Exercise

The role of basial epithelial cells for small airway loss and epithelial injury in chronic lung disease.

- **Design a suitable folder structure for this research**

Think about data files (raw / processed), documentation files, source code, publications, results.

- **What would be useful elements for file names and/or folder names?**

Abstrqct: Small airways play a key role in maintaining optimal gas exchange in the alveoli but why, where and how they disappear in chronic lung diseases remain unknown. Disturbed airway homeostasis caused by repeated injury-induced excessive activation of the repair process leading to exhaustion of the (basal) progenitor cells may result in abnormal airway remodelling and loss of small airways. We hypothesize that alterations of small airways and airway epithelium represent the initial step in early lung disease. Understanding the small airway organization, the behaviour of the cells lining their epithelium, the regeneration potential and differentiation of progenitor cells (with a focus on basal cells) and their effect on the small airway physiology will provide key elements in chronic diseases like chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF). The aim of this project is to unravel the changes, destruction and disappearance of small airways and epithelial cells in healthy lungs and lungs with mild to severe COPD and IPF and validate the findings within in vitro models. Data from microCT scans of whole lungs and small cores will allow reconstruction of the airways. Data from lung tissue will be used to visualize structure and identify cells (histology) and to document cell behaviour on cell culture.

Data (just WP1)

Workpackage 1 will collect microCT scans of whole lungs (8-14 GB) and small cores (5-6 GB). These are collected in tiff format and reconstructed to jpg files. These jpg files are converted by ImageJ to an mha file for use in ITK-snap, NeuronStudio and ImageJ.

Overview of samples collected will be stored as Excel spreadsheet.

Documentation

Standard experimental procedures (SOPs):

- Lung collection and microCT scanning processing, airway segmentation and reconstruction
- Lung core sampling and small partition microCT scanning processing

A bit about the methodology

9 lungs will be examined for three groups: donor, COPD (Chronic obstructive pulmonary disease) and IPF (Idiopathic pulmonary fibrosis).

To assess the organization of the airways, whole lung MicroCT followed by reconstruction and airway segmentation will be performed on frozen lungs.

CT-images will be converted to MetaImage files (text-based) with ImageJ. ITK-SNAP will be used to segment using semi-automated segmentation and analysis by NeuronStudio will reconstruct the airway tree per generation.

This will allow detailed analyses and quantification of the number and length of airways per generation, amountof terminal bronchioles and the minimal diameter and area, alveolar attachments, lung volume, mass and density, mean linear intercept, percentage of tissue and surface area and fibrosis.

Small partition MicroCT will be used to create CT images for small airway segmentation to allow detailed study of small airway deformation.

In combination with whole lung MicroCT, the full airway, starting from the main bronchus to the alveoli will be mapped. The frozen lung will be cut in slices of 2 cm thickness with a band saw from apex to base and samples will be taken with a sharpened steel cylinder or hole saw: these lung cores will be used for subsequent analysis.

Pictures are taken before and after the sampling in order to visualize the location of the cores on the lung slice.

The cores will then be segmented by ITK-SNAP and analyzed by NeuronStudio. These data will be linked to the whole lung MicroCT to gain more insight into how larger airways affect small airways and vice versa.

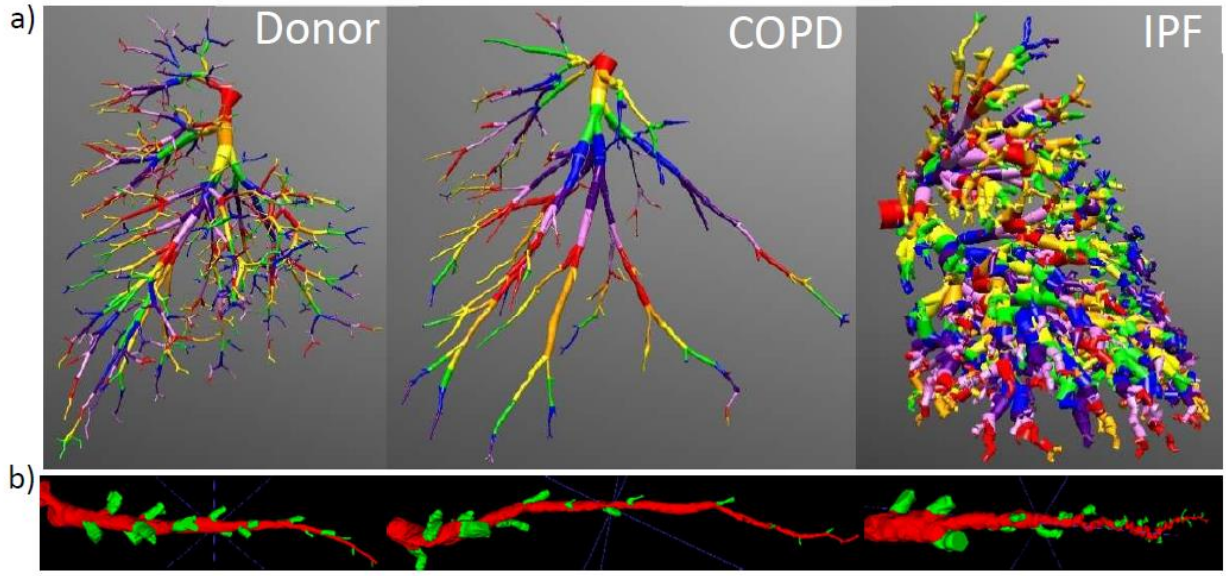
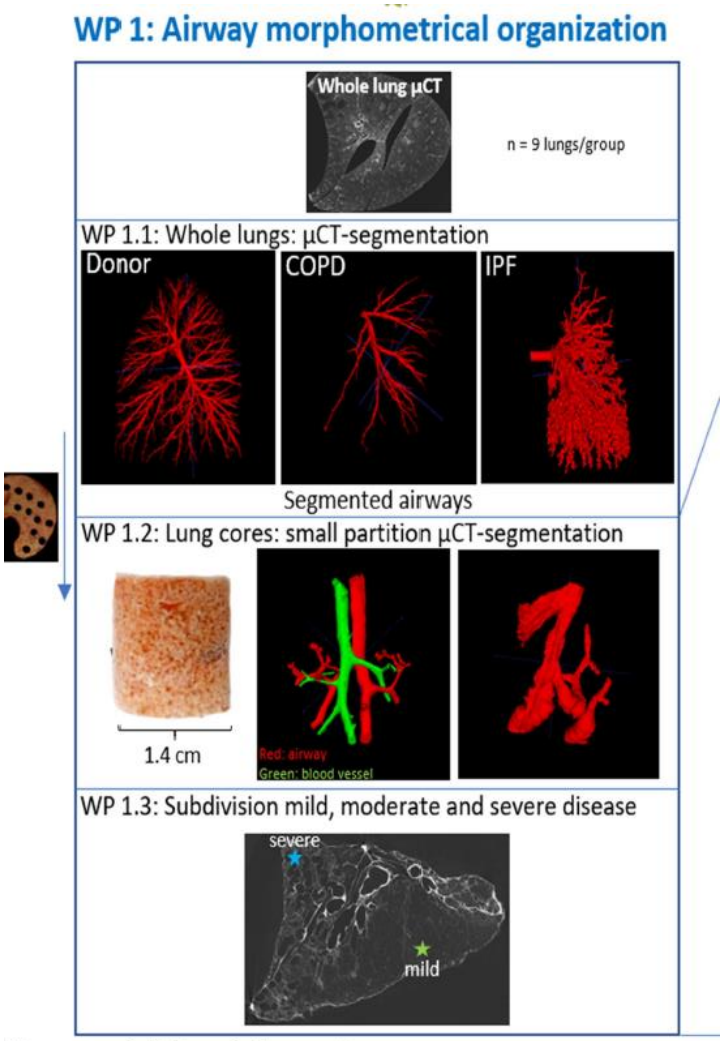


Fig.1: Airway segmentations of whole lung µCT of donor, COPD and IPF. (a) In COPD, less airways and longer branches are seen compared to donor lungs. In IPF, an enlargement of the air spaces is seen. Colors indicate subsequent generations. (b) Preliminary data of airway segmentations from the same branch to the lower lobe in donor, COPD and IPF lungs on which airway length, length between consecutive branches, angles and volumes have been measured resulting in two abstract submissions. Main branch is in red, bifurcations in green. CT: computed tomography



Measures at different disease stages:

- Number of airways, terminal bronchioles, alveolar attachments
- Angle, diameter and length
- Mean linear intercept
- Lung volume, mass and density