Four dimensional MR microscopy of respiratory mechanics in transgenic mice with emphysema: Lung motion quantification via a non-rigid registration algorithm

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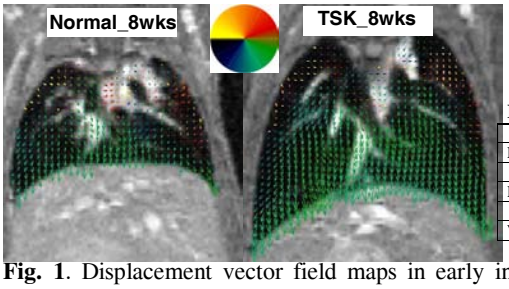
Introduction. When the lung is inflated, the fibers of collagen and elastin that can be seen in the alveolar walls and around the blood vessels and bronchi are stretched or distorted, so they have a tendency to return to their original shape and therefore develop elastic recoil. These biomechanical properties of the lung change in various pulmonary disorders such as chronic obstructive pulmonary disease (COPD) including pulmonary emphysema. Pulmonary function tests, which measure global lung function, have been widely accepted for the evaluation of COPD. In emphysema, there is increased lung distensibility due to destruction of alveolar walls with an accompanying increase in total lung capacity, functional residual capacity, and residual volume and a decrease in vital capacity [1]. However, it is known that the correlations of all these measures of the volume-pressure relationship with pathologic severity of emphysema are relatively weak. An important challenge in COPD is the development of more powerful, multi-variate methods for predicting individual outcome and individual responsiveness to particular therapies on the basis of clinical and laboratory characteristics. The objective of this study was to test if our four dimensional (4D) MR microscopy for regional parenchymal motion quantification could detect abnormal motions associated with morpho-pathologic changes observed in a transgenic mice model of emphysema.

Materials and Methods. Under anesthesia with 2% isoflurane, five normal mice (Balb/c) and four tight-skin (tsk) mice which has been proposed as a genetically determined model characterized by alveolar enlargement and physiologic evidence of emphysema [2], were tracheostomized in the supine position; and the trachea was cannulated using a 20-gauge non-metallic cannula, about 1 cm long. The cannula was connected via a 1.6 m-long tube to a small animal ventilator (FlexiVent, SCIREQ, Quebec, Canada), and all animals were placed with a respiratory sensor in the 4.7 T MRI (Biospec 47/40, Bruker BioSpin, Karlsruhe, Germany). The animals were mechanically ventilated at a frequency of 120 breaths/min (500 msec/breath). In each animal, the serial 3D gradient echo MRI, which was gated using a respiratory triggering system, was conducted in cine-mode (thus, this is a 4D MRI). TR was selected as 1/10 of one respiratory cycle (50 msec) to obtain the 10 serial phase images over the respiratory cycle. Other scan parameters were: FOV = 2.6×2.6×2 cm^3, matrix = 128×128×100 (zerofilled to 128^3), minimum TE (= 1.8 msec), and NEX = 1. All data were computed to generate volume rendered (VR) images to calculate the lung volume. Subsequently, on a resliced coronal image of the 3D data sets, four different phase images over a respiratory cycle (end- and mid-inspiratory, and end- and mid-expiratory phases) were selected. A non-rigid registration algorithm was applied to generate the displacement vector field map between successive images in the sequence. A quantitative analysis was performed to localize motion differences in the anatomic regions (right and left, upper and lower for coronal, or ventral and dorsal for sagittal). Within each region, the mean pulmonary displacement magnitude was calculated. To assess the orientation distribution of the voxelwise displacements in each region, the percentage of the number of vectors in each span of 60 degrees (angle group I to VI), relative to the total number of vectors in each region were computed. Additionally, Lagrangian strains in each anatomical region were computed as described [3]. All the pathologic changes were validated by histological examination.

Results and Discussion. The tsk mice showed overinflated and barrel shaped chest, elevation of the ribs and narrow mediastinum at the endexpiration as observed in patients with emphysema (Fig. 1). The parenchymal regional motion was heterogeneous, demonstrating greater movement in the left and right lower areas at any respiratory phases in both groups. The magnitude of the parenchymal motion in this area was grater in the tsk group in the early inspiratory phase ($p<0.05$, Fig. 1) but no difference in the other respiratory phases. The orientation distribution of displacement vectors showed a significant difference in early inspiration (Fig. 2), implying the imbalanced motions between the diaphragm and chest walls. These averaged values calculated within the whole lung did not show any differences. The calculated finite strain (Table 1) indicated the higher distensibility in most of the regions in the late inspiration of the tsk group. The results showed that our MRI-based method for regional parenchymal motion may provide grading of severity of the progression of emphysema and response, which is essential for testing potential pharmacological agents for treatment of emphysema.



Mean magnitude of each region (mm)

	Normal (n=5)	Tsk (n = 4)	p<
Left upper	1.38 ± 0.13	2.33 ± 0.35	.0008
lower	0.66 ± 0.15	0.88 ± 0.27	.1638
Right upper	1.55 ± 0.14	2.45 ± 0.41	.0024
lower	0.84 ± 0.15	0.92 ± 0.06	.3399
Whole lung	1.34 ± 0.30	1.66 ± 0.19	.1036

Fig. 1. Displacement vector field maps in early inspiratory phase in the 8 week-old normal and tsk mouse. Each vector is colored depending upon its direction as indicated in the scale. The tsk group showed larger magnitude of parenchymal motion in the lower areas.

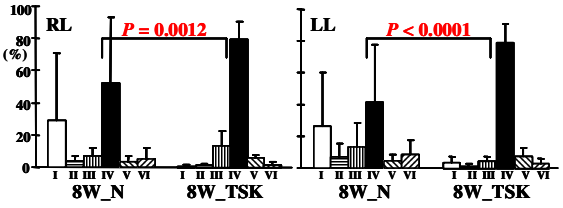


Fig. 2. Histograms of the displacement orientation of parenchymal voxels during early inspiration phase in normal and tsk mice. The motion along the body axis (IV) is prominent in left and right lower areas in the tsk.

Table 1. Mean finite strain in each region in the late inspiration phase.

	Left lower	Left upper	Right lower	Right upper	Whole lung
Normal	0.13 ± 0.03	0.09 ± 0.02	0.17 ± 0.04	0.11 ± 0.02	0.13 ± 0.02
tsk	0.10 ± 0.02	0.04 ± 0.02*	0.08 ± 0.01*	0.06 ± 0.02#	0.07 ± 0.0*

#p< 0.05, *p< 0.005 by ANOVA

References

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