Parametric Mapping of Ex-vivo Mouse Lung at 9.4 Tesla with Air-Inflation Fixation Method

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Introduction:

MR imaging of lung parenchyma has not been explored due to intrinsic low proton density, respiratory and cardiac motion, pulmonary blood flow and molecular diffusion, and severe susceptibility caused by alveolar air / soft-tissue interfaces. In order to avoid these artifacts that degrade image quality, MR imaging of an isolated lung was attempted in the depiction of various lung pathologies (1). We hypothesized that MR imaging of an isolated lung would produce a considerable signal from the lung parenchyma, and that we could characterize T1 and T2 relaxation times of various lung disorders.

Materials and Methods:

Five wild-type mice and 5 transgenic sickle mice that produce human sickle hemoglobin were included. Upon exposure of these transgenic sickle mice to hypoxia (5% oxygen), these mice died from sickling-dependent pulmonary sequestration (2). After euthanasia, the lungs were inflated by tracheotomy to 20 cm H_2O pressure with air. Lungs were excised en bloc, then subjected to MR imaging.

All experiments were performed on a 9.4 T MR system (Bruker). For high resolution MR images, two-dimensional spin echo (SE) MR images (repetition time (TR)/ echo time (TE)/ number of excitations (NEX): 4000/ 3.45 ms/ 4) were obtained using a 12.8 mm x 12.8 mm field of view (FOV), a 256 x 256 matrix and a 0.5 mm slice thickness (voxel sizes of 50 x 50 x 500 mm). For T1 measurement, single-section SE images were obtained at increasing TR (0.3, 0.6, 1, 1.5, 2, and 5 s, TE: 4.1 ms, NEX: 1). The T2 values were measured using the Carr Purcell Meiboom Gill technique with a TE of 4.1 ms and echoes varying in number from 1 to 10 (TR: 4000 ms, NEX: 2).

Parametric T1 and T2 maps were produced as shown in Figs 1 and 2. The regions of interest were placed on the parametric map to measure the T1 and T2 values. Statistical analysis of the data was performed using the Mann-Whitney U-test.

Results:

MR images show excellent visualization of lung vasculature, bronchi, and the lung parenchyma in both groups. In transgenic mice, the inflation of the pulmonary arteries and the diffuse signal increase of lung parenchyma were demonstrated. No such findings were observed in the lungs of wild-type mice. The T1 and T2 values of the wild-type mouse lung were 1.69±0.72 s and 0.028±0.005 s, respectively. The T1 and T2 values of the transgenic mouse lung were 0.89±0.55 s and 0.005±0.004 s, respectively. The T1 and T2 values of the transgenic mouse lung significantly decreased compared with those of the wild-type mouse lung ($P<0.01$). The reduction in T1 and T2 values of the transgenic mouse lung were visually apparent in the parametric map (Fig 2). In the histology of the transgenic mice lung, the capillaries and small vessels were occluded by numerous deformed red blood cells as shown in Fig 2.

Discussion and Conclusion:

To the best of our knowledge, this is the first report describing the correlation among the high-resolution MR images, relaxation times and pathologic changes of the lung parenchyma. The inflation of the pulmonary arteries and the diffuse signal increase of lung parenchyma were demonstrated in the transgenic mice. These findings were supported by histological analysis, in which numerous deformed red blood cells occupied the capillaries and small vessels, causing significant reduction in the T1 and T2 values due to deoxy-Hb. In conclusion, MR images combined with isolated lungs demonstrated considerable signals from lung parenchyma. T1 and T2 relaxation times may provide additional information about lung disorders.

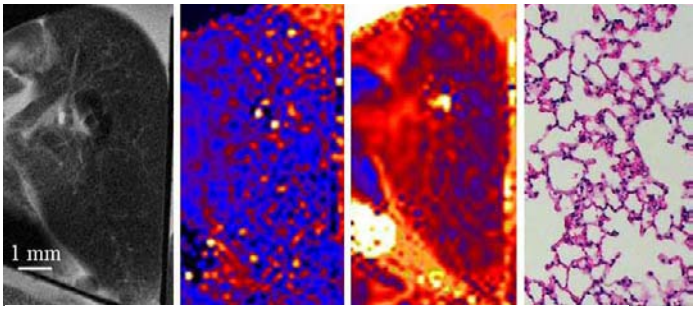

Figure 1. Representative MR images of the wild-type mouse lung. From left to right: anatomical SE MR image, corresponding T1 map, T2 map and histology of the section (HE staining, x200).

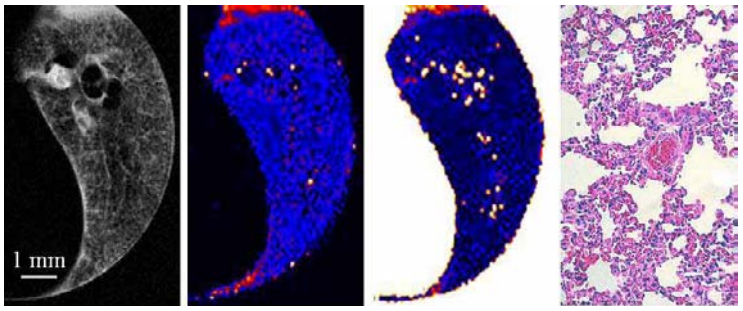

Figure 2. Representative MR images of the transgenic sickle mouse lung. From left to right: anatomical SE MR image, corresponding T1 map, T2 map and histology of the section (HE staining, x200). The reductions in T1 and T2 values are visually apparent compared with those in the wild-type mouse lung. Note that blood vessels including capillaries are occluded by massive abnormal-shaped red blood cells.

References:

1. Hatabu H, et al. Eur J Radiol 2002; 44: 210-215
2. Reilly MP et al. Exp Hematol 1994; 22: 501-509