In vivo assessment of fatty diabetic lung by ultra-short TE (UTE) MRI in rats

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Target audience: Researchers and clinicians studying imaging-function correlates in the lung.

Purpose: Obesity mechanically restricts lung volume and causes lipid deposition in non-adipose lung tissue, which increases pro-oxidant and pro-inflammatory cellular stress and alters lung structure (ref). Although the effects of obesity on ventilatory control and airway mechanics are known, few studies have examined the effect of obesity on lung structure and ventilatory function. The Zucker diabetic fatty (ZDF) rat (*fa/fa*) carries the mutation that causes leptin insensitivey, leading to hyperphagia, diet-related obesity and diabetes mellitus. Our group observed lipid deposition and progressive hyperplastic changes within the alveolar septa of *fa/fa* animals associated with pulmonary dysfunction (1). We have previously shown that signal intensity (SI) and short transverse relaxation time (T2*) measured by an ultra-short TE MRI (UTE-MRI) in lung parenchyma have close correlation to lung tissue density in animal and human (2,3). Further, we have utilized these biomarkers to detect regional distribution of ventilation in a murine model of pulmonary embolism (4). The purpose of this study was to investigate the ability of in vivo UTE-MRI in assessment of pulmonary microstructure and ventilatory function in ZDF rats in comparison with physiological global measures and histomolphology.

Materials and Methods: We used 8 month-old male ZDF fatty diabetic (*fa/fa)* and matched lean control (+/+) animals (n=4 per group). MRI: MRI studies were conducted in a 3T whole-body human scanner (Achieva™, Philips Medical Systems, Best, Netherlands) with a small solenoid coil (I.D. 63 mm). Under anesthesia with 1.5-2% isoflurane mixed in either 100% oxygen or medical grade air (21% oxygen) and breathing spontaneously through a respiratory mask, all animals were subjected to the following MRI protocol. Under 100% oxygen, the entire lung was imaged in supine position with an UTE sequence at two different TEs (90 μs and 1.2 ms). The other imaging parameters were: TR = 10 ms, FA = 10º, FOV=70^3 mm^3, matrix size=100^3 (reconstructed to 260 μm isotropic resolution), NEX=1, affording a total scan time of 3.3 min. Subsequently, the UTE-MRI was performed with FA = 30º and NEX=2 for oxygen-enhancement, which was repeated 5 min after the inhalation gas was switched to 21% oxygen. The total scan time was approximately 6.5 min per imaging. Data analysis: We first applied a pixel-by-pixel based analysis on the 3D UTE-MRI data in which the lung field is automatically identified and segmented in each image as contiguous regions having SI less than a specified threshold value to provide 3D parametric maps of T2* and % change of SI. On the 3D maps, six regions of interest (ROIs) were placed on the lung parenchyma avoiding pulmonary vessels and abnormal high SI to measure T2* and % change of SI between the images (ref). An average value of six T2*s and % change of SI were defined for each animal to compare the physiological pulmonary functions . Following MRI and on separate days, pulmonary function was measured in the awake unsedated condition via a respiratory mask and body chamber, and repeated under anesthesia using an established rebreathing method (4).

Results and Discussion: Blood glucose levels were 145.3 ± 15.4 and 438.0 ± 230.5 (P<.05) in the +/+ and *fa/fa* groups. The total lung volume (mL) on the MR images is lower in the *fa/*fa (5.0 ± 0.6) than that in the +/+ (3.2 ± 0.4, P<.05). Compared to +/+ rats, *fa/fa* rats show hazy increased signals in lung parenchyma, which was more obvious at a long TE (Figure 1). The T2* (ms) in the parenchyma in +/+ and *fa/fa* groups (1.02 ± 0.04 and 1.10 ± 0.13, respectively), were consistent with the value previously observed in rodents (4) and not significantly different between groups (P = 0.24). Figure 2 shows representative maps of % change in SI after inhalation of 100% oxygen. The enhancement of SI (%) in *fa/fa* rats (5.2 ± 3.4) was ~65% lower than that in +/+ rats (13.9 ± 5.8, P<.05), indicating lover ventilation. The *fa/fa* rats showed lower values than the +/+ in physiological measures in mean lung volume, ventilation and DLco at 90% O_2 (Table 1). The results on the UTE-MRI were comparable to physiological measures and consistent with the our previous results (4) that ZDF rat had higher volumes of interstitial collagen fibers, cells, and matrix and exhibited a strain-specific increase in resistance of the air-blood diffusion barrier, especially in *fa/fa* lungs.

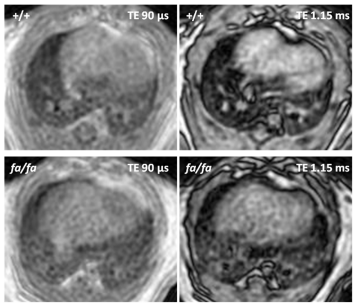

Fig 1. Typical UTE images of lung parenchyma at TE of 90 μs (left) and 1.15 ms (right). SI was increased in the *fa/fa* group (bottom), especially at long TE.

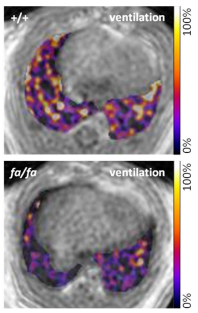

Fig 2. Typical maps of % change in SI on UTE imaging following inhalation of 100% oxygen in +/+ (upper) and *fa/fa* rat lung (bottom).

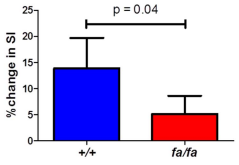

Fig 3. Comparison of % change in SI following inhalation of 100% oxygen. P value, by student's t-test.

Table 1. Residual functional volume (FRC), ventilation and DLco at 90% O_2 in physiologic measures. *p<.05 by student-t test.

Rebreathing	awake		anesthetized	
	+/+	*fa/fa*	+/+	*fa/fa*
FRC (mL)	12.5±1.7	6.2±1.8*	14.7±1.0	10.3±0.7*
Ventilation ($mL.min^{-1}$)	686±83	489±91*	305±25	206±14*
DLco ($mL[min.mmHg]^{-1}$)	0.21±0.04	0.07±0.02*	0.14±0.01	0.06±0.02*

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