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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 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 4D reconstruction may allow further insights, particularly with regard to sptatial 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 the 4D X-ray technique.

Adult female Balb/c mice (n=12) were subject to an ovalbumin sensitization / challenge model of allergic airways disease or saline control protocol. Computed tomography was performed on the anaesthetized mice under mechanical ventilation using a laboratory-based X-ray source, without need for a contrast agent. Baseline measurements and measurements at four ascending concentrations of methacholine bronchoconstrictor were taken on each mouse. Mice were then euthanized and lung tissue taken for histology – H&E, Masson trichrome, and Alcian blue periodic acid Schiff stains.

Histological analysis showed airway inflammation, and goblet cell metaplasia in the diseased mice.
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 location across lung lobes and throughout the respiratory tree to the small airways with excellent resolution.

The 4D instrument allowed us to perform lung function in asthma model mice with a similar data collection throughput to invasive plethysmography and without additional animal welfare burden. Data analysis is ongoing but we were able to perturb clear differences between the mice groups in airway calibre and flow even in smaller airways. Is uniform protocols can be adopted, these temporo-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)

Lung, asthma, 4D, X-ray, methacholine, mouse model

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No

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No

Are you an ECR? (<5 yrs</br>since PhD/Masters)

No

What is your gender?

Male

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