In vivo optical coherence tomography of the nasal mucosa

Usama Mahmood, B.S., James Ridgway, M.D., Ryan Jackson, M.E., Shuguang Guo, Ph.D., Jianping Su, B.S., William Armstrong, M.D., Terry Shibuya, M.D., Roger Crumley, M.D., M.B.A., Zhongping Chen, Ph.D., and Brian Wong, M.D., Ph.D.

ABSTRACT

Background: Optical coherence tomography (OCT) is an emerging imaging modality that uses light to produce in vivo high-resolution cross-sectional images (7 μm) of tissues to depths of up to 3 mm. OCT is analogous to ultrasound, but relies on interferometry and low-coherence optical sources to produce images of tissue structure at the histological level.

Methods: In this study, OCT was used to image the mucosa overlying structures in the nasal cavity to obtain information regarding normative in vivo tissue microstructure. An OCT system using a Michelson interferometer and a 1.3-μm broadband light source was incorporated into a fiber-optic imaging device that was inserted into the nasal cavity. Cross-sectional tomographic images of the anterior and posterior nasal septum, turbinates, and vestibule were acquired in 44 patients in either the office or the operating room during surgical endoscopy.

Results: OCT images of the nasal mucosa identified the distinct boundaries between the epithelium, lamina propria, and underlying bone/cartilaginous tissue. Within the lamina propria, features consistent with glands, ducts, and blood vessels were clearly identified. In patients who underwent decongestant therapy, before and after images showed distinct morphological changes in the mucosa. The thickness of the epithelium was tabulated, as well.

Conclusion: This study establishes the potential of using OCT to produce high-resolution images of the nasal mucosa. As an in vivo tissue microstructural imaging modality, OCT may be valuable in studying the impact of allergic and infectious disease on the nasal mucosa and monitoring its response to pharmacologic therapy. (Am J Rhinol 20:155–159, 2006)

Rhinitis is a significant health care problem that affects between 10 and 25% of the population and results in more than $5 billion in annual health care expenditures in the United States alone.1,2 Despite its significance, rhinitis is frequently dismissed or mistreated by physicians. A recent survey, e.g., found that only one-third of those patients with seasonal rhinitis and 17% of those with perennial disease were satisfied with their treatment.3 One difficulty with the management of rhinitis is that there are no effective tools to follow the progression of disease over time. Although patient symptoms and physical examination are indispensable in the management of rhinitis, they do not yield quantifiable data and are mostly subjective criteria by which to follow the affects of disease or therapy over time. Currently available objective tests, on the other hand, including nasal airway tests such as rhinomanometry, acoustic rhinometry, and nasal inspiratory/expiratory peak flow, are not widely used by physicians because they are limited by instrumentation costs and numerous operator-dependent factors that lead to poor reproducibility.1

An emerging technology that may prove useful in the management of rhinitis is optical coherence tomography (OCT). OCT is an imaging modality that combines light from a low-coherence source with a Michelson interferometer to produce cross-sectional images of tissue structures.3 Conceptually, OCT is analogous to ultrasound with the exception that broadband near-infrared light, rather than sound, is used to create images with a resolution approaching that of light microscopy (7 μm). Similar to how ultrasound resolves differences in the acoustic properties of biological structures, OCT relies on detecting differences in tissue optical properties, which includes the effects of both absorption and scattering. Furthermore, OCT is a real-time, noninvasive imaging modality that operates without the need for cytotoxic fixation, dyes, or ionizing radiation. Hence, it is an ideal imaging technique for living tissue and monitoring the response of superficial tissues to pharmacologic interventions.4 Even though OCT has a limited depth of penetration (~2 mm depending on the tissue being examined), it can be performed using flexible single-mode fiber-optic imaging probes, allowing access to many clinically relevant tissues, including those of the upper aerodigestive tract.

Currently, OCT systems are used clinically in ophthalmology5 with further applications being sought in numerous medical disciplines including dermatology,6 gastroenterology,7 cardiology,8 and urology.9 In otolaryngology, most efforts have focused on the application of this technology toward the early detection of cancer of the laryngeal and oral cavities10,11 and in experimental studies of the cochlea.12 Regrettably, there has been limited discussion concerning the application of OCT toward the assessment of the human nasal mucosa. The only previously published literature regarding OCT of this region showed architectural changes of the nasal septal mucosa before and after septoplasty using a holmium: YAG laser in 15 patients.13 To date, however, no systematic study of the normal in vivo microanatomy of the nasal mucosa has been performed using OCT.
In this study, we used an OCT system to image the nasal cavity of subjects during surgical endoscopy and in the office setting. This study attempted to evaluate the ability of OCT to image normal nasal mucosal microstructure. In so doing, we hope to assess OCT’s potential to detect pathological or therapeutic changes in the nasal mucosa.

METHODS

OCT Imaging Instrumentation

Imaging is performed using an OCT system along with a fiber-based handheld probe. The fundamental elements of the system have been described previously\(^\text{14}\) and only a brief overview is provided here.

A photograph of our OCT system as it is used is provided in Fig. 1 with a schematic representation of the working parts in Fig. 2. The system used in this study uses a low-coherence light source (central wavelength \(\lambda_0 = 1310\) nm, full width at half maximum \(\Delta \lambda = 80\) nm, AFC BT 1310; JDS Uniphase, San Jose, CA) and an optical delay line which allows the acquisition of A-line scans at a rate of \(-500\) Hz. Signals backscattered from the sample arm are obtained by phase-resolved processing with the interference fringes. Cross-sectional images are obtained by performing successive scans across the tissue of interest using a fiber-based handheld probe.

The handheld probe (Fig. 3) consists of an OCT imaging fiber with a gradient refractive index lens and prism mounted to the end using ultraviolet cured glue (detailed in Fig. 4), which allowed for the delivery and collection of light from the target tissue. Scanning is achieved by linearly translating the fiber optic along its axis using a motorized stage (Model 663.4pr; Physik Instrumente, Tustin, CA). The fiber optic and optical elements are enclosed by a transparent plastic tube (inner diameter, 1.5 mm), which is mechanically supported and protected by an outer stainless steel cylinder. To assist the user in positioning the probe, colored markings were made along one side of the optic fiber opposite the light exit.

The axial resolution of the system is \(~7\) \(\mu\)m and the lateral resolution is \(20\) \(\mu\)m. Image size was set at \(6\) mm in length by \(1.6\) mm in depth. Total acquisition time for a single image is \(~1\) second.

Imaging

Subjects were imaged using our OCT system at the University of California Irvine Medical Center and Beckman Laser Institute in accordance with a protocol approved by the Institutional Review Board at the University of California, Irvine. Patients were imaged either while awake in an office setting or while under general anesthesia during surgical endoscopy.

All equipment, including the OCT system and handheld probe, were assembled, calibrated, and properly sterilized before data acquisition. To acquire images, the scanning tip of the handheld probe was inserted into the subject’s nasal cavity and oriented toward the specific region of interest. OCT images from the various anatomic sites were then recorded to the workstation. The OCT images along with other relevant subject information were used to construct a database of normative in vivo tissue microanatomy of the nasal cavity.

OCT images were analyzed for the presence of various nasal mucosal structures, including the epithelium, basement membrane, lamina propria (LP), and underlying cartilaginous and bony structures. Moreover, characterization was performed of tissue microstructures residing within the LP. Because tissue biopsy of the nasal mucosa is rarely indicated, analysis of OCT images was performed in reference to previously published literature regarding nasal mucosal microanatomy.\(^\text{15}\) Additionally, whenever possible, nasal mucosal architecture as imaged using OCT was compared before and after application of Neo-Synephrine (phenylephrine hydrochloride 1%) when decongestion was required for indications relevant to the patients’ clinical care.

Digital micrometry was performed to attain data regarding normative nasal mucosal epithelial thickness using a workstation running Adobe Photoshop 7.0 (Adobe Systems, Inc., San Jose, CA). Measurements of epithelial thickness were obtained at five evenly spaced points separated by 1 mm in each. These data were used to determine an average nasal epithelial thickness per subject, which was then used to calculate an overall average of our study group. Measurements were not taken from those images in which the demarcation between the epithelium and underlying LP could not be identified clearly.

RESULTS

Forty-four subjects were examined. The average age of our subjects was 60.1 years (range, 18–89 years) with a gender distribution of 63.6% male patients and 36.4% female patients. The nasal mucosa of 38 subjects (86.4%) was imaged using OCT while under general anesthesia in the operating room, and 6 subjects (13.6%) were imaged in the office. Although the majority of patients in our study had
no history of nasal mucosal disease, six subjects (13.6%) were taking medication for allergic rhinitis at the time of imaging.

A total of 224 OCT images were obtained from various structures in the nasal cavity, including the cartilaginous and bony septum, the inferior turbinate, and the lateral vestibule. OCT images depicted regions of varying signal intensity consistent with expected microstructures of the nasal mucosa. One of the more consistent microstructures identified was the pseudostratified columnar epithelium (PCE). As shown in Fig. 5, the PCE normally displayed a relatively low signal intensity in comparison with the underlying LP, allowing a clear demarcation between the two layers at the expected position of the basement membrane. The LP had relatively higher signal intensity, most likely because of its more abundant connective tissue elements. Moreover, as depicted in Fig. 6, the LP displayed regions of decreased signal intensity consistent with seromucinous glands. Of note, glandular elements were particularly prominent in the mucosa overlying the inferior turbinate. As seen in Fig. 7, OCT images of the LP also contained structures consistent with blood vessels. Blood, as opposed to seromucinous fluid, had the tendency to absorb optical signal and create a shadowing of underlying tissues. Finally, in some subjects, OCT images displayed a high signal intensity structure underlying the LP consistent with the perichondrium of the supporting cartilaginous framework (Fig. 8).

In patients that underwent nasal decongestant therapy, before and after OCT imaging revealed distinct morphological changes in the nasal mucosa (Fig. 9). Prededcongestant images displayed variations of signal intensity within the LP consistent with the presence of glandular elements, such as
seromucinous ducts, whereas postdecongestant images lacked such structural features. Instead, the LP displayed a pattern of uniformly increased tissue density as evidenced by an increased optical backscattering. Of note, some OCT images displayed a blurred appearance at one edge as a result of a motion artifact created by a change in direction of the translational stage (Figs. 5, 6, 8, and 9a). Measurements from digital micrometry resulted in an average nasal septal epithelial thickness of 102 ± 38 μm (n = 36; average, 1.88 ± 1.34 images per patient). No significant gender difference in epithelial thickness was seen.

**DISCUSSION**

This study shows the value of OCT as a high-resolution imaging modality capable of delineating nasal mucosal microanatomy. In addition to being able to identify the boundaries between the PCE, LP, and underlying cartilage or bone, OCT also was able to identify microstructures within the LP (such as glandular elements and blood vessels). Moreover, we were able to detect distinct morphological changes within the LP after the application of a nasal decongestant.

Other commonly used imaging modalities, such as computed tomography, magnetic resonance imaging, and ultrasound, have the ability to image subsurface architectures, but none offer the soft-tissue resolution of OCT (7 μm). Hence, these methods can not be used to depict reliably changes in the nasal mucosal as these occur at nearly a microscopic level. Novel endoscopic imaging techniques such as contact endoscopy, on the other hand, have remarkable soft-tissue resolution (10 μm); however, they require substantial training and, more importantly, suffer from an inadequate depth of penetration (<100 μm). As such, they can not be used to image structures beyond the nasal mucosal epithelium, which was found to average 102 μm in our study. Of current imaging modalities, only OCT offers a unique combination of high resolution (7 μm) and a depth of penetration (~2 mm) that is adequate for imaging nasal mucosal microanatomy. Moreover, unlike other imaging modalities, OCT does not employ the use of in vivo staining or ionizing radiation and, as such, is safe to be used repeatedly to follow the progression of disease or therapy over time.

Given the in vivo imaging capabilities of OCT, it has the potential to someday become an invaluable tool in the field of rhinology. A variety of potential applications for this technology can be envisioned within this field. For one, it may be used as an office-based tool to document rhinitis disease progression or its response to drugs or immunotherapy over time. Indices that potentially could be followed include the amount and nature of vascular and glandular structures present in the LP, the overall tissue density of the LP, or the thickness of the entire mucosa. The specific measurements used will depend on which type of rhinitis is present, because each displays unique histopathological features. OCT may even potentially be used to help make diagnostic decisions among the various forms of rhinitis. For example, OCT could be used to detect the characteristic changes of the mucosa in atrophic rhinitis or, with improved resolution and acquisition rate, the ciliary changes associated with primary ciliary dyskinesia. Moreover, OCT could potentially be used to help elucidate the poorly understood pathophysiology of various forms of rhinitis. Finally, OCT could be used as an "optical biopsy" to increase the efficacy of—or in place of—the rare instances of nasal mucosal biopsy (i.e., for vasculitis or benign or malignant neoplasms). To OCT’s advantage, it can be performed without the changes in tissue architecture that occur as a result of the excision, fixation, and microtoming involved with histological processing.
Clearly, more investigation needs to be performed before OCT can be used routinely in the management of nasal mucosal disease. Clinically, the study population will need to be both broadened to include patients with various pathological processes and followed over a longer duration. The limited number of patients in our study presenting with rhinitis precluded the formation of any conclusions regarding this group. Also, although our OCT imaging detected immediate changes in the nasal mucosa postdecongestant therapy, it would be necessary to evaluate changes induced by other drugs, including antihistamines, steroids, decongestants, anticholinergics, and antileukotrienes, over time. Parallel efforts need to be placed toward the further development of OCT technology. Faster image acquisition rates, increased depth of penetration, and, most importantly, improved resolution will all render OCT an even more powerful imaging modality.

REFERENCES