SPI measurement of MR signal and T2* in order to characterize emphysema type changes in a tight skin mouse model

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Emphysema is characterized by the breakdown of the alveoli walls, increasing the volumes of air sacs, and decreasing the overall density of the lungs. The density will be directly reflected in the MRI signal intensity. The breakdown also results in a different ratio of tissue/air interfaces, which may affect the susceptibility and thereby T2*. The T2* for lung tissue is very short (~ 1 ms) and will also have a considerably effect on the MRI signal unless very short detection times are used. Recently, single point imaging (SPI) was suggested for respiratory studies in animals, with improved signal from the lung tissue compared to conventional imaging techniques (Price et al., 2005). SPI detection time with td below 0.1 ms is possible. The aim of this study was to apply SPI to evaluate signal intensity for short td (reflecting density changes) and measure T2* (reflecting alveoli size) of mouse lung tissue in vivo for emphysema vs controls. Micro CT and histology were used as reference methods.

Materials and Methods: Tight skin (TSK) mice have an autosomal dominant mutation in the fibrillin 1 gene and rapidly develop emphysematous lesions. The cause of lung lesions in TSK mice is not fully understood but it is likely that both mechanical and biochemical defects contributes to the destruction of lung tissue, mimicking the emphysema found in patients. One group (n=6) of 8 weeks old TSK mice and a corresponding control group of 8 weeks old CB57BL/6 were studied. Mice were scanned with a 3D SPI sequence on a 4.7 T MR scanner (Bruker, Ettlingen, Germany) with short detection times, td=0.2 ms and 0.4 ms. The repetition time was 1.5 ms, FA=4°, FOV=30x30x50 mm^3, 96x96x32 matrix, BW=125 kHz, and 4 averages. The animals were freely breathing during image acquisition. Immediately following the MRI session the animal was moved to the CT-scanner (MicroCAT II, ImTek Inc, Knoxville, TN, USA). The CT scan consisted of 540 individual acquisition steps (110 kV, 0.4 mA and 125 ms) to complete a full 360° rotation. Each step was acquired during end expiration using respiratory triggering. The evaluation of MRI and CT images was performed by region of interests (ROI). In one central transaxial slice of the lung a ROI was drawn manually in the parenchyma of the right lung lobe. Larger vessels and bronchi were not included in the ROI. T2* was calculated from the two SPI detection times. After sacrifice the lungs were perfused with 4% formaldehyde at 25 cm H2O pressure, dehydrated and embedded in paraffin. Lung sections were cut on a microtome (5 μm thickness) and stained with hematoxylin and eosin. The mean linear intercept (MLI) was calculated with an ocular grid by a modified method used for the assessment of emphysema.

Results: The MRI signal at td=0.2 was significantly lower in TSK mice than in matched controls. Signal (relative to a reference source) was 0.18±0.03 (a.u.) and 0.32±0.03 (a.u.) for TSK and controls (p<10E-4), respectively. The signal ratio between lung and muscle tissue was 0.34±0.05 and 0.50±0.06 in TSK mice and controls, respectively. T2* was significantly shorter in TSK mice, 0.24±0.05 ms than matched controls, 0.46±0.05 ms (p<10E-5). Density in the lung measured with CT was significantly (p<10E-6) lower in the TSK mice 0.34±0.04 g/cm3 compared to the matched controls 0.58±0.03 g/cm3. The MLI was significantly larger in the TSK mice than the matched controls. The MLI was 73.0±9.6 um and 35.8±2.0 um for TSK and controls (p<10-7), respectively. There was a significant correlation (Pearson) between MLI and T2* (p<0.0001, r=-0.91, Fig. 1) and CT density and MRI signal (p<0.0001, r=0.96, Fig. 2).

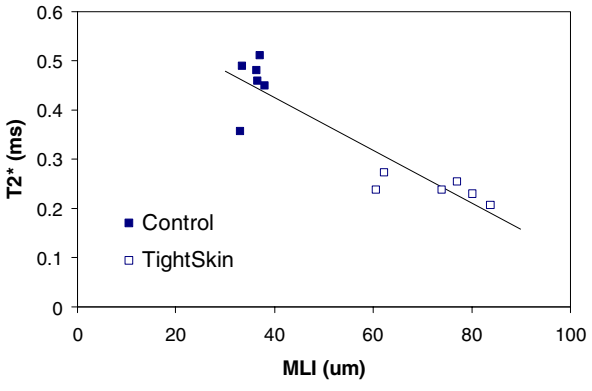

Figure 1. The correlation between MLI and T2*

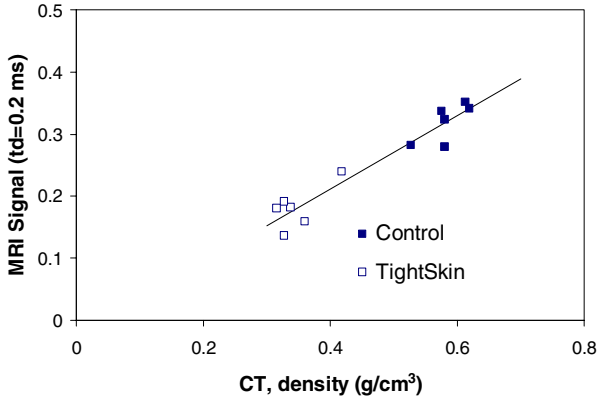

Figure 2. The correlation between CT density and MRI signal

Discussion: T2* correlated with alveoli size and MRI signal correlated with CT density and both were considerably smaller for TSK mice than controls. The decrease in tissue density seen on MRI, uCT and histology results in an increased air/tissue ratio in TSK mice leading to an increase of the internal susceptibility gradients and a reduction in T2*. Although, signal intensity at td=0.2 ms will not only reflect proton density but to a certain extent be influenced by T2*, there is still a good correlation between density measured by CT and MR signal intensity. The findings in this study indicate that the signal intensity (measured at short detection times) and T2* can be used as imaging biomarkers to characterize parenchyma density and alveoli sizes.

Reference: Price A et al., Single point imaging (SPI) of lung tissue. Proc Intl Soc Magn Reson Med 2004;11:858.