



Contribution ID: 239

Type: Oral

Capturing lung health in animal models of ventilator-induced lung injury and cystic fibrosis using 4D X-ray imaging

Thursday, 19 November 2020 13:30 (20 minutes)

Introduction:

Lung disease, including chronic respiratory conditions and thoracic cancers, is Australia's second leading cause of death [1]. Furthermore, the current COVID-19 pandemic has acutely highlighted the importance of understanding acute respiratory distress syndrome and mechanical ventilation. Lung health is typically measured in the clinic by functional measures such as spirometry and structural measures from CT images, but neither can identify regional changes in lung function. The regional manifestation of lung disease and the dynamic nature of the lung means that experimental in vivo 4D X-ray imaging is ideal for detailed analysis of the lung in health and disease. The imaging and medical beamline (IMBL) at the Australian Synchrotron provides a wide, monochromatic X-ray beam, with suitable flux for high-speed in vivo imaging of small animals such as mice and rats. Here, we demonstrate the methods and preliminary results from two studies of dynamic lung imaging and X-ray velocimetry (4DXV) [2] analysis of mouse models of ventilator-induced lung injury and rat models of cystic fibrosis-like lung disease.

Methods:

The X-ray beam was set to an energy of 25 - 30 keV, with exposure lengths of between 0.02 - 0.04 seconds, suitable for the imaging of lung tissue in either mice or rats (respectively). The sample-to-detector distance was 3 metres, for capturing propagation-based phase contrast images of the lungs. Animals were anaesthetised, surgically intubated (according to University of Tasmania and University of Adelaide animal ethics committee approvals), and attached to a small animal ventilator (4DMedical) to acquire breath-cycle gated images.

A four-dimensional computed tomography image acquisition was conducted with 12133 projection images of the lungs captured over a 182 degree rotation for one 4DCT scan. This resulted in 15 phases (CT images) in the 4DCT sequence and took 3.5 - 11 minutes, depending on the mechanical ventilation rate. The Ruby X-ray detector was used with a pixel size of between 19 - 24 μm . The X-ray beam width (field-of-view) was set to either 2.4 cm (for mouse lungs) or 4 cm (for rat lungs).

Projection images were captured as hierarchical data format version 5 (hdf5) and binned into the phases of the breath cycle on the Australian Synchrotron's computing infrastructure environment (ASCI). Customised code provided integration of the projection images with the CSIRO X-TRACT CT reconstruction software [3], whereby images were reconstructed using the transport-of-intensity equation (TIE) phase retrieval algorithm [4]. The reconstructed CTs from both studies were transferred to MASSIVE, a dedicated computing cluster environment for image processing and visualisation [5], and the 4DXV analysis [2] was applied to the data.

Results:

An example of a resulting CT of a mouse lung is shown as a slice image in panel (c) of the figure. 4DXV results are shown in the figure from a normal rat (a) before, and (b) after delivery of sterile agar beads into a single lobe of the lung. The colour bar represents the lung tissue expansion (in voxels), whereby the dark blue region indicates a region of low expansion, due to the agar beads blocking the airways, in a similar manner to the mucus obstructions that are a hallmark of cystic fibrosis disease. Panel (c) shows the lung detail from a CT slice of mouse lungs from the ventilator-induced lung injury study, taken at the beginning of mechanical ventilation, with a peak inspiratory pressure of 12 cmH₂O and zero positive end-expiratory pressure. The

scale bar represents 2 mm. The anatomical detail of the lung can be seen as airways (1), blood vessels (2), lobe fissures (3) and fat and muscle layers (4).

Conclusions:

We have successfully performed dynamic in vivo CT imaging and 4DXV analysis of lungs on the Australian Synchrotron IMBL. We have investigated two pre-clinical models: a rat model of cystic fibrosis-like disease, and a mouse model of ventilator-induced lung injury. In addition to the ongoing studies of ventilator-induced lung injury, new pre-clinical studies are planned for testing the efficacy of novel drugs for the treatment of antibiotic-resistant bacterial lung infections.

Acknowledgements: MASSIVE HPC facility (www.massive.org.au), ARC DECRA (SD), ARC Future Fellowship (KM), NHMRC APP1160774 (GZ, KM, SD), NHMRC APP1160011 (DP, MD, KM), Australian Synchrotron beamtime grants (14690, 11727, 12061, 12926).

Keywords: 4DCT, X-ray velocimetry, small animal imaging, lung imaging, mechanical ventilation, ventilator-induced lung injury, cystic fibrosis.

References:

- [1] Australian Bureau of Statistics –Australia’s leading causes of death, 2016.
- [2] Dubsky S, Hooper S, Siu KKW, and Fouras A, “Synchrotron-based dynamic computed tomography of tissue motion for regional lung function measurement”. J. R. Soc. Interface 9, 2213-2224, 2012.
- [3] Gureyev TE, Nesterets Y, Ternovski D, Thompson D, Wilkins SW, Stevenson AW, Taylor JA, “Toolbox for advanced X-ray image processing. Advances in Computational Methods for X-Ray Optics II”, 8141, 1-14, 2011.
- [4] Paganin, D, Mayo SC, Gureyev TE, Miller PR, and Wilkins SW. “Simultaneous phase and amplitude extraction from a single defocused image of a homogeneous object.” Journal of microscopy 206, no. 1: 33-40, 2002.
- [5] Goscinski, WJ, Hines C, McIntosh P, Bambery K, Felzmann U, Hall C, Maksimenko A, Panjikar S, Paterson D, and Tobin M. “MASSIVE: An HPC Collaboration To Underpin Synchrotron Science.” 15th International Conference on Accelerator and Large Experimental Control Systems (ICALEPCS 2015), Melbourne, 2015.

Primary author: PREISSNER, Melissa (Monash University)

Co-authors: Dr DONNELLEY, Martin (University of Adelaide); Dr WERDIGER, Freda (Melbourne Brain Centre); Dr SONG, Yong (University of Tasmania); Ms SMALLEY, Ella (University of Tasmania); Dr CMIELEWSKI, Patricia (University of Adelaide); Mr THOMPSON, Darren (CSIRO); Dr KLEIN, Mitzi (ANSTO); Dr SCOTT, Clare (ANSTO); Dr MAKSIMENKO, Anton (ANSTO); Dr HAUSERMANN, Daniel (ANSTO); Dr PARSONS, David (University of Adelaide); Prof. ZOSKY, Graeme (University of Tasmania); Dr DUBSKY, Stephen (Monash University); Dr MORGAN, Kaye (Monash University)

Presenter: PREISSNER, Melissa (Monash University)

Session Classification: Session 4 - Biomedicine & Health

Track Classification: Biomedicine and Health