Micro-CT of Airway Remodelling in the Cigarette Smoke Model

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Aims

Exposure to chronic cigarette smoke in the mouse results in changes in lung histology which model emphysema found in chronic obstructive pulmonary disease (COPD). Computed tomography (CT) is used in the clinic to assess COPD and other lung diseases, and micro-CT allows smaller specimens to be scanned at microscope resolution and in 3D throughout the lung. Micro-CT findings may therefore have an impact which translates to CT in the clinic. In this pilot study, micro-CT has allowed us to image and measure airway remodelling in 3D throughout the lung, and quantify the effects of smoke, without physical sectioning of the tissue.

Method

Small groups of mice (n=3) were exposed to cigarette smoke or forced air (sham control) for 25 weeks. The animals were killed and the lungs were fixed by inflation with paraformaldehyde fixative. They were then dehydrated and chemically dried for micro-CT scanning using a method kindly given to us by Jeroen Hostens, SkyScan. The lungs were enclosed in a tightly fitting polyethylene plastic container and scanned in the SkyScan 1072 scanner at 40kV without filtration and with 11µm voxel resolution (1,000 sections per lung). Regions of interest for the whole lung and peripheral lung tissue were defined in the Skyscan CT analysis software, thresholds applied to detect tissue from background, and volumetric and densitometric measurements made.

Results

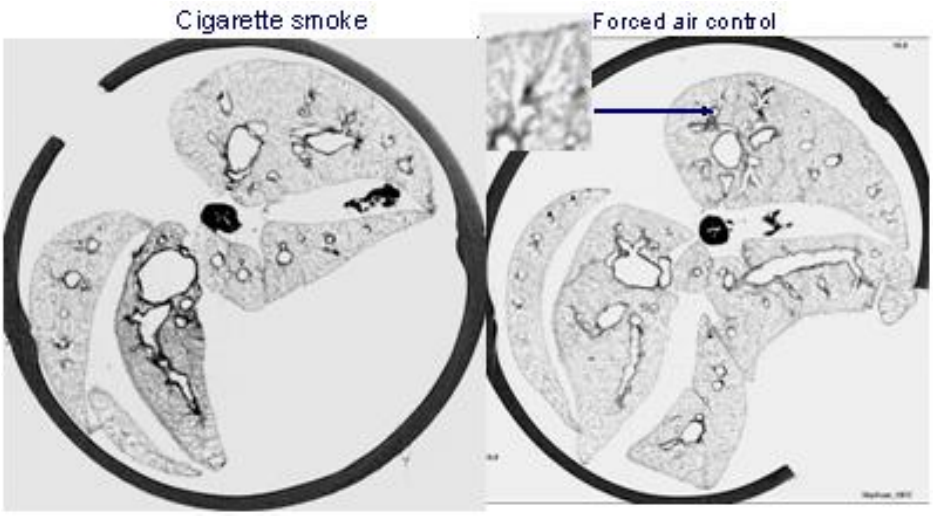

Figure 1: Micro-CT sections at mid-lung level showing detailed lung anatomy

The new micro-CT preparation method resulted in highly detailed micro-CT sections, resolving structure down to the alveolar level, without tissue damage (Fig. 1 inset shows airway branching to alveoli at high magnification). In the micro-CT sections the airway wall appears dense compared to other lung tissue and was quantified for volume, thickness and density.

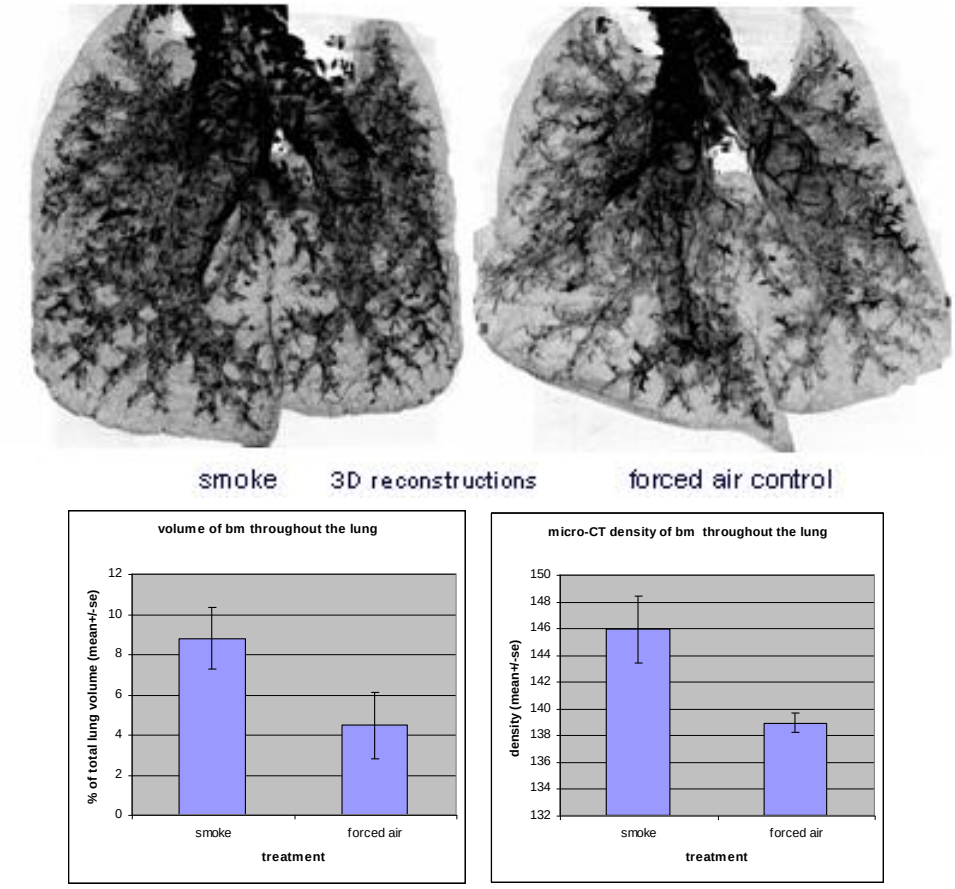

Figure 2: 3D images and graphs showing increased airway wall volume and density in response to cigarette smoke

In the lungs of the smoke exposed animals we found an increase in relative volume and density of airway wall in the peripheral lung compared to controls which suggests that remodelling is taking place. This has not been described before in this mouse model and may represent fibrosis of the small airways which occurs in human COPD (Chung and Adcock, 2008).

Conclusion

Micro-CT has demonstrated new remodelling changes in response to cigarette smoke in a mouse model of COPD. We are now investigating how these relate to fibrosis of the lung tissue. The new method of preparing the lungs has resulted in consistent highly detailed micro-CT scans.

Reference:

K.F. Chung and I.M. Adcock, “Multifaceted mechanisms in COPD:inflammation, immunity, and tissue repair and destruction”, Eur Respir J, 31: 1334–1356, 2008.