Imaging lung motion to detect lung disease

Lung diseases restrict the airflow into or out of the lungs during breathing due to increases in airway resistance or to changes in the mechanical properties of lung tissue. For example, pulmonary fibrosis increases the stiffness of tissue surrounding the distal airways, asthma increases airway resistance and emphysema reduces lung tissue recoil thereby increasing its compliance. Although these diseases vary markedly in both cause and consequence, by altering the movement of air into and out of the diseased regions they must also alter lung motion within those regions [1,2].

Little is known about the dynamics of lung motion during breathing, particularly how different regions move in relation to other regions during both inspiration and expiration. For instance, it is unknown whether the lung expands and deflates uniformly, whether specific regions lead or trail other regions due to differences in local compliances or due to their proximity to the diaphragm or chest wall. Similarly, it is unknown how these diseases affect regional lung motion and whether motion in healthy regions is altered to compensate for diseased regions. Although regional information is best provided by imaging the lung *in vivo*, until recently it has not been possible to image the lung with sufficiently high spatial and temporal resolution.

Previous techniques used to measure lung motion have relied on the inhalation of contrast agents or other techniques that utilize invasive procedures [3]. More recently, MRI and X-ray CT techniques have been developed to assist in radiotherapy treatment planning or the development of lung biomechanical models. However, these approaches are limited, particularly by the need to image the lung while it is stationary to minimize blurring. Thus, interpolation is required to deduce lung motion between two steady state positions within a breath and assumes that lung motion between these positions follows a linear or defined path.

Although standard X-ray imaging has the capacity to identify diseased regions of the lung, substantial changes in lung tissue characteristics are required to provide sufficient contrast (e.g. changes in X-ray absorption) between diseased and healthy regions. Thus, for diseases like asthma, which affect airway caliber and resistance, standard imaging techniques offer little benefit in identifying diseased airways. To improve the detection, assessment and management of most lung diseases, there is a need to develop techniques that provide accurate measures of regional lung function.

In this study, we demonstrated that the combination of Particle Image Velocimetry (PIV) and Phase Contrast X-ray Imaging (PCXI) can produce quantitative measures of regional lung motion which can be used to differentiate between normal and abnormal lung tissue. PIV utilizes a cross-correlation analysis to track the movement of lung tissue between consecutive frames allowing the reconstruction of velocity fields that define speed and direction of regional lung motion throughout a breath (Fig. 1). Reconstruction of the velocity fields throughout a breath demonstrates that motion is very heterogeneous across the lung and that the speed and direction of motion within a region is highly position dependent. To control for the regional differences in motion across the lung, regional maps of expansion (Fig. 2) and average time of expansion can be generated, revealing regions with abnormal movement caused by disease. Experimental induction of non-uniform lung disease, specifically pulmonary fibrosis in mice, caused abnormal motion in both diseased and healthy regions within the same lung. In particular, we discovered that

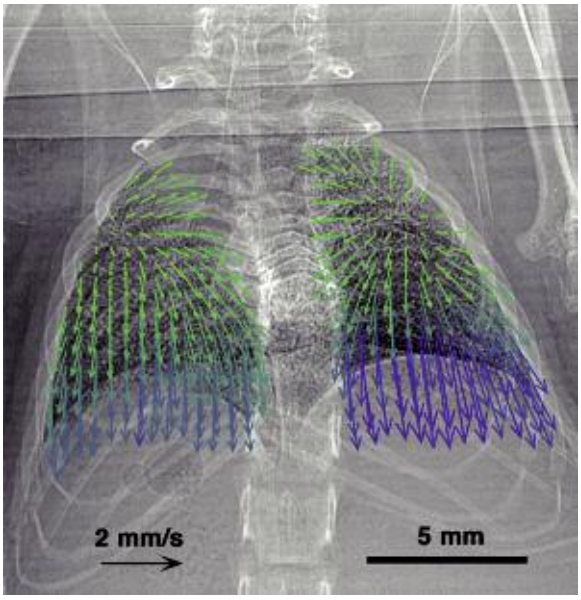

Fig. 1. *In vivo* detection of lung tissue motion. Instantaneous velocity of a healthy mouse lung, ~14 ms after start of inspiration, shown as a vector field. Vectors are reduced in number (293 of 2640 displayed) for clarity. Vectors are colored according to magnitude (from lowest; green, to highest; blue) of velocity.

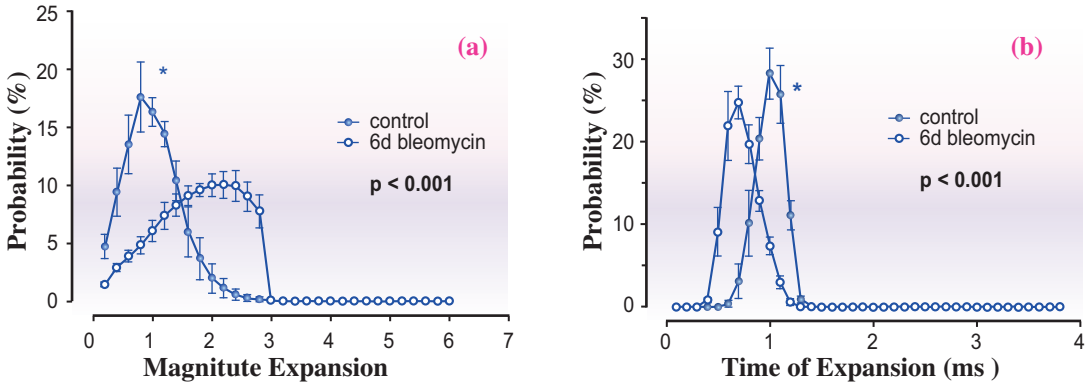

Fig. 2. Velocimetry measures of lung pathology after bleomycin exposure. **(a)** Frequency distribution of the magnitude of expansion (normalized to the average of controls) is compared for treated groups (n=4) with controls (n=3). Data are normalized by the average of the controls. Treated mice have 76% greater expansion on average and 47% of treated lungs expand at over 2× the control average compared with less than 4% for control lungs. Frequency distributions of the average time of expansion **(b)** in control and treated mice. Asterisks indicate significant differences between control and treated animals ($p<0.001$).

motion in healthy regions increased to compensate for slower moving diseased regions (Fig 3). We conclude that X-ray velocimetry can quantify regional lung motion and detect lung disease by identifying regions with abnormal movement. Furthermore, this technology is more sensitive and quantitative for disease detection than other conventional measures such as global lung function and histological changes.

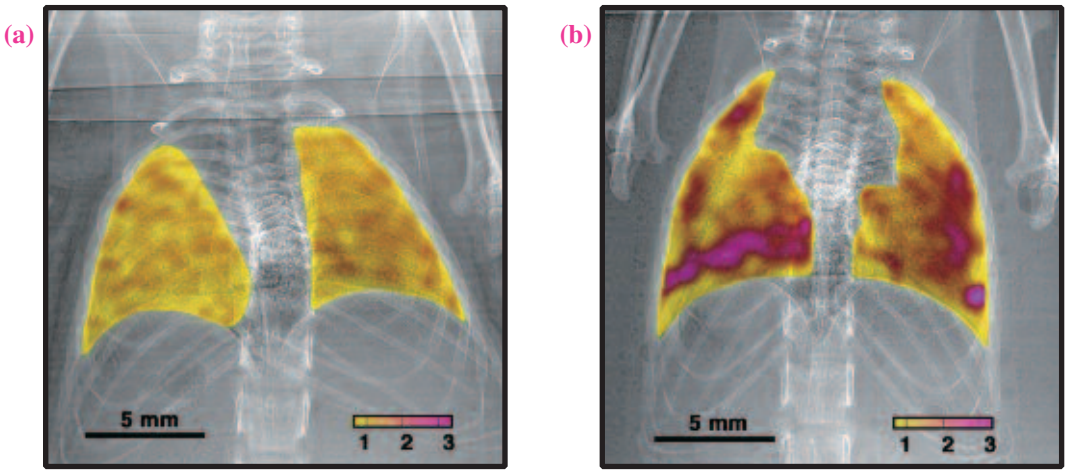

Fig. 3. Regional expansion within the lung. Color maps of regional lung expansion determined using PIV for typical: **(a)** control and; **(b)** bleomycin-treated mice. Data are normalized by the average regional expansion across the control group and color maps were generated using the same color-scale (see legend). The mice treated with bleomycin **(b)** have dramatic regional alterations in the pattern of lung expansion.

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