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Optical Coherence Tomography of Laryngeal Cancer

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Objectives: **Optical coherence tomography (OCT) is a high-resolution optical imaging technique that produces cross-sectional images of living tissues using light in a manner similar to ultrasound. This prospective study evaluated the ability of OCT to identify the characteristics of laryngeal cancer and measure changes in the basement membrane, tissue microstructure, and the transition zone at the edge of tumors.** ***Materials and Methods:*** **One hundred thirty-three patients underwent OCT examination during surgical endoscopy of the head and neck. Twenty-two patients with laryngeal cancer or a history of laryngeal cancer were imaged with a fiberoptic OCT system. Tumor and adjacent transition zones were imaged along with uninvolved subsites. OCT images were correlated with histopathology.** ***Results:*** **Twenty-six OCT examinations were performed in 22 patients. Basement membrane disruption was seen in 18 subjects, all of whom had histology showing classic features of cancer. A transition zone to uninvolved epithelium at the tumor periphery was also often observed. In six studies, benign or premalignant processes were histologically confirmed. In three thin, superficial lesions, an intact basement membrane was observed. The basement membrane could not be identified in three other bulky exophytic, premalignant lesions, primarily because of increased superficial signal backscattering observed in pathologic tissues.** ***Conclusions:*** **OCT clearly identifies basement membrane violation from laryngeal cancer and can identify transition zones at the cancer margin. In bulky exophytic lesions, OCT signal may not penetrate deeply enough to show the basement membrane, but for many suspicious lesions that require exclusion of cancer, OCT shows potential for assisting in diagnostic assessment.** ***Key Words:*** **Optical coherence tomography, larynx, vocal cord, laryngeal cancer, endoscopy, optical biopsy, laryngology.**

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INTRODUCTION

Optical coherence tomography (OCT) is a rapidly evolving imaging technology that combines a broadband, low coherent light source with interferometry and signal processing to produce high-resolution images of living tissues.[1] OCT relies on analysis of phase and intensity differences in backscattered light to discern differences in tissue structure. Current OCT devices used in clinical studies have a resolution of approximately 10 μm and a depth of penetration of up to 2 mm in most soft tissues, depending on the turbidity of the media.[2] In a manner analogous to ultrasound technology, OCT uses near-infrared light waves to produce cross-sectional images oriented in the same plane as histologic preparations from tissue biopsies. The first clinical applications of OCT were in ophthalmology to obtain measurements of structures within the globe and to image retinal pathology.[3] More recently, OCT applications have expanded to include imaging of solid tissues, and the technology shows promise for evaluating epithelial and subepithelial structures throughout the body.[4–8]

The ability to provide high-resolution cross-sectional images of turbid media such as living tissues provides the opportunity to characterize both normative microanatomy and disease.[9] In particular, OCT imaging has the potential to impact clinical management whenever detailed information about surface and subsurface microstructure is essential for accurate diagnosis or treatment, and when a

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surgical biopsy has the potential for producing significant morbidity. OCT images with a resolution of 10 μm can be routinely obtained, and the capabilities of advanced laboratory-based systems may even exceed 1 μm.[10–13] Images can be obtained immediately in the operating room and at video or near-video frame rates. The technology is noninvasive, using safe low-power, near-infrared light to interrogate tissue. The technique does not rely on tissue contact (as ultrasound does), therefore there is potential for development of noncontact devices mounted on a surgical microscope or of office-based systems combined with rigid or flexible endoscopes, both of which our group is actively working to develop.

Previously, we have described the in vivo microanatomy of the larynx for both normal and benign pathologic conditions.[2] In this companion article, we focus on the use of OCT in imaging laryngeal cancer, which is a much more technically challenging task because to distinguish benign lesions from malignant neoplasms, structural features such as the basement membrane must be clearly identified. This is critical in distinguishing early invasive cancer from premalignant or benign lesions. Hence, validating the integrity of the basement membrane is paramount. Previous investigations have demonstrated that OCT can be used to clearly identify the basement membrane within the vocal fold.[2,4,14–19]

In this study, we performed OCT on patients undergoing operative endoscopy for the diagnosis or staging of laryngeal cancer or patients with a history of laryngeal cancer undergoing surgery for complications of treatment or suspected recurrence. The goals of this project are to define our ability to accurately characterize basement membrane involvement with OCT and to better define OCT image characteristics in patients with laryngeal cancer.

MATERIALS AND METHODS

This study was performed with the approval of the Human Subjects Institutional Review Board at the University of California, Irvine. Informed consent was obtained from each patient before OCT imaging.

Patient Population

OCT imaging has been performed in 133 patients undergoing upper airway endoscopy under general anesthesia at the University of California, Irvine Medical Center. The study population consisted of 22 patients with a diagnosis of carcinoma involving the larynx or patients with a history of laryngeal cancer who underwent operative endoscopy for suspected recurrence or airway stenosis. Four patients were imaged on two separate occasions with OCT. The majority of the subjects were male (18 of 22 [82%]). The mean age of the subjects was 71 years (range, 51–87 years).

Optical Coherence Tomography Equipment

Details of the time-domain OCT device used in this study have been described previously[20,21] and are only briefly reviewed here. The system used in this study used a low-coherence light source (central wavelength λ = 1310 nm; JDS Uniphase, San Jose, CA, USA).[5] Raster scanned images were generated by controlled translation of the imaging fiber using a precision piezoelectric translation stage (model 663.4pr; Physik Instrumente, Tustin, CA, USA). The optical fiber and optical elements are enclosed by a transparent plastic tube, which is, in turn, surrounded by a second 2-mm diameter metal tube for mechanical support and protection. Details of the probe design and probe tip conformation can be found in Hanna et al.[5] Two probe lengths were used in this trial. A shorter 20-cm probe was used during imaging with the operating microscope and a 48-cm-long probe was used when rigid telescopic visualization was performed.

The axial resolution of the imaging system is approximately 9 μm and is determined by the coherence length of the light source. The lateral resolution is diffraction-limited (10 μm). The region of interest scanned using the system was 1.6 mm in depth (although image signal intensity decreased markedly with depth) and 6 mm laterally. The lateral extent of each image was controlled by distance traversed by the translation stage.

Optical Coherence Tomography Imaging Technique

In all subjects in this group, the larynx was exposed using surgical laryngoscopes with suspension. Biopsies or surgical excisions were performed only when indicated clinically. Photographs of clinical lesions were obtained in most patients for correlation with OCT images, and when available, histology was correlated as well. The OCT findings were not incorporated into clinical decision-making in this study.

Images were obtained by inserting the OCT probe through the lumen of the surgical laryngoscope. The probe tip was placed directly adjacent to the area to be imaged and its position monitored with a rigid telescope or the operative microscope. OCT images were acquired from the lesion, at the margins of the lesion, and in adjacent normal laryngeal structures. Images were acquired in a coronal plane and 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. The images on the monitor were used to adjust probe position and refine OCT parameters to improve image quality. Images were captured continuously and recorded for further detailed analysis.

Image Analysis and Correlation

OCT videos, still OCT images, endoscopic photographs, and histologic data were reviewed by three study investigators (WBA, DEV, JMR). Image quality and characteristics were analyzed at the site of pathology and laryngeal subsites in each patient. Overall image quality, the presence or absence of a definable border between the epithelium and lamina propria or submucosa, represented as the basement membrane, the thickness and signal intensity of epithelial layers, and the characteristics of the submucosa were noted. Image quality for each subject was rated by consensus on a 1 to 4 scale as follows: 1 (poor) = unable to interpret adequately; 2 (adequate) = able to discern tissues/planes but pixelation, limited depth of penetration, or other artifact compromises the image data; 3 (good) = good signal penetration, able to distinguish subsurface structures with minimal artifact; or 4 (excellent) = outstanding imaging detail and signal penetration with minimal to no artifact. The OCT images were compared with the endoscopic images and histologic findings.

The depth at which backscattering was still identified was measured as a means to gauge the extent that this technology can image the deeper submucosal regions in pathologic lesions. In each study, the deepest signal penetration depths were recorded to provide a range through which the present OCT device could image the laryngeal mucosa.

All images in this study were 6 mm wide by 1.6 mm deep. Digital micrometry was performed on bitmap image data using Photoshop (Adobe Photosystems, Inc. San Jose, CA, USA). Tissue

TABLE I.
Pathologic Diagnoses for Patients Undergoing Optical Coherence Tomography (n = 22*).

	Diagnosis						
Primary site	Inflammation	Dysplasia	Tumor In Situ	T1	T2	T3	T4
Larynx							
Supraglottic					3	2	
Glottic	1	3	1		3	3	2
Hypopharynx							
Pyriform sinus					1	2	

*One subject not included in table did not have biopsy at optical coherence tomography (see text for details).

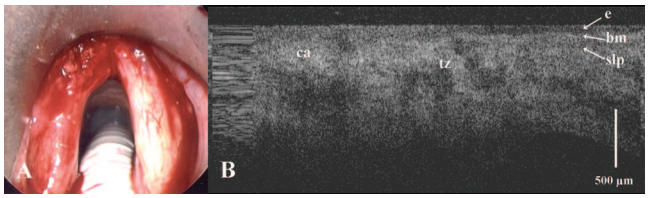

Fig. 1. T2 squamous cell carcinoma of the left vocal fold; recurrent postradiation therapy. (A) Endoscopic photograph. (B) Optical coherence tomography image demonstrating normal epithelium with an intact basement membrane on the right of the image, and invasive cancer with increased backscattering and loss of the basement membrane on the left. A transition zone is seen between these two areas. Note the area of motion artifact on the left of the image. bm = basement membrane; ca = invasive cancer; e = epithelium; tz = transition zone; SLP = superficial lamina propria.

layer thickness and depth were ascertained by measuring the distance along a line perpendicular to the mucosal surface.

Histopathology

Specimens were fixed in 10% neutral-buffered formalin and embedded in paraffin. Tissue blocks were sectioned at 5-μm-thick slices followed by hematoxylin–eosin staining. Specimens were oriented to provide histologic sections that were in close registry with the OCT imaging plane.

RESULTS

The 22 patients in this report underwent a total of 26 OCT studies. Sixteen patients (18 OCT studies) had confirmed laryngeal or hypopharyngeal cancer involving the larynx. Two patients (three OCT studies) with a history of laryngeal cancer underwent endoscopy with OCT for evaluation of airway compromise. One patient was found to have severe dysplasia. Two patients (two OCT studies) with possible recurrences of laryngeal cancer were found to have reactive atypia and moderate dysplasia. One patient (one OCT study) with a new vocal fold lesion was found to have carcinoma in situ. One patient underwent a second OCT study to evaluate radiation therapy response during the course of management of simultaneous primary tumors of the supraglottic larynx and oral cavity.

Biopsies or surgical resections were performed in 21 of 22 patients (24 of 26 OCT studies). Histopathologic results from biopsies or surgical excisions performed at the OCT examinations included invasive laryngeal cancer in 13 patients (all SCC except one case of mucoepidermoid carcinoma), pyriform sinus SCC in three patients, carcinoma in situ of the glottis in one patient, dysplastic lesions of the glottis in three patients, and inflammation with atypical cells (without dysplasia) in one patient. Four patients underwent two OCT examinations. Two of these patients had biopsy-confirmed cancer at both procedures, making 18 total invasive cancers examined by OCT. Details of tumor site and stage are found in Table I. The predominance of advanced T stage tumors and recurrent disease reflects the tertiary referral pattern of our institution.

Image Quality

The image quality for the collected images for each OCT examination was rated using the grading system described previously. OCT results produced the following distribution based on the quality of the images: poor = 1, adequate = 12, good = 9, and excellent = 4. A grade of "adequate" or "better" was obtained in 25 of 26 studies. In 25 cases, the presence or absence of basement membrane integrity in pathologic lesions could be ascertained with confidence. In the single study with "poor" quality, overall signal penetration depth was limited and the quality of individual images was variable. This limited the ability to completely evaluate individual images, albeit analysis of the series of images when viewed together and as a video clip demonstrated the basement membrane was not present.

Optical Coherence Tomography Signal Penetration

OCT signal penetration depth for each study was estimated by measuring the distance from the tissue surface to the point at which no detectable signal could be visualized (i.e., black pixels) from images obtained from both pathologic lesions and clinically normal regions. The depths of penetration for each study were tabulated. The mean maximum signal penetration in pathologic lesions was 0.65 mm (range, 0.2–1.2 mm). In regions of the larynx without significant abnormal clinical findings, the mean maximal signal penetration was 0.81 mm (range, 0.2–1.3 mm).

Histologic Correlation

Invasive carcinoma was histologically diagnosed by a pathologist in 18 of 26 studies. The lesion in one patient was diagnosed carcinoma in situ, three patients with moderate or severe dysplasia, and one patient with inflammation and mild atypia but no dysplasia or invasive cancer. In the 16 patients (18 examinations) with invasive cancer, the basement membrane boundary between the epithelium and the lamina propria was not visualized. In many of these specimens, a transition zone between the tumor and normal epithelium was identified. The transition zone appeared as gradual thickening of the epithelial layer and loss of delineation between the epithelial layer and the submucosal structures.

A representative OCT image of an invasive SCC is presented in Figure 1. Normal-appearing epithelium is on

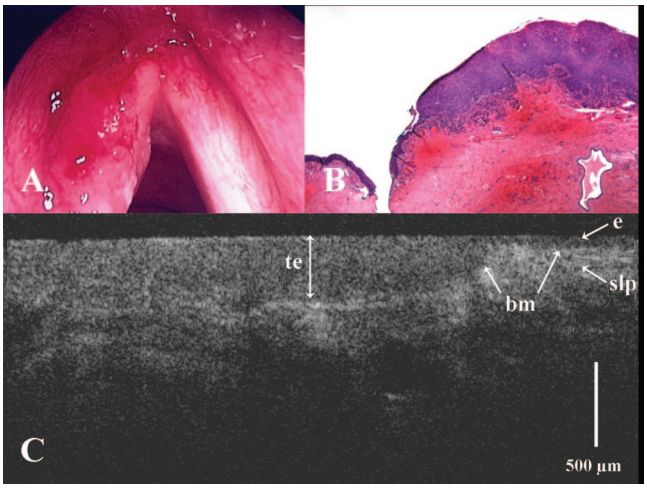

Fig. 2. Left vocal fold lesion 3 years after transoral excision of squamous cell carcinoma on the left vocal fold. (A) Endoscopic photograph. (B) Histopathologic specimen demonstrating mild cellular atypia and inflammation with no evidence of dysplasia. (C) Optical coherence tomography image demonstrating thickened epithelium with an intact basement membrane. bm = basement membrane; e = epithelium; te = thickened epithelium; SLP = superficial lamina propria.

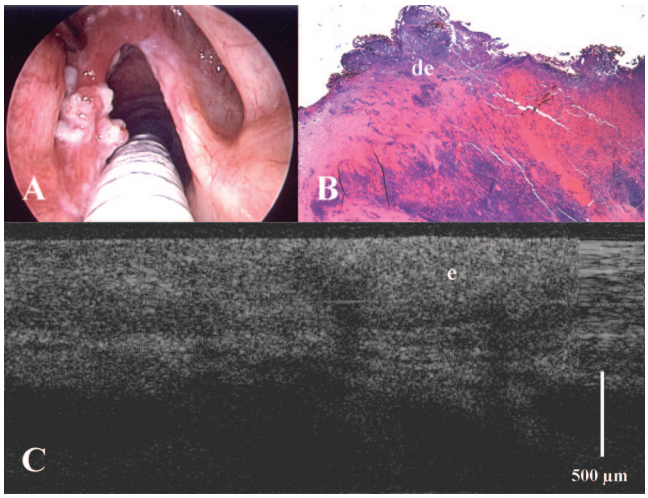

Fig. 3. Exophytic lesion of the left vocal fold with extension to the right vocal fold. A biopsy at another institution showed squamous cell carcinoma. (A) Endoscopic photograph. (B) Histopathologic section demonstrating severe dysplasia with no evidence of invasive carcinoma. (C) Optical coherence tomography image demonstrating increased backscattering from the epithelium. No basement membrane is visible. Note the motion artifact on the right side of the image. de = dysplastic epithelium; e = epithelium.

the right side of the image. There is low signal intensity (low backscattering) in the epithelial layer, and the boundary between the epithelium and superficial lamina propria (SLP) is clearly visible. Toward the middle of the OCT image at the margin of the cancer, a transition zone from normal-appearing epithelium to invasive tumor is seen. The epithelial thickness increases and the boundary between the epithelial layer and SLP disappears on the left half of the image. There is also increased backscattering from the area of the tumor on the left side of the image, suggesting a difference in optical properties between tumor and normal tissue.

In eight OCT examinations in seven patients with a history of laryngeal cancer, no invasive cancer was identified. Biopsies were performed based on clinical indications in six of the eight examinations, demonstrating: carcinoma in situ (1), severe dysplasia (2), moderate dysplasia (1), inflammation and mild atypia (1), and normal histology (1). In three of these six patients, the basement membrane was clearly identified using OCT. Figure 2 shows the OCT and endoscopic images as well as the corresponding histology of the suspected abnormal region in a subject with a history of T1 glottic SCC (previously treated by microsurgical resection 3 years before the present OCT examination and biopsy). The left anterior true vocal fold demonstrated raised granular appearance with areas of leukoplakia, and the overall visual appearance was very suspicious for recurrent cancer. The OCT images showed thickened epithelium with preservation of the junction between the epithelium and SLP, the locus of the basement membrane. Histology revealed acanthotic squamous mucosa with reactive atypia without evidence of dysplasia or invasive carcinoma.

The second patient in this group had simultaneous primary SCCs of the mandibular alveolus and aryepiglottic fold. After initial radiation therapy, at the time of composite resection, operative endoscopy with biopsies and OCT were performed to confirm complete response to radiation therapy treatment. Clinical examination indicated complete regression of the aryepiglottic fold tumor. OCT was able to clearly delineate a border between the epithelium and submucosa, and biopsies did not demonstrate any remaining cancer. The third patient, with a history of radiation therapy 10 years previously, presented with laryngeal stenosis and superior migration of his tracheostomy tract into the cricoid region. Friable mucosa on the left true and ventricular folds was identified and diffuse inflammation and edema of the larynx was visible. OCT of the area of ulceration and granulation tissue demonstrated a thickened superficial layer with a definite change in signal characteristics at the basement membrane zone. Biopsy of the imaged region demonstrated severe dysplasia.

In three other cases, however, basement membrane integrity could not be reliably ascertained. Figure 3 displays the OCT and endoscopic image of a left T1b N0M0 glottic SCC in a 78-year-old man. The patient was referred to our institution by a surgeon who performed a biopsy that demonstrated invasive carcinoma. At the time of transoral laser resection, the tumor clinically appeared to be an invasive carcinoma, and on OCT examination of the basement membrane was not identified. Histology from the surgical resection, however, showed severe dysplasia with no evidence of invasive squamous cell carcinoma.

The endoscopic and OCT images of an exophytic hyperkeratotic lesion of the left vocal fold suspicious for an early T1 glottic SCC in a 72-year-old man are shown in Figure 4. The lesion was excised microsurgically and oriented to allow histologic sections to maintain the same plane of registry with the OCT images. OCT images show

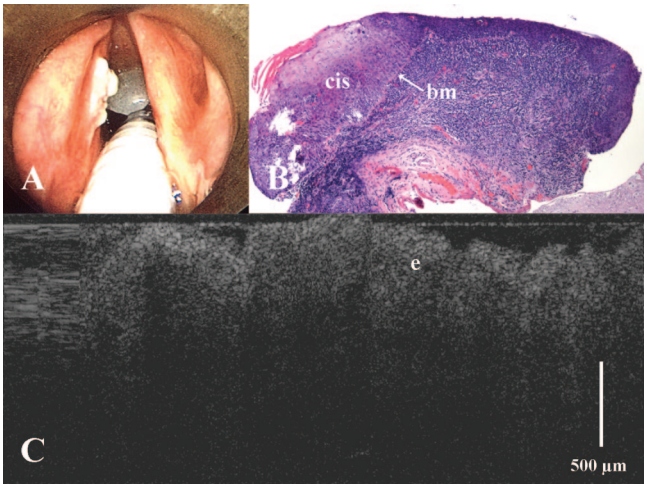

Fig. 4. Carcinoma in situ in the left vocal fold. (A) Endoscopic photograph. (B) Histopathologic specimen demonstrating carcinoma in situ. The basement membrane is intact. (C) Optical coherence tomography image demonstrating increased backscattering from the epithelium. No basement membrane is visible. The irregular surface of the lesion is visible as the probe is not in full contact. Note the motion artifact on the left side of the image. bm = basement membrane; cis = carcinoma in situ; e = epithelium.

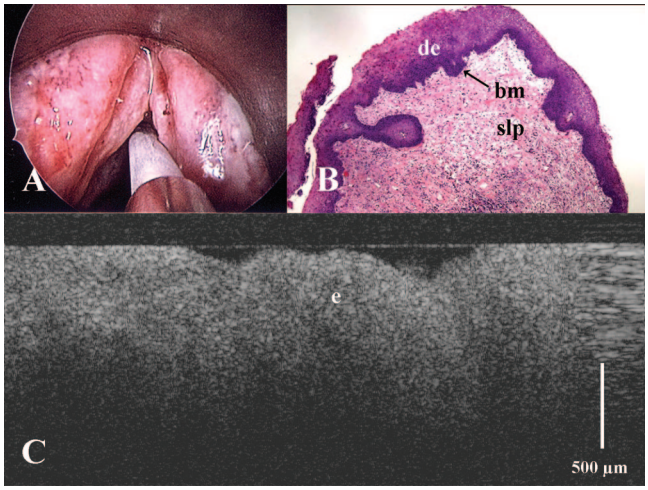

Fig. 5. Right vocal fold lesion post radiation therapy for a T2 squamous cell carcinoma of the supraglottis. (A) Endoscopic photograph with optical coherence tomography probe in contact with the right vocal fold. (B) Histopathologic specimen demonstrating moderate epithelial dysplasia and radiation changes in the lamina propria with fibrosis, hyalinized blood vessels and many plasma cells. (C) Optical coherence tomography image demonstrating increased epithelial backscattering. No basement membrane is visible. Note the motion artifact on the right side of the image. bm = basement membrane; de = dysplastic epithelium; e = epithelium; SLP = superficial lamina propria.

a transition zone and loss of basement membrane with increased backscattering (a brighter image) in the superficial layers. Histology showed carcinoma in situ of the left true vocal fold.

The third case of a noninvasive lesion that did not demonstrate intact demarcation between the epithelium and SLP (indicating the basement membrane) using OCT was a 64-year-old woman who had been treated with radiation therapy for a T2N0M0 supraglottic SCC. She reported persistent hoarseness and mild difficulty breathing. At microlaryngoscopy (Fig. 5A), she had diffusely edematous, inflamed, and granular-appearing laryngeal mucosa. OCT imaging of the right vocal fold did not identify the basement membrane. The biopsy of the right vocal fold revealed atypical squamous cells consistent with moderate squamous dysplasia. On the left aryepiglottic fold, mild dysplasia was found. OCT images at this site showed a markedly thickened epithelial layer and intact basement membrane. Biopsy of the right ventricular fold demonstrated squamous mucosa with ulceration and atypia that was felt to be consistent with radiation changes.

DISCUSSION

In this series of 22 patients imaged with OCT, loss of the demarcation between the epithelium and the submucosal tissue was demonstrated in all cases of invasive cancer. In many of the cases of invasive cancer, a transition zone was visualized at the periphery of the tumor. In several cases with bulky tumors and difficult exposure, transition zones were not imaged. Characteristically, progressive thickening of the epithelial layer was observed with loss of demarcation between the lesion and the lamina propria or submucosa. Visualization of these findings at the edge of the lesion added confidence to our assessment that the basement membrane was disrupted as opposed to failure to visualize the basement membrane because of poor signal transmission or technical factors. Because of the tertiary referral nature of our center, many of the patients in this series had prior radiation therapy, recurrent tumors, or advanced disease. A limitation in the applicability of these results is the preponderance of advanced tumors, which limits our ability to comment directly on superficial T1 cancers. We have performed OCT on several T1 lesions using an early prototype of our microscope-mounted OCT system but have not included cases imaged with this device because the image quality with this device is significantly different from that of our handheld probe. Our experience with this OCT microscope system will be reported in the future.

OCT was performed on six patients with a history of laryngeal cancer, but no invasive cancer was identified histologically. In three of these patients, the basement membrane was visualized. All three lesions in these patients were relatively thin lesions. The case depicted in Figure 2 is representative of these three subjects. In contrast to the three subjects demonstrating an intact basement membrane with OCT, the three subjects (Figs. 3–5) in whom the basement membrane could not be clearly identified all had bulky lesions. One patient diagnosed with invasive cancer at an outside institution was referred for management of a clinically bulky lesion (Fig. 3). The failure to identify the basement membrane with OCT could be the result of insufficient light penetration through a very thick lesion, or because of increased optical absorption or scattering from a hyperkeratotic lesion that limited the penetration of light and backscattering from the deeper structures, or even to tissue disruption from the previous biopsy. In this case, because of the prior

biopsy indicating invasive cancer, it is also possible that improper orientation and processing of the endoscopic resection of this lesion contributed to the failure to identify invasive cancer on histopathology at our center. Thorough review of the processed and sectioned pathology specimen demonstrated severe dysplasia, submucosal fibrosis with a very cellular stroma. The technical quality of the histologic specimen was very good without evidence of inadequate specimen processing.

The second patient (Fig. 4), with a bulky mid left vocal fold lesion suspicious for carcinoma who did not have basement membrane visualized on OCT examination, was found to have carcinoma in situ. Measurements obtained from the surgical excision of the specimen indicated a lesion thickness up to 1.1 mm. The markedly increased thickness and hypercellularity of the epithelial layer produced increased backscatter of the OCT signal, which eliminated light penetration to the deeper structures. Thus, the failure to delineate the basement membrane most likely resulted from decreased signal penetration.

The third patient (Fig. 5) had diffuse laryngeal edema, inflammation, and swelling approximately 1 year after radiation therapy. Radiation perichondritis was suspected; however, recurrent cancer needed to be excluded. With OCT imaging, no basement membrane was identified in the images of the right ventricular fold, and signal was visible to a depth of 1 mm. In the histologic preparations, the epithelium was measured to be as thick as 450 μm in some areas. In other areas of the larynx, OCT imaging revealed inconsistent presence of a basement membrane and areas of markedly thickened epithelium. In the areas where the basement membrane was visible on OCT images, the epithelial thickness was as great as 400 μm. Several general observations about OCT imaging of laryngeal disease merit discussion. First, in many of the pathologic lesions observed in this study, the backscattering of light from the lesions is increased over that of normal epithelium and appears on the scans as increased signal intensity in the superficial region. This may be a reflection of the increased cellularity of the tissues because backscattering is a reflection of turbidity. The increased backscattering at the surface results in decreased signal penetration into the deeper tissues and lowers the effective imaging depth. We noticed less signal penetration in pathologic lesions, and measurements of maximum depth of signal penetration in normal tissues and tumor tissue appear to support this hypothesis. A more detailed evaluation of image penetration depth in normal laryngeal tissues at each subsite of the larynx to obtain normative values for each subsite is a topic of future investigation in our laboratory.

With very bulky benign lesions, OCT did not reliably identify the basement membrane layer. In bulky nonmalignant lesions, thick, hypercellular tissues increase backscattering at the surface and limit the propagation of light into deeper layers of the specimen. This results in a limited capability to both identify the basement membrane and image deeper tissue structures. Regardless, such lesions would undergo biopsy on clinical criteria alone; hence, this limitation of OCT has limited clinical impact.

The lamina propria in general shows increased backscattering compared with the thin translucent epithelium. Often glands, their ducts, and blood vessels can be seen with distinct signal characteristics as darker structures within the stroma.[2,22] When there is radiation fibrosis or inflammation, the cellularity of the lamina propria is markedly increased along with collagen content, creating increased optical turbidity, which translates into increased backscattering. The OCT and histologic images in Figure 5 demonstrate this concept. The optical properties of the epithelium and lamina propria may appear similar after radiation therapy or with other processes that produce inflammatory response, edema, or fibrotic reaction in the lamina propria. In situations in which there is hypercellular epithelium and the lamina propria is hypercellular from inflammation and fibrosis, the ability to differentiate the lamina propria from epithelium may be impaired. A recent presentation of OCT of the oral mucosa observed similar changes in the epithelium and submucosa with loss of the basement membrane, indicating the onset of mucositis during radiation therapy.[23]

In addition to bulky hypercellular lesions that can block signal penetration, we have also observed that difficulties in interpretation of OCT signal can occur in a few other pathologic conditions. Granulation tissue or ulcerative lesions in which there is no epithelial layer will not demonstrate a basement membrane. Also, bulky laryngeal papillomas can block signal transmission and the basement membrane will not be seen. It is important to note, however, that these types of abnormal lesions that deform the vocal structure would undergo biopsy or excision on clinical grounds alone and that this potential limitation of OCT would not be a clinical limitation. OCT will most likely be of greatest value in evaluating subtle lesions in which the appearance is atypical, but there remains uncertainty about features of invasion.

A number of technical issues affect the ultimate quality of images obtained with OCT. There is a definite learning curve to the procedure, and with the current devices, the ability to manipulate the probe, position it correctly, hold it steady with one hand, and visualize the probe with a telescope through the operating laryngoscope takes practice. At the same time, recognition of normal and abnormal findings requires knowledge gained from repeated performance of OCT. This is analogous in many ways to the learning curve experienced in standard ultrasound.

Motion artifact can be problematic. Images with the system used in this study are acquired at 1 Hz; therefore, instrument motion and patient motion can affect signal quality. Probe stabilization and ergonomic probe design improvements have decreased the effects of motion artifact in our examinations. The use of new high-speed systems that can acquire images at video frame rate will eliminate motion artifact. Because the probe design is perpendicular to the visual axis of the surgeon, probe placement can be difficult for some lesions. Development of small probes that image in a longitudinal direction to produce en face images greatly will simplify image acquisition. Recent advances in micromechanical systems (MEMS) may solve this technical challenge. One group has recently evaluated a prototype MEMS mirror

sheathed in a 4-mm housing that was able to produce high-quality images and could be delivered through an operating endoscope.[24]

Faster image acquisition rates, higher resolution, and improved probe design are constantly improving the capabilities of OCT. Use of OCT in ophthalmology is well established, particularly for retinal imaging, and the pilot studies performed by our institution and others have provided encouraging results that OCT may have clinical use in the head and neck as well. OCT has potential use in assisting the diagnosis and staging of early laryngeal cancers, determining the presence or absence of invasion, selecting sites for biopsy in diffuse lesions that may have areas of invasion, as a guide for margin selection with resections, and for monitoring of treatment effect and surveillance for recurrence.

The most important group of patients to evaluate with OCT is patients with potential T1 tumors of the larynx who may have dysplastic lesions or early microinvasive tumors. The current system has a resolution of approximately 10 μm. This is outstanding, but even at this resolution, OCT cannot distinguish subcellular details such as presence of nuclear abnormalities, which will be necessary to distinguish reactive or hyperplastic lesions from dysplasia and carcinoma in situ. This will require the use of ultrahigh-resolution OCT devices, which for the most part are currently limited to laboratory investigations.[11,12] Regardless, OCT in otolaryngology will likely follow the same adoption curve dynamics as computed tomography and magnetic resonance imaging in previous decades with increased use following reductions in cost and increases in capabilities.

CONCLUSION

In this study, OCT was used to reliably identify the loss of basement membrane integrity in patients with laryngeal cancer. Bulky exophytic lesions can interfere with OCT signal propagation, limiting the ability to image the basement membrane and submucosal structures, but in thin lesions, OCT was able to clearly confirm basement membrane integrity. Further study in a larger cohort of patients with early T1 lesions, carcinoma in situ, and benign but clinically suspicious lesions will be necessary to further define the diagnostic use of OCT. OCT is a rapidly advancing imaging modality and improvements in probe design, speed of image acquisition, and image resolution will undoubtedly result in improved ability to acquire and properly interpret OCT findings.

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