HIGH FRAME RATE IMAGING OF NASAL FLUID DOSING DYNAMICS

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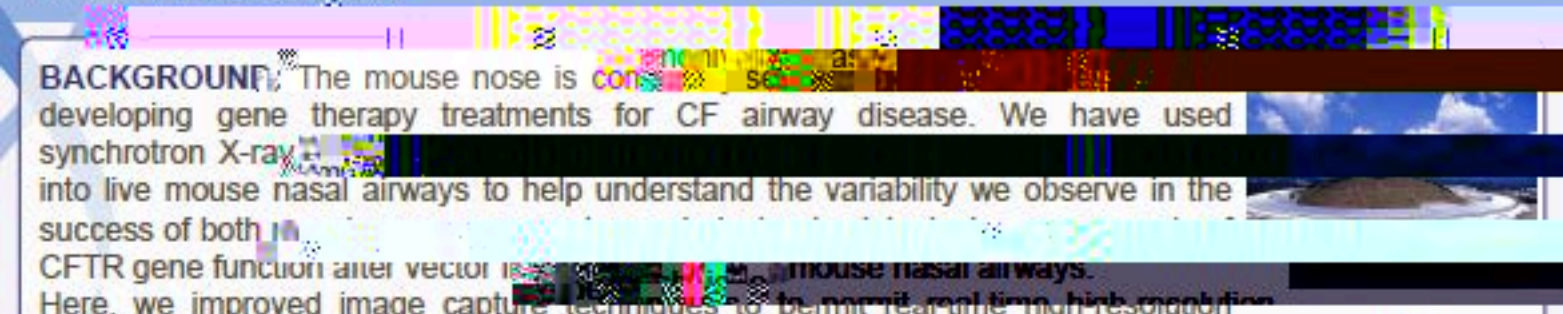
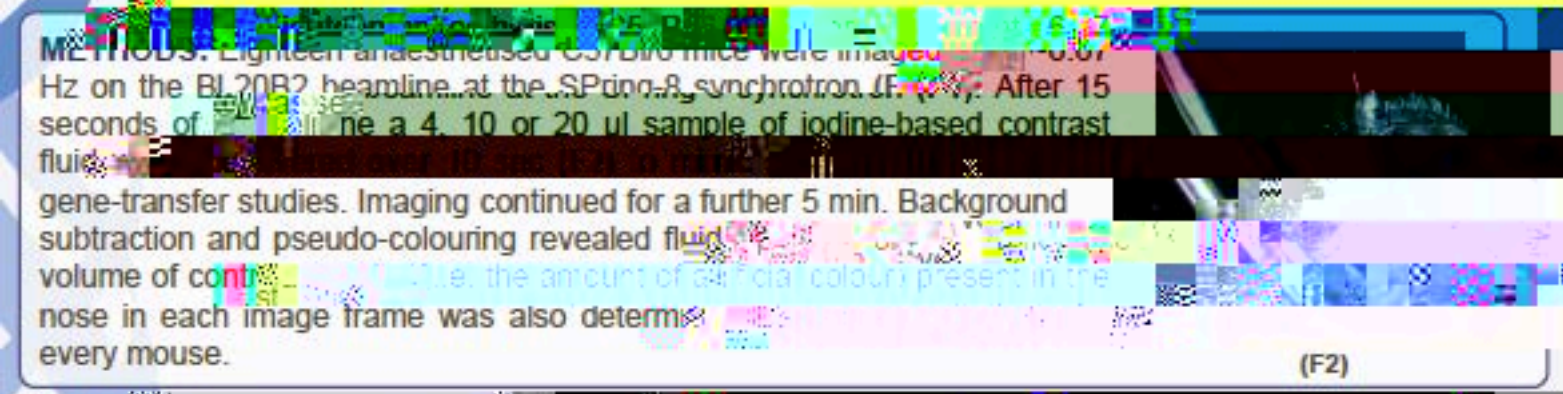
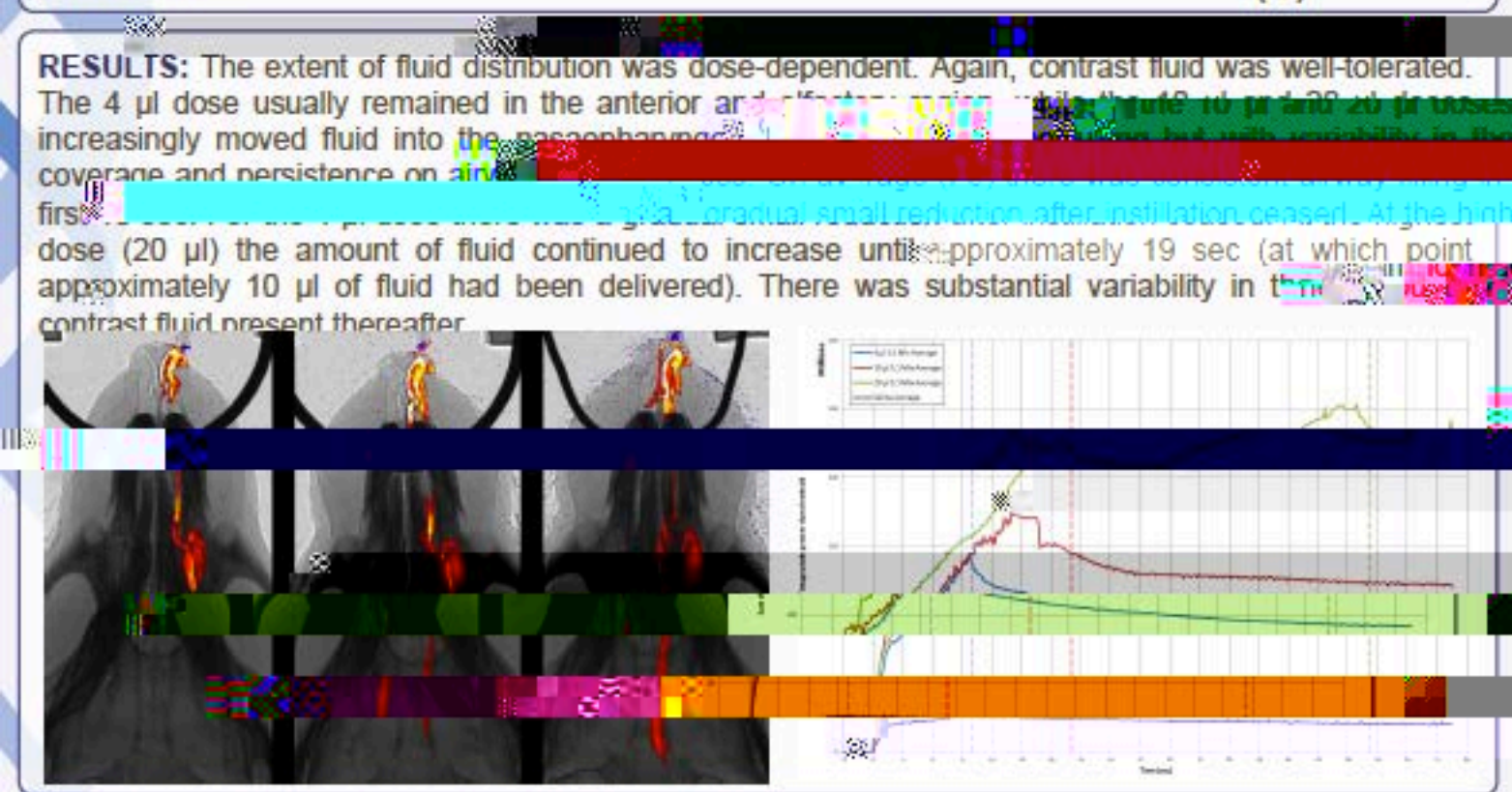


BACKGROUND: The mouse nose is commonly used as a [illegible] developing gene therapy treatments for CF airway disease. We have used synchrotron X-ray [illegible] into live mouse nasal airways to help understand the variability we observe in the success of both [illegible] CFTR gene function after vector [illegible] mouse nasal airways. Here, we improved image capture techniques to permit real-time high-resolution monitoring and document the detailed dose movement in live mouse nasal airways. (F1)



METHODS: Eighteen anaesthetised C57Bl/6 mice were imaged [illegible] Hz on the BL20B2 beamline at the SPring-8 synchrotron (Fig. 2). After 15 seconds of [illegible] ne a 4, 10 or 20 µl sample of iodine-based contrast fluid [illegible] gene-transfer studies. Imaging continued for a further 5 min. Background subtraction and pseudo-colouring revealed fluid [illegible] volume of cont[illegible]. the amount of artificial colour present in the nose in each image frame was also determ[illegible] every mouse. (F2)



RESULTS: The extent of fluid distribution was dose-dependent. Again, contrast fluid was well-tolerated. The 4 µl dose usually remained in the anterior and [illegible] while the 10 µl and 20 µl doses increasingly moved fluid into the nasopharynx [illegible] but with variability in the coverage and persistence on airw[illegible] first [illegible] sec. For the 4 µl dose there was a gradual gradual small reduction after instillation ceased. At the high dose (20 µl) the amount of fluid continued to increase until approximately 19 sec (at which point approximately 10 µl of fluid had been delivered). There was substantial variability in t[illegible] contrast fluid present thereafter.

(F4)

(F5)

CONCLUSION: High [illegible] X[illegible] reveal the real-time dynamics of this commonly used dosing technique in mice. Clear in vivo visualisation of nasal airways reveals that outcome variability may be influenced by the heterogeneous dose distribution that occurs in these anatomically complex nasal airways.

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