Hyperpolarized Xenon-129 Gas-Exchange Imaging of Lung Microstructure: Preliminary Results in Subjects with Obstructive Lung Disease

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Introduction: There currently exists no clinical method for measuring regional gas exchange within the lung. However, early diagnosis, phenotyping and monitoring of lung disease would greatly benefit from such a tool. Hyperpolarized xenon-129 (HXe129) is a non-invasive contrast agent for lung MRI. Upon inhalation, HXe129 follows the functional pathway of gas exchange in the lung by diffusing from the alveolar air spaces into the alveolar septa and capillary blood. The purpose of this study was to develop and test a method, Multiple exchange time Xenon polarization Transfer Contrast (MXTC) MRI, to non-invasively assess the functional lung microstructure.

Methods: MXTC is an extension of the XTC technique (1-3) to 4D, i.e., 3D gas-phase depolarization maps ($f(\tau)$) are collected for several exchange times (τ) (Fig. 1). Two lung-function parameters are obtained by fitting the MXTC data to a 1D diffusion model (Eq. [1]) (1) including: MXTC-F, the long exchange-time depolarization value, which is proportional to the ratio of the functional lung-tissue volume ($V_{\tilde{t}}$) to the alveolar volume (V_a) (Eq. [2]); and MXTC-S ($S = \sqrt{\tau_c}$), which is proportional to the functional alveolar wall thickness $L_{\tilde{t}}$ (Eq. [3]):

$$f(\tau) = F\left(1 - 8\pi^{-2}\exp\left(-\tau/\tau_c\right)\right) \quad [1] \qquad V_{\tilde{t}}/V_a = F/\lambda \quad [2] \qquad L_{\tilde{t}} = \sqrt{\tau_c D_m}\cdot\pi \quad [3]$$

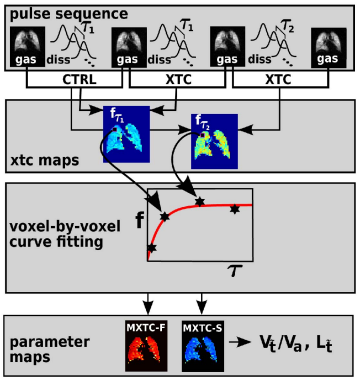

Figure 1: MXTC acquisition and data analysis schematic.

Three healthy volunteers (H1-H3), two subjects with COPD (C1, C2) and one with asthma (A1) were recruited for MXTC studies, which were performed on a whole-body 3T MRI system (TIM Trio, Siemens Medical Solutions, Malvern, PA) using a custom-built 32-channel receive array with integrated asymmetric birdcage transmit coil (4). Informed written consent was obtained and a physician supervised each study. The imaging parameters for gas-phase acquisitions were: TR/TE 7.7/2.5 ms, resolution 9.2 x 9.2 x 21-24 mm^3, matrix 48 x 30 x 10, acceleration R = 3, BW 260 Hz/pixel. Image excitation RF pulses were 500-µs, non-selective rectangular pulses with flip angles of 1°, 1°, 2° and 4° for the four 3D image acquisitions per breath hold. Contrast-generating pulses were 75º, 3-ms Gaussian RF pulses. MXTC maps were corrected for the use of 75º saturation RF pulses by a multiplication factor of 1.5, determined from 90º XTC spectroscopy measurements. A total of four to six breath holds were performed; each used identical xenon doses and breath-hold maneuvers to minimize registration errors due to different breath-hold positions. In subject C2, we also compared functional lung-tissue density maps derived from MXTC to CT and HXe129 ADC imaging. CT data were obtained from a routine clinical scan using a standard clinical protocol. HXe129 ADC imaging used a standard interleaved, two *b*-value (0 and 10 s/cm^2) slice-selective 2D-GRE implementation with a diffusion time of 3.2 ms.

Results: The MXTC-S parameter was found to be elevated in all subjects with lung disease (e.g., Fig. 2d, f) relative to results in healthy volunteers. In COPD subject C2, the MXTC-F parameter maps exhibited regional areas with relatively low values, indicating loss of functional lung tissue; these regions were consistent with both CT and ADC findings (Fig. 3). The sensitivity of MXTC is further illustrated by its capability of depicting gravity-induced anterior-posterior (AP) parameter dependence in healthy volunteers (Fig. 2a, b). In COPD subject C1 this effect was absent (Fig. 2c, d).

Conclusion: The functional tissue-density parameter map MXTC-F showed excellent agreement with CT imaging. However, since MXTC-F is based on xenon gas exchange, the parameters derived from MXTC represent true functional information, whereas CT represents structure, which only indirectly yields information about lung function via the structure-function relationship. The newly introduced parameter MXTC-S, which characterizes the alveolar wall thickness, has potential as a novel biomarker for regional parenchymal inflammation, fibrosis or other processes that impair gas transfer across the alveolar wall.

References: [1] Ruppert K, et.al., MRM 2000;44(3):349-357. [2] Ruppert K, et.al., MRM 2004;51(4):676-687. [3] Patz S, et.al., Acad Radiol 2008;15(6):713-727. [4] Dregely IM, ISMRM 2009, p.4918

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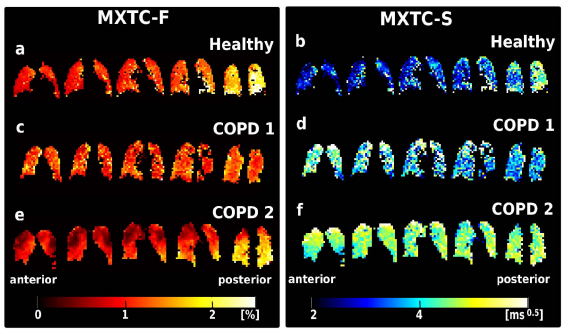

Figure 2: MXTC maps for healthy subject H1 and the two COPD subjects. The healthy subject shows homogeneous parameter distributions within each image and higher parameter values in dependent (posterior) images. This effect is absent in subject C1. Subject C2 exhibits regional loss of functional tissue density (MXTC-F). For both COPD subjects, the septal wall parameter (MXTC-S) is elevated compared to healthy subjects.

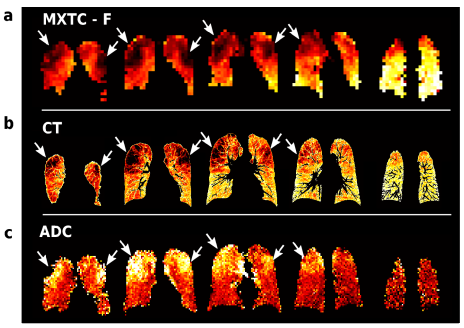

Figure 3: MXTC-F maps (a), CT images (b) and HXe129 ADC maps (c) for subject C2. A regional comparison shows excellent correlation of areas with emphysematous lung destruction (white arrows).