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Pulmonary computed tomography using a laboratory-based X-ray source in murine asthma models.

Rodent models of allergic airways disease largely replicate the pathophysiology of asthma and are widely used in basic science and in preclinical drug evaluation.The phenotype of allergic airways disease rodents with a genetic deficiency or their response to pharmacological treatment can be assessed according to clinically relevant endpoints including lung function tests.This often takes the form of invasive plethysmography where airway resistance and dynamic compliance are determined from flow and pressure measurements in anesthetised tracheostomized mice with a bronchoconstrictor challenge.However, as in human medicine, the technology is advancing, and techniques such as X-ray imaging with computed tomography (CT) 4D reconstruction and X-ray velocimetry (XV) may allow further insights, particularly with regard to spatial localization of responses in the regions of the lung.

The aim of the current study was to compare normal and allergic airways disease mice using four dimensional x-ray velocimetry(4DXV).

Adult female Balb/c mice(n=12)were subject to a model of allergic airways disease. In-vivo 4DCT was performed on the live anaesthetized mice under mechanical ventilation using a 70 kV Excillum laboratory-based X-ray source, without need for a contrast agent. Images were acquired 30 frames per second, and image acquisition was gated to the breath cycle. XV was then performed on the 4DCT dataset to obtain 4DXV data. Baseline measurements and measurements at four ascending concentrations of methacholine bronchoconstrictor were taken on each mouse.
Analysis of the functional data using particle-image velocimetry allowed us to observe and quantify preferential damage of airways and restriction of airflow in affected mice. These alterations in flow and airway size were most pronounced in the allergic airways disease mice during the highest dose of methacholine. Imaging shows the extent and longevity of response and its regional location across lung lobes and throughout the respiratory tree with excellent resolution to the small airways.

4DXV allows regional lung function to be observed in asthma model mice with a similar data collection throughput to invasive plethysmography.. Data analysis was much more complex and ongoing but we were able to perturb clear differences between the mice groups in airway calibre and flow even in smaller airways. If uniform protocols can be adopted, these temporal-spatial analyses may have many applications in measurement of anti-inflammatory, anti-remodelling and epithelial repair drug response and live monitoring of bronchodilator response in vivo.

Keywords or phrases (comma separated)

Asthma, imaging, mouse, 4D, histopathology

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No

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No

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No

What is your gender?

Male

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