Functional 1H lung MRI in healthy and emphysematous rats using a self-gated golden angle UTE

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Purpose: Several studies report using the ^{1}H MR signal difference in the lung parenchyma at inspiration and expiration for the assessment of lung function[1-3]. While initial results are promising, no study has been performed to assess the accuracy of this method over time. Animal studies, where disease progression can be properly controlled and assessed, could help validate the method, but has so far not been possible to perform due to the difficulties of self-gating in rodents. For the first time we demonstrate here the feasibility of the method in small animals by evaluating the lung function in rats with emphysema[4] using a self-gating golden angle 2D UTE sequence and a thorax-optimized phased-array coil.

Method: Twelve male WI rats (Charles River, 267 ± 7 g) were used in the experiment. Porcine pancreas elastase (PPE, Calbiochem, Germany) was intratracheally administered to anesthetized rats. The animals were separated into three groups of four; the control group (no administration of PPE), group 1 (75 U PPE/100g BW in the left lung dissolved in 0.2 mL saline), and group 2 (75 U PPE/100g BW in both lungs, dissolved in 0.2 mL). Baseline images were acquired from all animals before administration of PPE, with a follow-up scan 2 weeks after the administration.

All images were acquired during anesthesia using a 2D golden angle ultra-short echo time (GA UTE)[5] sequence at 7 T Biospec spectrometer (Bruker, Ettlingen, Germany), with an in-house developed thorax 4 Rx phased-array coil of 48 mm inner diameter[6]. Twelve consecutive slices of 1 mm thickness were acquired (TE=0.343 ms, TR=120 ms, FOV=5 cm x 6 cm, FA=30 degrees, 20 fold oversampling, total acquisition time of about 30 minutes). The self -gating signal was extracted from the k-space center and filtered between 0.5 and 3.5 Hz to extract the respiratory signal. Inspiratory images for each slice were reconstructed from data corresponding the lowest 10% of the signal, and expiratory images were reconstructed from the highest 50%. Micro-CT images (90 kV, 160 µA, FOV 60 mm, 4.5 min acquisition, respiratory gating) were acquired as gold-standard to assess the development of the emphysema.

Lung volumes at inspiration were registered to expiration at both time points using a fluid image registration model[7]. Expansion maps were then created by comparing the relative difference in signal intensity[1], $E = (S_{exp} - S_{insp})/\,S_{exp}$, where S_{exp} is the signal intensity at expiration and S_{insp} the signal intensity at inspiration. The lungs were then semi automatically segmented using an active contour method[8] and the mean expansion calculated for each lung volume at each time point. Values below zero were set to zero and values above 0.5 were considered artifacts and removed from the calculation.

Results: One animal died between the scans during the inflammatory phase that follows the PPE administration. Two weeks after administration the control group showed an average (both lungs) expansion of 97% of the baseline expansion, group 1 had 89% of the baseline and group 2 had 54%. In total, an average group reduction of 27% was found for the afflicted (PPE-treated) lungs, with a significant reduction (student's t-test, p<0.05) found between the baseline expansion and the expansion at the 2 week time point for all the afflicted lungs individually, as well as group wise (Figure 1). No group average reduction of expansion was seen in the healthy lungs. Images demonstrating the reduction of expansion can be seen in Figure 2a with MR and CT images in Figure 2b.

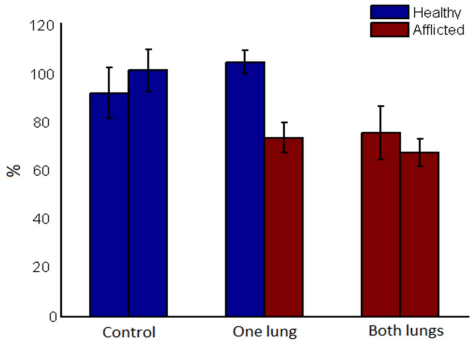

Figure 1. Mean percentage of baseline expansion at 2 weeks in both lungs for the three groups. A significant reduction of expansion can be seen in the afflicted lungs (p<0.05).

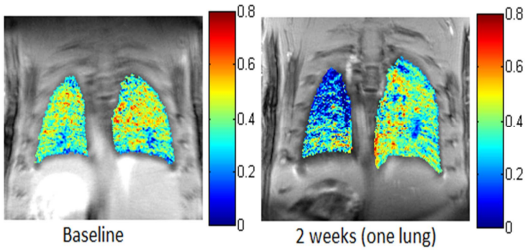

Figure 2a. Expansion maps at the baseline (left) and after two weeks (right). Note the clear reduction of expansion in the afflicted left lung.

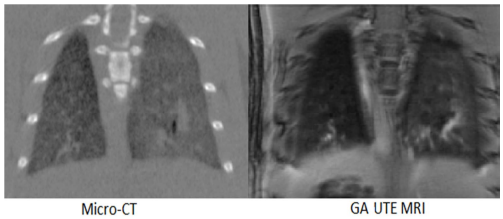

Figure 2b. Micro-CT (left) and GA UTE MRI (right) at the 2-week point. Emphysema is clearly visible in the left lung of both images.

Discussion: The expansion method yielded the overall expected results from all three groups. A significant reduction of expansion from baseline was found in 10 of 10 afflicted lung volumes and no significant reduction found in 9 of 12 healthy lung volumes. This indicates a good sensitivity to reduced lung function, but lower specificity. These measurements were made possible thanks to the high signal intensity of lung parenchyma in both inspiratory and expiratory phases, resulting from the synergic employment of the GA UTE and the phased-array coil optimized for thorax imaging. This method will especially benefit from any improvements in coil design and increases in SNR. Since only a small part of the respiratory cycle is in the inspiratory phase the SNR of these images suffer from less acquired signal as well as a lower proton density in the lung, disproportionally affecting the image analysis.

Conclusion: We have proven for the first time the feasibility of inspiration-expiration imaging in small animals and demonstrated that the resulting expansion maps are capable of tracking changes in lung function over time in emphysematous rats. This opens up new possibilities for functional ^{1}H lung MRI in animals and the method may become a useful quantitative tool for the investigation of selected lead compounds in relevant models of lung disease.

References: [1]: Zapke, Respir Res 2006, 7, p. 106; [2]:Kjørstad, Magn Reson Mater Phy 2014,*in print*; [3]:Pennati, Radiology 2014, 273(2):580-90; [4]: Quintana, Magn Reson Med 2006, 56:1242-50; [5]: Yu, Magn Reson Med 66.1 (2011): 248-254; [6]: Berthel, Proc. Intl. Soc. Mag. Reson. Med. 22 (2014):2310 [7]:D'Agostino, Med Image Anal 2003,7(4):565-75; [8]:Chan, IEEE Trans Image Process. 2001;10(2):266-77. **Acknowledgement**: Parts of this work was funded by EU FP7 (ITN-FP7-2010) 264834 (PINET) and Boehringer Ingelheim Pharma GmbH & Co. KG.