The Mechanism of Ring Enhancement in Malignant Hepatic Tumors on SPIO-Enhanced T1-Weighted Images: An Investigation Into Peritumoral Kupffer Cells

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Synopsis: To investigate the mechanism of ring enhancement on SPIO-enhanced T1W-GRE in malignant focal hepatic lesions, MR imaging findings and Kupffer cell (KC)-stain sections of 18 hepatocellular carcinoma were reviewed. Ring enhancement was noted in 13 of 18 HCC (72%). Peritumoral KC density significantly increased in ring enhancement (+) group as compared with ring (-) group. In ring (+) group, tumor size on T2W was smaller than those on T1W and T2*W, suggesting sustained T1 effect and decreased T2* effect in peritumoral region. Ring enhancement on SPIO-enhanced T1W may correlate with increased KC density and decreased SPIO clustering in KC.

Introduction: Differentiation between malignant and benign lesions is of primary importance in clinical settings. Ring enhancement of focal hepatic lesions on SPIO-enhanced T1-weighted GRE images has been known as a sign of malignancy [1-2]. There have been a few reports about the mechanism of ring enhancement [3], but little is known about the relevance of Kupffer cell (KC) density and its function to this phenomenon. We investigate the mechanism of ring enhancement on T1W-GRE for focal malignant hepatic lesions.

Methods: Between April 2001 and March 2002, 18 consecutive patients underwent SPIO-enhanced MR imaging for assessment of hepatocellular carcinoma (HCC) before surgery. All of 18 patients with 18 HCC were pathologically proved to have HCC. Resected specimens were prepared for KP-1 stain (KC stain) sections. A pathologist reviewed KC density of the HCC itself, peritumoral liver parenchyma, and outer liver parenchyma (far from the tumor), without the knowledge of MR imaging findings. The KC density of HCC itself and peritumoral liver parenchyma was categorized into 5-point scale; 5: markedly increased, 4:slightly increased, 3: same density, 2: slightly decreased, 1: markedly decreased, as compared with KC density of outer liver parenchyma. MR images were obtained at 1.5 T (Signa Horizon LX). All patients underwent breath-hold T2-weighted FSE (2500/80), T1-weighted FSPGR (130/2/90^o), and moderately T2*-weighted FSPGR (130/8.6/60^o) after SPIO administration (10 μmol Fe/kg of ferumoxides). To assess the relationship between the actual tumor size and ring enhancement, the maximum size of the area showing decreased phagocytic activity (high signal intensity as compared with surrounding liver parenchyma) on T2W and T2*W, and that of the area showing ring enhancement on T1W were measured. Every effort was made to reproduce the measurements on MR films using a vernier micrometer.

Results: On SPIO-enhanced T1W-GRE, 14 of 18 HCC showed low signal intensity, two showed iso-intensity, and two high signal intensity as compared with the liver. Thirteen of 18 HCC showed ring enhancement on T1W-GRE (Fig. 1). Peritumoral KC density significantly increased in ring enhancement (+) group as compared with ring (-) group (Fig. 2, Table 1). In terms of tumor size measured on each pulse sequence, the size on T2W-FSE was significantly smaller in ring enhancement (+) group than that on T1W-GRE (ring included) and T2*W-GRE, but the same in ring enhancement (-) group (Table 2).

Discussion and Conclusion: Kanematsu et al [3] presumed that ring enhancement correlated with sinusoidal congestion surrounding malignant hepatic tumors, but they did not refer to KC density and KC function in liver parenchyma bordering the tumor. The mechanism of ring enhancement could be argued differently from their assumption. Mass effect of malignant lesions may compress the surrounding sinusoids and increase KC density but may decrease phagocytic function of KC. Assuming that increased number of KC and smaller size of intracellular SPIO clusters than the outer liver parenchyma occur in peritumoral tissue, water molecules can diffuse in the vicinity of SPIO clusters more frequently than in outer liver parenchyma [4]. T2 relaxation effect is caused by the same manner as T1 relaxation effect, and is maintained in peritumoral tissue. Thus, SPIO clusters in KC close to malignant lesions are smaller than outer KC and cause decreased T2*effect and prominent T1 effect, resulting in ring enhancement on T1W-GRE [Fig. 3]. The fact that tumor size seen on T1W-GRE (ring enhancement included) and T2*W-FSE is larger than that in T2W-FSE, could support this hypothesis. In contrast, mass effect is weak in benign "soft" lesions and HCC without capsules, resulting in the lack of ring enhancement. Ring enhancement on SPIO-enhanced T1W may correlate with increased KC density and decreased SPIO clustering in KC.

References:

1. Mergo PJ, et al. AJR 1996; 166: 379-384.
2. Reimer P, et al. Eur Radiol. 1998; 8: 1198-1204.
3. Kanematsu M, et al. JMRI 2003; 18: 40-48.
4. Tanimoto A, et al. JMRI 2001;14:72-77.

Fig. 1: 71M, HCC: A hypointense mass with ring enhancement (arrow).
T2W (size: 51mm) T1W (57mm) T2*W (56mm)

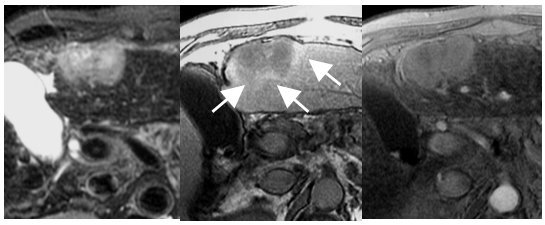

Table 1: Peritumoral and intratumoral KC density (comparison with outer parenchyma)

	Peritumoral KC density (p<0.01)	Intratumoral KC density (NS)
scale	5 4 3 2 1	5 4 3 2 1
ring (+)	4 9 0 0 0	0 0 0 4 9
ring (-)	0 1 4 0 0	0 0 1 0 4

Table 2: Tumor size measured with a vernier micrometer on each pulse sequence (*: size including "ring")

(mm)	T2W	T1W	T1WI*	T2*W	P
ring (+)	43.6	43.2	48.4	47.9	<0.001
ring (-)	26.0	25.3	26.2	26.5	NS

Fig.2: KP1-stain: Peritumoral liver tissue is compressed and KC density is increased (arrows).

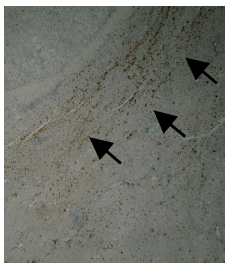

Fig.3: Schematic representation of ring enhancement on T1W.

Peritumoral KC density is increased but intracellular SPIO clustering is suppressed. T1 relaxation effect is maintained (A) but T2* effect is decreased (B) in peritumoral tissue. As a result, a prominent positive enhancement is noted in peritumoral tissue on T1W (C).