Imaging Local Tissue Strain Using *In Vivo* 4D Synchrotron X-ray µCT in Bleomycin-Induced Lung Injury in Rats

Richard T. Deyhle Jr. (1,2), Luca Fardin (3), Irma Mahmutovic Persson (1,4, Jose Luis Cercos-Pita (5), Gaetano Perchiazzi (5), Lars E. Olsson (1,2), Sam Bayat (3)

1. *Lund University, Medical Radiation Physics, Department of Translational Medicine, Lund, Sweden*
2. *Skåne University Hospital, Malmö, Sweden*
3. *Université Grenoble Alpes, Inserm UA07 STROBE Laboratory, Grenoble, France*
4. *Lund University BioImaging Center, Faculty of Medicine, Lund University, 221 42 Lund, Sweden*
5. *Uppsala University, Hedenstierna Laboratory, Uppsala, Sweden*

Introduction

Pulmonary fibrosis is characterized by excessive and heterogeneous deposition of extracellular matrix (ECM) components, particularly collagen, altering the local lung tissue stiffness. There is evidence that changes in ECM micromechanics significantly impact cell function [1]. However, there are no techniques to assess the local ECM micromechanics in lungs, *in vivo*. We applied a time-resolved synchrotron radiation phase contrast µCT technique (4D-µCT) to investigate local ECM deformation under controlled ventilation in bleomycin-induced lung injury [2], with an effective pixel size of 6 µm. Here, we computed and qualitatively compared images of local lung strain distribution within the lung tissue in normal and bleomycin-injured rat lungs.

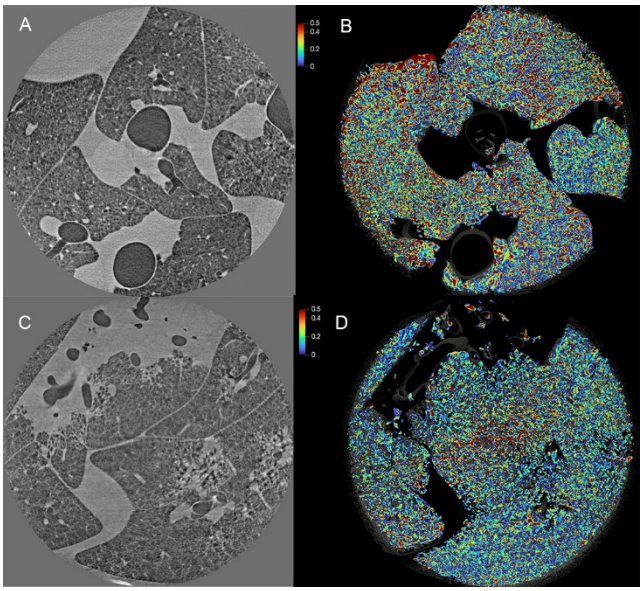
Methods

The experiments were performed in 6 control and 7 bleomycin-injured anesthetized, muscle-relaxed and mechanically ventilated adult rats at 7 days post intratracheal instillation. X-rays from a synchrotron source were monochromatized at 38 keV. A free propagation phase-contrast setup was used with a sample to detector distance of 3.5 m. Images were reconstruction using the Paganin phase retrieval algorithm. Projection images were acquired at a constant frame rate using a fast camera (PCO Edge), coupled with optics determining a pixel size of 6 µm and 10 ms time resolution. The ECG signal was recorded and image reconstruction was retrospectively gated to both breathing and cardiac activity. Quantitative maps of local lung strain were computed using a previously described image-registration based processing pipeline [3].

Results

Figure 1 shows sample phase-contrast CT and composite strain maps in a representative control and bleomycin rat with lung injury. Further quantitative analysis of the local strain data is underway.

Figure 1: Sample phase-contrast (A, C) and local strain maps (B, D) in a representative control (A, B) and bleomycin-injured lung (C, D), under positive-pressure ventilation. Note the reduced tissue deformation particularly in fibrotic regions, and strain magnitudes comparable to control in normal appearing regions in bleomycin-induced lung injury. Color scale range (B, D) is 0 to 0.5.



Conclusions

Here, we show a first comparison of quantitative images of local strain acquired in normal and bleomycin-injured *in vivo* rat lungs, based on registration of dynamic 4D-µCT synchrotron phase-contrast images obtained at 6 µm voxel resolution. This approach will allow to investigate how the ECM micromechanical alterations influence fibrogenesis and vice-versa. Assessing the involved mechanisms will provide insight for developing new therapies.

References

1. Deng, Z., et al. Int J Biochem Cell Biol, 2020. 126: p. 105802.
2. Mahmutovic Persson, I., et al. Front Physiol, 2020. 11: p. 584.
3. Cercos-Pita, J.-L., et al. Scientific Reports, 2022. 12(1): p. 1-11.

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