**Idiopathic pulmonary fibrosis: a study using volumetric imaging and functional data in a computational lung model**

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**Introduction**

Idiopathic pulmonary fibrosis (IPF) is an aggressive idiopathic interstitial pneumonia, and often occurs in elderly adults. In IPF, fibrosis typically develops preferentially in posterior-basal lung regions, and often co-exists with emphysema. Currently it is not clear how - or whether - the spatial distribution of tissue abnormalities in IPF (including classifications of tissue type) correlate with pulmonary function tests (PFTs) and their change over time. This work aims to develop a new quantitative tool that integrates data from volumetric imaging, PFTs, and computational models for lung function, to understand differences between IPF and normal older lungs.

**Methods**

Routinely-acquired volumetric HRCT data was acquired retrospectively from 8 patients (aged 43-82) at diagnosis of IPF with follow up scans between 5-20 months and PFTs acquired more frequently. A geometric mesh was fitted to the shape of each subject’s lung and lobes and compared with a statistical shape model (SSM) quantifying the average normal lung shape and its principal modes of shape variation. Tissue was classified as normal, reticular, ground glass, or emphysema using CALIPER (Computer-Aided Lung Informatics for Pathology Evaluation and Ratings) software. The spatial distribution of classified tissue and its mean density (TD) and volume were calculated and mapped to lung models. Ventilation (V) and perfusion (Q) and gas exchange were simulated in vascular and airway models generated to lung shape models and coupled to spatial distributions of tissue density, assuming increased and decreased tissue stiffness in regions of fibrosis and emphysema, respectively.

**Results**

Fibrosis had higher TD=0.34/0.41 for reticular/ground-glass) compared with normal tissue TD=0.28, and presented predominantly basally and posteriorly. In contrast, emphysema (TD=0.08) was predominantly in upper lobes. The first principal SSM mode (>20% of the shape variation in normal lungs) was significantly different between IPF and normal (p=0.001). This shape mode relates to the anteroposterior diameter of the lung, and the ratio of apical and basal diameters; differences from normal in IPF potentially result in impaired diaphragmatic movement. V/Q mismatch as a result of tissue abnormalities was not predicted to be sufficient by itself to reduce gas exchange to measured values.

**Conclusion**

Statistical shape analysis suggests quantifiable differences from normal in lung shape are present in IPF at diagnosis. Simulation of V, Q, and gas exchange in a model that includes spatial mapping of tissue classifications suggests that V/Q mismatch (impaired gas exchange) is present in ‘normal’ tissue as well as regions that are classified as abnormal.