Evaluation of Gd-DTPA contrast enhancement of lung and metastatic tumor with ultra-short echo-time imaging

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Introduction In a previous study, we administered nanoparticles containing a MR contrast agent, a fluorescence dye and an anticancer drug to successfully detect and visualize subcutaneous and deep-seated tumor in the back muscle of a mouse cancer model [1, 2]. The tumor appeared as a signal enhancement in T_1-weighted MRI. As the next step, it is desired to apply the nanoparticle to lung tumors and other pulmonary disease. Imaging of the lungs is difficult because of the low proton density, short T_2* and respiratory motion. However, ultra-short echo-time (UTE) imaging [3, 4] has recently been utilized to evaluate signal changes in lung parenchyma for various animal disease models [5, 6]. Moreover, quantitative assessment of pulmonary perfusion with dynamic contrast-enhanced MRI has been performed for pulmonary embolism and tumor in humans [7, 8].

As a preliminary step toward visible disease therapeutics using nanoparticles, the present study evaluated changes to the signal intensity in lung parenchyma and metastatic tumor using a positive contrast agent (Gd-DTPA) and UTE imaging.

Materials and Methods Female BALB/c nude mice were used for *in vivo* experiments (N=8). B16-F10 melanoma cancer cells (2.5×10^5 cells) were administered via the tail vein to make metastasis models in the lung, liver and skin. All MRI acquisitions were performed on a 7.0 Tesla animal MRI (Magnet: Kobelco, Japan; Console: Bruker Biospin, Germany). Measurements were made with a 35 mm inner-diameter transmit/receive volume coil (Rapid Biomedical, Germany). T_2-weighted images using a rapid acquisition with relaxation enhancement (RARE) sequence were acquired to detect tumors in the body area. Imaging parameters were: TR/effective TE = 2000/40 ms; FOV = 38.4 × 38.4 mm, Matrix = 256 × 256, RARE factor = 4.

In order to compare the effects of a contrast agent on signal intensity in lung parenchyma, normal liver and metastatic liver tumor, 3D UTE images at flip angles (FAs) of 5º, 10º, 15º and 20º were acquired before and after administration of 0.50 mmol/kg Gd-DTPA (Magnevist, Bayer HealthCare, Germany) via the tail vein. Other imaging parameters were: TR/TE = 8/0.02 ms; FOV = 38.4 mm × 38.4 mm × 44.8 mm, Matrix = 128 × 128 × 128, Projection number = 51360. After the experiments, regions-of-interest (ROIs) that avoided blood-rich areas were selected to assess signal intensity changes in the lung, liver and metastatic liver tumor.

Results Figure 1 presents 3D-UTE images of the lung for several FAs before and after Gd-DTPA administration. For all FAs, the signal intensity in lung parenchyma after administration was greater than that before. Also, the signal intensity for small FA (5º and 10º) was higher than that for FA ≥ 15º. Figure 2 compares the ratio of signal changes in lung parenchyma and liver before and after Gd-DTPA administration for several FAs. In lung parenchyma, the ratio was significantly higher for FA = 10º (paired–t test, $p<0.05$). There was no significant difference between FAs for the normal liver tissue. Figure 3 presents a T_2-weighted image (a) and 3D UTE images (FA = 10º) of metastatic tumor in liver (b) before and (c) after Gd-DTPA administration. The signal intensity of the tumor after administration increased from that before administration. For the metastatic tumors in liver, the signal intensity ratio for FA ≥ 10º was approximately 1.5 times larger than that for FA = 5º (Figure 4).

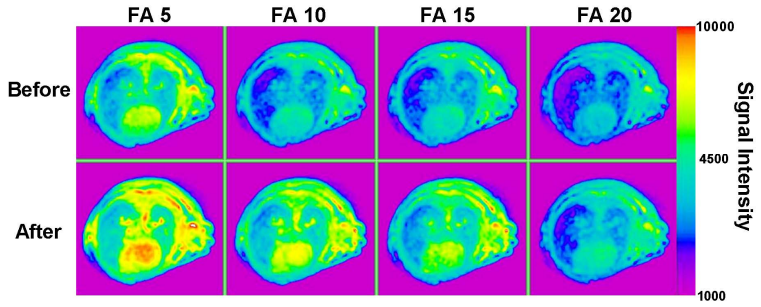

Figure 1 3D UTE images of mouse lung before and after Gd-DTPA administration for FAs 5-20º.

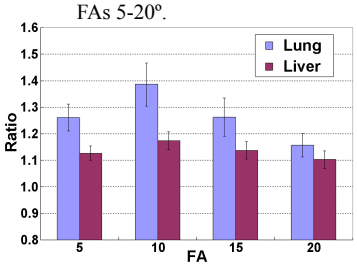

Figure 2 Comparison of the signal intensity ratio in lung parenchyma and liver for FAs 5-20 º.

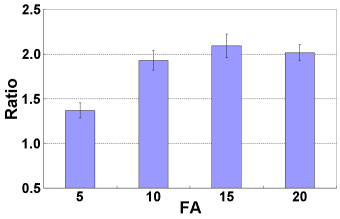

Figure 4 Comparison of the signal intensity ratio in metastatic tumor of liver for FAs 5-20 º.

Discussion According to a previous study [2], the signal intensity in lung parenchyma for FA = 5º was higher than that for FA ≥ 10º, which is similar to the results shown in Figure 1. On the other hand, the results in Figure 2 demonstrated that the before/after signal intensity ratio for lung parenchyma was largest for FA = 10º. Furthermore, the ratio in tumor was much larger for FA ≥ 10º (Figure 4). This indicates that using FA ≥ 10º will produce more favorable results than a smaller FA when using UTE imaging with a positive contrast agent.

Conclusion The results of this study demonstrated that tumor can be observed in UTE images using a positive contrast agent and the contrast between before and after Gd-DTPA administration can be compared. This suggests that tumors in lung parenchyma can be detected using a similar technique. In future work, changes to the contrast caused by early-stage parenchymal pulmonary diseases may be detected using contrast-enhanced UTE imaging with MRI-visible tumor-targeting nanoparticles.

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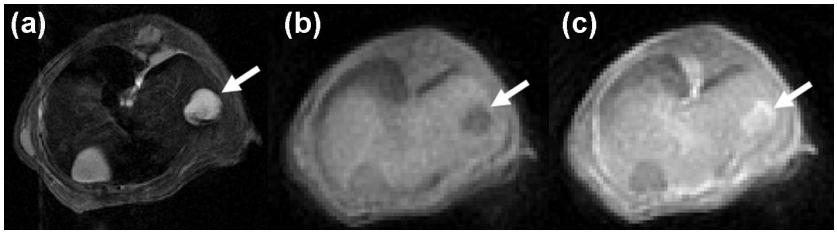

Figure 3 Typical (a) T_2 weighted image and 3D UTE images (FA = 10) (b) before and (c) after Gd-DTPA administration. The signal intensity in the tumor area (white arrows) increased after administration.