| **X-ray Velocimetry functional lung imaging identifies the origin of ventilation defects in Hurler Syndrome (MPS I) mice** |
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| **Introduction/Aim:** Mucopolysaccharidoses (MPS) are a subset of Lysosomal storage diseases characterised by the storage of glycosaminoglycans (GAG). Almost all MPS patients have respiratory dysfunction with varying symptoms and severity during disease progression. The accumulation of GAG in the trachea and bronchi results in both obstructive and restrictive airway disease including diffuse tracheomalacia, tracheal stenosis and tortuosity. However, middle and lower airway involvement is an understudied aspect of clinical manifestations in the MPS. Here we aimed to characterise airway disease in an MPS I (Hurler syndrome) mouse model. **Methods:** We used non-invasive X-ray Velocimetry (XV) functional lung imaging technology, combined with gold-standard flexiVent lung mechanics assessment, to comprehensively analyse respiratory function in the MPS I mouse model. This included, for the first time, providing information on regional lung function across the breathing cycle. **Results:** MPS I mice showed a reduction in the mean specific ventilation that was predominantly due to a reduction in ventilation in the inner region of the lung. In addition, an increase in lung heterogeneity suggested patchy ventilation across the lung. MPS I mice exhibited an increase in lung compliance and reduced tissue elastance as well as reduced airflow likely due to higher central airway resistance. **Conclusions:** Together these results are consistent with an obstructive disease phenotype that can be attributed to not only the upper airways, but specifically intrinsic pulmonary alterations involving the central airways and parenchymal component of the peripheral lung. **Grant Support:** This work is supported by a National MPS Society Research Grant, and Medical Research Future Fund Grant RFRHPSI000013. |