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Long-range Fourier domain optical coherence tomography of the pediatric subglottis

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ABSTRACT

Background: Acquired subglottic stenosis (SGS) most commonly results from prolonged endotracheal intubation and is a diagnostic challenge in the intubated child. At present, no imaging modality allows for *in vivo* characterization of subglottic microanatomy to identify early signs of acquired SGS while the child remains intubated. Fourier domain optical coherence tomography (FD-OCT) is a minimally invasive, light-based imaging modality which provides high resolution, three dimensional (3D) cross-sectional images of biological tissue. We used long-range FD-OCT to image the subglottis in intubated pediatric patients undergoing minor head and neck surgical procedures in the operating room.
Methods: A long-range FD-OCT system and rotary optical probes (1.2 mm and 0.7 mm outer diameters) were constructed. Forty-six pediatric patients (ages 2–16 years) undergoing minor upper airway surgery (e.g., tonsillectomy and adenoidectomy) were selected for intraoperative, trans-endotracheal tube FD-OCT of the subglottis. Images were analyzed for anatomical landmarks and subepithelial histology. Volumetric image sets were rendered into virtual 3D airway models in Mimics software.
Results: FD-OCT was performed on 46 patients (ages 2–16 years) with no complications. Gross airway contour was visible on all 46 data sets. Twenty (43%) high-quality data sets clearly demonstrated airway anatomy (e.g., tracheal rings, cricoid and vocal folds) and layered microanatomy of the mucosa (e.g., epithelium, basement membrane and lamina propria). The remaining 26 data sets were discarded due to artifact, high signal-to-noise ratio or missing data. 3D airway models were allowed for user-controlled manipulation and multiplanar airway slicing (e.g., sagittal, coronal) for visualization of OCT data at multiple anatomic levels simultaneously.
Conclusions: Long-range FD-OCT produces high-resolution, 3D volumetric images of the pediatric subglottis. This technology offers a safe and practical means for *in vivo* evaluation of lower airway microanatomy in intubated pediatric patients. Ultimately, FD-OCT may be applied to serial monitoring of the neonatal subglottis in long-term intubated infants at risk for acquired SGS.

1. Introduction

Acquired subglottic stenosis (SGS) in a neonate or child is most commonly a result of prolonged endotracheal intubation for mechanical ventilation [1]. In these intubated patients, the endotracheal tube (ETT) may impose pressure and/or exert a shearing effect against the delicate and pliable subglottic mucosa. This may induce necrosis and trigger a wound healing cascade which, if undiagnosed, culminates in granulation and stenosis [2–4]. Furthermore, the cricoid is the only complete cartilaginous ring of the pediatric airway, preventing airway expansion in the event of subglottic injury and edema [4–6]. While the current incidence of acquired SGS in neonatal intensive care unit (NICU) settings is approximately 0.24–3.0% [6–8], SGS remains a diagnostic and therapeutic challenge for otolaryngologists. High-grade SGS often requires multi-staged surgical intervention which

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is associated with increased morbidity and risk for long-term voice impairment or dysphonia [9,10].

At present, clinicians have limited options for diagnosing SGS. High-resolution computed tomography (CT) has spatial resolution up to 0.5 mm, but exposes patients to ionizing radiation [11]. Direct laryngoscopy and rigid endoscopy remain the gold standard for diagnosis of SGS. However, this procedure is often performed after patients fail extubation in the ICU with clinical or radiographic signs of SGS. By this point, mature scar tissue has often developed, requiring endoscopic or open surgical intervention. Furthermore, rigid endoscopy is limited to a visual assessment of the luminal dimensions and mucosal surface of the airway, entails the use of general anesthesia and carries risk of mucosal trauma from airway instrumentation. Hence, there exists a need for a less invasive imaging modality with the capability of evaluating the substructural anatomy of subglottic tissues while children are intubated. This may help identify early signs of epithelial and subepithelial injury secondary to the ETT and alert the otolaryngologist and intensivist prior to the onset of fibrosis and cicatrization.

Optical coherence tomography (OCT) is a minimally invasive imaging modality that couples non-ionizing near infrared light (laser or super luminescent LED) with principles of low coherence interferometry [12]. OCT acquires high resolution (~10 μm), three dimensional (3D) cross-sectional images of living tissue at video rate imaging speeds. OCT is analogous to ultrasound B-mode imaging, however, instead of measuring acoustic echoes, OCT measures back-reflectance of light from biological tissue (up to 2 mm penetration depth) based on optical scattering properties of tissue structures. Previous reports have described OCT of the neonatal and pediatric subglottis [13,14]. However, these studies used time-domain (TD-OCT) systems which were limited by slow imaging speeds (0.33 frames/s) and linear, two-dimensional (2D) image acquisition methods. A derivative of conventional OCT, known as anatomic or long-range OCT, has been shown to image airway lumens up to 30–40 mm in diameter [15,16]; systems used in these studies also had low imaging speeds (1–5 frames/sec). Frequency, or "Fourier", domain swept source OCT (FD-OCT) is an advanced OCT technology which exhibits higher sensitivity and imaging speeds (25 frames/s) than TD-OCT systems, allowing for real-time, dynamic monitoring of the airway. In 2012, Jing et al. described *in vivo* high-speed long-range FD-OCT of the adult upper airway [17]. Their system utilized a rotary endoscopic probe which allowed 360° scanning of the airway (axial imaging range ~15 mm) and demonstrated the capability of long-range FD-OCT to acquire anatomic and substructural images of the airway in a 3D volumetric format. Additional reports of swept source anatomical OCT imaging of *ex vivo* (swine) airways and pediatric airway phantoms in a volumetric format (helical scanning) are available in the literature [18,19]. Those FD-OCT systems consisted of a fiber-optic probe integrated with a small-bore flexible endoscope for quantification of airway lumen geometry.

The objective of this study was to evaluate the feasibility and methodology of long-range FD-OCT imaging of the subglottis in intubated children undergoing minor upper airway surgery. A controlled, operative setting with adequate personnel and resources for airway management allowed for safe evaluation of trans-ETT OCT imaging of the airway and simulation of bedside OCT imaging of intubated patients. While the patients included in this study were not at risk for acquired SGS, FD-OCT was used to identify normal structural microanatomy within the subglottis. This is the first report of *in vivo* long-range (~9 mm axial imaging range) FD-OCT in the pediatric lower airway. This investigation is a step towards the use of long-range FD-OCT in the NICU to acquire volumetric images of the intubated neonatal airway. In anticipation of this future application, the current study served as a pilot to optimize specifications of the OCT sampling probe and trans-ETT imaging methodology.

2. Material and methods

2.1. Study design

Approval for this study was obtained from the human subjects Institutional Review Board at the University of California Irvine (HS# 2003-3025) and Children's Hospital of Orange County (IRB #1211115). We conducted a prospective clinical trial to evaluate long-range FD-OCT of the subglottis in pediatric patients undergoing minor upper airway surgery (e.g., tonsillectomy and adenoidectomy). The study was temporally divided into two phases (Phases I and II); alterations to OCT probe design, rotational and translational speeds were made between phases. All patients reported no history of subglottic injury or prolonged endotracheal intubation. Patient age, weight and pertinent medical history were recorded from the medical record.

2.2. OCT system

A long-range swept source FD-OCT system was designed and constructed (Fig. 1A). The interferometry unit specifications are previously described [17]. Near-infrared light is generated from a 1310 nm swept source laser (Axsun Technology, Billerica, MA, USA) operating at 50 kHz A-line scan rate. Light is split by a 90:10 coupler into a sample arm (biological tissue) and reference arm (mirror), respectively. In the reference arm, an acousto-optic modulator (AOM; Brimrose, Sparks, MD, USA) generates a frequency shift (150 MHz) which allows for the removal of mirror terms that arise from Fourier transform processing and utilization of the complete coherence length of the laser. For our system, this amounts to an increase in imaging range by a factor of 2, as compared to a standard OCT system utilizing the same light source. The 6 dB system sensitivity range as measured with a collimated beam in the sample arm was reported previously to be 12.8 mm [20]. Based on unique optical scattering properties of tissue structures, OCT signal is back-reflected from the sample arm and recombined with the reference arm to generate a reflectivity profile (A-line). Two thousand A-lines are aligned to form a single frame, with axial resolution of approximately 10 μm.

Two types of custom-built, flexible endoscopic OCT probes (75–80 cm length) were constructed with outer diameters (OD) of 1.2 mm (Phase I) and 0.7 mm (Phase II). In Phase II of the study, a slimmer probe was built to simulate trans-ETT imaging of the neonatal subglottis. In NICU settings, endotracheal intubation is typically conducted with uncuffed 2.5–3.5 Fr ETTs. Hence, 0.7 mm OD probes more suitable for the luminal dimensions of neonatal ETTs and ventilation circuits were tested.

Probes consisted of a single-mode optical fiber encased in a stainless torque coil (Asahi Intecc; Santa Clara, CA, USA). Fibers were coupled distally with a gradient refractive index (GRIN; Go!Foton, Somerset, NJ, USA) lens used to focus the laser beam on a 45° gold-coated mirror which reflected the signal at a 90° angle. The GRIN lens and mirror were enclosed in a custom designed metal housing to protect these fragile components (Fig. 1B). The 1.2 mm OD probe had a focal length of ~9 mm and a Rayleigh range of 5.2 mm. The 0.7 mm OD probe had a focal length of ~3 mm and a Rayleigh range of 850 μm. While the reduced Rayleigh range of the smaller probe reduces the overall imaging range, these probes were designed to cover the majority of radial distances to tissue surfaces encountered in the neonatal subglottic airway. The overall sensitivity roll off with respect to depth for the FD-OCT system and a 9 mm focal length probe is shown in Fig. 2. A 6 dB sensitivity roll-off is demonstrated at a total imaging range of 8 mm which is less