MUCOCILIARY TRANSIT BEHAVIOUR OF POLLUTANT AND MARKER PARTICLES ON LIVE MOUSE AIRWAYS

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BACKGROUND:

- Airborne pollutants are a considerable health concern and have the potential to impact on respiratory diseases such as cystic fibrosis (CF)
- We have previously described synchrotron imaging techniques for examining the mucociliary transit (MCT) behavior of particulates in the nasal airways and trachea of anaesthetised mice
- Our previous studies delivered particulates in a fluid bolus, however the presence of the carrier fluid perturbed the airway surface and would have altered both the manner of deposition and post-deposition MCT behaviour that we sought to measure
- The **aim of this study** was to verify that synchrotron phase contrast X-ray imaging (PCXI) can be used to detect, monitor and compare the deposition and MCT behaviour of pollutant and marker particles after dry deposition into the trachea of live mice

METHODS:

- Intubated (flexiVent ventilation) C57Bl/6 mice (n=8) were imaged on the BL20XU beamline at the SPring-8 synchrotron in Japan
- Particles of fibreglass, quarry dust and lead ore, as well as reference 14 µm hollow glass beads were delivered to the trachea via the ET tube using a dry powder insufflator and air pump (PennCentury, Wyndmoor, PA, USA)
- Images of the trachea (1.8 x 1.2 mm) with an effective pixel size of 0.45 µm were captured at a rate of one per breath (in an end-inspiratory pause) for five minutes using a high-resolution camera
- Images were enhanced post-experiment (Matlab, The Mathworks, MA, USA), assembled into movies showing particle motion and also analysed using X-ray velocimetry (XV)

RESULTS:

- The first movement of particulates tended to appear approximately 2-3 minutes after delivery
- As in previous studies the particle transit was heterogeneous: after deposition some particles did not move, while others transited the field of view rapidly
- The big and heavy particles lead and tantalum moved substantially less than the other particulates after deposition
- Most particles did not follow a linear path along the airway: many followed seemingly random, tortuous paths
- There was more movement of particles along the bottom quarter of the tracheal surface than the remainder of the trachea, possibly due to the quantity of fluid present and gravitational effects
- In some animals we also saw radial and axial contraction of the tracheal airway throughout the imaging period

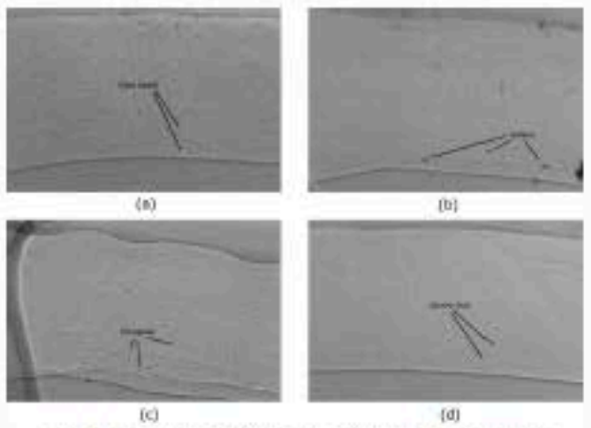

FIG 1: Particle visibility on the airway surface of four mice (a) **silver coated hollow glass beads**, (b) **lead**, (c) **fibreglass fibres**, and (d) **quarry dust**. In these static images it is hard to clearly identify some of the particles (excluding the large lead particles and fibreglass fibres), but in the image sequences the dynamic behaviour of the particulates is clear. Images are 1.8 x 1.2 mm and the imaging location is just above the main carina.

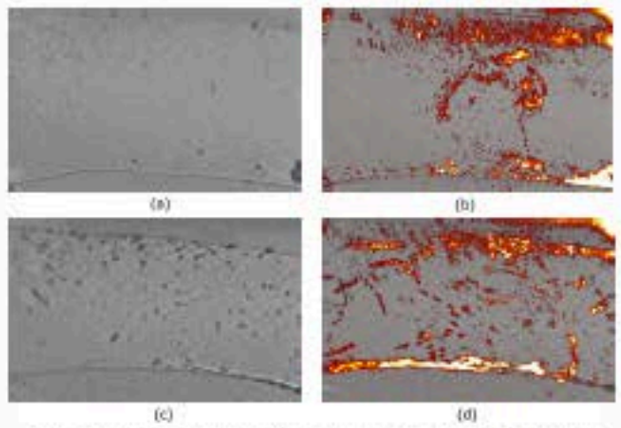

FIG 2: Image sequences from two animals (a) and (c) were analysed to show the sites of all **lead** particle movement (b) and (d) on the airway surface over the 5 minute imaging period. The yellow and white regions contained the most particle movement. Movement in the top third of the frame resulted from X-ray beam instability not particle motion. Figure orientation and location is the same as in FIG 1.

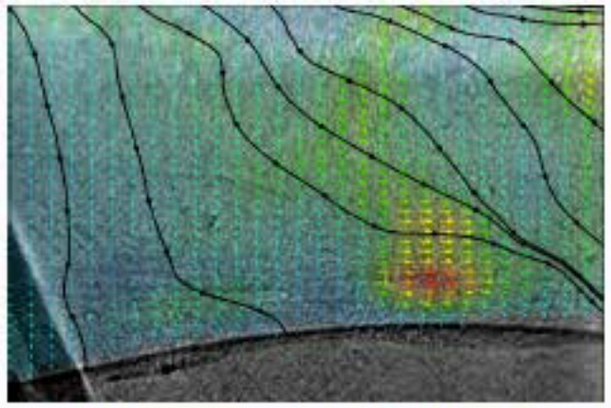

FIG 3: X-ray velocimetry (XV) analysis – a Mechanical Engineering flow measurement technique – shows that, on average, there is more particle MCC of **hollow glass beads** along and towards the dorsal quarter of the tracheal surface. A grid of the average movement vectors (green to red pseudo-coloured arrows) with black streamlines reveals overall particle motion over the entire imaging period. Figure orientation and location is the same as in FIG 1.

CONCLUSION:

Synchrotron PCXI permits detection of particle transit via MCT along live mouse trachea. We are continuing with studies to improve our direct and non-invasive MCT assessment methods to assist our understanding and treatment of respiratory diseases such as CF.

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