OCT in the field of laryngology - further perspectives

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ABSTRACT

Early detection of cancerous lesions of the larynx may be the best method of improving patient quality of life and survival rates. New in-vivo technologies may be of great clinical relevance in improving the accuracy of sampling during microlaryngeal surgery. Optical coherence tomography (OCT) is an optical imaging technique that clearly identifies basement membrane violation caused by laryngeal cancer. With a microscope-based spectral domain OCT (SD-OCT) we reached in vivo a fairly accurate assessment of benign and dysplastic laryngeal lesions.
Recent improvements in OCT technology have led to the development of high-speed OCT systems displaying millions of pixels per second. These systems allow non-contact real-time imaging of large sections of laryngeal tissue. Polarization contrast OCT (PS-OCT) may provide additional information about the lamina propria of the true vocal cord because of the birefringence of connective tissue.
We present microscope-based high-speed SD-OCT images with and without polarization contrast and 3D volumes of selected laryngeal pathologies in order to demonstrate our current concepts for the intended intraoperative application. High-speed SD-OCT and polarization contrast can also be complemented by our recently developed rigid confocal endoscopic system to obtain cellular and sub-cellular information about the tissue. Further perspectives will be presented.

Keywords: Optical coherence tomography, laryngology, in vivo imaging, vocal cord

1. INTRODUCTION

Optical coherence tomography (OCT) is widely accepted as a new imaging technology for the early detection of laryngeal lesions of unknown dignity. OCT is applied either with a flexible probe/endoscope[1-3] or using a microscope[3,4] during microlaryngoscopy. In the latter case, the OCT system is attached onto the camera port of the microscope. The microscopic-based version allows for visualization of pathological lesions of the larynx in the center of the microscopic field of vision and precise visualization of the scanning plane by means of a green pilot beam. During OCT measurements, surgical instruments and laser systems for tumor resection can be used. Currently, real-time imaging and visualization of volumetric data are possible.[5] Preliminary experiments demonstrated the feasibility of real-time 3D-OCT for guided interventions.[6,7] In the literature, when OCT was used during microlaryngoscopy, data with a sensitivity and specificity of 100% and 95% were reported to differentiate between malignant laryngeal and benign lesions (pre-malignant lesions included).[8] These data are based on epithelial thickness. Our own data revealed sensitivity less than 90%. OCT allows for a fairly accurate differentiation between benign and dysplastic and malignant laryngeal lesions. However, in epithelium with pronounced hyperkeratosis, the basal membrane is not visible or is blurred, and a accurate diagnosis of invasion cannot be made.[4] For example, carcinoma in situ, an intraepithelial carcinoma with intact basal membrane[9], cannot be differentiated from a micro-invasive carcinoma, where the basal membrane is interrupted.[10]
This paper addresses two questions: Firstly, how can we improve the visualization of the basal membrane? Secondly, how can we improve the OCT system so that sampling during microlaryngoscopy will be more accurate? To accomplish this, the applicability of high-speed SD-OCT with polarization contrast is demonstrated. Then we describe our approach to combine OCT as an optical method that provides cross-sections of the tissue with confocal endoscopy. The latter method provides en-face images of the laryngeal tissue. Finally, a prospective application of OCT in laryngology will be presented.

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2. METHODOLOGY

Optical coherence tomography system, imaging

Different OCT systems were used. For intraoperative imaging an OCT camera based on spectral-domain (SD)-OCT with a central wavelength of 840 nm (OptoMedical Technologies GmbH, Lübeck, Germany) was connected to an operating microscope (MÖLLER Hi-R 1000, Möller Wedel GmbH, Wedel, Germany) (Fig. 1). This system allows for OCT scans of any object in the center of the field of view of the microscope. Details of the microscope with integrated OCT technology have been published elsewhere[3,11] and are only briefly reviewed here. The scan head of the OCT camera was connected to the camera port of the microscope. The lateral resolution depends on the magnification (zoom) of the microscope. The OCT system is able to automatically adjust to working distances between 220 and 490 mm by computer-controlled adjustment of the reference arm length. The newly developed OCT camera provides 10,000 single A scans per second and allows 2D scans and 3D volume scans of the laryngeal tissue. Polarization contrast was obtained by subtracting two OCT images taken with different polarization states between sample and reference radiation. From these data cross sectional images of the intensity and the polarization change in the backscattered irradiation were calculated. A depth range of up to 5.2 mm in air can be visualized in one A-scan. Because of strong light scattering in most biological tissues, real measurement depths varied from 0.5 to 2 mm depending on the tissue type.
Endoscopic OCT images were measured with a specially developed rigid GRIN lens endoscope (diameter 3 mm, length 300 mm; Richard Wolf GmbH, Knittlingen, Germany) which was adapted to a 1300 nm time-domain OCT (Sirius 713; 4 Optics AG, Lübeck, Germany). Details are given elsewhere.[12]

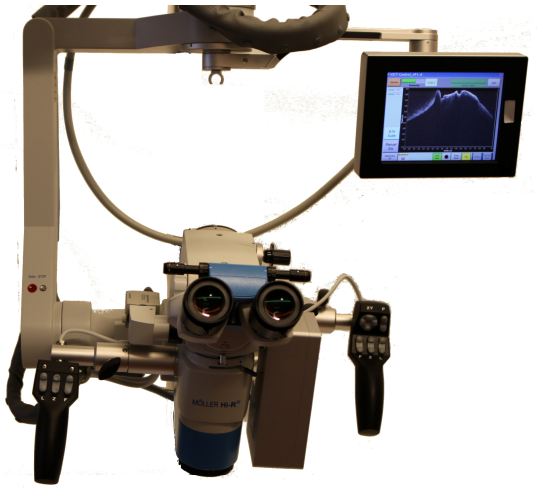


Fig. 1. Operating microscope (MÖLLER Hi-R 1000, Möller Wedel GmbH, Wedel, Germany) with MÖLLER Medis Touchscreen and with attached OCT camera (OptoMedical Technologies GmbH, Lübeck, Germany) for intraoperative measurement of the larynx. Volume scans and 3D reconstruction of the vocal cord can be taken.

Intraoperative application of OCT

The larynx is exposed during microlaryngoscopy using laryngoscopes. Suspicious lesions are identified with the operating microscope or with conventional endoscopes (0°, 30° or 70°). Using the operating microscope, a nominal working distance of between 220 and 300 mm was used for OCT measurements (magnification between x4.0 and x7.0). OCT measurements can be started manually, and images are displayed on a dedicated touchscreen. A pilot beam indicates the scanning field.

Rigid confocal endoscopy, imaging

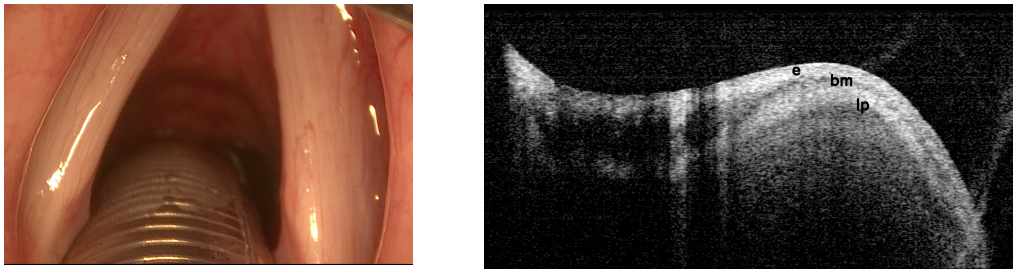
OCT provides optical cross sections of the tissue. In contrast to OCT, laser-scanning microscopy provides en-face images of the laryngeal tissue. Recently, a rigid confocal endoscope has been developed as a complementary diagnostic

tool for detection of premalignant lesions in vivo. A modified Heidelberg Retina Tomograph II (HRTII) (Heidelberg Engineering GmbH, Heidelberg, Germany) is used. The rigid endoscope is connected to the scanner. Polarized light travels through a λ/4 plate. Reflections may occur at the water immersion objective and the endoscope. Illumination is delivered by a 670-nm diode laser.[13] For endoscopic use, the λ/4 plate of the HRTII is removed to avoid strong reflections. This leads to a certain reduction in the image quality. The maximal penetration depth is about 300 µm and ranges from 100 to 450 µm. The acquisition time for a volume scan is about 6 s. In sequence acquisition mode, up to 100 images are stored. In section mode, single images can be stored. The prototype of the custom-made endoscope (length: 23 cm, diameter: 5 mm) consists of a steel endoscope shaft with integrated rod lenses and one microscope objective at the end-side of the endoscope (diameter 3.5 mm). A flexible, transparent solid piece of cement is used to connect two adjacent rod lenses. This flexible material reduces the risk of damage to the rod lenses. The cement is non-scattering and does not impair the light transfer and image quality. The numerical aperture of the system is 0.9 and is limited by the endoscope. A connector has been developed (KARL STORZ GmbH & Co. KG; Tuttlingen, Germany) to connect the HRTII to the rigid endoscope. The devices (HRTII, adapter, and endoscope) supply images of 400 x 400 µm and reach average penetration depths of 100–300 µm (λ/4 plate of the HRTII was removed). The lateral and axial resolutions are about 1–2 µm and 2 µm, respectively.

3. RESULTS

Normal true vocal cord

An in vivo OCT image of the healthy true vocal cord is shown (Fig. 2). The demarcation between epithelium and superficial lamina propria represents the basal membrane. However, there is non-malignant tissue where the border between epithelium and lamina propria cannot easily be detected with OCT. Figure 3 shows a healthy larynx specimen. The specimen was posteriorly dissected. For better orientation CO_2 laser spots were applied on the epithelium (diameter of 1.0 mm, 2 W). The corresponding OCT images (Fig. 4A) show the cavities produced by CO_2 laser within the healthy true vocal cord but no demarcation of the epithelium (compare Fig. 2B). The entire true vocal cord of both sides was imaged. The basal membrane could not be detected. A polarization contrast image of the left true vocal cord is shown in Fig. 4B. The polarization effect, the change from color blue to red, of the superficial lamina propria leads to better differentiation of the border between the epithelium and the lamina propria.



A B

Fig. 2. A Photograph of a healthy true vocal cord.
B Intraoperative in vivo OCT image with OCT camera of the healthy true vocal cord. The epithelium (e) can be identified, and the border (basal membrane – bm) between the epithelium and the lamina propria (lp) is also evident (image size: 6.5 mm x 3.5 mm in air).

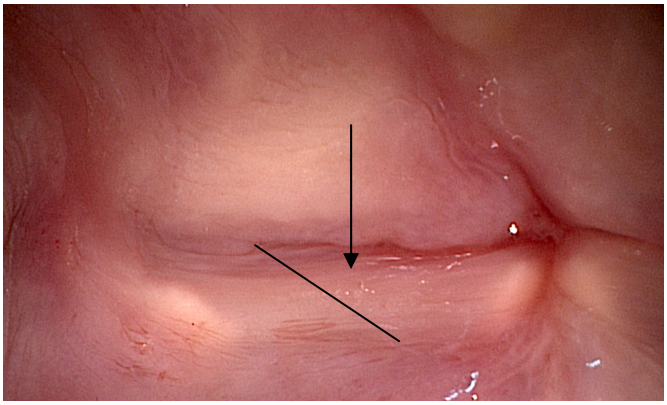


Fig. 3. Photograph of a healthy true vocal cord. Arrow indicates laser spots applied with a CO_2 laser (2 W). Laser spots were applied to improve the accuracy of measurements and for better orientation (Line – scanning plane).

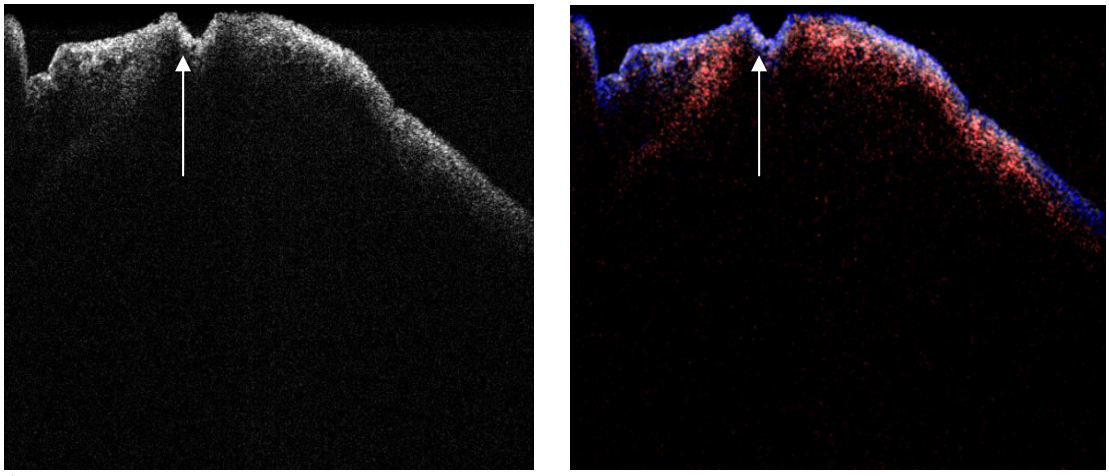


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Fig. 4. SD-OCT (A) and PS-OCT (B) images of a healthy true vocal cord (same specimen as Fig. 1) measured by OCT camera. The arrow demonstrates the laser spot (original OCT image size: 6 mm x 5.2 mm in air).

Volumetric measurements of the true vocal cord allow one to identify the basal membrane and to assess the integrity of the membrane. Figure 5 shows the internal structures of the vocal cord (arrow). In the video clip, these structures can be easily identified with moving cross sections. The CO_2 laser induced tissue lesions improve the orientation within the tissue.

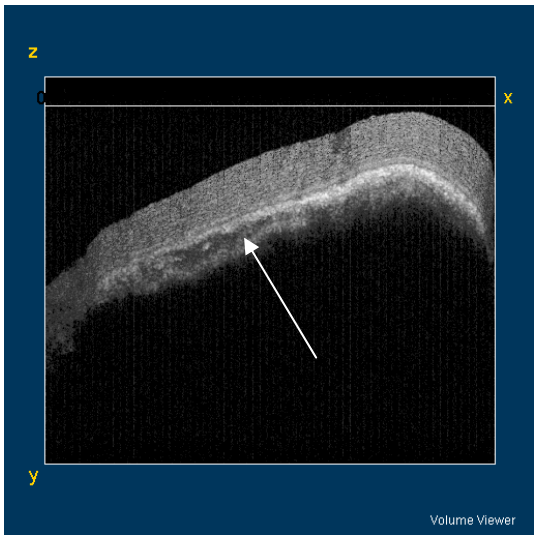


Fig. 5. Three-dimensional reconstruction of the true vocal cord from optical coherence tomography scans. Arrow indicates internal structures underneath the epithelium.

Malignant lesion

A wide-field image of suspicious findings for both true vocal cords is shown in Fig. 6. On the left true vocal cord a micro-invasive carcinoma was found by histopathology. The right side revealed severe dysplasia. Figure 7 shows a representative scan. Loss of integrity of the basal membrane is a sign of tumor invasion into the lamina propria and can be monitored with moving cross sections.

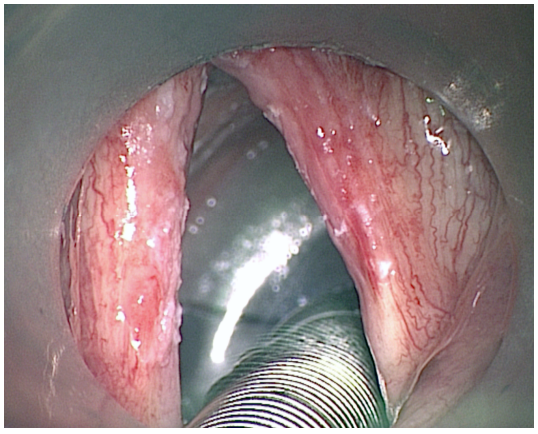
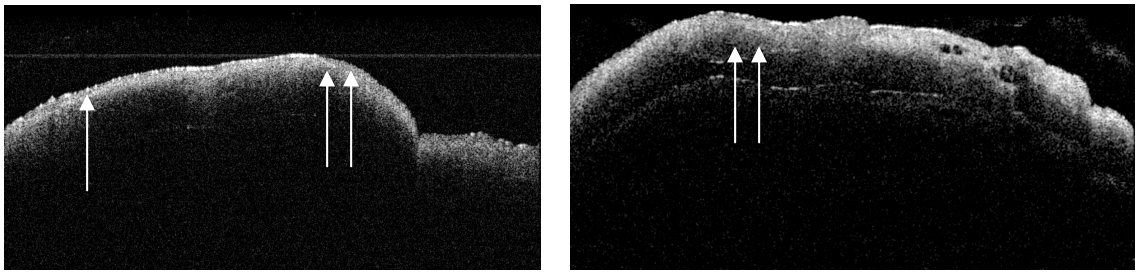


Fig. 6. Photograph of a micro-invasive carcinoma of the left true vocal cord and severe dysplasia of the right true vocal cord. Diagnosis based on conventional histopathology.

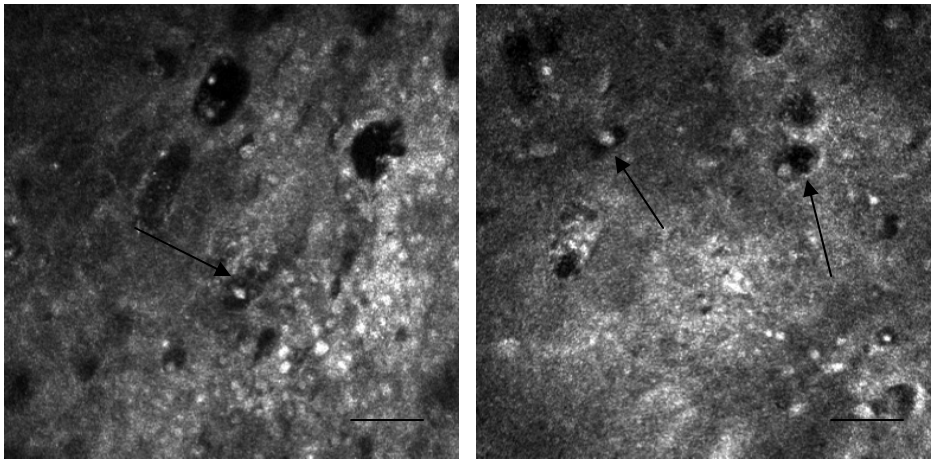


A B

Fig. 7. Corresponding SD-OCT images of volume scans of the anterior (A) and posterior (B) part of the left vocal cord (Fig. 6) reveal a basal membrane (single arrow) and a loss of basal membrane integrity (double arrow) measured by OCT camera (image size: 6 mm x 5.2 mm in air).

Rigid confocal endoscopy

Figure 8 shows two selected images of a volume scan through the epithelium of a micro-invasive carcinoma of the left vocal cord with confocal endoscopy (same case as Fig. 6). Epithelial changes can be detected with rigid confocal endoscopy. Representative images of a volume scan demonstrate enlarged cells with variable shapes, cluster of cells, increased nucleus/cytoplasm ratio, and irregular cell architecture. These are criteria for dysplasia. In contrast to OCT, confocal endoscopy cannot detect the basal membrane.
The combined application of both confocal endoscopy and high speed OCT/PS-OCT may lead to improved accuracy in the diagnosis of laryngeal diseases during microlaryngoscopy.



A B

Fig. 8. Confocal microscopic images of a micro-invasive carcinoma of the left true vocal cord (same case as Fig. 6). Arrows indicate dysplastic cells at a depth of 15 μm (A) and 25 μm (B) (scale bar 50 μm).

5. CONCLUSION AND FURTHER PERSPECTIVES

PS-OCT improves the detection of the basal membrane (border between epithelium and lamina propria) especially in healthy laryngeal tissue. Kim et al.[14] reported that a loss of birefringence was found in several lesions.[14] In contrast to SD-OCT, PS-OCT seems to improve the differentiation between benign and malignant lesions but fails to differentiate among different laryngeal lesions (mild, moderate and severe dysplasia, carcinoma in situ). The authors used a MEMS scanning catheter in conjunction with a multi-functional SD-OCT. [14,15] Clinical studies are needed to test the early findings.

Volumetric scans of the vocal cords enable the clinicians to assess the integrity of the basal membrane with moving cross sections. Applying laser spots to the surface of the epithelium improves the orientation within the tissue. Real-time OCT imaging can be used to improve the precision of surgical interventions.[5] In small carcinoma of the larynx, several authors propose safety margins of less than 5 mm after tumor resection.[16] Real-time OCT and volumetric OCT may improve the accuracy of tumor resection in phonomicrosurgery. Integration of this technology into laryngoscopes will lead to a further application option of real-time-, 3D-, and PS-OCT in the clinical routine. Stroboscopy was thought to detect early malignant lesions of the larynx, but when applied preoperatively, this method fails to reliably predict the presence of cancer and to determine the penetration depth of the laryngeal cancer. Stroboscopy and laryngoscope-based OCT may help to improve the accuracy in the diagnosis of laryngeal cancer.

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