**TSANZ presentation speech draft**

**Slide 1**: Good morning, everyone, I’m Yuwen Zhang, from Auckland Bioengineering Institute. Thank you very much for coming to my presentation. Next, I will introduce my research project, it’s about CT-based characterization analysis of idiopathic pulmonary fibrosis

**Slide 2**: IPF is one of the most aggressive and frequent forms of idiopathic lung disease. Idiopathic means that the cause is unknown. For people more than 75 years old, IPF is estimated to occur in more than 200 cases per 1000,000. That is a large number of people, and a mean survival of only approximately 3 years. The aetiology of IPF remains elusive and there is no known cure. The rate of progression of IPF is quite variable and unpredictable between patients. However, there are currently no reliable biomarkers that can indicate the likely progression of IPF disease.

**Slide 3**: With the development of radiological imaging techniques, high-resolution computed tomography (HRCT) has played an essential role in evaluating lung disease. Based on the criteria set by members of ATS / ERS [5], the diagnosis of IPF usually associates with the presence of a usual interstitial pneumonia (UIP) pattern on HRCT. Honycomb, reticular and ground-glass are all typical CT patterns of fibrosis disease. In addition, in the past ten years, some researchers suggest that combined IPF and emphysema (CPFE) should be regarded as a distinct clinical entity other than emphysema or IPF alone. Therefore, our research also involves in quantitative analysis of emphysema region on HRCT image.

**Slide 4**: In the past few years, there has been effort to provide quantitative analysis on CT scans of lung parenchymal abnormalities, and also some statistical analysis of clinical data from IPF patients, such as PFT data, airway resistance, tissue compliance and ventilation/perfusion ratio. But, currently, there are few researches involves in relating spatial distribution of abnormalities to the functional data. And there is no established quantitative tools exist to assess the progression of IPF. So the aim of our study is to develop a new method for quantitative assessment of the IPF lung that brings together volumetric imaging, pulmonary function tests, and computational models for lung function.

**Slide 5**: The clinical CT data used in this study was acquired from 8 patients diagnosed with IPF at Auckland City Hospital. The slice thickness of these clinical CT images are from 1.25 to 3.00mm. Among these data, 5 patients have one time point, 1 patient has 2 time point data, 2 patients have time point data. The time interval between different time point is between 5 to 20 monts.

**Slide 6**: Tissue regions were classified using CALIPER (Computer-Aided Lung Informatics for Pathology Evaluation and Ratings) software, developed at the Mayo Clinic. This software is able to classify every lung parenchymal voxel into several kinds of CT patterns, including normal (N), reticular (R), honeycomb (HC), ground-glass (GG), mild low attenuation areas (LAA), moderate LAA and severe LAA. In addition, emphysema areas were extracted through detecting the voxels whose Hounsfield Unit is under -950.

**Slide 7**: Lung surface data was extracted from the classified data and fissure surfaces were defined manually using the open-source visualization software CMGUI by an expert user. A bi-cubic Hermite finite element surface mesh was fitted to the shape of the lung and its fissures. Since there is lung shape variation between different subjects and often between clinical images obtained at different times. Classified volumetric lung data was then mapped to a statistical shape model (SSM) of the ‘normal’ older human lung. The statistical shape model was constructed based on principle component analysis derived from a set of training meshes. The gaps on the mapped data was filled using KNN searching to make it easier for the further quantitative analysis.

**Slide 8**: The average tissue density of each classified CT pattern was calculated. From the result, we can see fibrosis has a consistently higher tissue density (0.34/0.41 for reticular/ground-glass) over time compared to normal tissue (0.2752). In contrast, emphysema has lower density (0.0784).

**Slide 9**: In order to analyze the spatial distribution of abnormalities, the volume percent of each kind of disease pattern was averaged withinin 5% lung height in the direction from base to apex. Also, the volume percent of each disease pattern for each lobe was calculated to provide a lobar distribution of disease. We can see from the result that fibrosis mostly located in lower lobes (72%, 58%, 65% for honeycomb, reticular, ground-glass). In contrast, Emphysema mostly located in upper lobes (73%).

**Slide 10**: Next, we used fractal dimension as a measurement to analyze the heterogeneity of IPF lungs. With a specific size window, we can divide the whole lung into a set of same sized voxels. For each voxel, the average density is calculated, as shown in the left figure. A straight line is fitted to build a relationship between the coeffient of variance of density and the shampling window size. The fractal dimension equals to 1 minus the graident of the fitted line. As we can see from the result, although the spatial position and percentage of abnormalities keep changing all the time, the heterogeneity seems not change too much with the development of the disease.

**Slide 11**: Next, we compared the IPF lung shape to the old normal ones. In order to analyze the lung shape difference, we also used the PCA-based SSM which is constructed using the same way as we introduced previously. The only difference is here we used 35 old normal subjects as the training set. By making use of PCA analysis, we are able to decompose lung shape into a set of mode, each mode represents a kind of shape variation. Here, we projected each IPF lung to the SSM, so that we can get the weight value for each mode. Through comparing the mode weight between IPF lungs and old normal lungs, we found that there is a significant differece of the first mode between these two groups. The first mode captures over 20% of the entire shape variation, it mainly describes the change of the anteroposterior diameter of the lung, and the ratio of apical and basal diameters. Also, we found there is a strong relationship between the first mode and the fibrosis percentage. That means with the progression of IPF, the abnormalities could cause a shape change of lung, and this kind of change has a relationship with the fibrosis overall percent.

**Slide 12**: In the next stage, our work is to use the previous quantitative CT based analysis on our computational models. Before that, a patient-specific airway tree geometry is needed to be created. Firstly, the upper airway tree was manually digitized using cmgui. Then, for each patient, generate full airway tree of the first time point, map this airway tree to the lung volume mesh of other time points, this can make sure the same airway tree geometry was used for different time point. Next, the airway tree terminal acinar unit was labelled with different CT disease patterns through matching the airway tree to the classified data. When label the airway tree, both the disease spatial location and volume percentage were taken into consideration. After that, we scaled the airway tree, from image volume to its FRC volume.

**Slide 13**: With the labelled and scaled airway geometry, we used our ventilation model to simulate forced inspiration from FRC to TLC. For each subject, we can get a corresponding normal FRC and TLC volume as reference and a real reduced FRC and TLC volume. Simulate forced inspiration from reference FRC to TLC, we can set a needed muscle pressure, then use the same muscle pressure to drive the disease ventilation on real FRC to TLC. Here, we decreased the compliance of the disease labelled acinar unit into a very small value, in order to make sure the disease region is stiff enough. We found, for most subjects, the fibrosis area extracted from CT image is not sufficient to match the real inspiration curve. There must be some tissue become stiffer on CT “normal” regions.

**Slide 14**: For the patient-specific perfusion analysis, we generated the full vessel tree matching and surrounding by the airway tree. The vessel radius of the disease labelled region were decreased so that we can get a reduced perfusion of the abnormal regions. Using the ventilation and perfusion as input of the gas exchange model, we can get a V/Q ration distribution of IPF patient. We can observe from the result that V/Q mismatching could occur not only around the disease location but also happen on normal region. Currently we are still working on this part, more factor need to be taken into consideration, which leads to our future work.

**Slide15**: In the next stage, we may take the transfer factor into consideration. As for emphysema regions, the aveolar-capillary membrane has a larger area, for fibrosis tissues, the membrane thickness will become bigger, both of them will influce the transfer factor. We also plan to use more PFT data to parameterize our model, e.g. use FEV1 and FVC value to parameterize the forced expiratory model. And use the density and shape analysis results on our tissue mechanical model to analyze the stress distribution of IPF lungs. Our further goal is to integrate all the analysis to make a prediction of IPF progression at an early stage in order to help with a clinical treatment.