In-Vivo Assessment of Pulmonary Fibrosis in Rodents Using Ultrasound Multiple Scattering

Kaustav Mohanty[1], John Blackwell[2], Mir Ali[2], Stephanie A. Montogomery[3], Hong Yuan[4], Thomas Egan[2], Marie Muller[1]
[1]Department of Mechanical and Aerospace Engineering, NC State University, Raleigh, NC-27695
[2]Division of Cardiothoracic Surgery, Dept. of Surgery, UNC Chapel Hill, Chapel Hill, NC-27599
[3]Dept. of Pathology and Laboratory Medicine, UNC Chapel Hill, Chapel Hill, NC-27599
[4]Dept. of Radiology, UNC School of Medicine, UNC Chapel Hill, Chapel Hill, NC-27599

Background, Motivation and Objective

Idiopathic pulmonary fibrosis (IPF) causes *changes in the micro-architecture of the lung parenchyma, and thickening of the alveolar walls, which reduces compliance and elasticity. IPF affects 200,000 patients in the U.S. annually. Computed Tomography (CT) can diagnose pulmonary fibrosis. However, CT is inappropriate for monitoring IPF due to cost and ionizing radiation. Lung is highly complex from the point of view of ultrasound propagation, due to the presence of air-filled alveoli. We present an ultrasound method capable of detecting and quantifying pulmonary fibrosis in-vivo in rodents by taking advantage of ultrasound multiple scattering due to air-liquid interface scatter. We calculated the diffusion of ultrasound waves characterized by the scattering mean free path (L*). L* provides a quantitative assessment of the micro-architectural changes of the lungs due to IPF.*

Statement of Contribution/Methods

Pulmonary fibrosis was created in Sprague-Dawley rats by instilling bleomycin into the airway. Rats were studied in groups of n=6 (3 male, 3 female): no bleomycin (control) and 2, 3, and 4 weeks after bleomycin administration, to provide a range of severity of pulmonary fibrosis. Anesthetized rats, ventilated after tracheotomy had a sternotomy to expose both lungs. Impulse response matrices were acquired in-vivo using a 128-element linear array transducer operating at 7.8MHz, applied directly to lung allowed estimating the incoherent backscattered intensity. L was calculated by measuring the rate of growth of the diffusive halo over time. Rats were euthanized and CT scans were performed on the inflated lung at 50 um resolution. The severity score from 0-4 was assigned to each lung in a masked manner based on the amount of fibrosis detected by CT. After CT, lungs were inflation-fixed. Severity of fibrosis was also evaluated from 5 micron H&E stained sections based on a modified Ashcroft. L* was then compared with the fibrosis severity scores obtained by CT and histology.*

Results/Discussion

At control, 2, 3 and 4 weeks post-bleomycin, the average severity scores from CT images were 0, 2.833, 2.28 and 2, and the average histology severity scores were 0, 2.6, 1.7 and 2.3 respectively. Significant differences were found between the L of Control (466±110 μm) and fibrotic rats (L* = 772±304 μm at 2 weeks, $p<0.001$), 690±191 μm at 3 weeks, $p<0.001$, and 713±171 μm at 4 weeks, $p<0.001$). A significant correlation was observed between the fibrosis severity scores obtained by CT and L* ($p=0.038$). Strong correlation was also observed between the histology fibrosis severity score and L* ($p=0.003$). These significant differences suggest the potential of this method to diagnose IPF. Serial assessment of multiple scattering in lung during a brief breath hold through multiple intercostal spaces may provide a reliable non-invasive adjunct to follow patients with IPF.*