Imaging of the Pediatric Airway Using Optical Coherence Tomography

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Objectives: Optical coherence tomography (OCT) is an imaging modality that uses a broadband light source to produce high-resolution cross-sectional images in living tissue (8–20 μm). A prospective study of normal, benign, and pathologic tissues in the pediatric airway was conducted to assess the utility of OCT technology in characterizing the microanatomy of the pediatric upper aerodigestive tract in vivo.

Study Design: Prospective clinical trial.

Materials and Methods: Fifteen patients from 1 to 17 years of age underwent surgical endoscopy and OCT for various airway disorders. OCT imaging was performed at a frame rate of 1 Hz using a 1.3-μm broadband light source to produce images 1.6 × 6 mm in vertical and horizontal dimensions. The epithelium, lamina propria, and unique tissue microstructures were visualized and then measured using digital micrometry. Direct comparison of OCT images with endoscopic photography was performed.

Results: Systematic imaging of the oral cavity, oropharynx, hypopharynx, and larynx was performed in all 15 patients. Normal microstructures identified included papillae, ducts, glands, and vessels, whereas pathologic conditions included distinct zones of mature scar, granulation tissue, edema, ulceration, and papillomatosis. Endoscopic photographs were well correlated with OCT images.

Conclusions: OCT is capable of obtaining high-resolution microanatomic images of pediatric airway in vivo tissue. OCT clearly identifies the epithelium and lamina propria while providing detailed structural information on normal and diseased tissues. OCT is a promising emerging imaging modality for use in current pediatric patient populations.

Key Words: Optical coherence tomography, pediatric airway, imaging.

INTRODUCTION

Optical coherence tomography (OCT) is a biomedical imaging modality that uses broadband, low-coherent light combined with interferometry to produce high-resolution images of living tissue. Similar to B-mode ultrasonography, this noninvasive, noncontact technique produces cross-sectional images of tissue with a resolution of approximately 10 μm. OCT imaging can distinguish the epithelium from underlying lamina propria and associated tissue microstructures based on the unique optical properties of each tissue as related to optical scattering, absorption, and anisotropy. The in vivo images produced by OCT are similar in resolution and orientation to those obtained using conventional microscopy but without the artifacts produced in mechanical biopsy and histologic tissue processing. Taken together, the ability of OCT to image and characterize in vivo tissue microstructure well exceeds the current resolution limits of computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound.

OCT imaging of various organs and tissues has considerably improved our understanding of biological, functional, and tissue disease states. Clinically, OCT has had the greatest impact in the study of retinal disease, in which the diagnostic capabilities have been used to study macular edema, choroidal neovascularization, and glaucomatous changes. The utility of this technology has led to the development of commercial OCT systems and reimbursement by third-party payors. Other fields of intense investigation include the study of cardiovascular, gastrointestinal, hepatobiliary, and pulmonary diseases. The preliminary use of OCT to study otolaryngologic disease states was first highlighted by Sergeev et al. Further studies involving cochlear imaging and monitoring for laryngeal laser surgery soon followed. Extensive investigations using OCT in the analysis of the aerodigestive tract of adult human subjects has been performed in...
normal, benign, and cancerous tissue states. These studies emphasized tissue microstructure and normative architecture and observed imaging changes in tissues of the oral cavity, oropharynx, nasal mucosa, and the human larynx.\(^9,10\)

Disorders of the larynx, and most notably of the vocal folds, can produce significant airway compromise as well as morbidity with regard to vocal function. The gold standard of airway evaluation remains direct laryngoscopy and bronchoscopy, often in tandem with rigid rod-lens endoscopy.\(^11\) Unfortunately, this form of evaluation provides limited information on the extent of subepithelial tissue involvement. If a disease process requires tissue biopsy, or even surgical resection to secure a patent airway, normal tissues may be sacrificed when the boundaries of laryngeal disease lack clear margins on endoscopic examination. Ultimately, the surgical challenge is to preserve healthy tissues and, accordingly, vocal quality while addressing the specific disease state.

OCT has a potential role in the management of superficial/epithelial disease during operative endoscopy. With the ability to resolve tissue depths up to 2 mm using current state of the art technology, OCT can provide vital histologic and structural information with near real-time frame rates. The current study reviews OCT imaging of pediatric patients undergoing operative endoscopy for a variety of medical conditions. The aims of this study were to use OCT to characterize normal tissue architecture as well as define tissue changes in pathologic conditions. We will discuss OCT image acquisition, interpretation, and operative instrumentation, followed by a review of our pediatric series of patients. To the best of our knowledge,

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**Fig. 1.** Optical coherence tomography (OCT) imaging system and oral cavity/oropharynx target. OCT system parameters: \(\lambda = 1310\) nm and full width at half maximum \(= 80\) nm; lateral resolution \(= 15\) \(\mu\)m; axial resolution \(= 10\) \(\mu\)m; frame rate 1 to 2 Hz. RSOD = rapid scanning optical delay line; A/D = analog to digital; DSP = digital signal processing.

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**Fig. 2.** Optical coherence tomography (OCT) handheld probe.
this is the first report of OCT imaging of the pediatric aerodigestive tract.

MATERIALS AND METHODS

Patient Population and Endoscopy

OCT imaging was performed on 15 patients undergoing surgical endoscopy at the University of California Irvine Medical Center under a protocol approved by the Human Subjects Institutional Review Board at the University of California, Irvine. Study subjects included patients with laryngeal papillomatosis, reflux, granulatation tissue formation, subglottic stenosis, and laryngomalacia. While patients were under general anesthesia, OCT imaging was performed with a handheld probe positioned manually or with endoscopic guidance. Multiple sites of interest were imaged including distal sites of the airway tract requiring laryngeal suspension. Digital photographs of imaged areas were obtained, and, only when clinically indicated, correlative biopsies were performed. In cases where biopsies were not performed, comparison of OCT images was made with previously published histology of the regions of interest.

OCT System and Instrumentation

The OCT system and instrumentation has been previously described. The components of our fiber-based OCT system are schematically illustrated in Figure 1. Near infrared light from a broadband light source (central wavelength \( \lambda = 1310 \text{ nm} \), full width at half maximum \( \Delta \lambda = 80 \text{ nm} \); AFC BT 1310, JDS Uniphase, San Jose, CA) enters a \( 2 \times 2 \) fiber optic coupler. In the reference arm, a rapid scanning optical delay line attains an A-scan at 500 Hz without phase modulation. The phase modulator generates 500 kHz phase modulation for heterodyne detection. Signals backscattered from the sample arm are obtained by phase-resolved processing with the interference fringes. The axial resolution of the system in tissue is approximately 7 \( \mu \text{m} \), whereas the lateral resolution approaches 10 \( \mu \text{m} \). The horizontal image window was set laterally from 2 to 10 mm in length, whereas detailed images of tissue microstructure were recorded up to a depth of 1.6 mm, depending on the turbidity of the media.

To image the pediatric airway in vivo, a custom flexible OCT probe was designed to accommodate specific anatomic structures. The probe consists of a 900 \( \mu \text{m} \) single mode fiber distally terminated by a gradient refractive index (GRIN) lens and a 0.7 mm right-angle prism (Fig. 2). The GRIN lens is 1.00 mm in diameter, 0.23 pitch, and works to focus light. Mounting of the prism and GRIN lens is accomplished with an optics grade, low-viscosity, wicking ultraviolet glue. Scanning is achieved by linearly translating the fiber optic along the long axis using a motorized piezo-driven stage (PI Line, model 663.4pr, Tustin, CA). The fiber optic and optical elements are enclosed within a transparent plastic tube (1.95 mm inner diameter, 0.21 mm thickness, fluorinated-ethylene-propylene material), which is mechanically supported and protected by a second slender outer stainless steel tube. To orient the user, colored markings were made along the sides of the optic fiber and opposite light exit along the fiber tip.

OCT Imaging

Images were obtained at the time of surgical endoscopy and were directed by the orientation of light propagation as it exited the tip of the OCT fiber and were confirmed with the use of a reference infrared sensor card (Newport Corp, Irvine, CA). The tip of the OCT probe was placed in near contact with the region of interest for OCT imaging. OCT was often performed in tandem with rigid endoscopy. OCT video files were subsequently transferred to a database in which still digital images were captured.

![Fig. 3. Optical coherence tomography image of normal tissues in the floor of mouth. E = epithelium; B = basement membrane; L = lamina propria. The bar in the lower right corner = 500 \( \mu \text{m} \).](image1)

![Fig. 4. Mucosal side of the lower lip. E = epithelium; B = basement membrane; L = lamina propria. Bar = 500 \( \mu \text{m} \).](image2)
and catalogued. Image orientation remained constant, with left and right sides of the images representing the proximal and distal regions of the area studied. Superior and inferior aspects of the image, respectively, illustrate the surface and the inner substance of the region of interest. Database images were reviewed, categorized, and partitioned into normal anatomic structures and pathologic states.

**OCT Image Analysis**

Images from multiple sites along the aerodigestive tract were obtained. Images were then sorted into three groups: 1) normal healthy tissues; 2) pathologic tissues; 3) transition zones at the borders of normal and pathologic tissue states. A tabulated review of images obtained at each anatomic subsite and pathologic conditions observed is given in Tables I and II. Of note, tissue images described in group 1 were found to reflect characteristic findings of tissues in normal healthy patients as well as the cumulative imaging experience of over 200 patients involved in laryngeal OCT studies at the University of California, Irvine.

Comparison of endoscopic and OCT imaging was performed with the use of ongoing OCT video capture, audio recording, and timed endoscopic photography. During endoscopic photography, both time and audio confirmation were performed while the OCT imaging probe was held stationary. This afforded correlation of OCT images and endoscopy image capture. Subsequent grading of OCT image quality was performed in the standard format by four independent reviewers, as previously described in our adult series.12

**Histology**

Specimens were fixed in 10% neutral buffered formalin, sectioned in 5-μm thickness, and then stained with hematoxylin-eosin followed by histologic examination with microscopy.

**RESULTS**

Fifteen pediatric subjects ranging from 18 months to 17 years of age participated in an OCT study of the pediatric aerodigestive tract with emphasis on various airway disorders. Cross-sectional images were collected from multiple sites during operative endoscopy. The anatomic distribution of images obtained is listed in Table I. Attention was also given to images demonstrating transitions from diseased to normal tissue architecture.

The following imaging series represents a survey of tissues in which epithelium, basement membrane, lamina propria, and other regional microstructures were clearly identified in normal tissues using OCT (group 1). Each OCT image represents a specific region of interest with common and unique characteristics. Figure 3 displays the floor of the mouth with clear identification of the stratified squamous epithelium along the mucosal surface, the underlying lamina propria, and the transition between these tissues along the basement membrane boundary. The variations of OCT grayscale intensity are directly related to the intensity of the reflected optical signal. Regions of darker appearance are less turbid and have lower optical scattering coefficients in comparison with regions of higher signal intensity. This allows for the differentiation between the less optically dense epithelium along the surface and the underlying interface of the basement membrane and lamina propria. Signal intensity also changes with further progression into the tissue and begins to diminish at a depth of 2 mm. Identification of seromucinous glands along the mucosal surface of the lower lip (Fig. 4), glandular characteristics of the false vocal fold (Fig. 5), and the cartilaginous ridges of the trachea (Fig. 6) is made with regard to changes in signal intensity, analysis of structural interface (outline), and known histology in the region of interest. Signal penetration to deeper tissue levels without intensity loss allows for the identification of structures consistent with ducts, glands, and lymphatic systems, which have low signal intensity (darker regions) that backscatter less photons than the surrounding tissues. By absorbing and scattering less light, the optical signal can propagate further into these tissues and still provide an adequate number of reflected coherent photons to produce a signal. Signal intensity is very high in turbid tissues that scatter light, whereas signal intensity is reduced when imaging substances that absorb the propagating or backscattered photons (blood). In tissues devoid of microstructural features (e.g., glands, ducts), there is a relative homogenous appearance in imaging, as seen in OCT imaging of the true vocal fold (Fig. 7). Tissues with glandular structures, and even more optically dense bone or cartilage, produce a more complex image with variable signal depth because of the variations of backscatter intensity (Fig. 8). OCT imaging of normal tissues provided a set of reference images for comparative analysis with other tissues (groups 2 and 3). In addition,
the placement of images in tandem was performed to offer a composite illustration of regional anatomy, as best exemplified in Figure 9.

Group 2 represents the data series of pathologic tissue states. Tissue microstructure was found to be considerably different in comparison with normal tissues. For example, the OCT image of a patient with subglottic stenosis reveals the normal landmarks of epithelium, lamina propria, and cricoid cartilage, but it also shows the dramatic tissue changes associated with diffuse scarring of this region. The considerable increase in signal intensity above the cricoid is likely caused by the dense collagen deposition that has replaced the glandular structures and native tissues as a result of chronic inflammation (Fig. 10). In other pathologic states, epithelial thickness and uniformity were markedly different as compared with group 1. As shown in Figure 11, OCT imaging of papillomatosis revealed a markedly thickened and irregular epithelium consistent with the classic irregular exophytic clusters that form along the vocal folds. Figure 12 shows images of granulation tissue produced by prolonged intubation from an endotracheal tube. The relatively homogenous signal of this tissue represents an amalgam of different cell types (inflammatory, vascular, and fibroelastic elements) devoid of any microstructural complexity. Notably, there is a lack of a basement membrane interface. Because of the thickness of the reactive tissue, no underlying boundaries (i.e., the basement membrane) were identified. In circumstances of tissue edema, reduction in signal intensity was observed along with an overall degradation of image quality. This is has been well described in other studies.9

Transition zones between laryngeal disease and normal tissues are represented in group 3. In Figure 13, the transition from normal epithelium to tissue hyperplasia associated with laryngeal papillomatosis can be clearly identified using OCT imaging. In addition, imaging of destructive pressure necrosis and reactive changes along the posterior subglottis reveal the transition between ischemic and viable tissues in an ulcer (Fig. 14). Finally, the transition between normal and reactive granulation tissue along the vocal folds is observed in Figure 15.

**DISCUSSION**

In this study, we present our experience in the imaging of 15 pediatric patients using OCT. With each patient studied, OCT was able to resolve surface epithelium, basement membrane interface, and supporting lamina propria in all normal tissues of the aerodigestive tract. In the majority of cases, we were able to visualize the interface of normal and pathologic tissues using this modality as well. The characterization of superficial disease is of exceptional value in head and neck surgery because operative endoscopy does not possess the ability to view into tissues, and CT, MRI, and ultrasound do not have the spatial resolution necessary to evaluate disease processes at the microscopic level. Although contact endoscopy has a resolution of 10 to 71 μm with the capability of observation of up to 100 μm below the tissue surface, this technique requires the use of in vivo staining with methylene blue,
acetic acid, or indigo carmine. In addition, contact endoscopy only provides visualization of the most superficial epithelium layers in an en-face plane. Presently, other noninvasive imaging methods are unable to characterize the tissue microstructures in the epithelium and subepithelial layers. A reliable means to noninvasively image living tissues at high resolution would add significantly to the diagnosis, treatment, and monitoring of diseases within the upper aerodigestive tract.

OCT is noninvasive technology that does not 1) require tissue staining; 2) produce ionizing radiation, or 3) image patients from only a fixed point or stage. In the current application, this modality operates in near real-time image production with the capacity for video production. OCT has been well established in multiple fields of laboratory and medicine research and provides the ability to microscopically view tissues without the limitations, complications, and artifacts inherent in surgical biopsy and histologic processing. It is important to reiterate that the OCT fiber used to produce the images in this pediatric series was only 1 mm in diameter, and, combined with the handheld instrument, the overall diameter did not exceed 2 mm. These relatively small dimensions, when compared with the diameter of pediatric rigid endoscopes (2.7 mm and 4.0 mm), make this technology ideal for the evaluation of the pediatric airway.

This study is the first to characterize normal tissue structures and common disease processes of the pediatric airway with OCT imaging. Correlation of OCT imaging with known histology revealed unique optical characteristics of various tissue layers as well as the complex microstructures that included glands, ducts, vessels, and cartilage. OCT imaging of pathologic conditions such as recurrent respiratory papillomatosis revealed changes in the epithelial density and tissue thickness while confirming the integrity of the basement membrane interface. In contrast, OCT images of granulation and ulcerated tissues revealed a complete absence of normal tissue microanatomy and the basement membrane. Further imaging of these and other lesions revealed transition zones between normal and disease processes of laryngeal tissues. One limitation discovered when applying this technology was the limitation in imaging large, bulky lesions. In these situations, the overlying tissue was found to reduce the optical signal that reached the basement membrane interface and the backscattered light from these areas. This was also observed in the study of granulation tissue, ulcerative lesions, and large, exophytic laryngeal papillomas. The diagnosis of such lesions is not subtle in pediatric populations and would often merit biopsy or excision on clinical grounds alone. What appears to be

Fig. 11. Optical coherence tomography imaging and endoscopic photograph of recurrent respiratory papillomatosis. H = epithelial hyperplasia; B = basement membrane; L = lamina propria. Bar = 500 μm.

Fig. 12. Optical coherence tomography imaging of granulation tissue. Note the absence of epithelium and basement membrane. G = granulation tissue. Bar = 500 μm.

Fig. 13. Optical coherence tomography imaging of transition zone between laryngeal papillomatosis and adjacent normal tissue. H = epithelial hyperplasia; E = epithelium; B = basement membrane; L = lamina propria. Bar = 500 μm.

Fig. 14. Optical coherence tomography imaging and endoscopic photograph along the posterior trachea revealing transition between ulceration and intact tissues. E = epithelium; B = basement membrane; L = lamina propria; C = cricoid cartilage. Bar = 500 μm.

Fig. 15. Optical coherence tomography (OCT) imaging and endoscopic photograph of granulation tissue along glottis. OCT image of transition zone between granulation and adjacent tissue. E = epithelium; B = basement membrane; L = lamina propria; G = granulation tissue. Bar = 500 μm.
one of the greatest potential applications of OCT is the ability to define tissues unaffected by disease processes. In these circumstances, OCT could aid in the guidance of surgical biopsy or tissue resection to optimize the preservation of sensitive tissues such as the vocal folds.

There are a number of challenges when applying this technology, each of which can compromise image quality. We have found a learning curve, as seen in many endoscopic techniques, in which the operator needs to become accustomed to applying endoscopy and OCT imaging at the same time. The surgeon must integrate the visualization of two surgical fields (one OCT, one traditional endoscope) with the appropriate probe and with endoscope positioning and stability. It is important to note that probe position must be adjusted “on the fly” to improve image quality and requires a working knowledge of image interpretation to determine when such actions are necessary.

Finally, because of the limited number of patients in the current study, further investigation is necessary to evaluate the usefulness of this modality in the imaging of the pediatric airway. These current findings are encouraging as to the feasibility of applying this imaging technology in such a young patient population and represent the basis of our ongoing pediatric investigations.

CONCLUSION

The ability to perform in vivo tissue imaging with a noninvasive, high-resolution modality could significantly alter the management of pediatric airway disease. With the capability to perform studies at or near video rates, this system could easily complement surgical endoscopy and allow performance of tissue biopsies or resections with greater precision. In addition, OCT is an evolving imaging modality in which improvements in light sources, electromechanical design, and high-speed frame production will lead to higher resolution images and greater ease of image acquisition.

The application of OCT imaging provides valuable information in characterizing diseases of the pediatric airway, guiding surgical therapy, and monitoring the progression of airway disease. Our current investigations are focused on the continuing development of applications of OCT in our pediatric population as well as in advancing the application of this promising modality in the imaging of the newborn patient.

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BIBLIOGRAPHY