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ORIGINAL RESEARCH—LARYNGOLOGY AND NEUROLARYNGOLOGY

Optical coherence tomography of the larynx in the awake patient

Ali Sepehr, MD, William B. Armstrong, MD, Shuguang Guo, PhD, Jianping Su, MS, Jorge Perez, BS, Zhonping Chen, PhD, and **Brian J.F. Wong, MD, PhD,** Irvine, CA

OBJECTIVE: To demonstrate the feasibility of performing optical coherence tomography of the human larynx on the awake patient with a novel flexible fiberoptic delivery system.
STUDY DESIGN: Prospective clinical trial.
SUBJECTS AND METHODS: Imaging was performed in 17 awake patients. A flexible optical coherence tomography probe was inserted through the nose and placed in near or gentle contact with laryngeal tissues under direct endoscopic visualization.
RESULTS: Images were successfully obtained from all laryngeal subsites and clearly identified laryngeal mucosal microanatomy. Several critical probe design modifications improved rotational and angular control of the distal tip while allowing linear translation of the probe and allowing more accurate apposition of the probe onto target tissues, which is critical for transnasal laryngeal imaging.
CONCLUSION: This study demonstrates the feasibility of awake transnasal laryngeal optical coherence tomography and identifies key instrumentation needed to obtain useful images.

The vocal fold consists of three anatomic layers, the epithelium, the lamina propria (LP), and the thyroarytenoid muscle.[1] The basement membrane is a microanatomic layer that separates the epithelium from the LP. Early laryngeal cancer is difficult to distinguish from benign disorders of the larynx, because, short of surgical biopsy under anesthesia, current examinations are unable to determine the presence of basement membrane (BM) invasion, which defines cancer.

Definitive diagnosis requires patients with questionable laryngeal lesions to bear the risks of general anesthesia, direct laryngoscopy, and biopsy. Patients may avoid the risks of surgical biopsy through the availability of office-based imaging techniques that are able to determine BM integrity.

Optical coherence tomography (OCT) is a new investigational imaging modality that uses near-infrared light to produce real-time, high-resolution (1 to 10 μm), cross-sectional images of in vivo tissue microstructure without tissue removal, cytotoxic fixation, or ionizing radiation.[2] OCT is analogous to ultrasound except that, instead of acoustic properties, it relies on differences in tissue optical properties, which produce phase and intensity differences in backscattered light, to produce images. OCT systems are currently used in ophthalmology.[3]

In otolaryngology, it has been used to identify BM integrity in laryngeal cancer patients under general anesthesia.[4] Otherwise its clinical applications have been limited in otolaryngology. It can become an indispensable clinical management tool whenever detailed information about subsurface microstructure is essential for accurate diagnosis or treatment and when a surgical biopsy has the potential to produce significant morbidity, such as laryngeal lesions seen in the office. However, implementing OCT as an office-based screening measure for laryngeal cancer has been challenging because of its inherent optical limitations as evidenced by three reported cases in the literature to date.[5] Because of its short focal length and need for steady positioning near target tissue, great control of the distal probe tip is required and has seemingly been elusive to date.

In the office setting, OCT has the potential to aid in diagnosing cancer, to monitor disease progression, and to direct biopsies. Its advantages include being performed without the need for general anesthesia or tissue removal. This study addresses the instrumentation designs necessary for reproducible imaging in this setting.

METHODS

Patient Population

Patients seen for other reasons in the office setting were examined in accordance with a University of California, Irvine IRB approved protocol.

OCT Core Instrumentation

The details of the core time-domain OCT device used in this study have been described previously[6] and are sum-

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marily described here. The system in this study used a low-coherence light source (central wavelength $\lambda = 1310$ nm; JDS Uniphase, San Jose, CA).[5] Raster scanned images were generated by controlled motion of the imaging fiber with a precision piezoelectric translation stage (model 663.4pr; Physik Instrumente, Tustin, CA). The optical fiber and optical elements, which comprise a small GRIN lens and prism, are enclosed by a transparent plastic tube. The axial resolution of the imaging system is determined by the coherence length of the light source and is approximately 7 μm. The lateral resolution is determined by diffraction and is approximately 10 μm. Signals were obtained up to a depth of 1.6 mm, whereas the lateral extent of each image was determined by the length over which the fiber was translated by the translation stage, typically 6 mm.

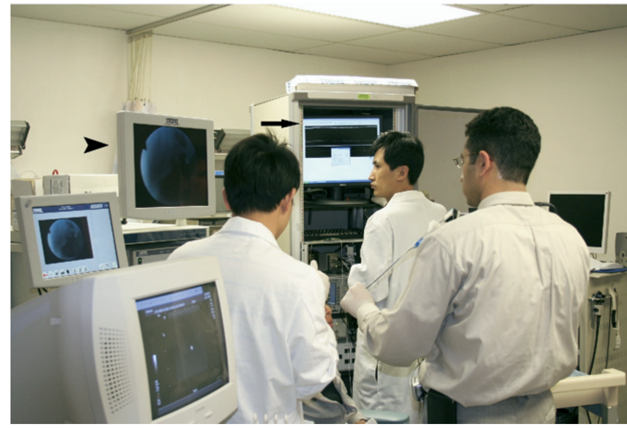

Figure 2 OCT imaging was performed in tandem with direct endoscopic visualization and allows simultaneous viewing of the endoscopic video (*arrowhead*) and the OCT image (*arrow*) on adjacent monitors.

OCT Flexible Fiberoptic Delivery System

A platform was constructed to couple the piezoelectric translation stage with a commercially available fiberoptic rhinolaryngoscope (Olympus ENF-P4, Center Valley, PA). The platform allowed the position of the translation stage to be fixed anywhere along a 5 cm axial distance relative to the rhinolaryngoscope. Furthermore, the platform provided for 360 degree rotation of the rhinolaryngoscope relative to the translation stage (Fig 1).

The OCT image plane is defined by the direction of light propagation, which is orthogonal to the long axis of the probe. This direction was marked just off of the distal tip of the probe. This tomographic image is analogous to the plane produced by a scalpel slicing through tissue, with the long axis of the probe represented by the handle of the scalpel, the axial translation of the probe tip represented by the to and fro movement of the blade, and the plane of light propagation represented by the angle of the scalpel on the tissue surface. Image quality is directly proportional to the proportion of reflected and back scattered light that could be detected, which required a near perpendicular plane to the tissue surface. This requirement made it necessary to accurately control the rotational orientation of the distal tip of the probe. To this end, the OCT optical fiber was passed through a flexible vertebrated tube. The distal tip of the vertebrated tube was glued to the optical fiber 5 cm removed from the prism and GRIN lens. This configuration permitted high-fidelity, accurate rotational control of the distal tip of optical fiber (inside the larynx) from a proximal location along its length (outside the nose).

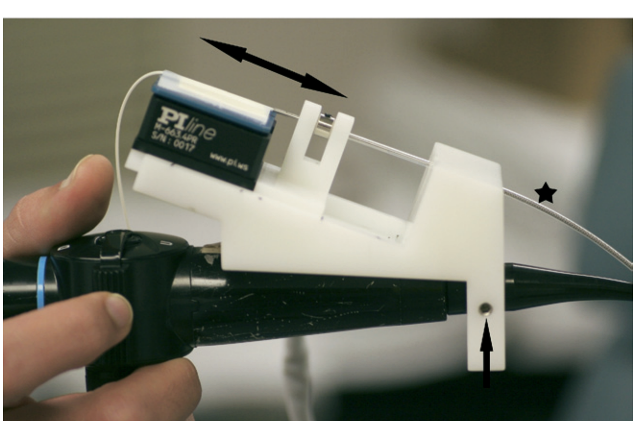

Figure 1 The platform used to couple the piezoelectric translation stage with the fiberoptic rhinolaryngoscope. (*Double headed arrow* indicates the to and fro motion of the translation stage; *star*, the optical plastic tube covering and the vertebrated tube that house the optical fiber; *single headed arrow,* the screw that allows rotation of the rhinolaryngoscope relative to the OCT probe.)

Images were displayed continuously on a monitor at a frame rate of 1 Hz. By convention, increased backscatter of OCT light was depicted as increased whiteness on gray-scale imaging. OCT imaging was performed in tandem with direct endoscopic visualization, which allowed simultaneous viewing of the video and the OCT image on adjacent monitors (Fig 2). The images on the monitors were used to adjust probe position to improve image quality. To allow efficient adjustment of probe position over the tissues, two separate modifications in the delivery instrumentation were used. First, the tip of the vertebrated tube/optical probe unit (OCT probe) was coupled to the tip of the rhinolaryngoscope with a disposable, slide-on channeled endosheath (Vision Sciences 33-4401, Orangeburg, NY). This coupling allowed radial control of the distal tip of the OCT probe (Fig 3). Furthermore, the OCT probe was coupled to the translation stage with o-rings that afforded simultaneous rotational control of the distal tip of the optical OCT fiber during imaging. In essence, the o-rings functioned in a fashion similar to ball bearings. These modifications allowed multiple degrees of freedom that provided for dependable imaging in each patient.