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

Yuwen Zhang

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This thesis is for examination purposes only and is confidential to the examination process.

Auckland Bioengineering Institute

The University of Auckland

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Abstract

Idiopathic pulmonary fibrosis (IPF), the most aggressive and frequent form of idiopathic interstitial pneumonias (IIPs), is a chronic and life-threatening disease of unknown cause. It is characterised by progressive worsening of dyspnea and lung function and is associated with a poor prognosis. IPF occurs primarily in middle-aged and elderly adults, and is more frequent in males than females. Even worse, the aetiology of IPF remains elusive, and its progression is variable and unpredictable, hence there are no biomarkers that can indicate the likely progression of the disease. A quantification scheme that allows recognition of disease consistently across radiology, pulmonary and pathology disciplines remains difficult. In this study, a combination of quantitative information extracted from HRCT, clinical knowledge, and computational modelling was developed to help with a better understanding of the progression of IPF and investigate strategies for patient-specific diagnosis and treatment planning for IPF patients.

First, an automatic lung lobe segmentation method from HRCT images was developed, which is guided by a statistical shape model that can predict the likely region of fissure locations. This new method was able to estimate the fissure location in 100% of cases including both normal healthy and IPF subjects, whereas two comparison segmentation softwares that use anatomy-based methods fail in several cases with lobes segmented. Second, tissue abnormalities in IPF lungs were classified, and then mapped

to a statistical shape model, and quantitative approaches were used to analyse lung shape, tissue density, tissue volume, the spatial distribution of abnormalities, and regional changes in tissue over time. Fibrosis was found to present predominantly basally and peripherally in the lung. In contrast, emphysema in these subjects mostly located in upper lobes. The first principal statistical shape mode ($> 20\%$ of the shape variation in normal lungs) is significantly different between IPF and normal and strongly correlated with fibrosis extent in IPF lungs. Finally, a computational model of lung function was developed which integrated quantification analysis from volumetric CT data and pulmonary functional test to understand differences between IPF and normal older lungs. Ventilation, perfusion and gas exchange models were parameterized to simulate $\dot{V}$, $\dot{Q}$ distribution and gas transport. The computational model can reasonably predict the patient-specific ventilation, perfusion and gas exchange in IPF lung, and quantify the difference of lung function between IPF patients and older normal people. However, abnormalities on volumetric CT imaging may be not able to provide enough information to explain the decline of lung function in IPF patient, and an individual impaired gas exchange appears to happen in not only abnormally tagged region but also in CT-visualized 'normal' tissues.

IPF is a complex and progressive disease that has multifarious physiological processes and significant individual differences. The methods and models presented in this thesis provide a basis for application to research in IPF lung function, and furthers investigations into the underlying relationship between physiology mechanisms and disease progressions of IPF.

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