| **X-ray Velocimetry functional lung imaging identifies the origin of ventilation defects in Hurler Syndrome (MPS I) mice** |
| --- |
| Martin Donnelley1-3, Patricia Cmielewski1-3, Ronan Smith1-3, Piraveen Pirakalathanan4, Nina Eikelis4, Kris Nilsen4, Jennie Louise5, Mark Lawrence6, David Parsons1-3, Kate Barratt7, Jessica Logan8, Ben Ung9, Doug Brooks8, Sandra Orgeig8 and Emma Parkinson-Lawrence8 |
| *1Robinson Research Institute, University of Adelaide, South Australia. 2Adelaide Medical School, University of Adelaide, South Australia. 3Respiratory and Sleep Medicine, Women's and Children's Hospital, South Australia. 44DMedical, Victoria, Australia. 5Biostatistics Unit, South Australian Health and Medical Research Institute. 6SCIREQ, Montreal, Canada. 7Faculty of Health and Medical Sciences, University of Adelaide, South Australia. 8Mechanisms in Cell Biology and Disease Research Concentration, Clinical and Health Sciences, University of South Australia. 9Quality Use of Medicines and Pharmacy Research Centre, Clinical and Health Sciences, University of South Australia.* |
| **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. |