PO Box 2345, Beijing 100023, China
Fax: +86-10-85381893
E-mail: wjg@wjgnet.com www.wjgnet.com

World J Gastroenterol 2002;8(1):82-86
World Journal of Gastroenterology
 ISSN 1007-9327

• LIVER CANCER •

Characterization of focal hepatic lesions with SPIO-enhanced MRI

Wei-Wei Zheng, Kang-Rong Zhou, Zu-Wang Chen, Ji-Zhang Shen, Cai-Zhong Chen, Shu-Jie Zhang

Wei-Wei Zheng, Kang-Rong Zhou ,Zu-Wang Chen, Ji-Zhang Shen, Cai-Zhong Chen, Shu-Jie Zhang, Department of Radiology, Affiliated Zhongshan Hospital, Medical College of Fudan University, Shanghai 200032, P.R.China
Supported by the Health Ministry Programme No.97030220
Correspondence to: Dr. Wei Wei Zheng, Department of Radiology, Zhongshan Hospital, Medical Center of Fudan University, 180 Fenglin Road, Shanghai 200032, China. Viviannc@online.sh.cn
Telephone: +86-21-64041990 Ext.2416
Received 2001-08-08 **Accepted** 2001-08-23

Abstract

AIM: **To evaluate the value of superparamagnetic iron oxide (SPIO) enhanced MRI in characterizing focal hepatic lesions.**

METHODS: **Forty-three patients (32 men, 11 women, mean age 51 years, age range 25-74 years) with previously identified focal hepatic lesions were enrolled into this study. All the patients underwent plain,Gd-DTPA enhanced MRI and the SPIO enhanced MRI 1-7 d later. The surgico-pathologic diagnosis was aestablished in 31 cases and the diagnosis in other 12 cases was made on the basis of clinical findings and biochemical tests. The signal changes of lesions were analyzed and the CNRs of lesion-to-liver were measured before and after SPIO enhancement. The data were analyzed by paired *t* test.**

RESULTS: **Focal hepatic lesions included primary hepatocellular carcinoma (HCC, *n*=22), hemangioma (*n*=5), cyst (*n*=4), metastases (*n*=5), cirrhotic nodule (*n*=4), focal nodular hyperplasia (FNH, *n*=5) and other miscellaneous lesions (*n*=6). After SPIO enhancement HCC demonstrated iso- or slight hyperintensity on T1WI and moderate hyperintersity on T2WI, hemangioma showed moderate hyperintensity on T1WI and obvious hyperintensity on T2WI, the SI of cyst had no change either on T1WI or on T2WI, cirrhotic nodules revealed iso-intensity on T2WI, and the SI of FNH decreased significantlyon T2WI. No specific manifestations were found in the other 6 miscellaneous lesions after SPIO enhancement.**

CONCLUSION: **SPIO enhanced-MRI can improve the characterization confidence for diagnosis of focal hepatic lesions.**

Zheng WW, Zhou KR, Chen ZW, Shen JZ, Chen CZ, Zhang SJ. Characterization of focal hepatic lesions with SPIO-enhanced MRI. *World J Gastroenterol* 2002;8(1):82-86

INTRODUCTION

Superparamagnetic iron oxide (SPIO) is a newly developed tissue-specific contrast material. Intravenously administrated SPIO particles can be specifically taken up by reticulo-endothelial system, and the signal intensities of normal hepatic and splenic parenchyma are significantly decreased on MR images. Therefore, it has been widely applied for lesion detection in the liver[1-6]. After SPIO-enhancement the detectablity of focal hepatic lesions smaller than 1cm could be increased from 65.9% to 97.5%. However, to our knowledge, the previously reported studies were mainly concerned about the detection of hepatic metastatic lesions and only a few studies focused on the characterization of focal hepatic lesions[4-13]. Thus, the purpose of this study is to evaluate the diagnostic value of superparamagnetic iron oxide in demonstrating benign and malignant focal hepatic lesions.

MATERIAL AND METHODS

Patients

Forty-three patients (32 men, 11 women, mean age 51 years, age range 25-74years) with previously identified focal hepatic lesions were enrolled into this study. The pathologically proven diagnosis was achieved in 31 cases and the other 12 cases were diagnosed on the basis of clinical findings and biochemical tests. Most lesions were smaller than 3cm. Three cases previously suspected of having focal hepatic lesion were finally confirmed as cirrhotic nodules after SPIO-enhancement. In the remaining 40 patients showed multiple hepatic lesions were found in 22 and solitary in 18, including malignant lesions in 29 cases and benign lesions in 11 cases. The malignant lesions included: primary hepatocellular carcinoma (HCC, *n*=22) associated with hemangioma or cyst in 4, cholangiocarcinoma with cysts (*n*=1),and cholangiohepatocarcinoma (*n*=1), metastases (*n*=5). The benign lesions included: multiple hemangiomas (*n*=2), focal nodular hyperplasia (FNH, *n*=5), angiolipoleiomyoma (*n*=1), inflammatory pseudotumor with hemangioma and cysts (*n*=1), multiple abscess (*n*=1) and focal inflammation with hemangioma (*n*=1).

Contrast agent

Gadopentetate dimeglumine (Magnevist; Schering, Berline, Germany) was manually administered through antecubital intravenous bolus of 0.1mmol/kg. Feridex (Advanced Magnetics, USA) is an iron oxide preparation coated with low-molecular-weight dextan available in 5mL vial containing 11. 2mg iron and 61.3mg mannitol/mL. Feridex at a dose of 0. 05mL·kg^{-1} (0.56mg Fe·kg^{-1}) was diluted with 100mL of 5g·L^{-1} glucose and infused intravenously at a rate of 3mL·min^{-1}.

Imaging procedure

The GE Signa 1.5T MR imaging system was used. The whole procedure including: ① non-enhanced images: SE T1-weighted (TR/TE=540ms/15ms), FSE T2-weighed with fat suppression (TR/TE=3000-4000ms/98ms); ② Gd-DTPA enhanced images: FMPSPGR with dynamic enhancement; and ③ SPIO-enhanced images: 1-7 d later, SE T1-weighed, FSE T2-weighed, FSE T2-weighed with fat suppressed sequences, were performed after SPIO administration. Transverse images were obtained with a slice thickness of 8mm, a section gap of 1-2mm, a field of view of 360mm and matrix size of 256×160.

Imaging analysis

The images were reviewed by 3 experienced radiologists. The signal intensities (SI) of normal hepatic parenchyma, hepatic lesions and

signal change of lesion-to-liver were measured before and after administration of SPIO. Regions of interest (ROI) with at least 50 pixels on homogeneous background free of artifacts. ROI were chosen to be representative of the tissue being evaluated. Measurements were made at the same anatomic level for unenhanced and enhanced images in each patient. If patient had multiple lesions with the homogeneous character, the typical one was selected, otherwise the lesions were analyzed individually.

RESULTS

Totally 12 kinds of benign and malignant diseases were observed in 43 patients. The CNR of lesion-to-liver was evaluated on each sequence (Tables 1 and 2). After SPIO-enhancement the ratios of lesion-to-liver were significantly raised on T1-weighed images except that of cyst, while on T2-weighed images the hepatic cirrhoticnodules and FNH's ratios of lesion-to-liver showed no significant difference before and after SPIO-enhancement.

Table 1 The CNR of lesion-to-liver on T_1WI

Lesion (cases)	T_1WI	SPIO-enhancedT_1WI	*P*
HCC (22)	-10.2±8.3	19.9±23.8	<0.001
Hemangioma (5)	-16.4±8.6	71±33	<0.05
Cyst (4)	-457±12.1	-33.7±17.9	>0.05
Metastases (5)	-15.4±9.3	6.8±28.1	<0.05
Cirrhosis nodules (4)	2.3±9.3	21.3±17	<0.05
FNH (5)	-4.3±14.1	18.8±18.6	<0.05
Cholangiocarcinoma (1)	-32	0	-
inflammatory pseudotumor (1)	-15	47	-
Hepatic abscess (1)	-19	1	-
Focal inflammatory lesion (1)	-17	12	-
Angiolipoleiomyoma (1)	16	85	-
Cholangiohepatocarcinoma (1)	-5	34	-

Table 2 The CNR of lesion-to-liver on T_2WI

Lesion (cases)	T_2WI	SPIO-enhancedT_2WI	*P*
HCC (22)	98.39±58.59	465.77±272.73	<0.001
Hemangioma (5)	354.57±119.78	1452.63±205.68	<0.001
Cyst (4)	509.48±145.02	1256.33±333.39	<0.001
Metastases (5)	104.36±52.02	416.11±324.94	<0.05
Cirrhosis nodules (4)	16.34±15.76	13.77±12.54	>0.05
FNH (5)	65.78±68.4	77.5±104.7	>0.05
Cholangiocarcinoma (1)	63.33	766.95	-
inflammatory pseudotumor (1)	45.58	618.01	-
Hepatic abscess (1)	114.97	587.55	-
Focal inflammatory lesion (1)	89.33	575.53	-
Angiolipoleiomyoma (1)	145.26	523.91	-
Cholangiohepatocarcinoma (1)	106.09	1390.6	-

HCC was found in 22 patients. The lesions were iso- or hypointense on T1-weighed images and slightly hyperintense on T_2-weighed images before enhancement. After SPIO administration, 11 cases of the lesions became slightly hyperintense, 10 were isointense and 1 was hypointense on T_1WI, while on T_2WI all lesions appeared hyperintense. The mean CNRs of lesion-to-liver on T1WI and T_2WI were greatly improved from -10.2±8.3, 98.4±58.6 to 19.9±23.8, 465.8±272.7 respectively after SPIO administration. The difference had statistical significance (P<0.001). After Gd-DTPA administration, 17 cases showed obvious enhancement while the other 5 cases enhanced mildly in early phase. Characteristically, the signal intensity or enhancement of the lesions decreased significantly in portal and delayed phases (Figure 1A-C).

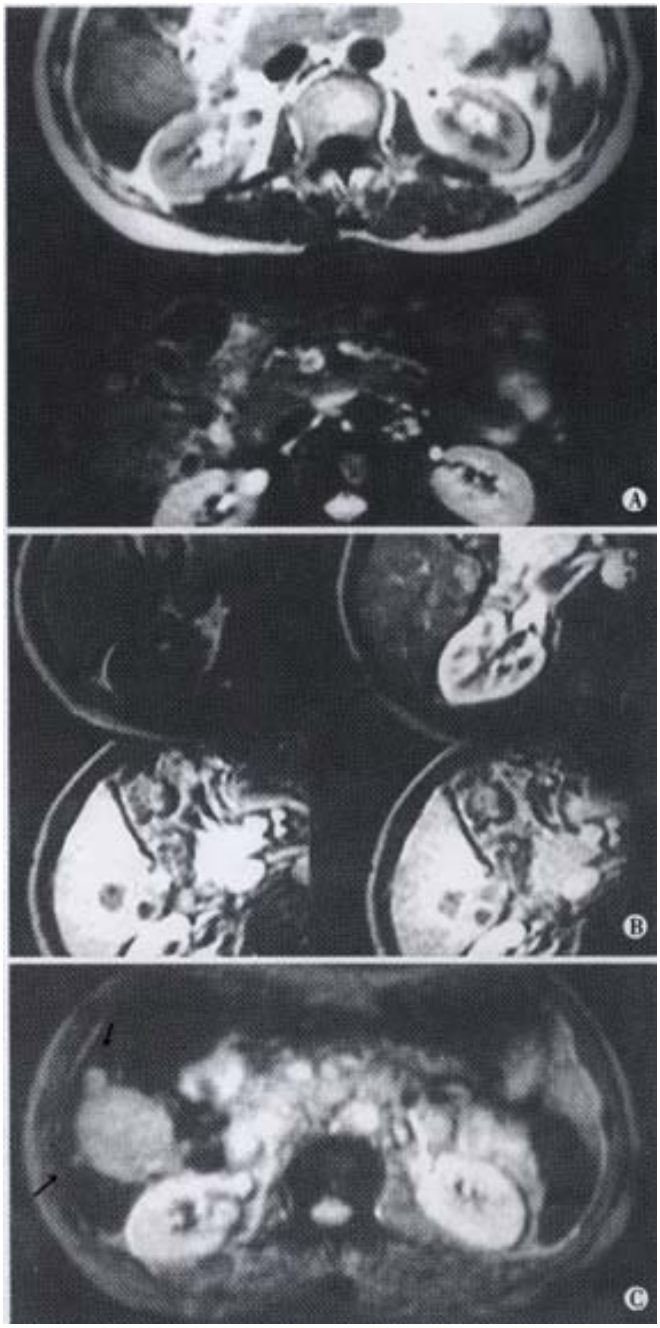

Figure 1 Primary hepatocellular carcinoma in posterior right lobe. The lesions appear hypointenity on T_1WI and mildly hyperintensity on T_2WI (A). On Gd-DTPA enhanced images, early enhancement can be seen in arterial phase and appear relatively hypointensity in portal phase.(B) On SPIO-enhanced image, the conspicuity is clearer than pre-contrasted and Gd-DTPA enhanced images. Two micro-lesions(arrow) are obviously showed (C).

Hepatic hemangioma was revealed in 5 cases. The lesions were iso- or hypointense on T_1WI and markedly hyperintense on T_2WI in pre-contrast images. After SPIO-enhancement distinct SI increase was noted and the CNR of lesion-to-liver increased from -16.4±8.6 to 71±33 (P<0.05) on T1WI. The signal intensity showed no perceivable change on T_2WI ,but the CNR of lesion-to-liver was greatly increased because of the signal loss of the background after SPIO administration (Figure 2A, B). After Gd-DTPA enhancement, the lesions were gradually filled by the contrast from peripheral to central area and were kept hyperintense in portal and delayed phases.

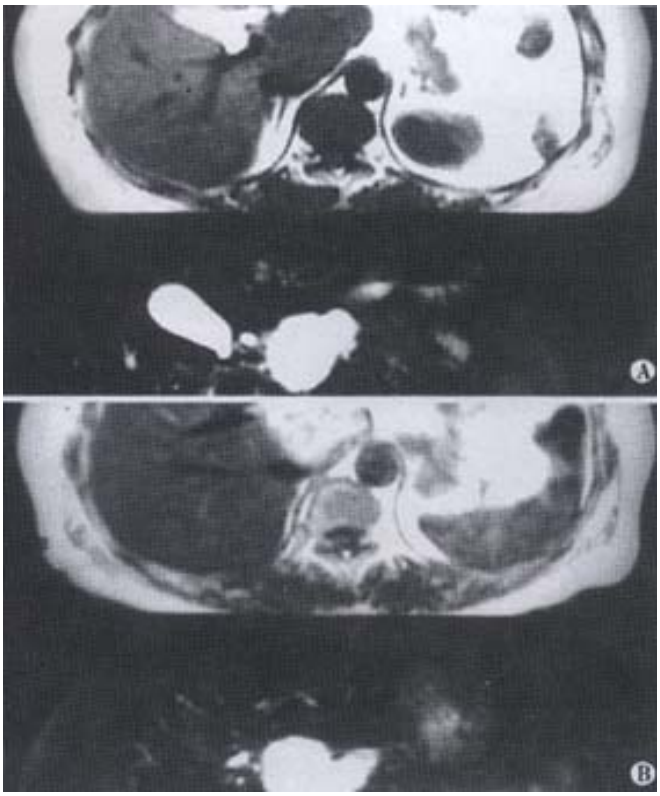

Figure 2 Hepatic hemangioma. (A) The lesion shows hypointensity on T_1WI and hyperintensity on T_2WI on pre-contrast images.(B) After SPIO administration, the lesion become hyerintense on both T1WI and T2WI (arrow).

Hepatic cyst was found in 4 patients. The SI of the cyst had no change after SPIO-enhencement. The hypointensity of cystic lesions on T1WI after SPIO-enhancement was characteristic,thus it could be distinguished from other focal hepatic lesions. The hepatic cyst showed no enhancement after Gd-DTPA administration.

Metastasis was observed in 5 cases. The lesions were hypointense on T_1WI pre-enhancement and iso- or hypointense during post-enhancement. On T_2WI they were mildly hyperintense before enhancement and relatively hyperintense after enhancement because of obvious signal decrease of adjacent normal liver parenchyma. Such change of SI had no diagnostic value because many other focal hepatic lesions could have the similar appearance after SPIO enhancement. The appearance of lesions varied after Gd-DTPA administration, most of them showed peripheral enhancement, or with " bull eyes" sign, or only slightly enhanced.

Cirrhotic nodule was found in 4 patients, which was associated with HCC in one patient. On pre-contrast T_1WI cirrhotic nodules appeared slightly hyperintense differing from other focal hepatic lesions. That the cirrhotic nodule contained Kupffer cells which could take up SPIO particles made it have the same SI as that of the surrounding liver parenchyma after SPIO administration. The cirrhotic nodules showed no early enhancement after Gd-DTPA administration and pertained iso- or hypo-intense in portal and delayed phases.

Focal nodular hyperplasia (FNH) was observed in 5 cases. The lesions were slightly hypointense on unenhanced T_1WI. The appearances of FNH on T_2WI were variable and could be hyperintense(n=2), heterogeneously intense(n=2) and iso-intense(n=1) which was unable to be detected. After SPIO-enhancement, SI of the lesion decreased markedly and appeared iso- or slightly hyper-intense on T_2WI,which was characteristic for FNH. On Gd-DTPA enhanced image, the manifestation was also characteristic: it was obviously enhanced in early phase and continuously kept hyperintense in portal and delayed phases (Figure 3A-C).

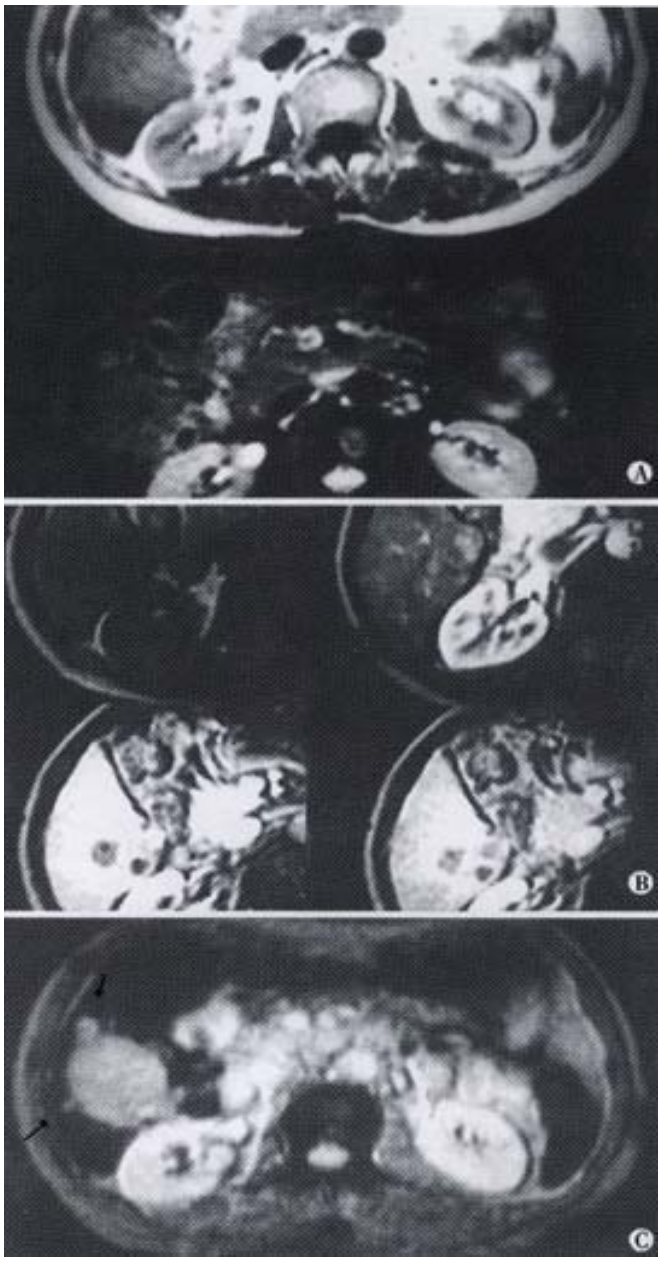

Figure 3 Focal nodular hyperplasia(FNH). Before enhancement, the lesion (arrow) presents hypointensity on T_1WI and heterogeneous hyerintensity on T_2WI (A). After Gd-DTPA administration, the lesion is obviously enhanced in arterial phase and remains hyperintense in portal and delayed phase (B). On T_2WI after SPIO enhancement, the lesion(arrow) has focal signal loss compared with the un-enhanced image (C).

Other focal hepatic lesions were found in 6 cases including cholangiocarcima (n=1), inflammatory pseudotumor (n=1), hepatic abscess (n=1), focal inflammatory lesion (n=1), angiolipoleiomyoma (n=1), and cholangiohepatocarcinoma (n=1). These lesions were hypointense on T1WI and slightly or moderately hyperintense on T2WI before enhancement. The appearances were non-specific after SPIO-enhancement although the contour of lesions was clear and the CNR of lesion-to-liver increased, which was helpful in improving the detectablity or conspicuity. The appearances of these lesions on Gd-DTPA enhanced images were also diversified.

DISCUSSION

As a non-specific extracellular contrast material, Gd-DTPA has been widely used in MR imaging of the liver. Dynamic Gd-DPTA-

enhanced MR images can provide much useful information of the blood supply of lesions and thus highly improving the accuracy of diagnose of focal hepatic lesions. However, Gd-DTPA has several disadvantages such as non-specific distribution, quickly reaching equilibrium throughout extracellular compartment and having slightly nephrotic toxicity. As a negative contrast material, namely reticulo-endothelial system specific contrast agent, the particles of SPIO can be taken up primarily by the hepato-splenic Kupffer cells. The collection of SPIO particles can produce a focal heterogeneous magnetic field which shortens T2 relaxation time predominantly, leading to a significant decrease of SI of normal hepatic parenchyma and remarkable improvement for the focal lesion detection. The prolonged half-life time and widened scanning time-window are also helpful in making examination more convenient[1,4,5,13-15,17].

The signal intensity of normal hepatic parenchyma decreased both on T_1WI and T_2WI after SPIO-enhancement, especially on T_2WI. The SI of HCC changed a little due to lack of Kupffer cells, but the signal loss of background inversely makes the HCC appear hyperintense. As a result ,the CNR of lesion-to-liver increased and the detection of HCC after SPIO-enhancement being improved. There are a few of reports dealing with the appearance of HCC on SPIO-enhanced MR images[9,14,17-22]. Grangier described HCC's feature in 10 cases after SPIO enhancement and concluded that the HCC presenting iso-intensity on TIWI was the key point for differentiating HCC from hemangioma and cyst[11]. However, we believe that it might be inappropriate because the appearances of HCC in our 22 cases on enhanced-T_1WI were slightly hyper-intense, isointense and hypointense which were 50% (11/22), 45. 5% (10/22) and 4.5% (1/22) respectively. This might be attributed to more examples in our study or the difference of HCC's differentiation between the two studies.The non-characteristic appearances of HCC on pre- and post-SPIO-enhanced T_2WI made it difficult to distinguish from other malignant lesions. Moreover, the signal changes on pre- and post-enhanced T_1WI can exclude the possibility of hemangioma and cyst. Accordingly, the accurate diagnosis of HCC must not merely rely on the appearance of lesion on SPIO-enhanced MRI but on the combination with the clinical findings and biochemical tests. After Gd-DTPA administration, the precise diagnosis in most cases can be made according to the enhancement pattern of the lesion. Typically, HCC is enhanced rapidly in arterial phase and the contrast agent is soon washed out in portal phase. So we believe that, only for those the diagnoses are indefinite or the appearances of lesion are untypical on Gd-DTPA-enhanced images, SPIO-enhanced MRI could be a method of choice to make further diagnosis[17-21].

The hemangioma had high SI on unenhanced T_2WI and showed no change on SPIO-enhanced T_2WI. The hemangioma presenting moderate hyper-intensity on T_1WI after SPIO-enhancement is a key point to distinguish it from cyst and other focal hepatic lesions. However, such typical appearance did not present, owing to the partial volume effect in tiny hemangioma in our study ,manifesting iso- or slight hyper-intensity on post-enhanced T_1WI which might make the diagnosis confused. Grangier and Hahn *et al* reported that on SPIO-enhanced T_2WI, the SI of hemangioma could decrease significantly and its enhancement pattern was as the same as that on Gd-DTPA enhanced T1WI (the lesion was filled with contrast agent gradually)[10,11]. Although the signal of lesion decreased a little, 11 lesions of 5 patients in our study had no such appearance and remained hyper-intensitive namely "Bright Bulb" on SPIO-enhanced T_2WI. Whether such difference is attributed to the different dosage of contrast agent used in studies (10(mol $Fe \cdot kg^{-1}$ in our group vs 15(mol $Fe \cdot kg^{-1}$ in others) needs further investigations.

SPIO has unique advantages in diagnosing liver cirrhotic nodules and FNH. Both contain Kupffer cells which can take up the SPIO particles. Accordingly, on post-contrast T_2WI, the former showed identical intensity to that of adjacent normal hepatic parenchyma and the latter had signal loss of different degree. Hepatic cirrhotic nodule and FNH were the only two diseases that had signal loss in our study.As hepatic cirrhotic nodules usually have a cirrhosis background, the lesion presented the SI similar to that of surrounding liver parenchyma after SPIO-administration and no early enhancement after Gd-DTPA administration is the key factorto make the accurate diagnosis. In our study there were 3 liver cirrhotic nodules, which had difficulty in characterization on pre- and Gd-DTPA enhanced MR images, accurate diagnoses were made after SPIO-administration. Thus, SPIO-enhanced MRI is supposed to be the first choice when the cirrhotic nodule is suspected to be associated with early stage of canceration and has no obvious early enhancement after Gd-DTPA administration[15]. FNH has no cirrhotic background with abnormally arrayed lobuli hepatis. The various appearances on pre-contrast T_2WI might be corresponding to its different cellular components. Most lesions were iso- or slightly hyperintense on T_2WI and had signal loss on SPIO-enhanced image. The CNR of lesion-to-liver had no statistical significance between pre- and post-contrast images in our study. This can exactly demonstrate that Kupffer cell in FNH uptake the contrast media and decrease the SI while the background has signal loss at the same time (the mean SI of lesion and liver decreased from 138.6 to 43 and 85.3 to 23.6 respectively on pre- and post-contrast images). The change of SI was different from other diseases and had statistical significance (P<0.05). The central scar was reported to present as mildly hyperintense and 2 cases in our study had this appearance. The characterized appearance of FNH on Gd-DTPA enhanced MR image demonstrated markedly early enhancement as homogeneous hyperintense and iso- to slightly hyperintense in portal or delayed phase. Central scarin 3 lesions enhanced in delayed phase. The results in our study were consistent with other report[24-29].

Cyst had no signal change on both pre- and post-contrast T_1W, and T_2W images. There were 4 inflammatory cases and 1 case of abscess in our study which had no visible difference on pre- and post- SPIO enhanced images. Diagnoses were made only by Gd-DTPA enhanced images and confirmed after clinical antibiotics treatment and follow-up. One case of inflammatory pseudotumor was pathologically proven[30]. One case of cholangiocarcinoma was diagnosed mainly on Gd-DTPA enhanced images which provided more information of the blood supply of lesions. Another case of angiolipoleiomyoma was misdiagnosed as HCC before surgery on both Gd-DTPA and SPIO-enhanced images because it had early enhancement and no SPIO uptake. When retrospectively reviewed, the patchy hyperintensity on T_1W and T_2W images corresponding to fatty component might suggest the diagnosis. Since there was no obvious difference of SI, SPIO-contrasted image had little specificity in diagnosing such hepatic inflammation, cholangiocarcinoma and angiolipoleiomyoma[30-33]. To characterize these lesions, SPIO-enhanced image was inferior to Gd-DTPA image although the lesions showed better circumscription.

As a specific MR contrast media, there is no doubt that SPIO has superiority in detection of hepatic micro-lesions. It is also useful in characterization of somelesions and is superior to unenhanced MR with Gd-DTPA enhanced image when differential diagnosis of HCC, FNH and cirrhotic nodule is needed. As most hepatic lesions could be precisely diagnosed by conventional MR combined with Gd-DTPA dynamic contrast enhancement, SPIO-enhanced image would be a supplementary modality to those which are difficult to be defined.

REFERENCES

1 Peter F, Sanjay S. Liver-specific MR imaging contrast agents. *Radiol Clin North Am* 1998;36:287-296
2 Anthony B, Janice W, Daniel W, *et al*. Hepatic lesion detection at MR imaging: A comparative study with four sequences. *Radiology* 1997; 203:759-765
3 Fretz CJ, Elizondo G, Weissleder R, Hahn PF, Stark DD, Ferrucci JT. Superparamagnetic iron oxide-enhanced MR imaging: Pulse sequence optimization for detection of liver cancer. *Radiology* 1989;172:393-397
4 Masayuke M, Kanematsu M, Itoh K, Maetani Y, Kondo H, Matsunaga N, Hoshi H, Shiraishi J. Detection of malignant hepatic tumors:

comparison of Gadolinium- and Ferumoxide-enhanced MR imaging. *AJR* 2001;177:637-643
5 Taylor PM, Hawnaur JM, Hutchinson CE. Superparamagnetic iron oxide imaging of focal liver Disease. *Clinical Radiology* 1995;50:215-219
6 Lwakatare F, Yamashita Y, Nakayama M, Takahashi M. SPIO-enhanced MR imaging of focal fatty liver lesions. *Abdom Imaging* 2001;26:157-160
7 Ros PR, Freeny PC, Harms SE, Seltzer SE, Davis PL, Chan TW, Stillman AE, Muroff LR, Runge VM, Nissenbaum MA. Hepatic MR imaging with ferumoxides: a multicenter clinical trial of the safety and efficacy in the detection of focal hepatic lesions. *Radiology* 1995; 196:481-488
8 Winter TC, Freeny PC, Nghiem HV, Mack LA, Patten RM, Thomas CR, Elliott S. MR Imaging with IV superparamagnetic ironoxide: efficacy in the detection of focal hepatic lesions. *AJR* 1993;161:1191-1198
9 Bluemke DA, Paulson EK, Choti MA, DeSena S, Clavien PA. Detection of hepatic lesions in candidates for surgery: comparison of Ferumoxides-enhanced MR imaging and dual-phase helical CT. *AJR* 2000;175:1653-1658
10 Bellin NB, Zaim S, Auberton E, Sarfati G, Duron VJ, Khayat D, Grellet J. Liver metastases: Safety and efficacy of detection with superparamagnetic iron oxide in MR imaging. *Radiology* 1994;193:657-663
11 Grangier C, Tourniaire J, Mentha G, Schiau R, Howarth N, Chachuat A, Grossholz M, Terrier F. Enhancement of liver hemangiomas on T1-weighted MR SE images by superparamagnetic iron oxide particles. *J Comput Assist Tomagr* 1994;18:888-896
12 Hahn RF, Stark DD, Weissleder R, Elizondo G, Saini S Ferrucci JT. Superparamagnetic iron oxide:Clinical application to imaging tissue perfusion in vascular liver tumors. *Radiology* 1990;174:361-366
13 Grandin C, Van Beers BE, Robert A, Gigot JF, Geubel A, Pringot J. Benign hepatocellular tumors:MRI after superparamagneticiron oxide administration. *J Comput Assist Tomogr* 1995;19:412-418
14 Parley MR, Mergo PJ, Torres GM, Ros PR. Characterization of focal hepatic lesions with Ferumoxides-enhanced T2-weighted MR imaging. *AJR* 2000;175:159-163
15 Clement O, Frija G, Chambon C, Schouman-Clayes E, Mosnier JF, Poupon MF, Balkau B. Liver tumors in cirrhosis: experimental study with SPIO-enhanced MR imaging. *Radiology* 1991;180:31-36
16 Krinsky GA, Lee VS, Theise ND, Weinreb JC, Rofsky NM, Diflo T, Teperman LW. Hepatocellular carcinoma and dysplastic nodules in patients with cirrhosis: prospective diagnosis with MR imaging and explantation correlation. *Radiology* 2001;219:445-454
17 Fernandez MDP, Redvanly R. Primary hepatic malignant neoplasms. *Radiol Clin North Am* 1998;36:333-348
18 Reimer P, Jahnke N, Fiebich M, Schima W, Deckers F, Marx C, Holzknecht N, Saini S. Hepatic lesion detection and characterization value of nonenhanced MR imaging,superparanagnetic iron oxide-enhanced MR imaging, and spiral CT -ROC analysis. *Radiology* 2000; 217:152-158
19 Arbab AS, Ichikawa T, Araki T, Toyama K, Nambu A, Ohsawa S, Kumagai H, Aikawa Y. Detection of hepatocellular carcinoma and its metastases with various pulse sequences using superparamagnetic iron oxide (SHU-555-A). *Abdom Imaging* 2000;25:151-158
20 Kondo H, Kanematsu M, Hoshi H, Murakami T, Kim T, Hori M, Matsuo M, Nakamura H. Preoperative detection of malignant hepatic tumors: comparison of combined methods of MR imaging with combined methods of CT. *AJR* 2000;174:947-954
21 Mori K, Yoshioka H, Itai Y, Okamoto Y, Takahashi N, Saida Y. Arterioportal shunts in cirrhotic patients: Evaluation of the difference between tumorous and nontumorous arterioportal shunts on MR imaging with superparamagnetic iron oxide. *AJR* 2000;175:1659-1664
22 Hahn PF, Stark DD, Weissleder R, Elizondo G, Saini S, Ferrucci JT. Clinical Application of superparamagnetic iron oxide of MR imaging of tissue perfusion in vascular liver tumors. *Radiology* 1991;174:361-366
23 Paley MR, Ros PR. Hepatic metastases. *Radiol Clin North Am* 1998;36: 349-368
24 Mergo PJ, Ros PR. Benign lesions of the liver. *Radiol Clin North Am* 1998;36:319-332
25 Mortele KJ, Praet M, Van Vlierberghe H, *et al*. CT and MR imaging findings in focal nodular hyperplasia of the liver: radiologic-pathologic correlation. *AJR* 2000;175:687-692
26 Carlson SK, Daniel JC, Bender CE, Welth TJ. CT of focal nodular hyperplasia of the liver. *AJR* 2000;174:705-712
27 Ji Y, Zhu XZ, Tan YS, Zeng HY, Ye QH, Tang ZY. A clinicopathological study of hepatic focal nodular hyperplasia. *Zhonghua Binglixue Zazhi* 2000;29:334-336
28 Yi Y, Zhu XZ, Sun HC, Tan YS, Ma ZC, Ye QH, Sujie A, Tang ZY. Hepatocellular adenoma and focal nodular hyperplasia: a series of 24 patients with clinicopathological and radiological correlation. *Chinese Medical Journal* 2000;113:852-857
29 Ruppert-Kohlmayr AJ, Uggowitzer MM, Kugler C, Zebedin D, Schaffler G, Ruppert GS. Focal nodular hyperplasia and hepatocellular adenoma of the liver: differentiation with multephasic helical CT. *AJR* 2001;176:1493-1498
30 Yan FH, Zhou KR, Jiang YP, Shi WB. Inflammatory pseudotumor of the liver:13 cases of MRI findings. *World J Gastroenterol* 2001;7:422-424
31 Ye HY, Xie ZF, Gao YG, Liang Y, Ji XL, Yu G. Hepatic angiomyolipoma: correlation of MRI and pathologic findings. *Zhonghua Fangshexue Zazhi* 2001;35:679-681
32 Braga HJ, Imam K, Bluemke DA. MR imaging of intrahepatic cholangiocarcinoma: use of Ferumoxides for lesion localization and extension. *AJR* 2001;177:111-114
33 Ahmadi T, Itai Y, Takahashi M, Onaya H, Kobayashi T, Tanaka YO, Matsuzake Y, Tanaka N, Okada Y. Angiomyolipoma of the liver: significance of CT and MR dynamic study. *Abdom Imaging* 1998;23:520 -526

Edited by Ma JY