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Clinical and surgical implications of intraoperative optical coherence tomography imaging for benign pediatric vocal fold lesions

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ABSTRACT

Introduction: Benign vocal disorders in children include an extensive list of abnormalities creating a variety of debilitating levels of dysphonia. Precise delineation of the benign lesion type and margins may have significant public health implications in children. An innovative technology such as optical coherence tomography (OCT) is being explored to delineate pediatric benign laryngeal lesions. An accurate assessment of the subepithelial morphology may help towards tailoring more personalized therapeutic treatments. This study was established to highlight key morphological and optical features of benign pediatric laryngeal lesions using intraoperative OCT and to suggest clinical implications that arise from such optical imaging.

Methods and materials: This in vivo study was performed at Massachusetts Eye and Ear Infirmary. Intraoperative imaging was performed on twenty-five pediatric patients ranging from 1 year to 16 years of age presenting hoarseness. Three-dimensional OCT images of benign laryngeal lesions or a subsite of the lesion were acquired.

Results: High-resolution OCT images of 25 patients with benign laryngeal lesions such as nodules, cysts, Reinke's edema, vocalis sulcus, and papilloma revealed distinct and specific morphological differences with normal tissue. Nodules show a symmetrical superficial remodeling of the vocal fold epithelial layer and the basement membrane. Cysts have oval-like shape and are either superficial or deeply located in the lamina propria. Sulcus vocalis OCT imaging allows characterizing if the lesion is shallow or deep according to Ford's classification system. Reinke's edema of the mucosa can be observed and quantified, which may lead to suspicion on the underlying social and medical conditions. Finally, the ability to assess margins and depth of invasion of papilloma lesions is demonstrated, raising the possibility to use OCT with angiolytic lasers for patient-tailored treatments.

Conclusions: OCT imaging of benign pediatric vocal lesions is promising as it could improve preoperative decision-making and possibly peroperative imaging-guidance for patient-tailored treatments. An assessment of the optical contrast between healthy and abnormal tissue may help towards a more qualitative and quantitative approach to current standard care, especially when diagnosis remains unclear.

1. Introduction

Childhood is a period of anatomical and physiological changes susceptible to affect the larynx and its respiratory, phonatory functions. Arising as a consequence a vast array of laryngeal disorders is affecting this population, which have significant public health implications [1]. Over 5 million children are affected in the United States. School-aged children from 8 to 14 years [2] are the most affected age group with a reported prevalence of 3.9–23.4 percent [3–5]. During this critical developmental period, where communication skills and psychosocial abilities are pillars of a child identity, voice disorders may adversely impact an individual life by generating poor self-esteem and self-image [6]. Furthermore, children with unresolved voice disorders often need additional ongoing treatments into adulthood adding a substantial burden on the medical system [1] with several billion dollars in productivity loss [7,8].

Unsurprisingly, functional assessment of pathological voices in children remains challenging. Often dysphonia can persist or reoccur over a five-year period after the initial assessment, suggesting the importance of an early and accurate intervention [9]. The essential rationale is to identify and distinguish among benign vocal fold lesions, and potential malignant tumors. However, the etiology can be challenging to establish, as the underlying laryngeal symptoms are often nonspecific, subtle or infrequent. Moreover, dysphonia may originate

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from multiple cofactors such as behavioral, environmental or inherited [10]. As such, obtaining a thorough patient history with laryngoscopy is fundamental for dysphonic children.

Although the evaluation of laryngeal lesions can be achieved with a rigid or transnasal fiberscope, videolaryngostroboscopy remains the primary clinical tool to evaluate possible abnormal vibratory motion of the vocal folds [11]. Functional and biomechanical features such as amplitude, asymmetry, abnormal closure patterns and vibratory behavior, can be assessed in this fashion [12]. These features may refine diagnoses and provide better postoperative planning and voice management [13]. However, stroboscopy or high-speed video [6] examination is challenging to perform on children and is largely subjective to interpretation as vibratory patterns have yet to be correlated with pathological conditions [14]. Moreover, a certain subset of children are either too young or non-compliant to allow for successful office endoscopy. For these children, suspension laryngoscopy remains the gold standard diagnostic tool, where dysphonia is pronounced and diagnosis must be procured.

As many laryngeal pathologies have subepithelial roots, some lesions may remain invisible or hard to distinguish with the above imaging techniques. An additional method of contrast may improve clinical management of patients with voice disorders. As such, optical coherence tomography (OCT) has been used to evaluate non-invasively the adult and pediatric laryngeal anatomy [12–18]. Its potential to image the pediatric laryngeal mucosa, cricoid cartilage and tracheal rings has been shown [15,16]. However, most studies so far have been focused on adult laryngeal diseases, and a very few have addressed pediatric benign vocal fold lesions such as vocal nodules, cysts, polyps, Reinke's edema and sulcus. The optical contrast between healthy and abnormal tissue may help towards a more qualitative and quantitative approach to current standard care, especially when diagnosis remains unclear. Clinicians should be aware of new and modern imaging modalities to aid therapeutic decision-making. The purpose of this study is to characterize the key morphological characteristics of benign pediatric vocal fold lesions using OCT and to correlate with clinical insights that correspond to intraoperative optical images of these lesions.

2. Materials and methods

2.1. Patient population

OCT imaging was performed on 25 dysphonic pediatric patients (n = 12 male, n = 13 female) ranging from 1 year to 16 years of age undergoing direct laryngoscopy under general anesthesia. Parents were informed, and written consents were obtained before intraoperative examination. As a comparative baseline, OCT images acquired on healthy laryngeal tracts from a previous study [17] were used. This study was performed at Massachusetts Eye and Ear Infirmary under the approval of the Institutional Review Board.

2.2. Instrumentation

The intraoperative OCT system used in this study was previously described [17,18]. The swept-source system is based on vertical-cavity surface-emitting laser source [19,20] centered at 1300 nm (SL1310V1, Thorlabs) with a tuning range of 110 nm (at full width at half maximum). Imaging of laryngeal lesions is achieved with a 3.6 mm handheld rigid scope, which is enclosed by a translucent disposable sterile sheath (0.2 mm thickness, Slide-ON Endosheath, Medtronic). The probe was designed for accurate positioning and rapid volumetric OCT imaging of the airway. Orientation laser marks along the stainless tube orients the clinician and fast galvanometers (6215H, Cambridge Technology) allow three-dimensional data to be acquired under 18 s (2, 2, and 5 mm, 1040 × 1040 x 1040 voxels). The system axial and lateral resolution is respectively 12 and 25 μm in tissue.

Table 1
OCT Intraoperative imaging of pediatric lesions.

Lesion	Patients		
	Male	Female	Total
Nodules	3	5	8
Cyst	2	1	3
Reinke Edema	1	1	2
Sulcus	1	1	2
Papilloma	6	3	9

2.3. Intraoperative imaging

Patients underwent a perceptual and a visual examination, before each intraoperative intervention. Conventional and OCT imaging were performed under suspension laryngoscopy. The glottis, including the anterior commissure, was exposed with a Lindholm laryngoscope for direct laryngoscopy (0°, 4 mm, Storz). Under endoscopic guidance, the handheld OCT probe tip was precisely positioned on each suspicious lesion or a subsite of the lesion. Positioning the probe and imaging both vocal folds extents the OCT imaging procedure by 45 s. When possible, lesion images were acquired with the surrounding tissue for delineation of margins. OCT cross-sections are displayed in logarithm scale (heat colormap, −84 dB) with the signal intensity proportional to the optical scattering coefficient. Endoscopic images were recorded and correlated with OCT for further analysis. All images are in the same orientation as acquired in the surgical setting. We used data previously obtained characterizing normal pediatric vocal fold with OCT [17] to compare with abnormal pathologies. This database represents a collection of longitudinal scans, which cover the true vocal fold and the subglottic region (up to 6 mm). Table 1 illustrates the gender distribution of patients imaged with laryngeal lesions in this study.

3. Results

All patients (n = 25) have been successfully imaged during suspension laryngoscopy with no follow-up complications. Clinical and optical observations are provided for different lesion imaged such as nodules (n = 9), cysts (n = 4), Reinke's edema (n = 2), vocalis sulcus (n = 2), and laryngeal papilloma (n = 8). As a baseline, a description of the normal laryngeal tract is first presented.

3.1. Intraoperative imaging of the glottis

A typical intraoperative view of a healthy 2-month-old aerodigestive tract (Fig. 1A) reveals both vocal folds pearly white and abducted, forming a V-shape structure. The free edges of the vocal folds are symmetrical with no appearance of lesions. The coronal schematic larynx section (Fig. 1B) highlights the most relevant structures of the human glottis and the subglottic region, which illustrates the stratified squamous nonkeratinized epithelium (SSE), pseudostratified columnar epithelium (PSE), lamina propria (LP), vocalis muscle (TA), mucoserous glands (MG), thyroid cartilage (T), cricoid cartilage (C), and cricothyroid muscle (CT).

The ability to delineate the mucosa layers based on the optical tissue properties is clearly demonstrated on the corresponding aerodigestive tract OCT cross-section (Fig. 1C). The vocal fold mucosa is characterized by a thin stratified squamous epithelial layer, predominantly cellular, and with its underlying lamina propria, mostly gelatinous. The basement membrane anchors the epidermis to the superficial lamina propria. This junction is of major interest as it is sensitive to trauma [21] and cancer cells [22]. Inferiorly to the vocal fold edge, the epithelium layer thickens. This thickening is attributed to the transition from SSE to PSE cells. This was confirmed with histopathology sections from previous ex vivo studies [18,23]. The TVF lamina propria is