

## Early Verification of Irradiated Field using Superparamagnetic Iron Oxide (SPIO) Enhanced MR Imaging

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**Introduction:** In radiation therapy, advanced technology and methods such as proton therapy, heavy ion therapy [1], fractionated stereotactic radiotherapy and so on are applied clinically. They make it feasible to deliver high radiation doses to the target volume while reducing the dose to adjacent normal tissues. It is important to irradiate the area precisely according to the therapeutic planning, and then to be able to verify the accuracy of the procedure. Hepatocellular carcinoma (HCC) is one of the difficult tumors for accurate setting the irradiated field because of respiratory movement. Recently, the area of radiation-induced liver injury was presented by superparamagnetic iron oxide (SPIO) enhanced MR images. The reticuloendothelial system (RES) was more sensitive to irradiation than hepatocytes, and SPIO-enhanced MR imaging was able to depict phagocytic functional abnormality in the early phase of injury. Morimoto et al. reported that SPIO-enhanced MR imaging was reliable for detecting the range and extent of liver injury a few days after low-dose irradiation using rats [2]. The purpose of this study is to apply SPIO-enhanced MR imaging to early verification of irradiated field after heavy ion (carbon ion) radiation.

**Methods:** Six patients with HCC were examined. Informed consent was obtained from all subjects prior to the study according to the guidelines of our institutional review board. They received carbon ion radiotherapy at a total dose of 52.8 Gy equivalent (GyE) in 4 fractions. Carbon-ion irradiation has a sharp Bragg Peak that permits accurate beam localization in the tumor [1].

The MR system used in this study was a VISION operated at 1.5T (Siemens-Asahi Medical Technologies, Ltd., Tokyo, Japan). A gradient echo pulse sequence was used (TR, 115 ms; TE, 4.1 ms; flip angle, 40). Slice thickness was 10 mm, and the image was not averaged. Matrix size was 512x512, and FOV was 350 mm. SPIO-enhanced MR imaging was performed within three days after carbon-ion irradiation. SPIO (Feridex, 5ml, Tanabe Ltd, Japan) was intravenously injected about 5 hours prior to MR imaging. A dynamic series of X-ray CT was performed in each patient 4-10 days after carbon-ion irradiation. The CT scans were acquired at pre-injection, arterial, portal, and delayed phases (Iopamiron 300, Schering AG, Germany, 150 ml/50 sec iv).

**Results:** The irradiated fields were clearly detected as higher intensity areas in all patients by SPIO-enhanced MR imaging (Fig. 1a), which were visually consistent with the physical dose distribution of treatment planning (Fig. 1c). Signal intensity in the irradiated field was significantly higher than that in non-irradiated tissue of the liver (paired-t test,  $p < .001$ ; Fig.2). The irradiated field was not detected visually by dynamic X-ray CT, and no significant difference in density between radiated and non-radiated areas was obtained in any dynamic phase (Fig. 2b)

**Conclusion:** SPIO-enhanced MR imaging can visualize the irradiated field immediately after radiation therapy for HCC. This may be useful for early verification of treatment planning.

### References

- 1, *J Clin Oncol* 20:4466-4471 (2002)
- 2, *JMRI* 9:573:578 (1999)

Fig. 1.

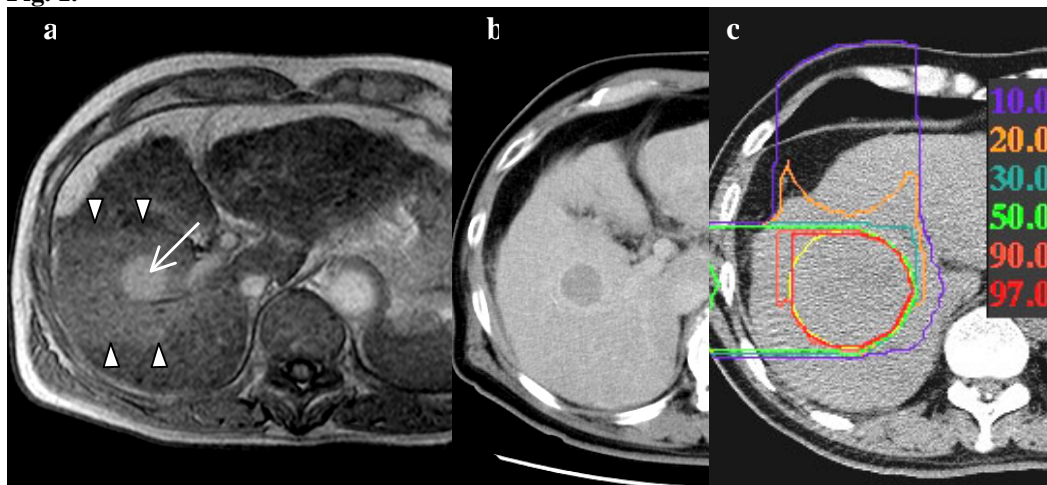
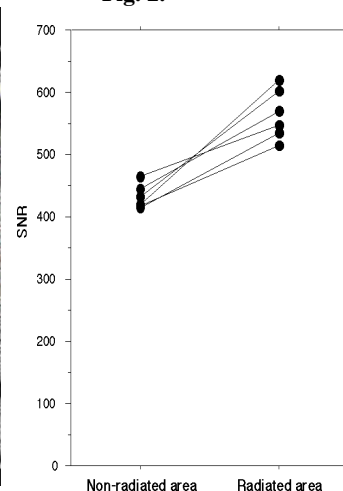


Fig. 2.



**Figure 1.** (a) SPIO-enhanced MR image. A irradiated field (arrowheads) is visualized (arrow shows HCC nodule). (b) Enhanced CT image at delayed phase. Early verification was impossible using dynamic enhanced X-ray CT. (c) Contour map of physical dose distribution. Color lines show relative radiation doses (%).

**Figure 2.** Signal-to-noise ratios (SNR) in non-irradiated and irradiated areas. Signal intensity in the irradiated field was significantly higher than that in non-irradiated tissue of the liver (paired-t test,  $p < .001$ ).