Morgan, Kaye

Abstract:

BACKGROUND: The manner in which fluid instillations into mouse nose and lung distribute through the airways is poorly understood. Many agents are delivered in this way for testing as therapeutics, or as challenges designed to establish infections or create systemic drug delivery effects. These agents are delivered into mouse airways with little knowledge of the manner in which doses move through the airways, how long they reside in each region, and where the instilled materials eventually reach.

METHODS: Synchrotron phase-contrast X-ray imaging (PCXI) was used to elucidate the primary controlling characteristics of mouse airway fluid dosing. High-speed image acquisition was used to track the movement of a range of bolus doses of an iodine-based contrast fluid through the nose (n=15) and lungs (n=10) of live anesthetized mice. For the lung studies, the mice were ventilated and paralyzed to control animal movement. Post-experiment image processing was used to visualize the fluid movement.

RESULTS: The maximum dose that could be retained in only the anterior nose was $\sim7.5 \text{ mL}$ (20 g mouse), and a range of dynamic dose behaviors was documented after delivery. In the lung, the use of mechanical...
ventilation in combination with a paralytic agent prevented confounding artifactual movement, improving visualization of fluid progression through the airways. In the lung, optimized image analysis using the high image capture rate revealed the presence of respiratory pauses that could not be visualized at slower acquisition rates. The variability in the outcome of identical dose deliveries in different animals indicates that uniform lung distribution cannot be expected to occur with tracheal fluid delivery.\n
CONCLUSIONS\n
With adequate imaging rate and fluid dose parameters, this study shows the utility of synchrotron PCXI for determining the post-delivery behavior and fate of fluid doses such as those used in in vivo gene transfer or pharmaceutical studies.

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