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Ultrahigh-resolution 3D full-field optical coherence micropscopy of the pulmonary airways ex vivo

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Visualizing the respiratory mucosa in pulmonary airways at the sub-cellular level could yield new insights into pathogenesis of many important diseases. However, current imaging modalities to study the respiratory mucosa lack the required resolution to visualize critical subcellular detail such as nuclei and respiratory epithelial cilia.

Full-field optical coherence microscopy (FFOCM) is an emerging technique capable of providing reflectance images in situ with high spatial resolution in all three dimensions.We have developed a FFOCM with an axial sectioning thickness of 1μm and a high transverse resolution of 0.6μm. The three-dimensional field of view was 256 (H) x 256 (W) x 400 (D) μm. Three-dimensional images of formalin-fixed, sectioned porcine bronchial segments were obtained immediately ex vivo. Images were compared to H&E stained histology at corresponding sites. Pilot images on fixed human airways from individuals with cystic fibrosis (CF) and Chronic Obstructive Pulmonary Disease (COPD) were also acquired.

Individual epithelial cells and goblet cells, including their subcellular morphologies, were easily seen. Cross-sectional views showed gland ducts containing mucus, cilia, the periciliary layer (PCL), and nuclei. Three-dimensional rendering of the trachea showed the presence of mucus droplets directly above non-ciliated goblet cells, tethered to the surface of these cells by a thin adherent mucus strand.

Our results demonstrate the potential of FFOCM to provide detailed microstructural imaging of pulmonary airways without administration of a contrast medium. The future development of a probe for in vivo monitoring of mucociliary transport, gland function, and airway surface liquid (ASL) depth could provide new avenues for improving our understanding of respiratory mucosal pathophysiology and enable longitudinal assessment of the response to novel drugs.

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