that can be moved along the propagation direction. At the proximal tip of the GRIN lens, a 90° prism is attached to fold the light path. At the distal tip of the GRIN lens, a customized prism is attached to reflect light 90° or 60° down to the larynx due to anatomy of the patient. The device is coupled to the laryngoscope by a carriage. The endoscope and the OCT device are held together in a “double-barreled” configuration. The collimator and the
lens L₃ are assembled onto a slider and can be moved back and forth together for working distance adjustment by the physician during the examination (Fig. 2b). Since all fixed optics can be considered as an optical relay, the optical delay of the focal point remains constant during adjustment of the working distance. During the examination both of the dual-channel endoscope and OCT signals are digitized and displayed on a single monitor. Figures 2(c-d) shows acquired frames of human lips captured with 40 frames (of 512 A-lines) per second, where the epithelium, the lamina propria and glands can be clearly identified. The image is comparable with images obtained in anesthetized patients during surgical endoscopy.

Fig. 2 (a-b) Picture of the OCT probe attached to the laryngoscope for office based laryngoscopy examination; (c-d) OCT frames from the video of the human lips.
During the examination of vocal cord, the patient is asked to sit straight up and hold the tongue with a gauze pad during the procedure. The back of the throat may be sprayed with a medicine that numbs the mouth and throat to eliminate the human gag reflection. As in conventional physical examination with a stroboscope, the patients are asked to make some sounds, so that the vocal cords will move and remains close to each other. Otherwise, patient’s vocal cord will remain open and become hard to image. Figure 3 shows the cross-sectional images of vibrating vocal cords of a male human subject during examination. The epithelium and basement membrane can be clearly identified. In the tested chest vibration mode the frequency of the vocal cord is about 120 Hz for the male volunteer. This is a perfect fit for the measured OCT image shown in Fig. 3. Since the OCT imaging speed is 40 frames per second, 3 cycles observed in Fig. 3 correspond to ~120Hz frequency. The precise dynamic vibration amplitudes can also be measured based on the above OCT image. Since the total imaging depth in the above figure is 2.6mm, the maximum vibration amplitude in the figure is estimated to be about 1.2mm.

**Conclusion**

In summary, we demonstrate video-rate *in-vivo* laryngeal imaging of 40 fps during a typical office based laryngoscopy examination with a swept-source OCT system. Taking advantages of being performed without the need for general anesthesia or tissue removal, office-based OCT has potential to guide surgical biopsies, direct therapy, and monitor disease. This is a promising imaging modality to study the larynx.

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