

# Potential of SPIO in the diagnosis of bone metastasis - preliminary examination for clinical application

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## Synopsis

In preliminary experiment using the model rabbits, we have reported that a superparamagnetic iron oxide (SPIO) enhanced magnetic resonance imaging (MRI) has a potential in the differential diagnosis of bone metastasis and inflammation. In this study, we clinically investigated optimal imaging parameters and scan timing of bone marrow with healthy volunteers as well as a potential of SPIO for the differential diagnosis with patients. Optimal imaging parameters and scan timing were short TI inversion recovery and at 3 hours after a ferucarbotran injection. SPIO enhanced MRI could detect bone metastasis in patients at a clinically approved liver imaging dose.

## Methods

### 1. Volunteer imaging:

The lumbar spines of three healthy male volunteers were examined before and at 15 minutes, 3, 24, and 48 hours after an intravenous ferucarbotran (Resovist, Schering AG) injection at a dose of 8 micro mol Fe/kg.

**MR imaging:** All volunteer were subjected to MR examination using a 1.0 T clinical imager (Magnetom, Harmony, SIEMENS) with the following sequences: short TI inversion recovery (STIR; TR / TE / TI = 3000 / 60 / 180 msec), T2 weighted turbo spin-echo with fat suppression (TSE FS; TR / TE = 3000 / 60 msec, ETL 7), 2-dimensional T2-weighted spoiled gradient-echo images (TR / TE = 184.2 / 8.0 msec, FA 15°) with and without fat suppression (2D-FLASH and 2D-FLASH FS). The parameters of those sequences were as follows: FOV 360 mm, Matrix 252 × 256. 11 slices of 5 mm thickness, 3 acquisitions.

**Data Analysis:** Signal intensity (SI) of bone marrow in each sequence was measured. All measurements were performed from the L1 through L5 vertebral body. The RE of bone marrow was calculated using the following formula:  $RE(\%) = [(SI_{post} - SI_{pre}) / (SI_{pre})] \times 100$ , where  $SI_{pre}$  and  $SI_{post}$  are the signal intensities of bone marrow before and after a ferucarbotran injection.

**Statistical Analysis:** Tukey test was used to compare the RE of each group.

### 2. Patient imaging:

The patients were examined before and at 3 hours after an intravenous ferucarbotran injection at a dose of 8 micro mol Fe/kg.

**MR imaging:** The patient was subjected to MR examination using a 1.5 T clinical imager (Intera, Philips) with TSE and STIR sequences using the same parameters as described above.

**Data Analysis:** SI of normal bone marrow and tumor metastasis were measured. The RE of bone marrow was calculated using the above formula. The contrast to noise ratio (CNR) between tumor metastasis and non-tumor region in bone marrow was calculated using the following formula:  $CNR = (SI_{tumor} - SI_{non-tumor}) / background$ , where  $SI_{tumor}$  and  $SI_{non-tumor}$  are the signal intensities of tumor metastasis and non-tumor region in bone marrow after a ferucarbotran injection.

## Results and Discussion

### 1. Volunteer imaging:

The typical STIR images of a volunteer are shown in Figure 1. TSE FS, fat suppressed 2D-FLASH, and STIR, the RE reached minimum at 3 hours after ferucarbotran injection. There were significant differences in each sequence ( $p < 0.05$ ). Only in 2D-FLASH without fat suppression, the RE reached minimum at 24 hours after a ferucarbotran injection. Our results show that ferucarbotran suppresses bone marrow signal the most in STIR ( $-47 \pm 14\%$ ). Therefore, it was suggested that ferucarbotran may be useful for clinical bone marrow imaging as well as the results of animal experiments (*Invest Radiol* 2005; 40: 10: 676-681).

### 2. Patient imaging:

The typical STIR images of the patient are shown in Figure 2. The SI of tumor metastasis in bone marrow (T10, T11, T12) did not change after a ferucarbotran injection, whereas the SI of normal bone marrow (T9, L1-L5) decreased at 3 hours after a ferucarbotran injection (Figure 2). The REs of tumor metastasis (the average of RE in T10, T11, T12) and non-tumor region (the average of RE in T9, L1-L5) in bone marrow were  $-22 \pm 9\%$  and  $-65 \pm 8\%$ , respectively. The RE of non-tumor region in bone marrow of patient was smaller than that of the volunteer, because the uptake of SPIO by Kupffer cells would decrease in patient. The CNR between tumor metastasis and non-tumor region in bone marrow after a ferucarbotran injection was increased (CNRs of pre and 3 hours after an injection were 2.8 and 3.9, respectively). Therefore, our results suggest that SPIO enhanced bone marrow imaging may be useful for the clinical diagnosis of bone metastasis.

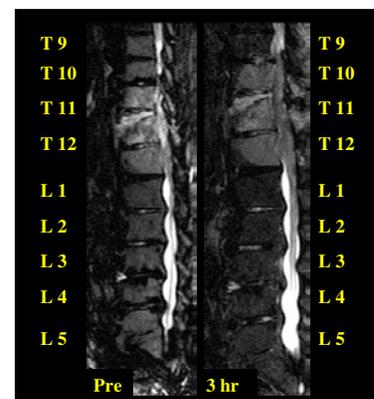
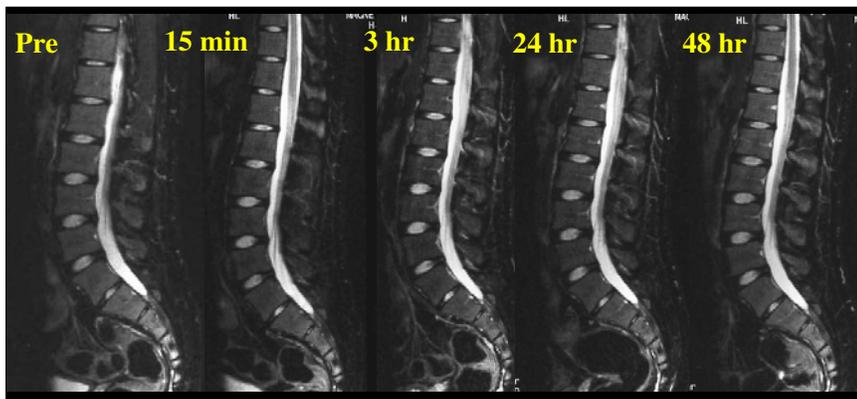


Figure 1 Signal change of bone marrow after a ferucarbotran injection a dose of 8 micro mol Fe/kg

Figure 2 Signal change of bone marrow in the patient metastasis with bone metastasis (67 age, male, HCC with cirrhosis) after a ferucarbotran injection at a dose of 8 micro mol Fe/kg.