Quantitative analysis of idiopathic pulmonary fibrosis abnormality from CT imaging

Yuwen Zhang
Supervised by : Prof. Merryn Tawhai
Dr. Alys Clark
Dr. Haribalan Kumar

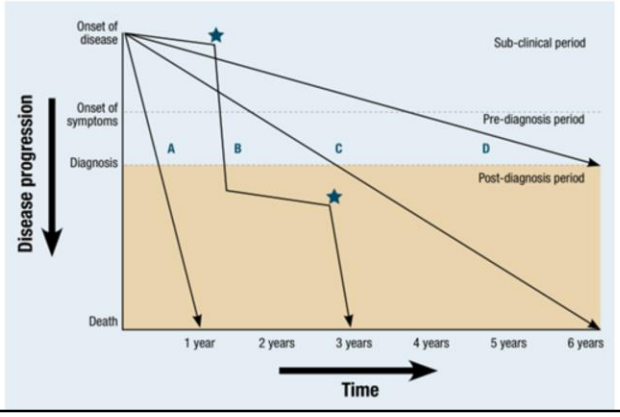
THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
AUCKLAND BIOENGINEERING INSTITUTE

Good morning, everyone, I'm Yuwen Zhang. In the next 15 minutes, I will make a introduction of my research, which is about quantitative analysis of idiopathic pulmonary fibrosis abnormality from CT imaging.

Background

AUCKLAND BIOENGINEERING INSTITUTE
THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

- A chronic and life-threatening disease
- Cause is unknown
- Aetiology remains elusive
- Progression is variable and unpredictable

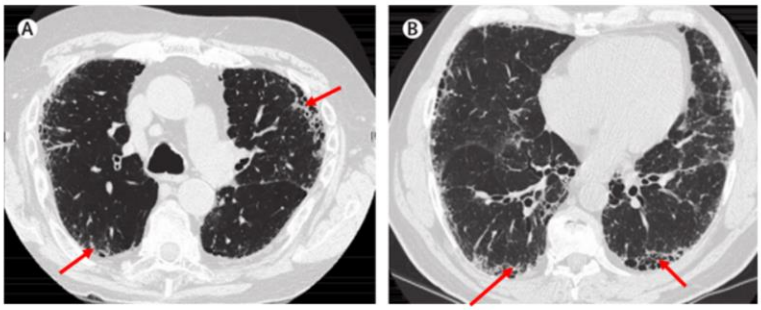


IPF is one of the most aggressive and frequent forms of idiopathic lung disease. Idiopathic means that the cause is unknown. For people more than 75 years old, IPF is estimated to occure in more than 200 cases per 1000,000. That is a large number of people with a disease that has no known cure, and a 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.

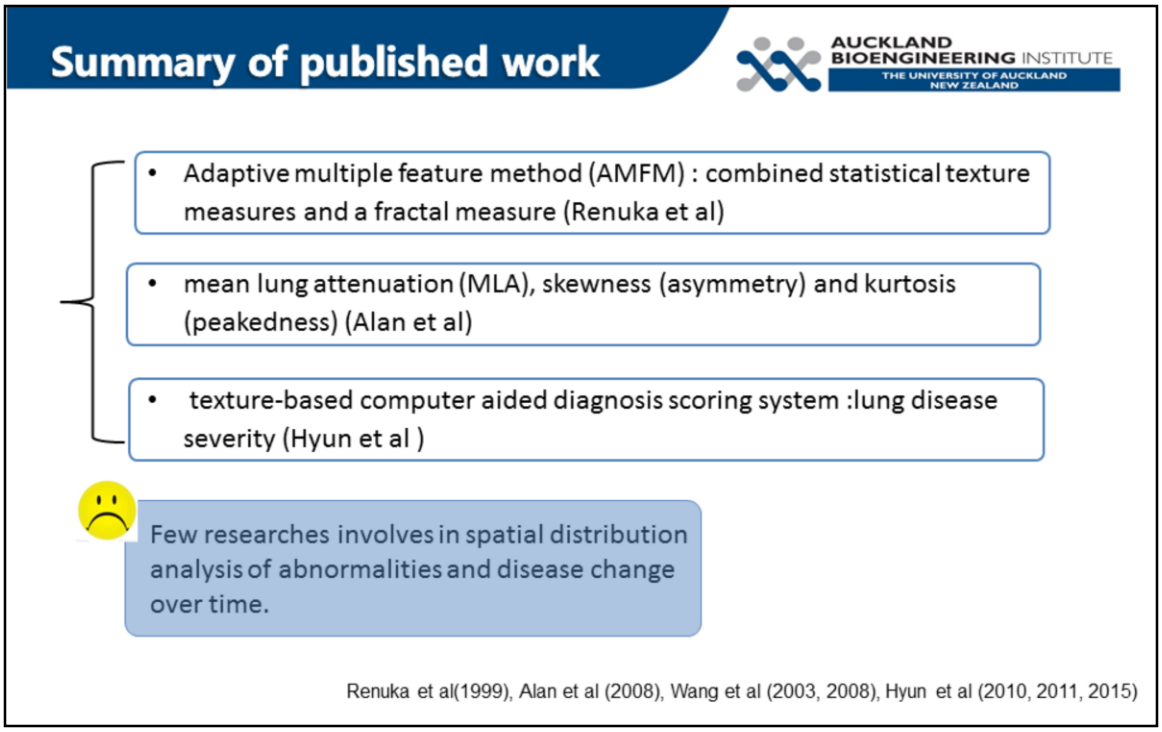
Background

AUCKLAND BIOENGINEERING INSTITUTE
THE UNIVERSITY OF AUCKLAND NEW ZEALAND

- HRCT is an essential tool in evaluating lung disease
- Associates with the presence of a usual interstitial pneumonia (UIP) pattern on HRCT (ATS/ERS criteria)
- Honeycomb, reticular, ground-glass
- combined IPF and emphysema (CPFE)



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.



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.

Imaging and clinical data

AUCKLAND BIOENGINEERING INSTITUTE
THE UNIVERSITY OF AUCKLAND NEW ZEALAND

Description	
Age years	43-82
Females/Males	3/5
Slice thickness	1.23-3.00mm
Scan month interval	5-20 month
Slice resolution	512*512
Number of slice	65-160

The clinical data used in this study comprised HRCT images obtained from 8 patients diagnosed with IPF at Auckland City Hospital, Auckland, New Zealand.

5 patients → 1 time point
1 patients → 2 time point
2 patients → 3 time point

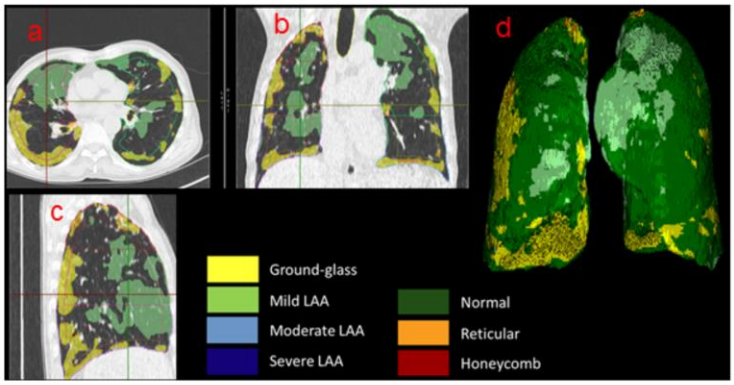
The clinical CT data used in this study was acquired from 8 patients diagnosed with IPF at Auckland City Hospital. The slice thickness of these clinical CT images are from 1.25 to 3.00mm. Among these data, 5 patients have one time point, 1 patient has 2 time point data, 2 patients have 3 time point data. The time interval between different time point is between 5 to 20 monts.

Pulmonary parenchymal classification

AUCKLAND BIOENGINEERING INSTITUTE
THE UNIVERSITY OF AUCKLAND NEW ZEALAND

CALIPER (Computer-Aided Lung Informatics for Pathology Evaluation and Ratings) software. Mayo Clinic (Rochester, MN, USA)

Each parenchymal voxel was classfied 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. Emphysema : Hounsfield Unit is under -950.



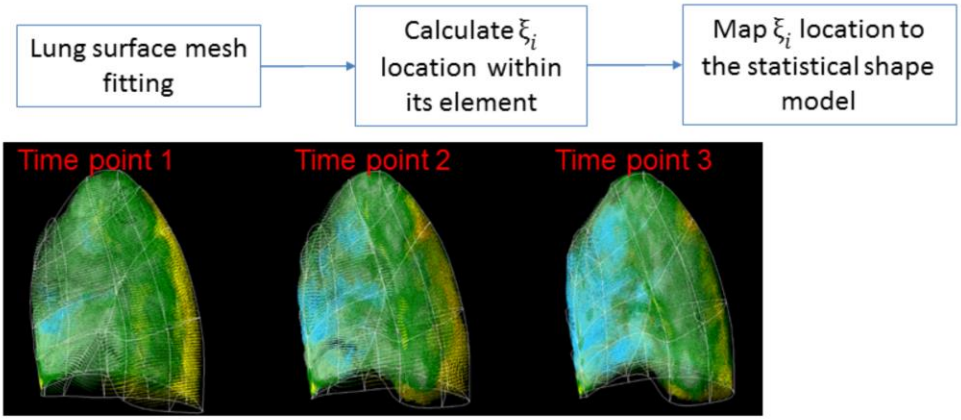
Color labelled classification result of case 7 on IPF HRCT by CALIPER. (a) Transverse plane. (b) Coronal plane. (c) Sagittal plane. (d) 3D color labelled lung.

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.

Normalization of classified data

AUCKLAND BIOENGINEERING INSTITUTE
THE UNIVERSITY OF AUCKLAND NEW ZEALAND

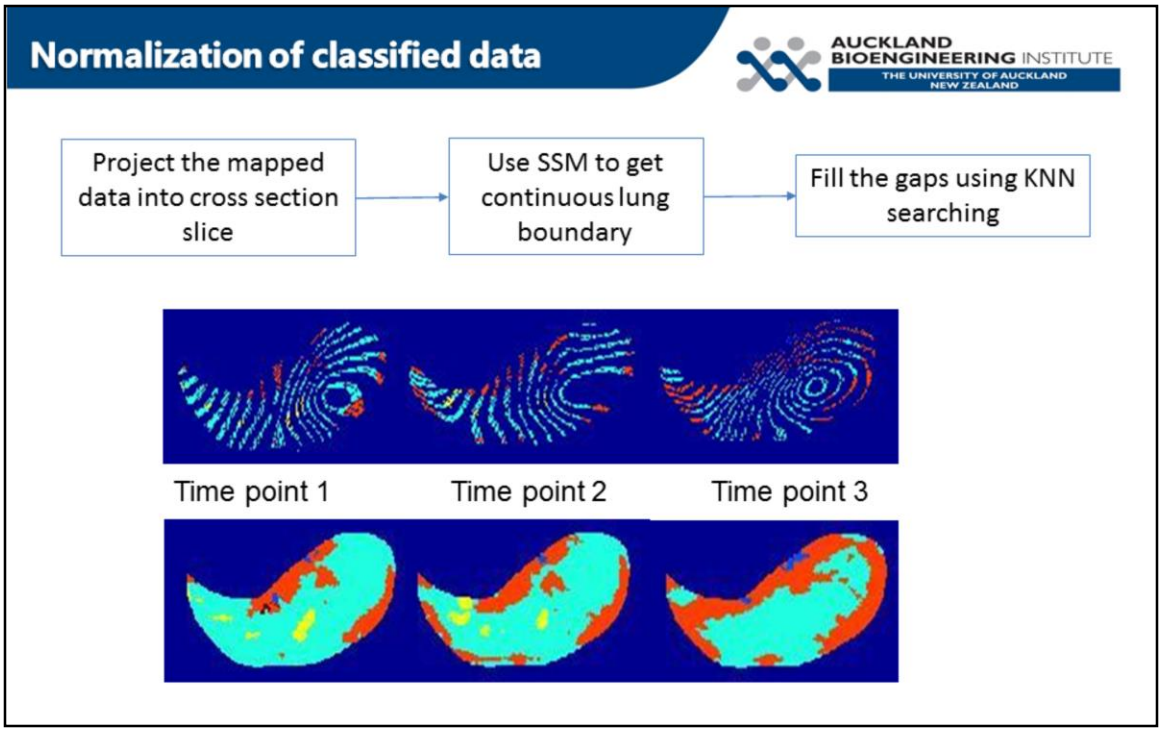
- Lung mesh : bi-cubic Hermite finite element surface mesh (left lung: 35 nodes and 44 elements; right lung: 50 nodes and 62 elements)
- Statistical shape model (SSM): 30 healthy normal subjects (15 males and 15 females), principal component analysis (PCA)



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.



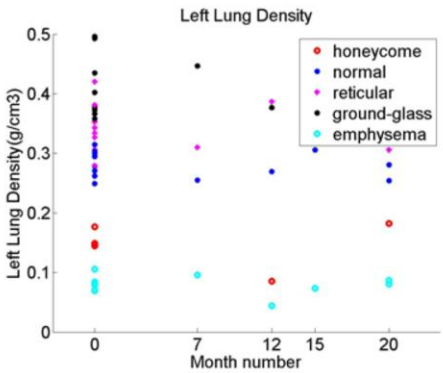
Next, we projected the mapped data into a series of cross section slices. From the first row image, we can see that there are some curved gaps within the mapped data, that is caused by the deformation during the mapping.

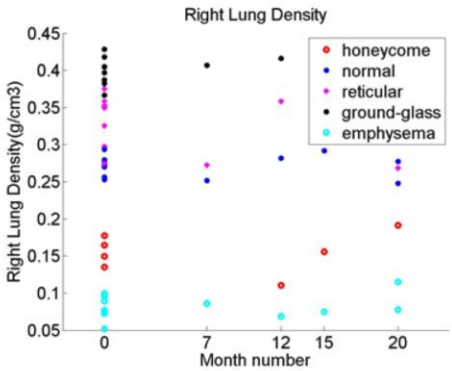
In order to make the data points distribute uniformly throughout each lung, the gap sin of the mapped data caused by the deformation. The gaps were filled to match their closest neighbor point among the classified data, so that it could be easier for the further volume and density quantitative analysis.

Density analysis

AUCKLAND BIOENGINEERING INSTITUTE
THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

- Average density for each CT pattern remains stable over time.
- 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 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).

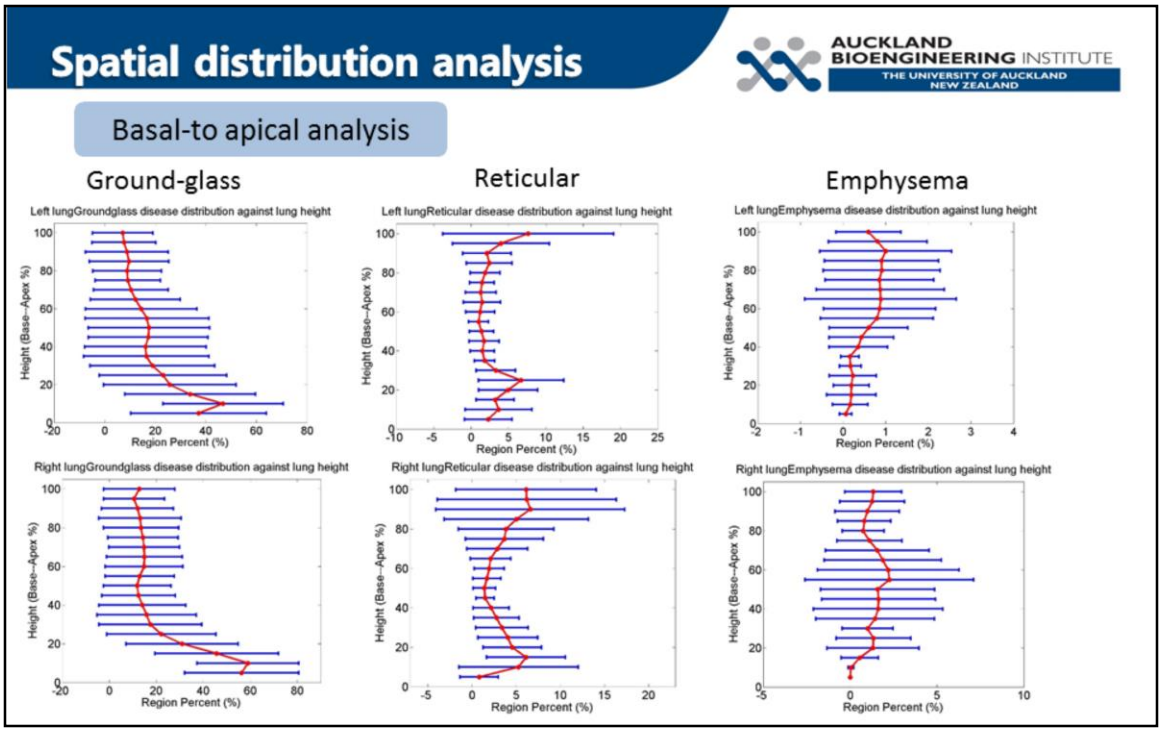
Volume analysis

AUCKLAND BIOENGINEERING INSTITUTE
THE UNIVERSITY OF AUCKLAND NEW ZEALAND

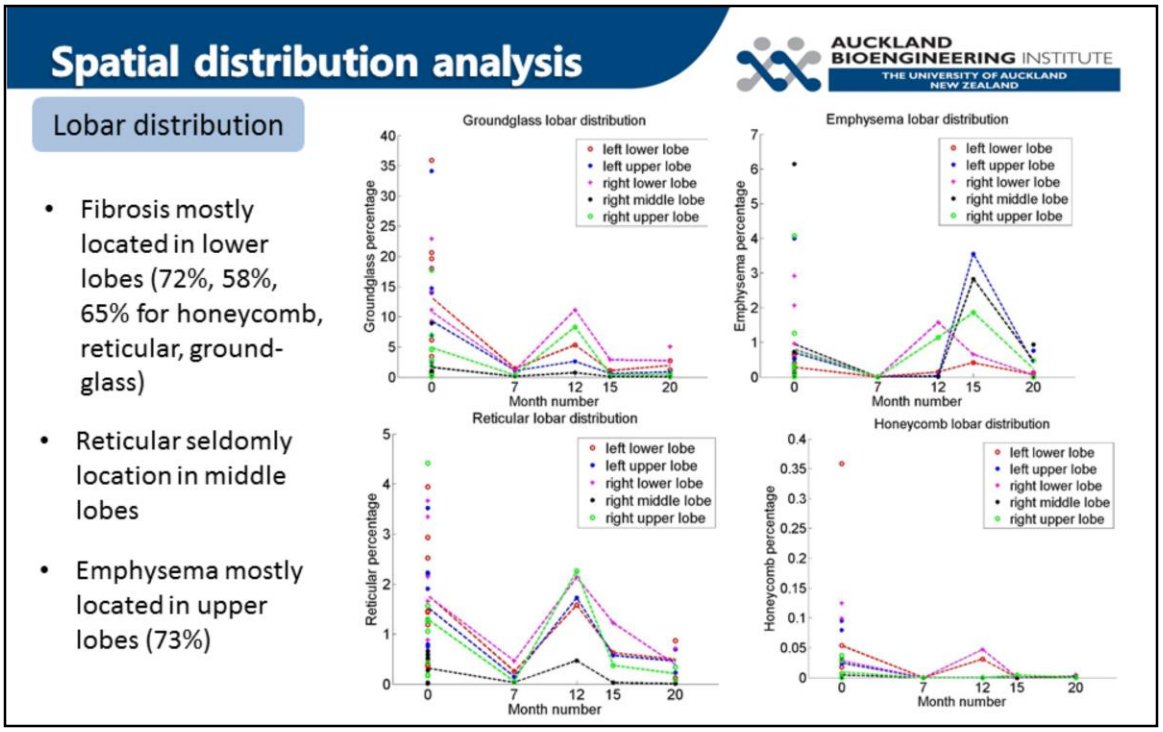
Sub No.	Time point	Date	Left Lung	Right Lung
IPF5	Time pint1	02/11/2013	4.3124	3.7212
	Time point2	12/11/2014	3.9457	3.2861
IPF6	Time point1	15/10/2012	2.4357	3.5879
	Time point2	30/01/2014	2.1505	3.0536
	Time point3	18/06/2014	2.0637	3.0962
IPF9	Time point1	24/12/2013	3.3798	3.7271
	Time point2	01/07/2014	3.0507	3.5815
	Time point3	12/08/2015	3.0814	3.8328

- The lung volume of IPF patient keeps an overall decreasing over time (11.85% off averagely).

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.

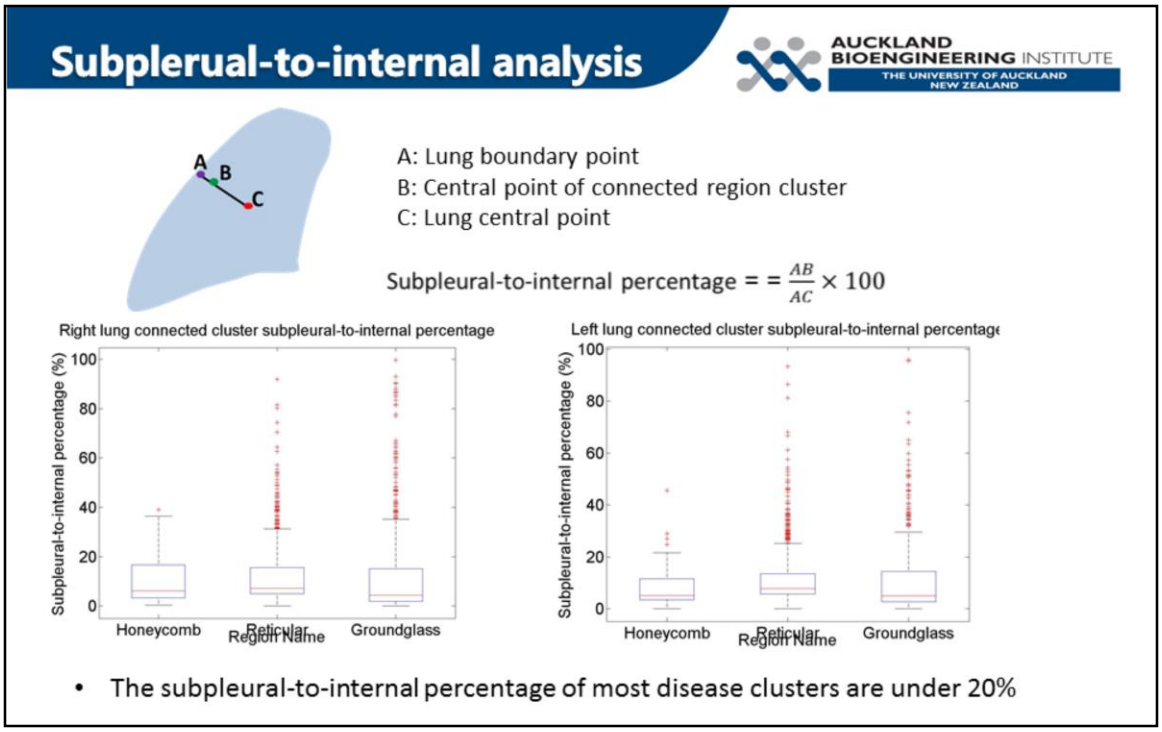


In the direction from base to apex, the volume percentage of each disease region was averaged in 5% percent lung height (along the dorsoventral axis). It can be seen from the result that ground-glass region mainly locates in the basal part of lung. The percentage of ground-glass decreases gradually with 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.



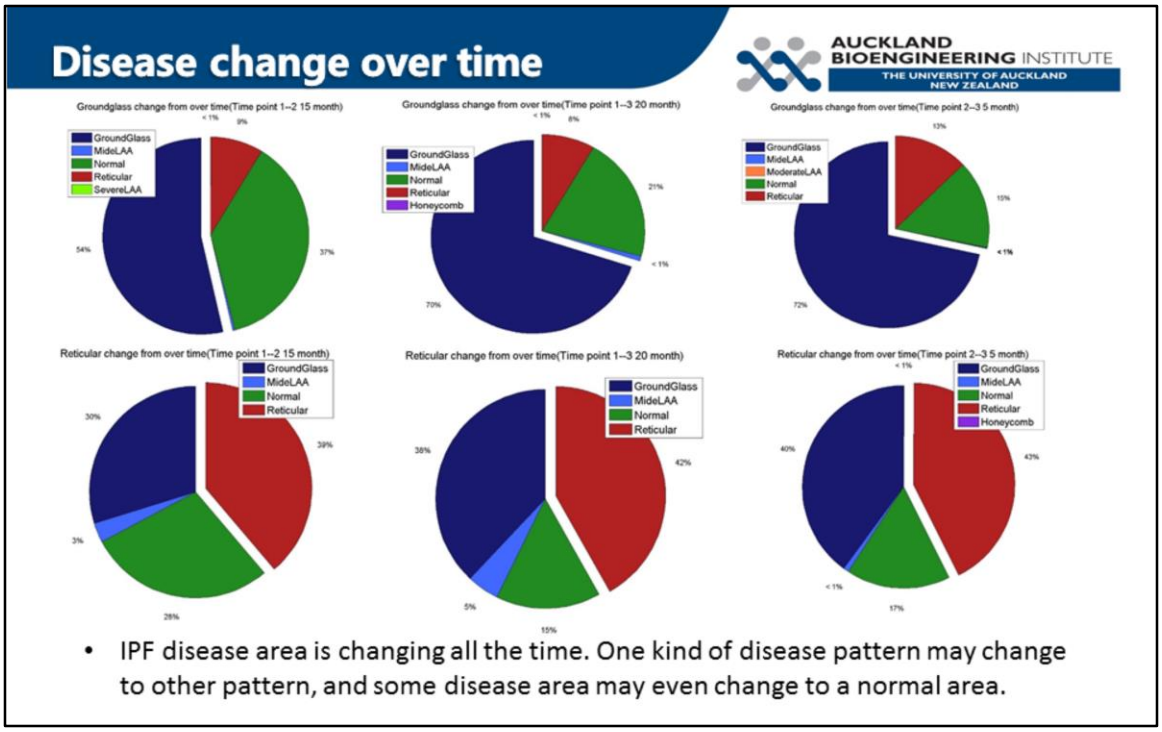
Also, the volume percentage of each disease region for each lobe was calculated to provide a lobar distribution of disease.

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.

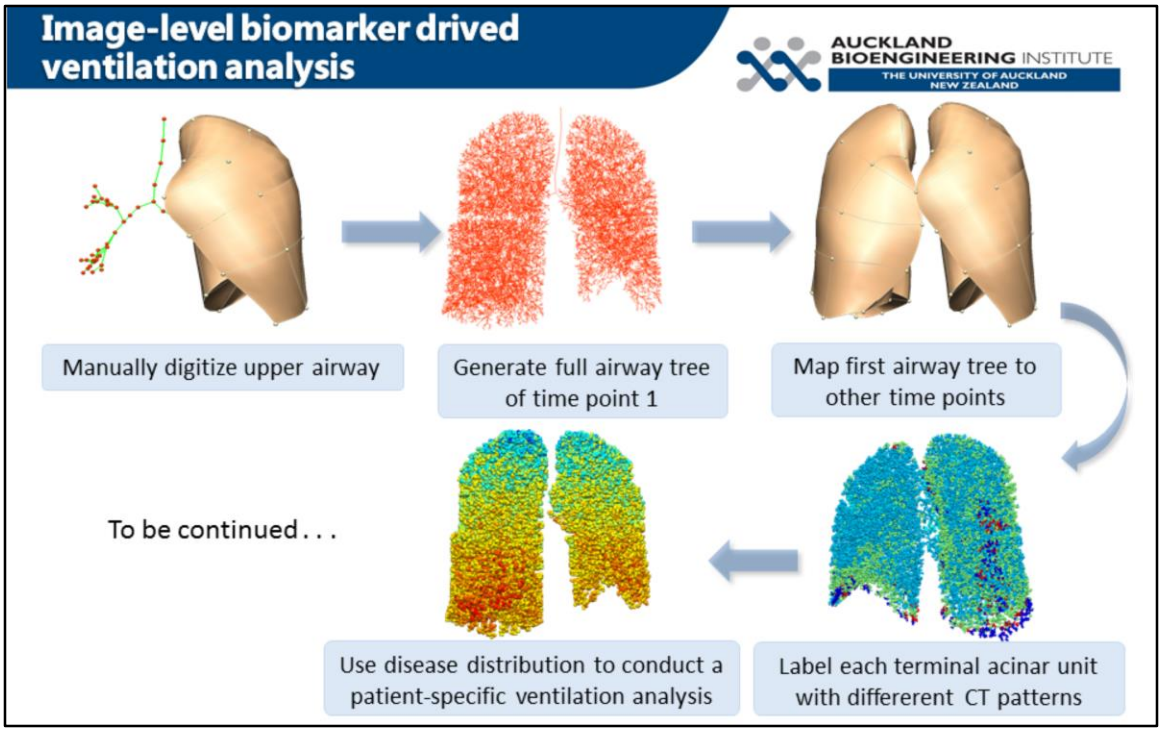


The percentage from the center of the lung to the boundary of the lung was used as a credible measurement to analyze the peripheral performance of disease. The center location of each connected cluster of disease pattern was firstly calculated. As the point position shown in Fig.3, the subpleraual to internal percentage of each connected cluster of disease region was calculated by:

Most of the disease clusters are peripheral performance. For both left and right lungs, the subpleural-to-internal percentage of most disease clusters are under 20%. That means the IPF disease are usually peripheral performance and mainly distributes surrounding the surface of the lung.



We analyzed the disease changes over time. These pie charts how the two characteristic disease CT patterns (ground-glass and reticular) change over time. It describes the percentage of each CT pattern which changes from ground-glass or reticular pattern of the previous time point. For ground-glass region of both left and right lungs, over 50% of this region still stays the same pattern over time, whereas there are also some area of ground-glass change to normal or reticular pattern as time goes by. The pattern changes is more significant for reticular region, although quite a number of reticular area didn't change over this period of time, a large proportion of it change to ground-glass, especially for right lung, and there is also about 10%-30% of reticular becoming normal during this time. In general, it seems that the IPF disease area is changing all the time. One kind of disease pattern may change to other pattern, and some parts of disease area may change to a normal one.



Our current work is to use the previous quantitative analysis as image-level biomarkers to drive a ventilation analysis. Here is a brief workflow of the model based analysis. 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.

Summary

AUCKLAND BIOENGINEERING INSTITUTE
THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

- We classified the pulmonary parenchyma representing IPF features, mapped the classified data to a PCA-based statistical shape model and performed quantitative analysis including density analysis, volume analysis, spatial distribution analysis and disease change over time.
- The results shows fibrosis usually has a consistently higher tissue density, whereas emphysema has lower density. The distribution of fibrosis is basal and peripheral (subplerual), though often patchy, while emphysema appears predominantly in upper lobes. The spatical location of disease keeps changing over time.
- This work could help to guide a future model based analysis, and point to new biomarkers as a clinical index for diagnosis and treatment planning.

This image based analysis will indicate potential tissue-level markers of lung function that could be translated to clinical indices for diagnosis and patient stratification into high and low risk groups. A further goal is to understand how the spatial distribution of each type of tissue abnormality translates to ventilation/perfusion mismatch and impaired gas exchange.

Acknowledgement

Clinical data for this study was provided by Drs ML Wilsher and DG Milne, Auckland City Hospital; CALIPER analysis was conducted by Dr Brian Bartholmai, Mayo Clinic.

I would like to thank my surpervisors for their great help and guidance with my project.
Prof. Merryn Tawhai
Dr. Alys Clark
Dr. Haribalan Kumar

Thank you

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

AUCKLAND BIOENGINEERING INSTITUTE