**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 the most aggressive and frequent form of idiopathic interstitial pneumonias with unknown cause. It is a lethal fibrosing lung disorder that occurs primarily in middle-aged and elderly adults. The progression of IPF is variable between individuals and no established quantitative tools exist to indicate the likely progression of the disease. The aim of this work is to develop a new quantitative method of the IPF that integrates information from volumetric imaging, pulmonary function tests, and computational models for lung function; and to conduct a quantitative assessment of IPF tissue characterisation and disease development over time.

**Method**

Tissue regions in HRCT images from 8 patients with IPF (aged 43-82) were quantitatively analysed. In the IPF cohort tissue abnormalities were classified using CALIPER (Computer-Aided Lung Informatics for Pathology Evaluation and Ratings) software. Mean tissue density (TD), volume and spatial distribution of tissue classified by CALIPER as reticular, ground glass, or emphysemawere calculated. The classified data were mapped to a statistical shape model, which allows consistent comparison between patients or within one patient at different time points. A computational representation airway tree was generated for each individual patient and deformed to fit the lung shape of each time point. A principal component analysis (PCA) was applied to assess lung shape and tissue heterogeneity differences between IPF lungs and a PCA derived average from a normal cohort aged X-Y. These quantitative tissue biomarkers combined with pulmonary functional tests were used to drive a non-uniform tissue property (density, stiffness, resistance and compliance) based stress distribution analysis gas exchange was simulated in the IPF lung to relate structural characteristics to function.

**Result**

Fibrosis usually has consistently higher TD (0.34/0.41 for reticular/ground-glass) compared to normal tissue (0.28), and presents predominantly in lower lobes basally and peripherally. In contrast, emphysema has lower density (0.08) and appears predominantly in upper lobes. Most IPF patients experience a decrease lung volume over time (on average 11.85% over a period of5-20 months). Lungg shape is signigficantly different between between IPF land normal lungs in the first mode of PCA analysis (p=0.001) which captures over 20% of shape variation. This shape difference is predominantly comprised of a change in the anteroposterior (AP) diameter of lung which results in impaired diagphramatic movement. There is a strong correlation between model predicted stress distribution and the distribution and development of disease (elastic recoil pressure of fibrosis is higher than normal whereas emphysema is lower). V-Q mismatchand impaired gas exchange is predicted in IPF lungs even in CT evaluated ‘normal’ tissue.

**Conclusion**

An image based analysis of IPF tissue characterisation and distribution combined with functional modelling techniques provides a set of tissue-level markers of lung decline in IPF. This could be a potential tool to help with assessment of IPF progression at the early stage of this disease.