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2017

Leung, H. M., Cui, D., Ford, T. N., Hyun, D., Dong, J., Yin, B., et al. (2017). Towards a clinical implementation of μ OCT instrument for in vivo imaging of human airways. Proceeding of SPIE 10056, Design and Quality for Biomedical Technologies X, 1005614-.

<https://hdl.handle.net/10356/89458>

<https://doi.org/10.1117/12.2253423>

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Towards a Clinical Implementation of μ OCT Instrument for *In Vivo* Imaging of Human Airways

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INTRODUCTION

We have previously reported the development of a micro-optical coherence tomography (μ OCT) imaging system that has a spatial resolution of 1-2 μ m and the application of that technology to the study of CF pathogenesis. The technology enables the capturing of the functional microanatomy and key metrics that characterize cystic fibrosis (CF) disease, such as airway surface liquid (ASL) layer, periciliary liquid (PCL) layer, cilia beating frequency (CBF), mucociliary transport (MCT), and epithelium thickness in a colocalized fashion.

Up till recently, the imaging technique is developed as a benchtop system that can be used to perform *in vitro* studies of CF pathogenesis in cultured cells and in animal explants. To translate this into a clinical technology and to allow the airways of CF patients to be observed directly, a clinical μ OCT system and flexible imaging catheters are being developed to perform *in vivo* imaging of human airways. We demonstrate for the first time the nasal imaging of human subjects using this technology.

(a) A schematic of the clinical imaging console. (b) A picture of a doctor handling a nasal probe to image the upper airways of a human subject. (c) A picture of the nasal probe installed onto an enclosed piezo stage that provides the linear beam scanning mechanism at 40 Hz. (d) A schematic of the distal tip of the catheter illustrating the orientation of illumination and scan direction. (e) A schematic of the optical elements within the imaging probe that provides the annular apodization of the beam required for this μ OCT imaging technique. (f) A diagram illustrating the optical setup of the imaging system. The use of a broadband illuminating beam provides the high axial resolution of this imaging technique, which is based on the principles of spectral-domain OCT.

μ OCT IMAGING INSTRUMENT COMPATIBLE WITH BRONCHIAL AND NASAL CATHETERS

FIRST *IN VIVO* μ OCT NASAL IMAGING OF CYSTIC FIBROSIS PATIENTS

μ OCT images of the nasal airways of cystic fibrosis patients. (a) The airway surface liquid (ASL, green bar) layer, which includes the striated mucus (mu) and periciliary layer (PCL, yellow bar), is seen overlaying the epithelium (ep). (b) A picture of a nasal gland duct (gl) and mucus around the region. (c) A distinct PCL can be seen overlaying the epithelium. (d) A heterogeneous mucus layer with globular components is observed over a distinct PCL. (e)-(g) In contrast to mucus seen in (d), the mucus in these regions contain long and striated components, suggesting a difference in mucus contents and possibly rheological properties. (h)-(j) Images of thick and heterogeneous mucus layers present in CF patients. Our imaging system allows live μ OCT images to be recorded at 40 fps and this in turn equipped us with the capability to study dynamical events such as cilia beating and mucociliary clearance *in vivo*, in addition to quantifying thicknesses of ASL and PCL.

μ OCT IMAGING IN SWINE

BRONCHIAL

NASAL

Bronchial and nasal μ OCT imaging obtained in swine studies. (a) Cilia and a distinct PCL are observed on the epithelium in the swine lungs. (b) A large mucus load over the ciliated epithelium. (c) An image of a gland duct in the swine lungs. (d) Similar to (b), a layer of mucus is seen overlaying a layer of cilia and PCL in the nasal airways of the swine. (e)-(f) In some other regions of the nasal, the mucus layer is comparatively less dense.

DISCUSSION AND SUMMARY

The very first μ OCT imaging of the human nasal airways has been successfully demonstrated and the technology allows the direct observation and analysis of various functional microanatomical features that characterize CF disease.

Numerous challenges remain to be overcome, the most significant of which is overcoming motion artifacts during *in vivo* imaging. Implementation of image registration algorithms is necessary to allow dynamical events to be quantitatively analyzed. Secondly, hysteresis in the scanning mechanisms, especially in bronchial imaging where the catheter has to be long, has often provided difficulties in obtaining stable and uniform scanning in the lower airways.

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ACKNOWLEDGEMENT

We are grateful for funding from the NIH (5R01HL116213-04) and CFF (Mucociliary Clearance Consortium). Special thanks to Joe Gardecki, Vladimir Vinarsky and Kengyeh Chu.

Design and Quality for Biomedical Technologies X, edited by Ramesh Raghavachari, Rongguang Liang, Proc. of SPIE Vol. 10056, 1005614 · © 2017 SPIE · CCC code: 1605-7422/17/\$18 · doi: 10.1117/12.2253423