European Respiratory Society
Annual Congress 2012

Abstract Number: 7182

Publication Number: 3308

Abstract Group: 4.1. Clinical physiology and Exercise

Keyword 1: Animal models **Keyword 2:** COPD - mechanism **Keyword 3:** Longitudinal study

Title: Lung structure and function in a rat model of emphysema: A longitudinal study

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Body: Our aim was to evaluate the long term structure-function relations in a rat model of emphysema. Rats were treated with porcine pancreatic elastase (50 UI, PPE, n=21) or saline (controls, C, n=19) intratracheally. Before the treatment (day 0) and 3, 10, 21 and 105 days thereafter, respiratory impedance was measured with forced oscillation technique and tissue elastance (H) was calculated. At 3, 21 and 105 day the lungs were fixed, sections were obtained and stained with hematoxylin and eosin, modified Movat's, Masson's and Alcian blue method to visualize elastin, collagen and proteoglycans. Randomly selected regions were photographed. The images were automatically segmented and the equivalent diameter of alveolar airspaces (D), mean elastin (Me), mean collagen content (Mc) and mean proteoglycan ratio (Mp) were measured. H decreased through the time-course in the treated animals ($p<0.001$). D was different between the control and the treated groups at 21 ($p=0.027$) and 105 days ($p=0.004$). Me increased in the treated groups (21 d, 105 d: $p<0.001$), Mc decreased in the treated groups (3 d, 21 d: $p<0.001$) and Mp was different between the 2 groups (21 d: $p<0.001$, 105 d: $p=0.016$). Multiple linear regression revealed significant correlations between H, D and Me/Mc/Mp ($r^2=0.7$, $p<0.001$; $r^2=0.712$, $p<0.001$; $r^2=0.547$, $p=0.042$). We conclude that the progression of emphysema in the PPE model occurs by gradual septal wall failures leading to enlarged airspaces, which in turn decreases the tissue elastance of the lung. This irreversible process results in strong functional and microstructural relations with the components of the extracellular matrix.