Comparison of MR lymphangiography with a G6 macromolecular contrast agent obtained at 1.5T and 3.0T Systems

Y. Hama1, M. Bernardo2, Y. Koyama1, C. A. Regino3, M. W. Brechbiel3, P. L. Choyke1, H. Kobayashi1

1Molecular Imaging Program, NCI/NIH, Bethesda, Maryland, United States, 2Molecular Imaging Program, SAIC-Frederick, NCI/NIH, Bethesda, Maryland, United States, 3Radiation Oncology Branch, NCI/NIH, Bethesda, Maryland, United States

Introduction
Higher field strength magnets are theoretically superior in signal to noise, which translates into better spatial and temporal resolution. Fortunately, small molecular weight imaging agents such as Gd-DTPA show little change in relaxivity between the field strengths of 1.5T and 3.0T. However, most of the macro-molecular contrast agents show more significantly decreased R1 and increased R2 relaxivities when the magnetic field changes from 1.5T to 3T. Since T2 and T2* effects should be enhanced on 3T system compared with those at 1.5T, T1 contrast induced by macromolecular contrast agents can be compromised at 3T as compared with 1.5T. Practical disadvantages caused by these effects have not been reported on a 3T system compared with 1.5T. In this study, MR lymphangiography (MRL) in mice with a G6 dendrimer-based macro-molecular contrast agent (~10nm in diameter; 204 Gd ions on a molecule) was compared at 1.5T and 3.0T. Images obtained using both T1-weighted 3D-fast spoiled gradient echo (3D-fSPGR) and T2/T1-weighted 3D-fast imaging employing steady-state acquisition (3D-FIESTA-C) with identical imaging parameters at both field strengths in order to evaluate the effect of high magnetic field on the detectability of macromolecular contrast agents.

Methods
Contrast agent: A polyamidoamine-G6 dendrimer (58 kD) based nano-size MRI contrast agent coupled with 2-(p-isothiocyanatobenzyl)-6-methyl-diethylenetriamine-pentaacetic acid (1B4M) and 204 Gd(III) ions (G6; 220 kD; ~10 nm in diameter) was synthesized to perform MRL. Relaxivity: To validate R1 and R2 relaxivities of G6 agent, we made a phantom, which consists of 0, 0.25, 0.5, 0.75, and 1 mM G6 in PBS together with 0.18 and 0.94 mM Gd-DTPA as internal controls. The phantom was examined with 2D- and 3D-fSPGR using flip angles 0-50° with 5° increments and R1 relaxivity was calculated. Then phantom was examined with multi-echo spin echo (TE; 15, 30, 45, and 60 msec) and R2 relaxivity was calculated on both systems.

Animal MRI models: Three groups of 10 week-old normal athymic mice (n=4) were used for; 1. A side-by-side comparison study between 3T and 1.5T system (both GE Signa systems LX at 1.5T and Excite at 3.0T) of the same mouse, 2. Dynamic scans for further optimization of timing and parameters on each system. All mice were anesthetized and injected intracutaneously with 0.005 µmol Gd of G6 into the middle phalanges in both upper extremities. All MR images were obtained with a modified Alderman-Grant resonator mouse coil fixed by an in-house constructed coil holder. For the comparative study, a T1-weighted 3D-FIESTA-C [TR/TE 10.8/2.2; bandwidth 41.7 kHz, flip angle 45°, frequency/phase: 384/256, slice thickness 0.6 mm, 2 NEX; scan time 3'42"] and a T2/T1-weighted 3D-fSPGR [TR/TE 14.3/7.0; bandwidth 31.2 kHz, flip angle 30°, frequency/phase: 512/256, slice thickness 0.6 mm, 4 NEX; scan time 4'38"] were used for obtaining coronal images of the contrast-enhanced MRL studies. A side-by-side comparison study was performed at 30 min post-injection of contrast agent. In addition, dynamic scans were obtained at 10, 20, and 30 min post-injection of the contrast agents to test shorter TE scans (TR/TE; 9.3/2.3) for 3D-fSPGR and larger flip angles (60°, 70°, 80°) for 3D-FIESTA-C were tested on both systems.

Results
The R1 and R2 relaxivity of the G6 contrast agent were 33 and 78 /sec/mM at 1.5T and 24 and 82 /sec/mM at 3T, respectively. The 1.5T system showed high axillary LN-to-fat ratios with both 3D-fSPGR (4.5±0.9 vs 3.5±0.9; 1.5T vs 3T, n=8) and 3D-FIESTA-C (2.7±0.2 vs 1.2±0.1; 1.5T vs 3T, n=8, p<0.001). Maximum intensity projections (MIP) obtained with 3D-fSPGR provided good enough contrast for both 1.5T and 3T systems (Fig. 1a, 2a). However, inadequate contrast between the enhanced LN and the surrounding fat tissue obtained with 3D-FIESTA-C on the 3T system compromised the visualization of the lymphatic system (Fig. 1b, 2b). Shorter TE scans with 3D-fSPGR helped to improve the LN-to-fat contrast especially on the 3T system. In contrast, changes of the flip angle with 3D-FIESTA-C did not improve the LN-to-fat contrast on the 3T system.

Conclusion
When comparing performance of the macromolecular G6 agent at 1.5T and 3.0T, the fat/opacified lymph node ratio was compromised with both 3D-fSPGR and 3D-FIESTA-C at 3T compared with the 1.5T system probably because of decreased R1 relaxivity of G6 agent and possible T2 and T2* effects. The lymphatic system was almost invisible on 3D-MIP MRL images taken with 3D-FIESTA-C on the 3T system.

Fig. 1. (a) 1.5T/ 3D-fSPGR (b) 1.5T/ 3D-FIESTA-C, Fig. 2. (a) 3T/ 3D-fSPGR (b) 3T/ 3D-FIESTA-C