C. Fink[1], M. Bock[2], S. Heckl[1], F. Kießling[1], S. Delorme[1]
Deutsches Krebsforschungszentrum (DKFZ), Heidelberg, Germany: [1] Dept. of Radiology (E0100), [2] Dept. of Biophysics and Medical Radiation Physics (E0200)

Abstract
The aim of this study was to evaluate the potential of Gadobutrol as a contrast agent for interstitial MR-Lymphography. Initial results in rats show that after the subcutaneous injection a marked enhancement of the lymphatic system can be observed, including the draining lymphatic vessels and subsequent lymph node groups. Additionally a rapid transit of the contrast agent into the vascular system and the subsequent renal elimination can also be seen.

Introduction
Various gadolinium chelates have been successfully utilized for interstitial lymphography in animals and humans [1-6]. Whereas most of these studies used macromolecular compounds, the use of conventional extracellular, micromolecular MR contrast media has recently been proposed [5,6]. Advantages are the long clinical experience with this agents and the known favorable toxicity profile. Gadobutrol is a highly concentrated (1 mol/L) gadolinium-based hydrophilic and neutral macrocyclic contrast agent. The aim of this study was to evaluate the potential of Gadobutrol for interstitial MR-Lymphography.

Methods
A reactive lymphadenopathy was induced by intramuscular injection of 0.1 mL Freund's complete adjuvant (Difco Laboratories, Detroit, MI, USA) in the thigh of six mature Copenhagen rats (Charles River, Sulzfeld, Germany). For MRI all animals were positioned in a prone position and anesthetized by mask inhalation of 0.5% halothane in a mixture of 40% nitrous oxide and 60% oxygen. A volume of 0.5 mL Gadobutrol was injected subcutaneously into the left hind leg at the level of the metatarsal bones. Massage of the injection site was not performed in order to avoid change of the positioning of the animal between the pre- and post-contrast series. MRI was performed on a clinical 1.5 T whole-body scanner with a maximum gradient strength of 25mT/m and a minimal rise time to maximum of 600 ms (Magnetom Vision, Siemens, Erlangen, Germany) using a custom-made radio-frequency coil for excitation and signal reception. The imaging protocol included repetitive acquisitions of a high resolution three-dimensional T1-weighted fast low angle shot (Flash 3D) sequence in coronal orientation: TR/TE=13.3/6.2 ms, FA=50°, FOV 110x55 mm, matrix 512x205, slab thickness 32mm, 100 partitions, voxel size 0.32x0.22x0.27 mm, TA 4:37 min). For the assessment of contrast kinetics immediately after the injection of the contrast agent a time resolved, two-dimensional T1-weighted fast low angle shot (Flash 2D) sequence (TR/TE=136/4.7 ms, FA=70°, FOV 90x56 mm, matrix 128x69, slice thickness 3 mm, voxel size 3.0x0.70x0.81 mm, TA 11 s) was employed in two animals. Image analysis included region of interests (ROI) analysis over various tissues (lymph nodes, kidney, liver, muscle).

Results
Immediately (Δt=11 s) after the injection of Gadobutrol a T2*-related loss of signal intensity was observed in the inguinal and iliac/paraaortic lymph nodes in the time resolved 2D T1-weighted sequence. Additionally, a rapid signal enhancement of the vascular system and parenchymal organs and a subsequent renal elimination could be observed (Fig. 1). The 3D T1-weighted sequence showed a continuous signal enhancement of the inguinal and iliac/paraaortic lymph nodes over the whole examination time (100 minutes) (Fig. 2). In addition, an enhancement of the regional lymph vessels, subsequent lymph nodes and the thoracic duct was visualized with this sequence (Fig. 3).

Discussion
Gadobutrol might serve as a potential contrast agent for interstitial MR-lymphography. Advantages compared to experimental macromolecular compounds are the high concentration which enable the use of small injection volumes and the known favorable safety profile.

References

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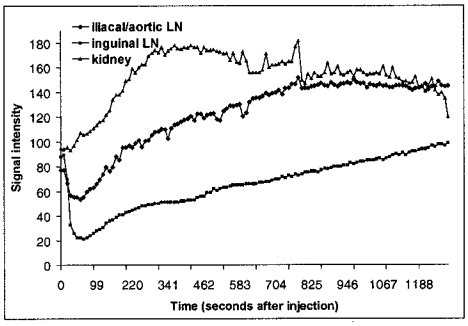

Fig. 1— Graph of signal intensity values of lymph nodes and kidney over time measured with 2D T1-weighted sequence.

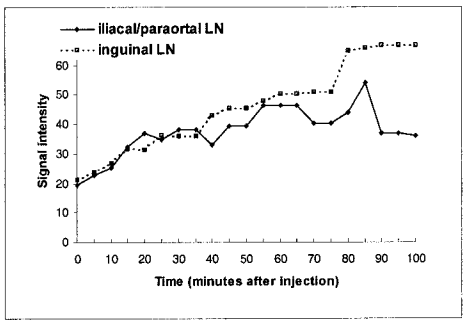

Fig. 2— Graph of signal intensity values of lymph nodes over time measured with 3D T1-weighted sequence.

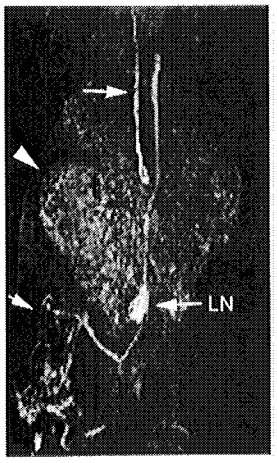

Fig. 3—Maximum intensity projection of 3D-T1-weighted series. Contrast enhancement in paraaortic lymph nodes (LN) and lymphatic vessels (arrows) 5 minutes after s.c. injection of 0.5 mL gadobutrol into left hindleg. Also minor enhancement of left kidney (arrowhead) as a sign of transfer of contrast agent into the vascular system.