High-resolution ZTE MR imaging of emphysematous lungs in rats

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Introduction: MR lung imaging is notably hampered by the intrinsic properties of this organ, with its low proton density and short T_2*. Nonetheless, the absence of ionizing radiation, the high soft tissue contrast and the good spatial resolution typical of MRI have motivated researcher to pursue in this challenge. One of the main open issues is how to provide full coverage of the lung while keeping good image quality in a reasonable acquisition time, with both high spatial resolution and significant signal-to-noise ratio (SNR) in lung parenchyma. These properties are of extreme importance especially in the detection and study of diseases like emphysema, where the alveoli sacs are disrupted and thus the local SNR further decreases. Weiger et al. [1] have recently showed that zero echo time (ZTE) MRI sequences can be a valuable instrument to image the lung of *healthy animals*.
We propose here for the first time the investigation of an emphysema model in rats using a ZTE sequence and a thorax-optimized phased-array coil. The results were validated against the gold-standard micro-CT and the standard measurement of T_2* using ultra-short echo time (UTE) MRI [2].

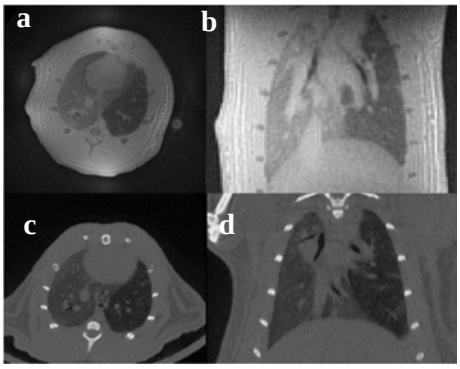

Fig. 1. *Typical (a) axial and (b) coronal ZTE MR images of a rat that received selective administration of PPE in the left lung. The respective (c) axial and (d) coronal CT images are shown as well.*

Material and methods: Twelve male WI rats (Charles River, 267 ± 7 g initial body weight (BW)) were used in the experiment. Porcine pancreas elastase (PPE, Calbiochem, Germany) was intratracheally administered to anesthetized mice. The rats were divided into three groups of four animals: the *control group* (no administration of PPE), the *one lobe* group (75 U PPE/100g BW in 0.2 mL saline selectively administered to the left lobe), and the *both lungs* group (75 U PPE/100g BW in 0.2 mL saline administered to both the lungs). MRI and micro-CT images were acquired 5 weeks after the administration of PPE.
MRI Protocol: Images were acquired on a 7 T Biospec spectrometer (Bruker, Ettlingen, Germany), using an in-house developed thorax 4 Rx phased-array coil of 48 mm inner diameter [3]. For each animal, a ZTE image was acquired with 126322 projections, isotropic matrix 200x200x200, 2 averages, FOV of 80x80x80cm^3, TR of 4.4 ms and FA of 1.3 degrees, for a total acquisition time of about 18 minutes. Similarly for each animal, six lower resolution 3D UTE images (isotropic matrix 128x128x128, FOV 50x50x50 cm^3) were acquired with different echo times (8µs, 0.05ms, 0.10ms, 0.25ms, 0.5ms, 1.5ms) to compute the T_2* in healthy and PPE-treated lobes.
MR image analysis: For each animal, lung parenchyma was identified in 3 different slices excluding the main vessels, and regions of interest *(ROI)* were manually segmented to measure the total average signal. The noise of the images was quantified as the standard deviation of the mean signal of a ROI selected in the image background and the signal-to-noise ratio in the parenchyma was calculated. T_2* values were computed on ROIs compassing the parenchyma, fitting with a non-linear least-squares algorithm the equation: $S(TE)= S_0*\exp(-TE/T_2*) + NL$, where NL is the noise level established from the dataset acquired at TE=1.5ms. Data from different groups were compared using Kruskal-Wallis test with Dunn's comparison using a 0.05 significance level.
CT imaging and analysis: Micro-CT (Quantum FX, Perkin Elmer, Waltham, MA-US) images were acquired on rats using 90 kV, 160 µA, FOV 60 mm, with cardiac and respiratory gating, for a total acquisition time of 4.5 min. Left and right lungs were segmented and Hounsfield Units (HU) histograms were obtained. The HU corresponding to the peak of the HU-histogram was used as a gold-standard measure of the emphysema development.

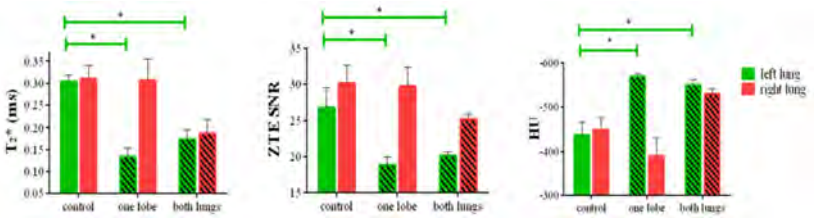

Fig. 2. *Bar plots showing the (a) T2* values obtained with UTE MRI, (b) the ZTE SNR and (c) the HU corresponding to the peak of CT HU-histograms for the three controls. Dashed lines indicate PPE-treated lungs. Asterisks indicate p<0.05.*

Results: Typical MR and micro-CT images for the group that underwent selective administration of PPE in the left lung are shown in *Fig. 1*. The measured values for T_2*, ZTE SNR and peak HU for left and right lungs are shown in *Fig. 2*. The decrease in SNR measured with ZTE in PPE-treated lungs excellently correlated (r=0.925, p<0.0001, Fig. 3a) with the decrease observed in the peak HU on the micro-CT histograms. Similarly, the decrease of T_2* in PPE-treated lobes well correlated with CT measurements (r =0.733, p = 0.0018, Fig. 3b). No significant statistical difference was observed in the right lung among the three groups across the three studied parameters (UTE MRI T_2*, ZTE MRI SNR, CT HU), even though a clear trend was observed (decrease of T_2*, SNR and HU in PPE-treated lobes).

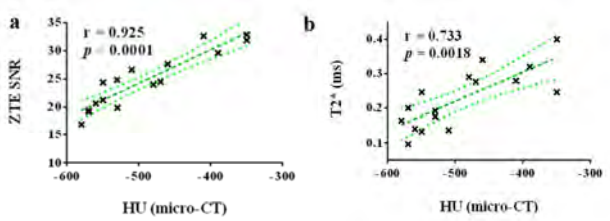

Fig. 3. *Correlations between (a) ZTE SNR and CT HU and (b) T_2* measured with UTE and CT HU.*

Discussion: As Zurek et al. previously showed [2], 2D UTE sequences are able to distinguish healthy from emphysematous lung tissues in an effective way. Nonetheless, 2D UTE sequences require the use of thick slices (e.g., 1.7 mm in Ref. [2]) in order to obtain sufficiently low TEs, which is mandatory in order to be able to visualize lung parenchyma changes. In this work, we were able to obtain *isotropic* three-dimensional ZTE images with high-resolution (400 µm), with absolutely negligible motion artifacts and significantly high SNR in lung parenchyma (>30 in healthy lungs), within a reasonable acquisition time. With respect to the somehow similar 3D UTE methods, ZTE doesn't suffer from eddy currents effects and doesn't require trajectory measurements [1], which makes the procedure simple and straightforward.
One of the animals of the group that underwent selective administration of PPE in the left lung showed both on CT and ZTE MR images signs of emphysema in the right lung. This fact, probably due to a non-perfect selective administration, clearly explains the lack of statistically significant difference in right lung among the three groups across the three studied parameters (UTE MRI T_2*, ZTE SNR, CT HU).
In conclusion, in this work we have clearly shown for the first time that ZTE MRI is a valuable non-invasive instrument to effectively detect and investigate the pathological changes in lung parenchyma, even at high magnetic fields, in a simple and precise way. Considering that ZTE was shown to be implementable on human scanners [4], the protocol proposed here is an excellent candidate for translational applications.

References: [1] Weiger et al., NMR Biomed. 2014; 27(9):1129-34 [2] Zurek et al., Magn Reson Med 2012; 68:898-904
[3] Berthel et al., Proc. Intl. Soc. Mag. Reson. Med. 22 (2014):2310 [4] Weiger et al., Magn Reson Med 2013; 70:328-332