In Vivo MR imaging of the Sequential Recruitment of Macrophages to the Soft Tissue Infection

J. S. Lee[1], H. J. Kang[2], H-D. Jung[3], K. H. Lim[3], S. T. Kim[3], T-H. Lim[1]

[1]Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea, Republic of, [2]Department of Laboratory Medicine, Hallym University College of Medicine, Seoul, Korea, Republic of, [3]Asan Institute for Life Sciences, University of Ulsan College of Medicine, Seoul, Korea, Republic of

PURPOSE: The development of new immunologic cell–based therapies requires a quantitative and qualitative assessment of cell distribution to target organs (homing) and engraftment. Magnetic resonance (MR) imaging is well suited for this task because it can enable both whole-body examinations and subsequent detailed depictions of host organs with near-microscopic anatomic resolution and excellent soft-tissue contrast. Therefore, the purpose of this study was to evaluate the feasibility of MR imaging to depict the in vivo sequential recruitment of iron oxide-labeled macrophages to experimentally induced soft tissue infection according to the time sequence.

METHODS: Experimental soft-tissue infection in 6 male C3H/HeN mice was induced by inoculation with a $5X10^7$ colony-forming unit of *Staphylococcus aureus* into the left lower leg. Peritoneal macrophages were harvested from thioglycollate-treated mice, cultured, and labeled with iron oxide nano particles in vitro. The iron oxide-labeled macrophage was administered through the tail vein 48 hours after inoculation of the bacteria. The left lower legs of the mice were imaged sequentially on a 4.7 T MR imaging unit before macrophage administration and 1, 2, 4, 6, 12, 18, 24, and 48 hours after administration. The imaging protocol was a T2*-weighted (356.5/10.3, 30° flip angle) gradient-echo (GRE) sequence. We chose a transverse (orthogonal to the tibia) section orientation to ensure anatomic reproducibility of the image position. The spatial resolution was as follows: 256×256; field of view, 2.18×2.06 cm; slice thickness, 0.67 mm; slice gap, 0.33 mm; 18 slices. The changes in relative MR signal intensity (SI) of the abscess wall and in the extent and pattern of contrast enhancement (macrophage distribution) were analyzed. The MR and histopathologic findings were compared.

RESULTS: The abscess showed slightly higher SI in T2*-weighted GRE images (Figure 1a). On sequential MR images after administration of macrophage labeled with iron oxide, the band-shaped lower SI zone was noted in the abscess wall (Figure 1). Intravenously injected macrophage began to be noted in the wall of the abscess within 6 hours after injection. The relative SI of the abscess wall progressively decreased until 24 hours after the injection of iron oxide-labeled macrophages (mean = 0.48) comparing to that before injection (mean = 1.24) ($p < 0.05$) (Figure 2). The lower SI zone corresponded with the distribution of the iron oxide–labeled macrophages on histopathology.

CONCLUSIONS: In this study we demonstrated that the sequential recruitment of intravenously administered iron oxide-labeled macrophage can be monitored with 4.7T MR imaging. This will provide a new and powerful tool to investigate the interactions between macrophages, the first-line defense of innate immunity and the invading pathogens.

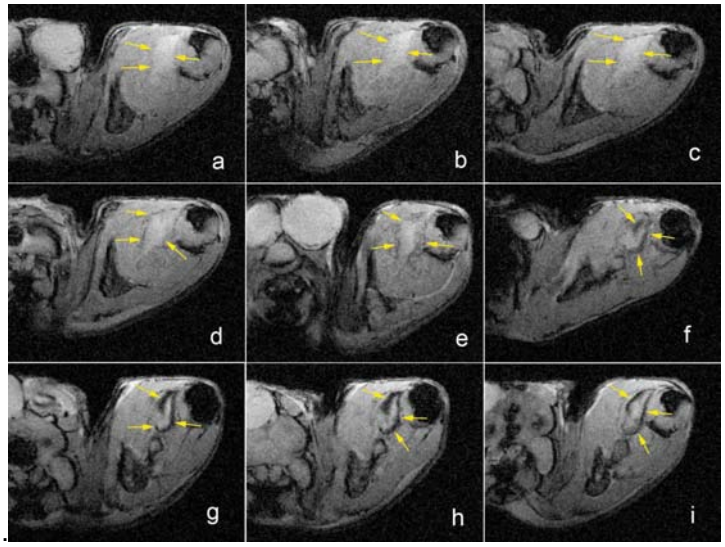

Figure 1. The left lower legs of the mice were imaged sequentially on a 4.7T MR imaging unit (a) before macrophage administration and (b) 1, (c) 2, (d) 4, (e) 6, (f) 12, (g) 18, (h) 24, and (i) 48 hours after administration. The band shaped lower SI zone was noted in the abscess wall (arrows).

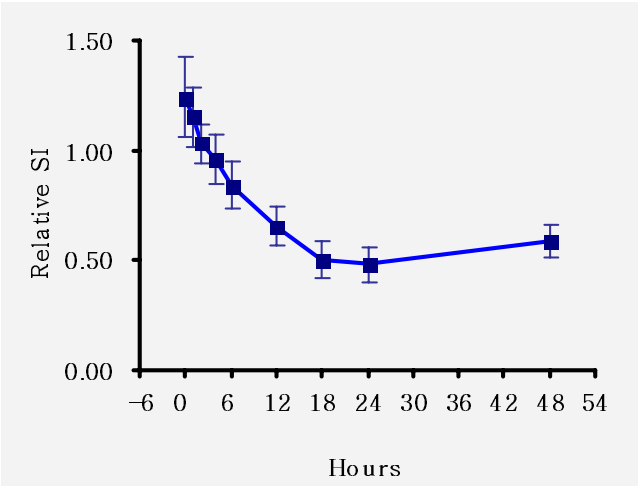

Figure 2. Changes of relative SI after intravenous injection of iron oxide labeled macrophages. The relative SI of the abscess wall progressively decreased until 24 hours.