

GADOLINIUM CONTRAST ENHANCED ULTRA-SHORT TE IMAGING OF LUNG IN MICE

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INTRODUCTION

High-resolution computed tomography (HRCT) is the standard imaging technique for assessing lung anatomy. However, it also leads to increased radiation exposure [1], a concern that has drawn wide attention. Although the susceptibility artifacts and respiratory motions in the lung present significant challenges for magnetic resonance imaging (MRI), the potentials of multi-modal and molecular imaging of lung with high soft tissue contrast have generated increasing interest in MRI of lung. Ultra-short echo time (UTE) imaging has shown promise as a technique for imaging tissues in the environment with high susceptibility [2]. It is capable of capturing signals from tissues with T2 values of a few milliseconds or less, such as tendons, menisci, and cortical bone or cells/organs targeted by the superparamagnetic iron oxide nanoparticle contrast agent [3], which are normally invisible in conventional MRI techniques. Recently, lung imaging using UTE were investigated in small animal [4] and human [5]. However, utilization of UTE MRI for lung imaging still needs further improvement in sensitivity. The current study investigated the feasibility of gadolinium contrast agent enhanced UTE MRI of lung in mice on a standard 3 Tesla clinical MRI system with the goal to improve the image quality of pulmonary MRI.

MATERIALS AND METHODS

Animal Preparation and Administration of Gadolinium Contrast Agent Animal protocol in this study was approved by the Institutional Animal Care and Use Committee. Female BALB/c (6 to 8 weeks old) mice (average 18-20 gram b.w.) were used in the study. They were anesthetized by i.p. injection of a ketamine-xylazine mixture (95:5 mg/kg) before being placed in an 8-channel wrist coil for MRI experiments. Animals were divided into different groups, in which different doses of Gadobenate dimeglumine (Bracco Diagnostics Inc.) were administered intravenously via tail vein injection. The concentration of the contrast agent is 0.5 M (Gadobenate dimeglumine, Bracco Diagnostics Inc.). Amounts of the contrast agent were: 150 μ l (high dose), 100 μ l (regular dose), 50 μ l (low dose), and 10 μ l (very low dose) for each group, respectively.

MR Image Acquisition MRI experiments were performed on a 3 T MRI scanner (Magnetom Tim Trio, Siemens). UTE images were obtained before and at the time points of 1 min, 15 min, 30 min, 45 min, and 60 min after i.v. injection of Gd-DTPA. A non-gated 3D radial UTE sequence [6] was performed with dual echoes of TE1 = 0.07 ms and TE2 = 4.11 ms. Other parameters included TR = 6.84 ms, FA = 14, voxel size = $0.5 \times 0.5 \times 0.5$ mm³, matrix size = $208 \times 208 \times 208$, radial views = 52000, bandwidth = 633 Hz/pixel, averages = 2, and total scan time = 11 min 51 s. The images were acquired in the coronal view. For contrast imaging, pre-contrast UTE Images were acquired as control images.

Image Analysis All image processing was conducted using imageJ software (National Institutes of Health, Bethesda, MD). Subtraction of two images from different TEs resulted in contrast enhanced lung images with low background. Regions of interest (ROIs) were manually selected as squares of 32 pixels (2.5 mm²) on upper and lower lung regions based on blood flow effects on the acquire images to measure signal intensity (SI). Mean SI of the lung was measured by calculating the mean signal intensity of all pixels within the ROIs in the right and left lung parenchyma on 3 continuous slices in the middle of the lung. SI of the lung parenchyma in each animal was measured in same regions at different time points before and after Gd injection. The standard deviation (SD) of the SI of all pixels within ROIs in the background was calculated for noise evaluation. Signal-to-noise ratio (SNR) was also calculated by dividing the mean SI of the ROIs by the SD of the noise.

RESULTS AND DISCUSSIONS

Fig. 1 shows selected coronal slices of UTE images of animals received different dosages of Gd-contrast agent. Comparing to the pre-contrast condition, gadolinium contrast enhanced UTE provided improved signal-to-noise ratio in imaging of the lung. The signal enhancement is optimal at the dosage of 50 μ l and 100 μ l in the current experimental condition. The contrast enhancement actually decreased at the dosage of 150 μ l. This is likely due to the increased T2 effect from the contrast agent at the higher dosage. ROI analysis suggested that the contrast enhancement is fairly homogenous throughout the lung as there is little difference in SNRs between upper and lower lung regions. Further examining the temporal changes of signal enhancement in the lung after the administration of the contrast agent revealed that contrast enhancement in the lung (at the dosage of 100 μ l injection) lasted more than 15 minutes before reducing to 70% of its highest level (Fig. 2).

CONCLUSIONS

The results from this study demonstrated that the administering gadolinium contrast agent combining with UTE acquisitions provide the high sensitivity and image contrast in MRI of lung. The gadolinium contrast enhanced UTE MRI of lung is dose-dependent. With the improved sensitivity and contrast, gadolinium contrast enhanced UTE MRI may be further improved to reduce imaging time and artifacts, and may be an important alternative imaging tool for imaging of lung diseases in patients.

References: [1] Maher MM, et al. *J Thorac Imaging*. 2004; [2] Kubo T, et al. *AJR Am JRoentgenol*. 2008; [3] Longjiang Zhang, et al. *J Magn Reson Imaging*. 2010; [4] Masaya Takahashi, et al. *J Magn Reson Imaging*. 2010; [5] Osamu Togao, et al. *J Magn Reson Imaging*. 2011; [6] Nielles-Vallespin et al. 17th ISMRM, 2009.

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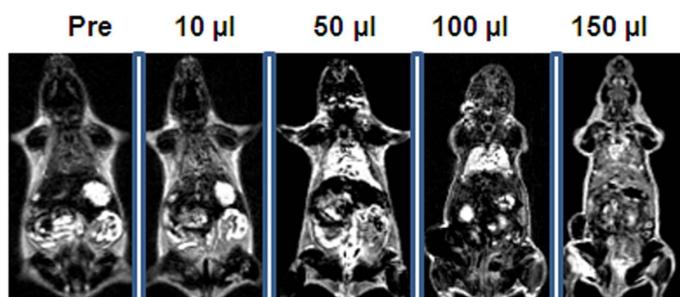


Fig.1 Lung images obtained from UTE MRI after i.v. injection of different dosages of Gd-contrast agent in mice. Images were recorded at 5 minutes after animals received Gd-contrast agent.

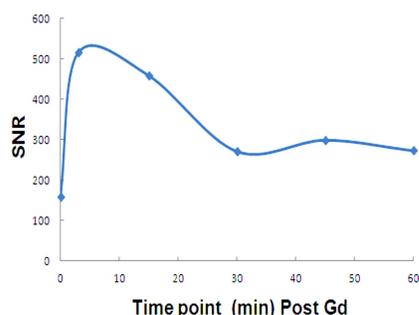


Fig. 2 SNR vs time curve for the mouse received dosage of 100 μ l.