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# Temporal correlation of optical coherence tomography in-vivo images of rabbit airway for the diagnosis of edema

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## ABSTRACT

Recently, full-range optical coherence tomography (OCT) systems have been developed to image the human airway. These novel systems utilize a fiber-based OCT probe which acquires three-dimensional (3-D) images with micrometer resolution. Following an airway injury, mucosal edema is the first step in the body's inflammatory response, which occasionally leads to airway stenosis, a life-threatening condition for critically ill newborns. Therefore, early detection of edema is vital for airway management and prevention of stenosis. In order to examine the potential of the full-range OCT to diagnose edema, we investigated temporal correlation of OCT images obtained from the subglottic airway of live rabbits. Temporally correlated OCT images were acquired at fixed locations in the rabbit subglottis of either artificially induced edema or normal tissues. Edematous tissue was experimentally modeled by injecting saline beneath the epithelial layer of the subglottic mucosa. The calculated cross temporal correlations between OCT images of normal airway regions show periodicity that correlates with the respiratory motion of the airway. However, the temporal correlation functions calculated from OCT images of the edematous regions show randomness without the periodic characteristic. These in-vivo experimental results of temporal correlations between OCT images show the potential of a computer-based or -aided diagnosis of edema in the human respiratory mucosa with a full-range OCT system.

**Keywords:** Optical coherence tomography, airway stenosis, edema, temporal correlation, inflammation

## 1. INTRODUCTION

Neonates or pediatric patients under prolonged endotracheal intubation are at risk for airway injuries. The early diagnosis of mucosal edema is clinically important, as this is the first step in a cascade of cellular events leading to scar formation and, in a severe case, airway stenosis. Stenosis of the airway at the supraglottic, glottic, and/or subglottic regions is a potentially life-threatening event for newborns. Imaging modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound, lack sufficient resolution to identify mucosal changes at a microanatomical level. The gold standard for diagnosis of airway stenosis in a clinical situation is surgical endoscopy, a procedure that requires general anesthesia and carries the disadvantage of further mechanical injuries to the airway. Furthermore, the diagnosis of edema during endoscopy is highly subjective and relies upon a trained surgeons' ability to visualize the airway clearly and palpate the tissue with an instrument. Furthermore, this method does not provide detailed information on the sub-epithelial structure of the airway where injury occurs.

Recently, full-range optical coherence tomography (OCT) systems have been developed for minimally invasive imaging of anatomic structures within the human airway [1,2]. The Fourier domain swept source OCT system with a fiber-based probe rotating in high speed can image an entire airway in three dimensions (3-D). Modern full-range OCT imaging systems typically generate hundreds of individual cross-sectional images during a single helical scan of the airway. Given that OCT light sources are non-ionizing and the probe diameter could be less than 1mm, the full-range OCT has the potential to safely and practically monitor the airway in intubated neonates, in whom the lumen can be less than 3mm in diameter. However, since the number of OCT images is very large with frequent noise contaminations, diagnosing edema on an OCT image with human eyes is challenging and highly subjective. Therefore, it is desirable to investigate algorithms for a computer-based or aided diagnosis of edema, which implements the clinical translation of

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the full-range OCT system. In this study, we demonstrate the potential for temporal correlation of OCT images to diagnose mucosal edema in the rabbit airway in vivo.

## 2. CONCEPT

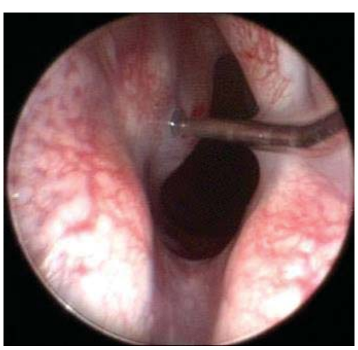
OCT is based upon the principle of low-coherence interferometry: light is split into a 'sample' arm (tissue of interest) and a 'reference' arm (mirror). Upon reflection and recombination of both arms, interference patterns between photons from both pathways are generated, which contains the microstructure information of the sample object. Since the photons reflected from the diffusive object (tissue) are randomly phased, speckle inherently exists in all OCT images [3]. Ideally, if an OCT system acquires images from the exactly same sample area, the randomly distributed speckle patterns are temporally stable. Although the systematic parameters of the OCT system and the portion of an imaged object could be slightly changed in a practical situation, the variation of speckle would be minimal. However, if the phase variation of reflected, diffused photons is temporally changed to a significant degree, the speckle patterns undergo vast changes in a short time.

As mentioned in the previous section, edema is a first physiological response in the inflammatory stage of wound healing. Following vasodilatation and increase in microvasculature permeability, accumulation of fluid occurs in interstitial tissue beneath the airway epithelium [4]. Because of the continuous secretion and movement of interstitial fluid within the injured mucosa, it is reasonable to consider that the temporal phase variation of photons reflected back from edematous tissue would be much faster and more abrupt than that from regions of normal airway tissue. Therefore, the degree of temporal correlation variation between the series of OCT images on a pathologic airway site could be the figure of merit for the diagnosis of edema.

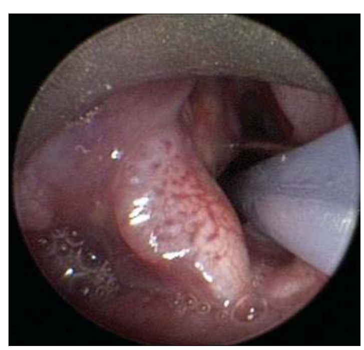
## 3. EXPERIMENT

For the in-vivo experiment, the customized, full-range swept source OCT system was constructed, the central wavelength of which is 1310nm. The system was coupled with a fiber-based probe that rotates 25 frames per second (fps) to acquire the airway images in a helical fashion. Each frame (i.e., B-scan image) is composed of 2000 A-lines, which covers an entire cross section of the airway. The probe was rotated within a sheath of transparent fluorinated ethylene propylene (FEP) to prevent contamination and direct contact between the probe and surrounding airway tissue. The details with respect to imaging and other systematic parameters for the full-range OCT system can be found in the reference [2].

The rabbit was induced with general anesthesia via intramuscular injection of ketamine (35mg / kg) and xylazine (5mg / kg) and placed in suspension microlaryngoscopy using an infant-sized Parson's laryngoscope. Nebulized lidocaine was applied to the larynx for additional topical anesthesia. A rigid, 0º surgical endoscope was inserted through the laryngoscope and used to visualize the larynx, subglottis and trachea. Using a 4.25", 25-Gauge spinal needle bent an appropriate degree at the tip, NaCl solution was injected in the subepithelium of the subglottis under endoscopic visualization (Figure 1 (a)). With the needle held in place at the subglottis, the OCT probe was inserted through the laryngoscope to the level of the proximal trachea, as shown in Fig. 2 (b). The needle was used as a reference point on OCT images to identify the location of the experimentally modeled edema.



(a)



(b)

Figure 1.In vivo endoscopic images of the rabbit subglottis. (a) Needle injection of saline into subepithelial tissue (b) The rotating OCT probe inside the sheath (shown as white) inserted past the needle, into the proximal trachea.

Figure 2 shows some examples of measured OCT images, where the correct location of edema could be estimated by the spinal needle image. Figure 2 (a) shows an originally acquired OCT image, and Figs. 2 (a) and (c) are circularized ones to make them look like real airway sections. As the first step of the in-vivo experiment, a single OCT data set was acquired by helical scanning, which is typically composed of several hundreds of 100μm apart consecutive OCT images like Fig. 2. For the acquired full OCT data set, OCT images of the edema region were identified and separated by the needle image. Once the airway location of the experimentally modeled edema is identified, the OCT probe tip was mechanically located on the airway section to measure multiple OCT images for the calculation of cross temporal correlation functions between them. The temporal gap for the same airway area between adjacent images was 0.04 seconds by the 25fps rotating OCT probe. The similar procedures were repeatedly conducted for the acquisition of multiple OCT images on different airway sections including normal regions.

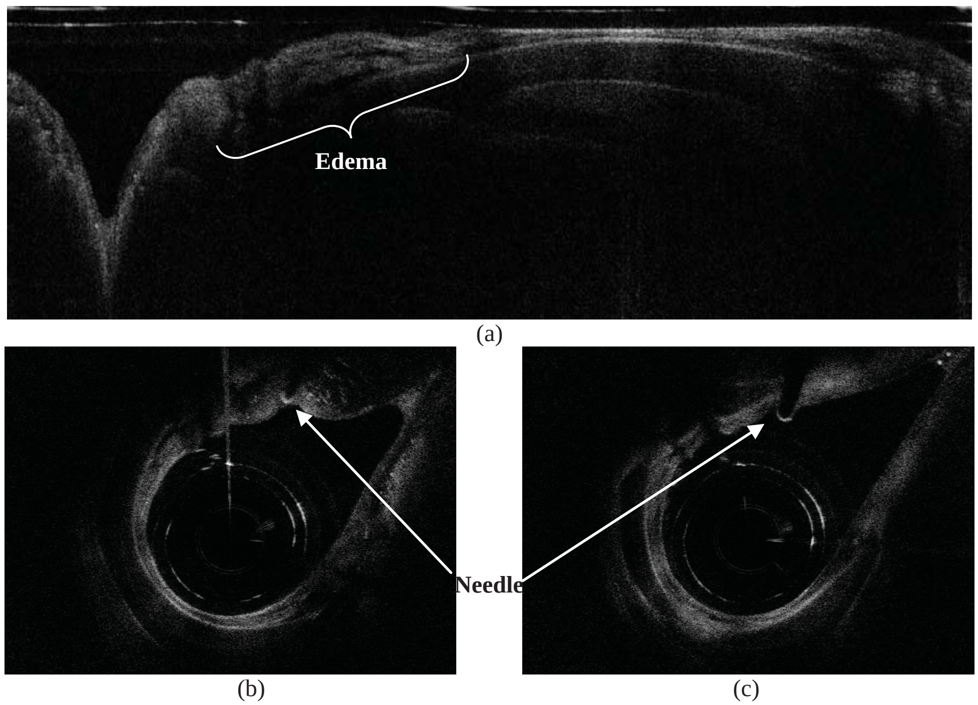



Figure 2. (a) Experimentally measured OCT image on the rabbit subglottic airway. (b) and (c) are circularized airway images of original linear ones, like (a), where the spinal needle used for injecting saline is clearly shown.

## 4. RESULT

More than 150 OCT images are acquired at each edema and normal airway section, where the cross correlation coefficients were calculated between the first and other consecutive images. Rather than considering an entire OCT image as in Fig. 2 (a), a subset of the entire image set was selected for the cross correlation analysis, which is equivalent to enhancing spatial resolution for the diagnosis of edema. Figure 3 shows some examples of the calculated temporal cross correlation coefficients for selected local regions in both normal and edema rabbit airway images. Each of those selected local areas is composed of 20 A-lines encompassing 200-pixel, which starts just below the airway surface. Because the axial resolution of the full-range OCT system is ~10μm, the actual depth of the selected regions is ~2mm. As shown in Fig. 3, the cross correlation functions of normal airway mucosa show periodicity that is not evident in the cases of edematous tissue. This periodicity is strongly correlated to the respiratory rate of the live rabbit in the *in-vivo* experiment, which is the physiological movement of the airway. The airway movement due to breathing generates low and high degrees on correlation coefficient functions between the temporally measured multiple OCT images. Although the similar movement exists on the edema region, the random phase variation of photons that are diffused back through the edema regions washes out this periodicity. Although not shown here, we verified that this characteristic is consistently observed for other sub-regions of the normal and edematous airway and even for experimental measured OCT images with another rabbit. Also, we've investigated intensities, signal-to-noise ratios, and gray-scale cooccurrence matrices [5] to differentiate the edema from normal mucosal tissue but none of them showed the clear difference as a good figure of merit for the diagnosis of edema.

## 5. CONCLUSION/DISCUSSION

A full-range OCT system has the potential of a ubiquitous device monitoring a human airway with the benefit of observing sub-surface airway regions. Especially, it may have multiple applications in imaging and monitoring changes in the airway during intubation. This is particularly important with respect to the early diagnosis of edema in airway that reduces the incidence of subglottic stenosis. To achieve computer-based or aided determination for this early diagnosis, we studied temporal variation of cross coefficients between OCT airway images, the result of which is promising as a strong figure of merit. For a normal airway mucosa, the temporal variation shows periodicity that is correlated to a physiological motion of the rabbit, such as a respiratory rate, but is not observed in edematous areas. However, for some local regions under examination, the periodic characteristic of cross coefficient functions is not clearly observed, as some signals intermediate to those illustrated in Figs. 3 (a) and (b), which makes the edema diagnosis ambiguous. Since the task of edema diagnosis is in the category of a binary statistical decision problem, it is required to develop a scalar figure of merit that is typically random called a test statistic [6]. For a given system (OCT), data (OCT images) and purpose (diagnosis of edema), an appropriate observer should be applied to the data to project the data to the space of the figure of merit for making a statistical decision between edema and normal. Future study will be focused on these subjects.

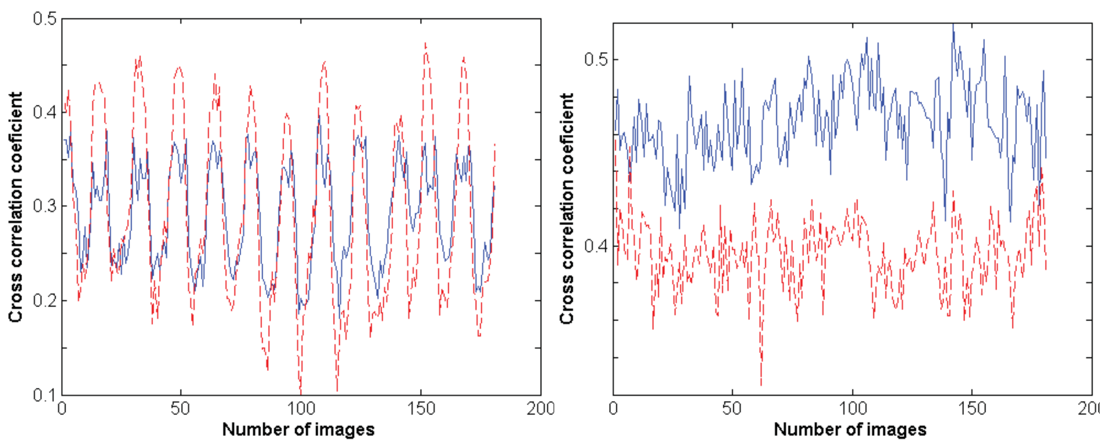



Figure 3. Temporal variations of cross correlation coefficients between OCT images are shown for (a) normal and (b) edema airway regions, respectively, which show the clear difference of periodicity.

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