TSANZ presentation speech draft

Slide 1: Good morning, everyone, I’m Yuwen Zhang, from the University of Auckland. Thank you very much for coming to my presentation. In the next 10 minutes, I will make a introduction of my research, 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 occure in more than 200 cases per 1000,000. That is a large number of people with a disease that has no known cure, 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, Some studies indicate that 15% of patients with IPF experience a rapid worsening of symptoms, insufficiency of pulmonary function and over 80% of these rapid progressive patients die of respiratory failure within 6 months. Most IPF patients deteriorate relatively slowly, and their pulmonary function usually decreases gradually over the months to years after the first clinical symptoms. However, there are currently no reliable biomarkers that indicate the likely progression of IPF disease.

Slide 3: Recent development in radiological imaging techniques offers exciting opportunities to provide radiological patient-specific biomarkers as important indicators of specific phenotypes. High-resolution computed tomography (HRCT) has played an essential role in evaluating lung disease through recognizing visual patterns and features of disease regions such as ground-glass opacities, reticular patterns and honeycombing. 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, combined IPF and emphysema (CPFE) has been mentioned and defined in the past ten years. Some researchers suggest that 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 considerable effort to provide quantitative analysis on CT scans of lung parenchymal abnormalities. Renuka et al [9-10] was an early group to present a computer aided diagnosis (CAD) method to quantify lung tissues based upon HRCT. An adaptive multiple feature method (AMFM) which combined statistical texture measures and a fractal measure was developed to assess CT features for classifying a tissue pattern. Alan et al [11-12] used mean lung attenuation (MLA), skewness (asymmetry) and kurtosis (peakedness) as quantitative CT indexes and furtherly used univariate and multiple correlation and regression statistical analyses to determine relationships between histogram features and results of PFTs. Hyun et al presented a texture-based CAD scoring system to assess quantitative lung fibrosis (QLF) as a measurement of lung disease severity and as a surrogate imaging marker. However, the current published methods mainly focus on the global analysis of each CT pattern or texture-based index as a whole lung (such as the percentile analysis or the correlation between indexes), but seldomly characterize the spatial distribution of each diseased region or the change extent of these abnormalities.

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 3 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. CALIPER is a computational image analysis platform developed by the Biomedical Imaging Resource Laboratory at the Mayo Clinic Rochester for the characterization and classification of lung parenchymal findings on CT images. CALPER classifies regions of the lung every parenchymal voxel into the following characteristic CT patterns: 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 via a least squares fit. The left lung mesh consists of 35 nodes and 44 elements, while the right lung mesh has 50 nodes and 62 elements.

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 to provide a consistent mapping of tissue abnormalities between and within individuals to a same lung shape. The statistical shape model was constructed based on principle component analysis derived from a set of training meshes. The training set consisted of data from 30 healthy normal subjects (15 males and 15 females) that was retrospectively selected from the Human Lung Atlas (HLA) database.

In order to map the data, we need to calculate the xi location of each data point within its correspond element, and then use this xi to calculate the global coordinates of the mapped data points.

Next, we projected the mapped data into a series of cross section slices. From the first row image, we can see that there are some curved gaps within the mapped data, that is caused by the deformation during the mapping.

In order to make the data points distribute uniformly throughout each lung, the gap sin of the mapped data caused by the deformation. The gaps were filled to match their closest neighbor point among the classified data, so that it could be easier for the further volume and density quantitative analysis.

Slide 8: The average density value of each classified CT pattern for each subject was calculated. From the result, we can see the average density of each region almost remains consistent over time, and for one region, the tissue density usually slightly fluctuates within a specific range. the average density of each region almost remains consistent over time, and for one region, the tissue density usually slightly fluctuates within a specific range. Fibrosis usually has a consistently

higher tissue density (0.34/0.41 for reticular/ground-glass) compared to normal tissue (0.2752) over time. In contrast, emphysema has lower density (0.0784).

The volume of left and right lung for each patient was calculated. From this table, we can see the lung volume of IPF patients keeps an overall decreasing over time. The lung volume decreased by about 11.85% averagely for these three patients.

Slide 9: In the direction from base to apex, the volume percentage of each disease region was averaged in 5% percent lung height (along the dorsoventral axis). It can be seen from the result that ground-glass region mainly locates in the basal part of lung. The percentage of ground-glass decreases gradually with the increasing of the lung height. In contrast, the percentage of emphysema roughly keeps a rising trend along with the increasing of lung height. The distribution of reticular region mainly focuses on the basal area and apex area. This kind of disease CT pattern seldom appears in the middle part of lung. The distribution of honeycomb seems not to have a regular distribution against lung height.

Also, the volume percentage of each disease region for each lobe was calculated to provide a lobar distribution of disease.

For ground-glass and honeycomb patterns, it can be seen from the figure that the disease regions mostly locate in the lower lobe of each lung. For reticular pattern, the percentage of middle lobe is significant lower than the percentage of other lobes, which probably means reticular pattern hardly locates in the middle part of lung. As for emphysema lesions, it commonly distributes in the upper lobes and with the increasing of time, it may also appear in the middle lobe.

Slide 10: Next, we used fractal dimension for density 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 are changing all the time with the development of the disease, the heterogeneity seems not change too much over time.

Slide 11: Next, we compared the IPF lung shape with the old normal ones. In order to analyze the lung shape difference, we also used the PCA-based SSM shape model 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. Through making use of PCA analysis, we are able to decompose lung shape into a set of mode, each mode represents each 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 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. 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. In the next stage, the airway tree terminal acinar unit was labelled with different CT disease patterns through matching the airway tree to the classified data. Different patient has different disease distribution, this patient-specific disease distribution can conduct a patient-specific ventilation analysis, such as change the resistance and compliance for different disease regions. Currently, we are working on the ventilation model, but a future goal is the use the quantitative analysis on our perfusion, gas exchange and mechanics model.

Slide 13: With the labelled and scaled airway geometry, we used our ventilation model to simulate the 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 region to a very small value, in order to make sure the disease region is stiff enough. We found, for most subjects, the fibrosis percent 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. This part of work we are still working on, we need to take more factor into consideration, which lead to our future work.

Slide15: In the next work, we may take the transfer factor into consideration. As for emphysema regions, the aveolar-capillary membrane area may become bigger, for fibrosis tissues, the membrane thickness 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 simulate the forced expiratory model. And use the density and shape analysis results on our tissue mechanical model to analyze the stree distribution of IPF lungs. Our further goal is to integrate all the analysis to make a prediction of IPF progression at an early stage to help with a clinical treatment.