Chapter 38
Clinical applications of OCT in laryngology

David Shamouelian, Tjoson Tjoa, Veronika Volgger & Brian J.F. Wong

Abstract

Here we discuss pertinent information on clinical applications of OCT in context of non-malignant laryngeal mucosal pathologies. We also demonstrate applicability of OCT to the studies of vocal fold (VF) kinetics.

Keywords: laryngeal OCT, lamina propria, basement membrane, true VF, subglottis, epiglottis, laryngeal hyperkeratosis, VF polyp, VF cyst, respiratory papillomatosis, VF granuloma, Reinke’s edema, Polarization Sensitive OCT, VF vibration, Doppler OCT, ex vivo, in vivo

Introduction

The evolution of laryngeal optical coherence tomography (OCT) was discussed in our previous chapter. In this chapter, pertinent clinical applications of OCT in the study of benign laryngeal pathologies are presented. Advances in OCT technology have also launched new applications in the study of vocal fold vibration.

OCT and histological tissue comparison

Several studies have investigated the correlation between OCT imaging and histology, assessing the reliability of its cross-sectional information of the larynx. In 2004, Bibas et al. [1] compared OCT images with corresponding histological sections from an ex vivo laryngectomy specimen. The epithelial layer, lamina propria, subepithelial structures, and basement membrane were readily identifiable. Wong [2] measured epithelial thickness at several laryngeal sub-sites via OCT and noted the epithelium was thinnest in the subglottis and thickest along the lingual surface of the epiglottis. The epithelial thickness of true and false VF was measured at about 125 micrometers. Kaiser and colleagues [3] examined the in vivo thickness of different layers of the laryngeal mucosa and compared them with histopathological specimens. Kraft’s study [4] on epithelial thickness in normal, dysplastic, and malignant lesions exhibited a direct relationship between OCT-derived epithelial thickness and the progression to malignancy. Conversely, benign lesions typically have only a slight increase in epithelial thickness. These studies laid the foundation for OCT’s potential utility to distinguish between benign and malignant pathology.

OCT of benign laryngeal pathology

In 2005, Wong and colleagues [2] offered the first comprehensive report systematically examining VF microstructure using OCT with an emphasis on benign pathology. Further expanding on the topic, Kraft [5] and colleagues published the definitive study in laryngeal OCT in 2008. The most significant OCT finding in benign laryngeal disease is the consistent identification of an intact basement membrane, separating the laryngeal epi-
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Epithelium from the underlying lamina propria. OCT imaging of the normal true VF exhibits epithelium that is identified as a thin, low signal intensity structure at the surface (Figure 1). Low signal intensity is a reflection of less optical scattering and is consistent clinically with the translucent appearance of the epithelium. In contrast, higher signal intensity is produced by the optically dense structures in the lamina propria such as blood vessels, lymphatics, and layers of collagen and elastin fibers. The basement membrane of the epithelium is clearly delineated separating the epithelium from lamina propria.

Figure 1. OCT image of true VF. The junction between the stratified squamous epithelium (e) and superficial lamina propria (slp) are very well defined, and arrow indicates the location of the basement membrane (bm). Courtesy of Brian J.F. Wong, MD, PhD.

The transition zone between the squamous epithelium of the VF and the gland-bearing ciliated pseudostratified columnar epithelium of the subglottis is presented in Figure 2. Arrows indicate structures consistent with seromucinous glands and ducts.

Figure 2. Subglottis. Image of transition zone between the stratified squamous epithelium (e) of the true vocal cord and the gland-bearing ciliated pseudostratified columnar epithelium of the subglottis. Basement membrane (bm); superficial lamina propria (slp); seromucinous glands (sg); and seromucinous ducts (sd). Courtesy of Brian J.F. Wong, MD, PhD.
The epiglottis (Figure 3) also demonstrates glandular properties. A sharp demarcation exists between the lamina propria and the smooth surface of the epiglottic cartilage.

![Figure 3. The Epiglottis. A sharp demarcation exists between the lamina propria (LP) and what is likely the smooth surface of the epiglottic cartilage (EC). Stratified squamous epithelium (SS); basement membrane (BM); seromucinous glands (SG). Courtesy of Brian J.F. Wong, MD, PhD.](image)

Nonmalignant pathologic processes of the VFVs demonstrate characteristic OCT features. In hyperkeratotic lesions of the larynx (Figure 4), the epithelial layer is markedly thickened, however the basement membrane remains clearly intact.

![Figure 4. Laryngeal hyperkeratosis. In hyperkeratotic lesions (hk) of the larynx, the epithelial layer is markedly thickened, whereas the BM was clearly demonstrated to remain intact. Corresponding endoscopic imaging and histopathology are presented. Basement membrane (bm); superficial lamina propria (slp). Courtesy of Brian J.F. Wong, MD, PhD.](image)

Vocal cord polyps (Figure 5) exhibit a normal to slightly thickened epithelium regionally with a loosely translucent lamina propria in contrast to normal VF, where the latter has more optical scattering.
**Figure 5.** OCT images of vocal cord polyps. Endoscopic image of an organized polyp, the corresponding OCT image, and corresponding histopathology after excision. There is good correlation between the *in vivo* OCT images and histopathology. Epithelium (E); basement membrane (BM). Courtesy of Brian J.F. Wong, MD, PhD.

VF cysts (Figure 6) demonstrate a thin translucent outer and inner epithelium as well as a more optically scattering intermediate connective tissue. The content of the cyst may vary from very translucent to intensely scattering, depending on its consistency.

**Figure 6.** Vocal cord cyst. The more scattering intermediate connective tissue is lying in between a thin translucent outer and inner epithelium. The content of the cyst (C) can vary from very translucent to intensely scattering, depending on its consistency. Epithelium (E). Courtesy of Brian J.F. Wong, MD, PhD.

Respiratory papillomas (Figure 7) present with a thickened mostly translucent epithelium and a typical fibrovascular core. The basement membrane remains intact and is clearly visible in superficial papillomas, whereas it cannot be identified in exophytic lesions due to the limited depth of penetration of OCT.

**Figure 7.** Respiratory papillomas. A thickened mostly translucent epithelium and a typical fibrovascular core. The basement membrane remains intact and is visible in superficial papillomas (P), whereas it cannot be identified in exophytic lesions due to the limited depth of penetration. Epithelium (E); basement membrane (BM). Courtesy of Brian J.F. Wong, MD, PhD.
In VF granulomas (Figure 8), the basement membrane is no longer recognizable due to an epithelial defect and the underlying granulation tissue shows a more regular pattern compared to invasive carcinomas that is more grainy and irregular.

**Figure 8.** Vocal cord granuloma. The basement membrane is no longer recognizable due to an epithelial defect. The underlying granulation tissue shows a more regular pattern than invasive carcinomas and no tumor plugs reaching to deeper tissue layers are visualized. Courtesy of Brian J.F. Wong, MD, PhD.

*Ex vivo* histologic sampling of Reinke’s Edema is limited as the fixative process fails to characterize edema and little is known about the true *in vivo* changes of VF structure with this disorder. Kraft & Glanz [6] investigated Reinke’s edema *in vivo* via OCT and devised a reproducible, objective classification system based on lamina propria morphology. This classification includes: Grade I – feathered structure; Grade II – lacunar structure; and Grade III – confluent structure.

There are several well-demarcated low-signal intensity regions within the lamina propria, which represent regions where clear fluid has collected. In Grade I, there is thin, feathery, fluid stranding of the lamina propria; in Grade II (Figure 9), there are distinct lakes of low intensity fluid regions; and in Grade III, there is a confluence of the lacunae with diffuse edema.

**Figure 9.** Reinke’s Edema. OCT imaging of Reinke’s edema (E) classification system based on lamina propria morphology. This is an image of Grade II (lacunar structure) with distinct lakes of low intensity fluid regions. Stratified squamous (SS) epithelium; basement membrane (BM). Courtesy of Brian J.F. Wong, MD, PhD.
Polarization Sensitive OCT (PS-OCT) and laryngeal scar imaging

A related form of OCT imaging, polarization sensitive OCT (PS-OCT) augments conventional OCT by detecting tissue birefringence. This occurs in molecules, such as collagen, that change the polarization state of reflected light. The presence of organized collagen fibers within VF tissue produces a characteristic “light-dark-light” banding pattern on PS-OCT. This pattern is disrupted or absent when collagen fibers are altered by pathologic changes within the layered microstructure. Polarization-sensitive images are generated concurrently with conventional OCT images and they provide complimentary information.

Burns and colleagues [7] performed PS-OCT imaging on eight patients with VF scarring. Images obtained from a scarred VF display absence of the superficial lamina propria, leaving epithelium attached directly to the ligament. Areas of scar typically show strong birefringence on PS-OCT imaging indicative of high collagen content. While conventional OCT imaging is similar for both normal and scarred VF, the PS-OCT banding pattern of scarred VF is more intense (i.e., the individual bands are narrower). Therefore, PS-OCT images can potentially map areas of scar within normal VF tissue, thereby identifying sites into which biomaterials could be injected to restore pliability. Using PS-OCT to precisely map scar can facilitate surgical efforts in restoring VF pliability.

OCT and laryngeal vibration

In 2006, Luerssen and colleagues [8] were first to demonstrate dynamic VF vibration in an ex vivo porcine model using OCT. The same year, Yu and colleagues [9] reported the first human OCT study to capture in vivo VF phonation. These early functional OCT studies had been limited to detailing basic phonatory parameters such as vibration frequency and magnitude. However, with faster, more advanced OCT technologies, applications of functional VF vibration have emerged as a promising new avenue of research. Kobler et al. [10] captured sequential snapshots of VF oscillation across the vibratory cycle using a novel continuous OCT image acquisition system. They were able to image a wave at a single cross-section and measure its amplitude, displacement, and frequency. Using OCT’s distinct ability to image sub-epithelial structure, it is possible to estimate local tissue dynamics and internal tissue strain. They noted a differential movement in the superficial lamina propria as a function of depth. This technology will facilitate testing basic tenets of VF function, such as the cover-body theory.

Liu et al. [11] introduced a Doppler OCT, a functional extension of OCT combining Doppler principles with OCT reporting high quality and cross-sectional velocity distribution images of vibrating vocal cords. Using an ex vivo porcine laryngeal model, they displayed variable wave velocity based on the location of the wave. Acceleration of the wave is highest at the peak and valley regions of the wave and lowest at the waist of the wave.

References
