European Respiratory Society
Annual Congress 2012

Abstract Number: 7135
Publication Number: P641

Abstract Group: 1.3. Imaging
Keyword 1: Imaging **Keyword 2:** Lung mechanics **Keyword 3:** No keyword

Title: Optical coherence tomography measurements of subpleural alveolar size compared to micro-CT and ray-trace modeling

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Body: Optical frequency domain imaging (OFDI) is a promising second-generation optical coherence tomorgraphy (OCT) modality for visualization of alveolar structure and function in vivo due to its microscopic resolution (~10µm) and fast imaging speed (>100fps). In order to enable quantitative conclusions about alveolar behavior under various ventilation strategies or pathologies, it was crucial to investigate the validity of alveolar size measurements obtained from OFDI images. Therefore, we compared the cross-sectional area, perimeter, volume, and surface area of matched subpleural alveoli from micro-CT (2.9µm resolution) and OFDI images of fixed air-filled swine samples. Furthermore, we developed a ray-tracing model that approximates the reconstructed alveolar size within OFDI images based on potential refraction effects that are not visible in micro-CT images. We discovered that the relative change in size between alveoli was extremely well correlated between the two imaging techniques ($r>0.9$, $p<0.0001$), but OFDI images underestimated absolute sizes compared to micro-CT images by 27% (area), 7% (perimeter), 46% (volume), and 25% (surface area) on average. Using our model and OFDI measurements of the refractive index for fixed and fresh lung tissue, the experimentally obtained OFDI measurements could be re-scaled to approximate the micro-CT measurements with dramatically reduced error (<10% for all size parameters). In this study, we have successfully validated relative alveolar sizes as measured within OFDI images and show the potential to obtain absolute size measurements with the use of predictive correction factors.