Assessing the Effect of Inhaled Particle Size on Mucociliary Transit Activity in Live Mice

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Background

- The CFTR ion channel defect in airway epithelial cells reduces airway surface liquid (ASL) depth and impairs mucociliary transport (MCT).
- We have created non-invasive, synchrotron imaging-based methods for quantifying ASL and MCT as direct measures of airway health.
- Our *in vivo* MCT quantification method relies on tracking the motion of deposited high refractive index (HRI) [redacted] have uniform size, shape and surface properties.
- Previous studies have suggested that MCT rate is dependent on particle material, but the effects of particle size were unclear.
- The aim of this study was to determine whether particle size affects MCT rate and behaviour.

Methods

- Intubated and ventilated C57Bl/6 mice (n=14) were imaged on the BL20XU beamline at SPring-8 Synchrotron in Japan (See Fig 1).
- A mix of two differently-sized HRI marker particles (10 µm and 33 µm dia, Corpuscular, USA) were delivered [redacted]
- Image[redacted] were captured using a scintillator and high-resolution camera.
- After baseline imaging (room-air respiration) an Aeroneb nebuliser was used to deliver aerosol (n=8 hypertonic & n=6 isotonic saline) for 15 msec on each inspiration (120 br/min) for 15 min.
- Images were collected at 5 Hz in 30 second blocks, every minute.
- Custom semi-automated image tracking software was used to tag part[redacted] and calculate individu[redacted] and bulk transit rates.

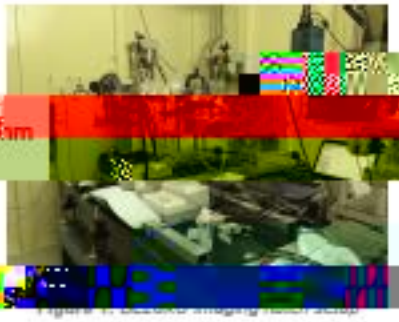

Figure 1: Beamline imaging hutch setup

Results

- Most HRI particles remained stationary throughout the imaging period. This effect was much more pronounced than with other particles that we have e[redacted] previously (quarry dust, fibreglass, asbestos, lead,etc).
- Moving particles were only detected in 6 mice treated with hypertonic saline, and 2 treated with isotonic saline.
- Most bead mo[redacted]
- When data wa[redacted] MCT rate between the large and small particle groups [redacted]y, p<0.05, t-test). Insufficient moving particles were detected at each individual time-point for statistical analysis.

Figure 2: Effect of HRI bead size on MCT rate

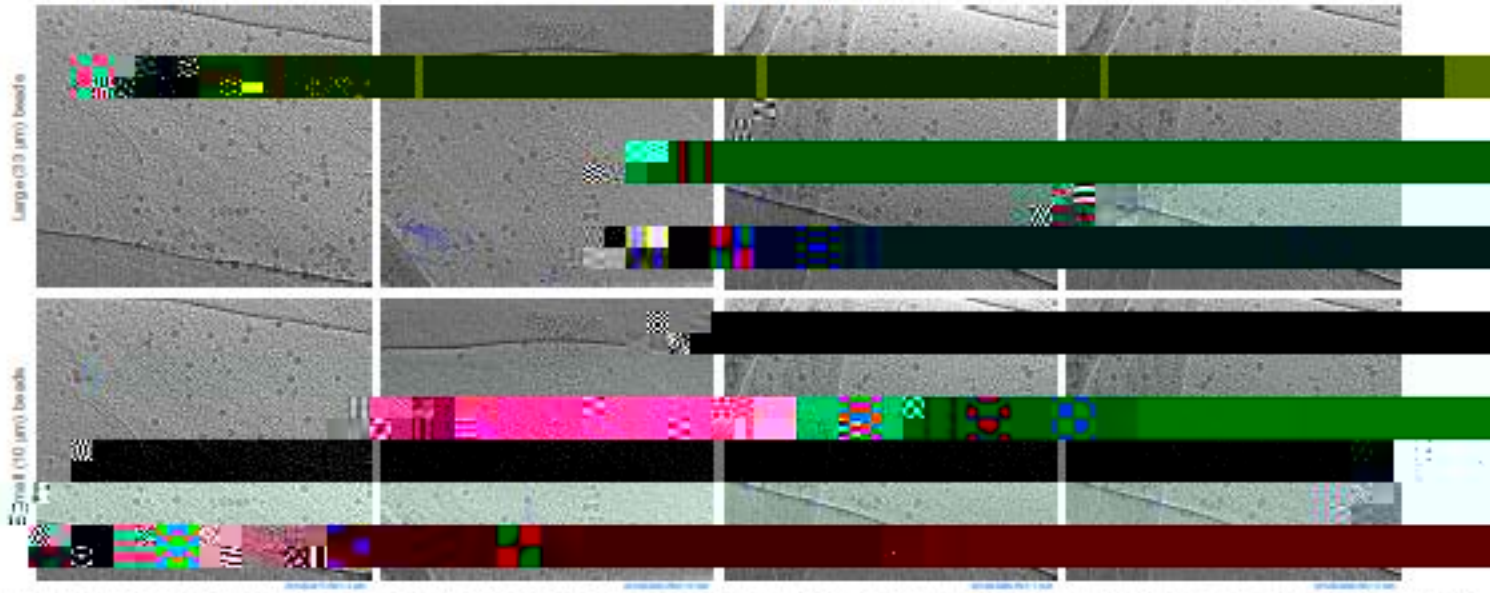

Figure 3: High mag[redacted] µm) beads, and th[redacted] the carina. Each moving particle is identified with a red mark, with [redacted] in subsequent frames identified with blue marks. Stationary particles are not marked. Images [redacted]

Conclusion

- MCT rate in live mouse trachea for these glass beads appears to be dependent on particle size, but surprisingly few of the introduced beads [redacted]
- We speculate that sub-optimal airway surface hydration and/or HRI bead surface properties may have influenced the ability of most particles to move during the imaging period.
- Future studies (Nov 2015) will examine the effect of changing inhaled air humidity and particle surface coating [redacted]

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