Prolonged signal decay in the ablated area after radiofrequency ablation in the ferucarbotran-administered liver: A basic experimental study for the visualization of ablative margins in a rabbit model

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Introduction: Radiofrequency ablation (RFA) is a promising method for the treatment of malignant hepatic lesions. Contrast-enhanced computed tomography (CT) is usually used to assess the effect of the treatment. However, because both the ablated tumor and liver parenchyma surrounding the tumor (ablative margin) do not exhibit contrast enhancement, it is impossible to objectively evaluate the ablative margin from these scans. This substantial disadvantage results in a relatively high incidence of local recurrence after RFA [1]. Ferucarbotran is a commercially available reticuloendothelial cell-specific contrast agent used for liver imaging. On T2*-weighted images, the signal intensity of the liver parenchyma is significantly decreased for 8 hours after ferucarbotran administration because of the susceptibility effect of superparamagnetic iron oxide particles phagocitosed by the Kupffer cells; malignant hepatic lesions lacking these cells are visualized as relatively hyperintense areas. The difference in the signal intensity of the liver parenchyma becomes insignificant after 3 days and the signal intensity reverts to a normal level after 3 weeks [2]. If RFA is performed within 8 hours after the administration of ferucarbotran, it is hypothesized that, several days later, the ablative margin will be visualized as a hypointense rim because of the impaired clearance of ferucarbotran (Figure 1). The purpose of the present experimental study is to prove the 2 following hypotheses in a rabbit model: if RFA is performed within 8 hours after the administration of ferucarbotran, **(**1) the signal decay of the ablated liver parenchyma will be prolonged and (2) iron deposition will occur in the ablated area.

Materials and Methods: A total of 7 male Japanese white rabbits aged 14–38 weeks (mean, 25 weeks) were divided into 2 groups: ferucarbotran group and control group. The rabbits in the ferucarbotran group were intravenously injected with 8 μmol/kg body weight ferucarbotran through the dorsal ear vein. After 3 hours, T2-weighted fast spin-echo (FSE) (retention time (TR)/effective echo time (TE) in ms, 4000/58; echo train length (ETL), 8; field-of-view (FOV), 22 cm; matrix, 256 × 160; slice thickness/gap in mm, 4/0.4; number of excitations (NEX), 4) and T2*-weighted gradient-echo (GRE) (TR/TE in ms, 440/10; FA, 30; FOV, 22cm; matrix, 256 × 160; slice thickness/gap in mm, 4/0.4; NEX, 8) images were obtained using a 3T MR imaging unit (Signa HDx 3T, General Electrics) equipped with a head coil. After 4 hours, RFA was performed under nitrous oxide/oxygen-isoflurane anesthesia. A small surgical incision was made in the left hypochondrial region and a 17-gauge electrode with a 1-cm-long exposed tip (Cool-tip RF system, Radionics) was inserted into the liver parenchyma. The electrode was connected to a 480-kHz RF generator. The power output was gradually increased from 5 W to a maximum of 19 W (8 min) at a rate of 2W/min. The ablation was terminated in 8 min or, when the impedance increased by 20 ohm over the initial impedance (roll off). In the control group, ferucarbotran was not administered, and RFA was performed in the same manner. In vivo MR imaging, including T2-weighted FSE and T2*-weighted GRE, were conducted on all rabbits at 1, 2, and 4 weeks after RFA. At 4 weeks after RFA, ex vivo high-resolution T2-weighted FSE (TR/effective TE in ms, 4000/57; ETL, 8; FOV, 22 cm; matrix, 512 × 256; slice thickness/gap in mm, 4/0.4; NEX, 4) and T2*-weighted GRE (TR/TE in ms, 440/10; FA, 30; FOV, 22 cm; matrix, 512 x 256; slice thickness/gap in mm, 4/0.4; NEX, 4) images were obtained immediately after euthanizing the rabbits by administering pentobarbital sodium. Two radiologists jointly assessed the in vivo MR images with respect to the reversion of the signal intensity of the non-ablated liver parenchyma and the complications due to RFA. They qualitatively assessed the ex vivo T2*-weighted images for the presence and distribution of hypointense areas in the ablated liver parenchyma as follows: no hypointense area; hypointense area in the periphery of the ablated area; and hypointense area in the center of the ablated area. For quantitative purposes, a region-of-interest (ROI) analysis was performed. The contrast-to-noise ratios (CNRs) of the ablated areas of the 2 groups were calculated and compared using the Student's *t* test. The liver specimens were histopathologically evaluated after hematoxylin-eosin and Prussian blue staining.

Results and Discussion: All the rabbits tolerated RFA and the pre- and post-procedural MR imaging. In all rabbits, the signal intensity of the non-ablated liver parenchyma reverted to sufficiently high values at 4 weeks after RFA. One rabbit in the control group developed hemorrhage in the ablated area leading to fluid level formation at 1 week after RFA. Qualitative analysis of the ex vivo images revealed that 3 of the 4 rabbits in the ferucarbotran group had central hypointense areas (Figure 1), and the remaining 1 had a peripheral hypointense area. Where as, 2 of the 3 rabbits in the control group had no hypointense areas (Figure 2), and the remaining rabbit had a peripheral hypointense area. The individual CNRs were –6.9, –12.8, –7.8, and –2.7 (mean, –7.6; SD, 4.2) in the ferucarbotran group and 9.9, 8.2, and 26.3 (mean, 14.8; SD, 10.0) in the control group. The mean CNR for the ferucarbotran group was significantly lower than that for the control group (P = 0.0472). In all rabbits the ablated area was identified as a central necrotic area surrounded by a fibrous capsule on histopathological evaluation. The hemorrhage observed in the above-mentioned rabbit was confirmed histopathologically and presumably resulted in the peripheral hypointense area observed in the MR images. In both the ferucarbotran and control groups, Prussian blue-positive macrophages were detected in the peripheral fibrous capsule. The presence of iron in the central necrotic tissue could not be proven for the ferucarbotran group. However, we did not observe any histopathological findings, including hemorrhage, that could have caused the signal decay observed on T2*-weighted images in the ferucarbotran group. Further investigation is required to confirm the presence of iron in the central necrotic tissue.

Figure 1

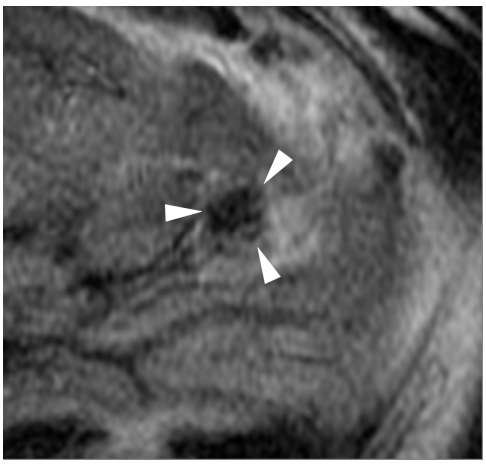
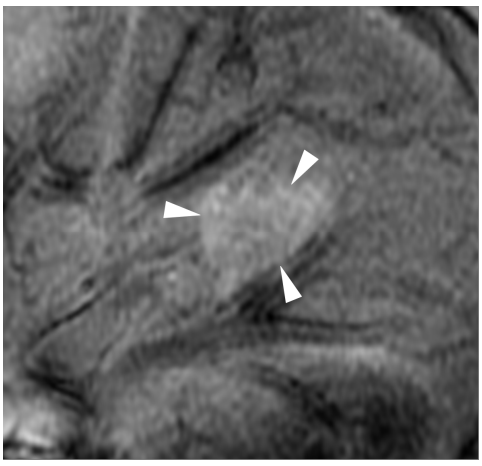


Figure 2



Conclusion: When ferucarbotran was administered before RFA, the signal decay of the ablated liver parenchyma was prolonged for at least 4 weeks. In our study, we could not prove the presence of iron in the ablated central necrotic tissue; however, the combination of MR imaging with the impaired clearance of ferucarbotran can potentially be used to visualize the ablative margin after RFA of the liver.

References:

1. Montorsi M et al. J Gastrointens Surg 2005; 9: 62–68.
2. Hamm B et al. J Magn Reson Imaging 1994; 4: 659–668.