

# Diagnostic Performance of Gadoteric Acid-Enhanced MR Imaging in the Diagnosis of Hepatocellular Carcinoma in Cirrhotic Liver

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**Objective:** To determine the diagnostic performance and the added value of hepatobiliary phase images in Gadoteric acid-enhanced magnetic resonance (MR) imaging in the evaluation of HCC in cirrhotic liver.

**Material and Method:** Between July 2011 and October 2012, 14 cirrhotic patients with 34 hepatic nodules underwent hepatic Gadoteric acid-enhanced MR imaging. Two radiologists reviewed in consensus, the two sets of Gadoteric acid-enhanced MR images in a retrospective fashion. Set 1 of MR images include unenhanced and Gadoteric acid-enhanced dynamic images, and set 2 of MR images include unenhanced, Gadoteric acid-enhanced dynamic, and hepatobiliary phase images. The diagnostic performance of the two sets of Gadoteric acid-enhanced MR imaging in the diagnosis of HCC were assessed. Comparison of sensitivity, specificity, and accuracy between the two imaging sets according to the lesion size were made.

**Results:** Higher sensitivity (between 95% and 75%) and negative predictive value (between 87.5% and 68.8%) were demonstrated on set 2 of MR images (addition of hepatobiliary phase images). No difference of accuracy (76.5%) between the two imaging sets were found. Excellent sensitivities (100%), specificities (100%), and accuracies (100%) in both imaging sets were shown in lesions more than 2 cm in diameter. Higher sensitivity (between 91.7% and 58.3%) were seen in the diagnosis of small hepatocellular carcinoma (HCC) group (less than 2 cm) with the addition of the hepatobiliary phase images.

**Conclusion:** Gadoteric acid-enhanced MR imaging has an excellent diagnostic performance for diagnosis of more than 2 cm-HCCs in cirrhotic liver; but still limited in small HCCs. Added hepatobiliary phase images in dynamic Gadoteric acid-enhanced MR imaging improve detection of small HCCs.

**Keywords:** Hepatocellular carcinoma, Gadoteric acid-enhanced MR imaging, Hepatobiliary phase images

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Hepatocellular carcinoma (HCC) is the most common primary liver cancer and the third leading cause of cancer-related death in the world<sup>(1)</sup>. Most HCCs develop in patients with underlying liver cirrhosis secondary to chronic viral hepatitis (B or C), alcohol intake, non-alcoholic fatty liver disease, and inherited metabolic diseases<sup>(2)</sup>. Early detection of HCC is of great importance, and the imaging examination plays a vital role for early detection and diagnosis. Recent clinical practice guidelines by the European Association for the Study of the Liver and the European Organisation for Research and Treatment of Cancer (EASL-EORTC) and the American Association for the Study of Liver Diseases (AASLD)<sup>(2,3)</sup> recommend that the surveillance programs should be performed in all

at-risk populations using abdominal ultrasound every six months. When any nodule larger than 1 cm is found in cirrhotic liver, cross-sectional imaging of liver including 4-phase multidetector computed tomography (MDCT) or/and dynamic contrast enhanced magnetic resonance (MR) imaging should be performed<sup>(2,3)</sup>. Non-invasive diagnosis is organized when the HCC radiological hallmarks (arterial hypervascularity and venous/late phase washout) are shown<sup>(2,3)</sup>. However, several previous studies<sup>(4-9)</sup> found that the detection and diagnosis of small HCC (2 cm or smaller) was still problematic by using multiphasic MDCT and dynamic contrast enhanced MR imaging. Poor and variable sensitivities of both imaging examinations were seen, ranging from 30 to 65% for multiphasic MDCT and 35 to 66% for dynamic contrast enhanced MR imaging. Atypical imaging appearances are frequently seen in small HCC and well-differentiated HCC. The previous investigators<sup>(10,11)</sup> found that 87% of well-differentiated HCCs and 41 to 62% of small HCCs showed either

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absence of arterial hypervascularity, venous washout, or both. Whenever, the diagnosis is based on vascular enhancement pattern alone, it may lead to under-detection and under-diagnosis of small or well-differentiated HCC.

A new combined extracellular-hepatobiliary contrast agent has been developed, gadolinium-ethoxybenzyl diethylenetriaminepentaacetic acid (Gd-EOB-DTPA), also known as gadoxetate disodium or gadoxetic acid (Primovist®, Bayer Schering Pharma, Germany)<sup>(12)</sup>. This contrast agent combines the properties of a conventional extracellular contrast agent that evaluating tissue vascularity, and a hepatobiliary agent that assessing hepatocyte function<sup>(12)</sup>. Accordingly, it may overcome some of the limitations of pure extracellular agents for detection and diagnosis of HCC with atypical enhancement pattern. Previous studies<sup>(4,5,8)</sup> reported that gadoxetic acid-enhanced MR imaging showed better diagnostic performance for detection and diagnosis of HCC, especially in cases of small HCC.

The purpose of the present study was to determine the diagnostic performance and the added value of hepatobiliary phase images in Gadoxetic acid-enhanced MR imaging in the evaluation of HCC in cirrhotic liver.

## **Material and Method**

### ***Study populations and standard of reference***

The present retrospective study was approved by the Institutional Ethic Committee, and informed consent was waived. Between July 2011 and October 2012, 55 consecutive patients with liver cirrhosis, suspected of having HCC [possible focal hepatic lesions at ultrasonography (US) or multiphasic MDCT, or elevated serum alpha-fetoprotein (AFP) level] underwent hepatic gadoxetic acid-enhanced MR imaging. Forty-one of 55 patients were excluded from the study by the following reasons: inaccessible medical records/incomplete MR imaging information (n = 1), lacks of pathologic confirmation and follow-up imaging by US, CT, or MR imaging performed at least one year after initial MR imaging (n = 39), known cases of HCC with treatment history of transarterial chemoembolization (TACE) or radiofrequency ablation (RFA) (n = 1). The remaining 14 patients were enrolled in the present study (8 men and 6 women, age range 44 to 79 years, mean age 61.5 years). All patients had cirrhotic liver, diagnosed by the combination of radiologic findings, clinical settings, and laboratory evidences. Five patients (5/14, 35.7%) had chronic

hepatitis B-related cirrhosis, six (6/14, 42.9%) had chronic hepatitis C-related cirrhosis, one (1/14, 7.1%) had autoimmune hepatitis and the remaining two (2/14, 14.3%) had cryptogenic cirrhosis.

Thirty-four nodules were found in 14 patients including 20 nodules that were HCCs. A diagnosis of HCC was based on pathological examination (n = 6, all were moderately-differentiated HCC), typical clinical history in combination with lipiodol uptake after TACE (n = 9), progression of the disease as depicted at 6-monthly follow-up imaging (n = 2), and typical HCC hallmarks<sup>(2,3)</sup> on dynamic contrast-enhanced MR imaging (arterial hypervascularity and washout on venous/equilibrium phase) (n = 3). The remaining 14 of 34 nodules were benign hepatocellular nodules. A diagnosis of all benign hepatocellular nodules was made by no interval change or less conspicuous without treatment at follow-up imaging (US, CT, or MR imaging) at least one year after initial imaging.

### ***MR examination***

MR imaging were performed by using a 1.5- or 3.0-Tesla systems (Intera Achieva, Phillips Medical Systems, Netherlands) with phased-array coils. The MR imaging examination comprised of dual-echo T1-weighted gradient-echo sequence, two dimensional T2-weighted turbo spin echo sequence, and contrast-enhanced dynamic sequences.

For contrast-enhanced dynamic MR imaging, 0.025 mmol per kilogram of body weight of gadoxetic acid (Primovist®, Bayer Schering Pharma, Germany) was injected as a rapid bolus and was immediately followed by a saline flush of 15 to 20 ml, through a 20-gauge intravenous catheter placed into a peripheral vein. A three-dimensional spoiled gradient-recall-echo sequences with fat suppression (THRIVE, Philips Medical system, Netherlands) was performed during suspended respiration at 30 seconds (arterial phase), 70 seconds (portovenous phase), and 120 seconds (equilibrium phase) after intravenous contrast administration. Additional hepatobiliary phase images were done at 20 minutes after contrast injection.

### ***Image analysis***

Two radiologists, with five and nine years of experience in abdominal imaging, reviewed in consensus of two sets of gadoxetic acid-enhanced MR images in a retrospective fashion and random order. Set 1 of MR images included unenhanced (precontrast T1- and T2-weighted images) and gadoxetic acid-enhanced dynamic images (arterial, portovenous, and

equilibrium phases), and set 2 of MR images included unenhanced (precontrast T1- and T2-weighted images), gadoteric acid-enhanced dynamic, and hepatobiliary phase images. The two readers were blinded to patient history, laboratory results, findings of other imaging modalities, and final diagnosis. To minimize the recall bias, the interval between the reviewed of the two sets of MR images was at least one month.

Readers categorized all detected lesions of the two image sets by using a 5-point confidence scale based on clinical practice guidelines by the EASL-EORTC, the AASLD, and the Asian Pacific Association for the Study of the Liver (APASL)<sup>(2,3,13)</sup> and Liver Imaging Reporting and Data System (LIRADS, version 1.0 March 2011, American College of Radiology [ACR])<sup>(14)</sup>. The scores were 1) benign, 2) probably benign, 3) intermediate probability for HCC, 4) probably HCC, and 5) definitely HCC. Confidence scores of 4 and 5 represented a positive diagnosis of HCC. Criteria for diagnosis of HCC were described as follow:

Confidence scale 5, definitely HCC: 1) size 2 cm or larger with arterial enhancement and portovenous or equilibrium phase washout; and 2) size less than 2 cm with arterial enhancement and portovenous or equilibrium phase washout, and one or more additional features that favor diagnosis of HCC including T2 hyperintensity, enhancing pseudocapsule, mosaic architecture (includes nodule-in-nodule, multi-nodule-in-nodule, presence of discrete internal compartments or elements within observation), fat deposition disproportionate to that in surrounding liver, and iron sparing in iron-overloaded liver.

Confidence scale 4, probably HCC: 1) size 2 cm or larger with, (a) arterial enhancement and no portovenous or equilibrium phase washout, and (b) no arterial enhancement and showed hypointensity on portovenous or equilibrium phase; and 2) size less than 2 cm with, (a) arterial enhancement and portovenous or equilibrium phase washout, (b) arterial enhancement and no portovenous or equilibrium phase washout, and one or more additional features that favor diagnosis of HCC, and (c) no arterial enhancement and showed hypointensity on portovenous or equilibrium phase, and one or more additional features that favor diagnosis of HCC.

When the readers interpreted set 2 images, a hypointense nodule seen on gadoteric acid-enhanced hepatobiliary phase images was considered HCC, on the basis of property of this hepatocyte specific agent. Confidence score was increased in equivocal cases

(4, probably HCC or 3, intermediate probability for HCC). However, a hypointense nodule seen on hepatobiliary phase images should not suggested to be HCC in cases of benign or probably benign categories, on the basis of their typical benign features<sup>(14)</sup>.

Moreover, morphologic features including location (adjacent to or apart to liver surface), outer margin (well-defined or ill-defined), shape (round, oval, irregular, or wedge-shaped), and size (longest diameter) were recorded. For patients with multiple lesions located in the same segment, the observers added further descriptions regarding the size and location of the lesion within each segment in order to avoid confusion during data analysis.

### **Statistical analysis**

The Fisher's exact test or Chi-square test was used to compare the location, shape, outer margin of HCCs and benign hepatocellular nodules. Comparison of the size difference was made using unpaired t-test. Regarding the MR imaging signal intensity (SI) and enhancement pattern on gadoteric acid-enhanced MR imaging in each group were compared using the Fisher's exact test.

The assigned confidence score of 1 to 3 and 4 to 5 was classified as benign and HCC, respectively. The diagnostic performance of the two sets of gadoteric acid-enhanced MR imaging in the diagnosis of HCC were assessed for all lesions.

A two sided *p*-value of less than 0.05 was considered to indicate statistical significance. Statistical analyses were performed by using statistical software (SPSS, version 13.0.1, SPSS, Chicago, Ill).

### **Results**

Twenty of the 34 detected nodules were HCCs. The mean diameter of HCCs in the present study was 1.76±0.56 cm in longest diameter (range 0.8 to 3 cm). Twelve of 20 (60%) HCC nodules were smaller than 2 cm. The mean diameter of 14 benign hepatocellular nodules was 1.29±0.39 cm in longest diameter (range 0.9 to 2 cm). No statistical difference in size between two groups was seen (*p*-value = 0.15). The location, margin, and shape of these nodules also showed no statistical differences between the two groups.

Regardless of lesion size, the diagnostic performance including sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of the two imaging sets were shown in Table 1. The sensitivity and NPV increased with the addition of hepatobiliary phase images, from 75 to 95%

and 68.8 to 87.5%, respectively. In contrast, the specificity and PPV decreased with the addition of hepatobiliary phase images, from 78.6 to 50% and 83 to 73%, respectively. The accuracy was not changed, when added hepatobiliary phase images, 76.5%.

Regarding to lesion size, the sensitivity, specificity, and accuracy of the two imaging sets were shown in Table 2. There was increase in sensitivity (58.3 to 91.7%) with the addition of hepatobiliary phase images in lesions smaller than 2 cm in diameter. However, decrease in specificity was observed (75.1 to 41.7%). The accuracy was unchanged. Excellent sensitivities, specificities, and accuracies in lesions equal or more than 2 cm in diameter in both imaging sets were depicted (Fig. 1).

**Table 1.** Diagnostic performance of gadoxetic acid-enhanced MRI for diagnosis of HCC in cirrhotic liver

	Sensitivity	Specificity	Accuracy	PPV	NPV
Set 1	75%	78.6%	76.5%	83%	68.8%
Set 2	95%	50.0%	76.5%	73%	87.5%

MRI = magnetic resonance imaging; HCC = hepatocellular carcinoma; PPV = positive predictive value; NPV = negative predictive value

The sets are defined in the Material and Method

**Table 2.** Comparison of sensitivity, specificity, and accuracy between the two imaging sets according to lesion size

Lesion size	Sensitivity	Specificity	Accuracy
<2 cm (n = 24)			
Set 1	58.3%	75.1%	67.67%
Set 2	91.7%	41.7%	67.67%
≥2 cm (n = 10)			
Set 1	100%	100%	100%
Set 2	100%	100%	100%

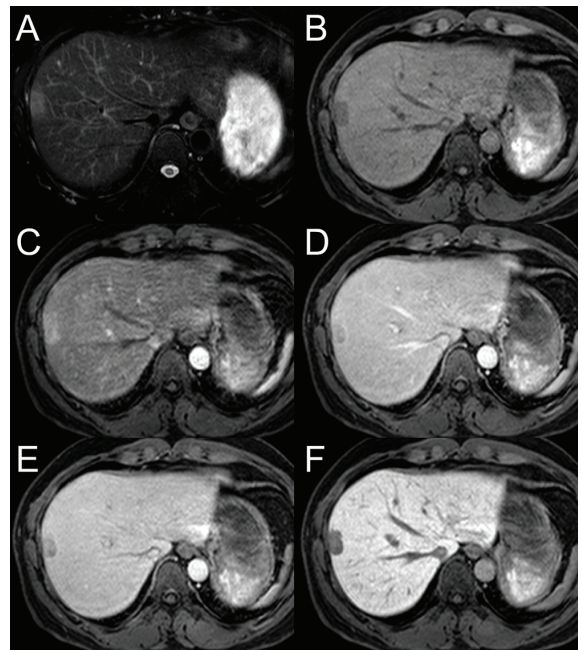
The sets are defined in the Material and Method

**Table 3.** Diagnostic performance of gadoxetic acid-enhanced liver MRI to differentiate between HCC and non-HCC

Gadoxetic acid-enhanced MRI	Gold standard		Sensitivity (95% CI)	Specificity (95% CI)	Accuracy	PPV (95% CI)	NPV (95% CI)
	HCC (n = 20)	Non-HCC (n = 14)					
Set 1: without hepatobiliary phase							
HCC	15	3	75% (0.5 to 0.9)	78.6% (0.48 to 0.94)	76.5%	83% (0.57 to 0.95)	68.8% (0.41 to 0.88)
Non-HCC	5	11					
Set 2: with hepatobiliary phase							
HCC	19	7	95% (0.73 to 0.99)	50.0% (0.24 to 0.76)	76.5%	73% (0.52 to 0.87)	87.5% (0.47 to 0.99)
Non-HCC	1	7					

Set 1: false positive 3 cases, false negative 5 cases

Set 2: false positive 7 cases, false negative 1 cases

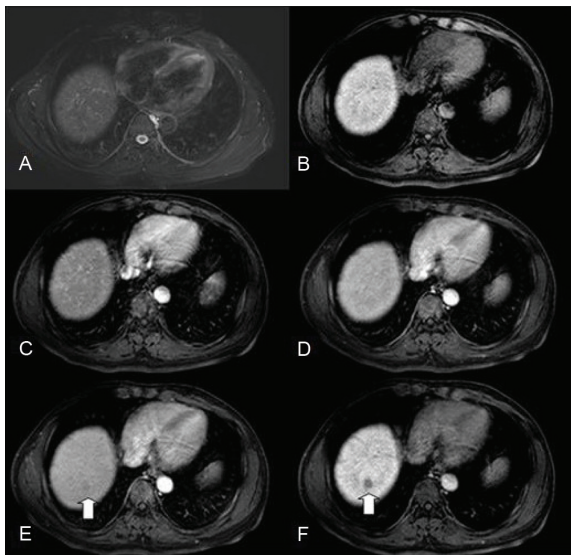


**Fig. 1** Gadoxetic acid-enhanced MR imaging of surgically verified HCC in a 44-year-old man with chronic hepatitis B. There is a 2.5 cm typical HCC nodule at hepatic segment 8 that shows high SI on T2-weighted image (A), low SI on T1-weighted image (B), arterial enhancement (C), and washout on portovenous (D) and equilibrium (E) phases images. At hepatobiliary phase image (F), the lesion is low SI to the surrounding liver parenchyma. Pathologic confirmation after hepatic resection was consistent with moderately-differentiated HCC.

The characteristics of the HCCs and benign hepatocellular nodules seen on gadoxetic acid-enhanced MR imaging were summarized in Table 3. Most HCCs showed high SI on T2-weighted images, whereas most benign hepatocellular nodules showed iso SI on T1- and T2-weighted images, with statistical

significance. Only one benign hepatocellular nodule demonstrated high SI on T2-weighted images. On dynamic MR imaging, most HCCs expressed arterial enhancement, however, only half showed portovenous or equilibrium phases washout. Five of 14 benign hepatocellular nodules revealed arterial enhancement. Statistically significant difference between two groups was shown only on arterial phase of dynamic contrast enhanced MR imaging ( $p$ -value = 0.014). There were 3 benign hepatocellular nodules and 1 HCC that contained microscopic fat component (showing high SI on in phase and low SI on opposed phase of T1-weighted gradient echo images). Nodule-within-nodule appearance was depicted in one case of HCCs.

Four HCC nodules were correctly diagnosed by additional hepatobiliary phase images. Three of them showed hypovascularity on dynamic gadoxetic acid-enhanced MR imaging (no arterial enhancement,

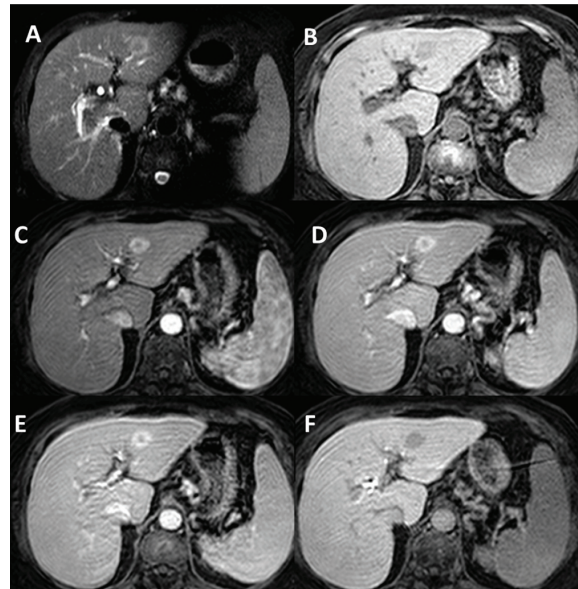


**Fig. 2** Gadoxetic acid-enhanced MR images of surgically verified HCC in 56-year-old man with chronic hepatitis C-related cirrhosis at hepatic dome (segment 8). No focal lesion is clearly visible on T2-weighted (A), T1-weighted (B), arterial phase (C), and portovenous phase (D) images. Equilibrium phase image (E) reveals 1-cm slightly low SI nodule (arrow). Two readers consider this nodule as intermediate probability for HCC (confidence score 3). At hepatobiliary phase image (F), the lesion shows markedly low SI (arrow) compared with surrounding liver parenchyma and is regarded as probably HCC. Pathological confirmation after hepatic resection was consistent with moderately-differentiated HCC.

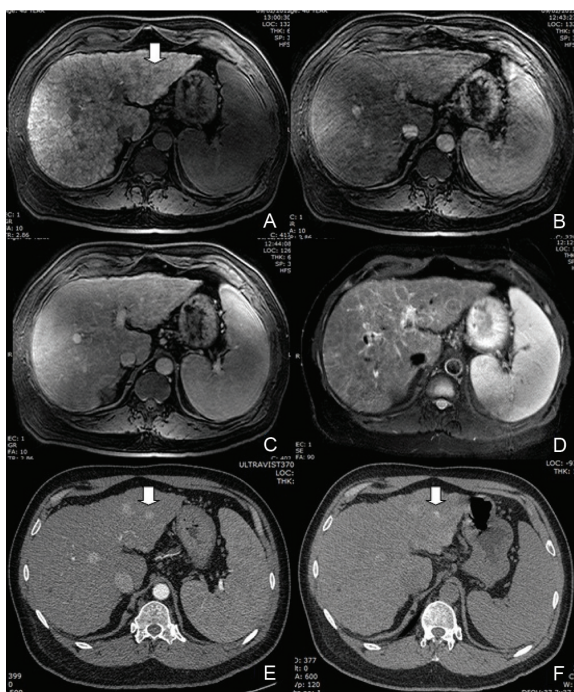
low SI on equilibrium phase) and iso SI on T2-weighted images, all measured less than 2 cm in size (range from 1 to 1.6 cm) (Fig. 2). The remaining one of them revealed 1.7-cm hypervascular nodule, however, no washout and no high SI on T2-weighted images. All of them depicted low SI on hepatobiliary phase images.

Added hepatobiliary phase images increased confidence in HCC diagnosis in two arterial enhancing nodules without washout on portovenous and equilibrium phases, that depicted low SI on hepatobiliary phase images (Fig. 3).

One of the 20 HCCs was misdiagnosed on both image sets. This nodule was 0.8 cm in longest diameter and showed iso SI on precontrast T1- and T2-weighted images, and dynamic gadoxetic acid-enhanced MR imaging. This lesion was depicted on hepatobiliary phase images but was not regarded as HCC because of its very small size and the lack of characteristic features on dynamic contrast-enhanced and T2-weighted images (Fig. 4).



**Fig. 3** Gadoxetic acid-enhanced MR images of surgically verified HCC in 79-year-old woman with chronic hepatitis C-related cirrhosis. There is a 2.1 cm nodule at hepatic segment 3 that shows high SI on T2-weighted (A), low SI on T1-weighted (B) with enhancement on arterial phase (C) images. No definite washout on portovenous (D) and equilibrium (E) phases is depicted. At hepatobiliary phase image (F), the lesion shows low SI and is regarded as HCC. Pathologic confirmation after hepatic resection was consistent with moderately-differentiated HCC.



**Fig. 4** A 48-year-old mass with cryptogenic cirrhosis. Gadolinium acid-enhanced MRI showed a 0.8-cm low SI nodule (arrow) at hepatic segment 3 on hepatobiliary phase image (A). No focal lesion was clearly seen on arterial phase (B), portovenous phase (C), and T2-weighted (D) images. This lesion was not regarded as HCC from both imaging sets. Follow-up multiphase MDCT on next 6 months, this lesion increased size (1.2 cm) and exhibited gross arterial enhancement (E, arrow). After TACE, there was small lipiodol staining in the lesion seen on precontrast CT image (F, arrow). Thus, this lesion was diagnosed as HCC.

There were increased in numbers of false positive cases, when interpreted MR images with additional hepatobiliary phase images. Four intermediate probability for HCC (confidence score 3) nodules seen on set 1 MR images were changed to probably HCC (confidence score 4) after low SI depicted on additional hepatobiliary phase images. All of them showed hypovascularity on dynamic contrast-enhanced and iso SI on T2-weighted images. There were measured range from 0.9 to 1.4 cm in longest diameter.

## Discussion

The present study showed improvement of sensitivity for diagnosis of HCC when adding hepatobiliary phase. All the correctly diagnosed HCC lesions by using hepatobiliary phases are small

HCCs, and show atypical enhancement pattern, either hypovascularity or hypervascularity without washout. According to previous reports<sup>(8,10,11,15,16)</sup>, small HCCs more often had atypical enhancement features, that seen either absence of arterial enhancement, venous washout, or both. These findings are explained by a few intratumoral or non-triadal arterioles and minimal decreased in numbers of portal tract in well-differentiated or small HCCs<sup>(17)</sup>. As small HCCs increase in size and become further dedifferentiated, the intratumoral arterioles develop<sup>(17)</sup>. Thus, assessment of tissue vascularity alone may miss the diagnosis of small HCCs. Besides the enhancement pattern, the size of lesion should be used for differentiating early HCC from benign cirrhotic nodules. Rhee et al<sup>(18)</sup> found that, the size threshold of more than 1.5 cm was demonstrated to be useful for the discrimination of early HCC and benign cirrhotic nodules. However, there is no statistical significant about the nodular size between HCC and benign cirrhotic nodules in the present study.

A small 0.8-cm HCC was misdiagnosed on both image sets. This lesion was found on hepatobiliary phase images alone. Although, there was not regarded as HCC, due to no characteristic findings according to our diagnostic criteria. However, as the previous investigator<sup>(8)</sup> said that any visible lesion on hepatobiliary phase images should not be ignored or dismissed. Rhee et al<sup>(18)</sup> found that hypointense in the hepatobiliary phase could be a useful predictor for differentiation between malignant and benign lesions.

Dynamic contrast-enhanced MR imaging have limitation for diagnosis of small HCCs in our results, but excellent for diagnosis of more than 2 cm-sized HCCs. Added hepatobiliary phase images could be enhance the sensitivity for diagnosis of small HCCs (from 58.3 to 91.7%). However, the specificity was decreased, from 75.1 to 41.7% and unchanged of diagnostic accuracy (67.67 to 67.67%) for diagnosis of small HCCs. Relatively high incidence of non-uptake gadolinium acid in benign cirrhotic nodules were seen, 64.3% (9 of 14 benign cirrhotic nodules).

Many of benign cirrhotic nodules showed low SI on hepatobiliary phase images, that mimic the malignant nodule. However, benign cirrhotic nodules including dysplastic nodules, may contain atypical hepatocytes and reduced portal tracts, depending on degree of differentiation. With progression of atypia, the number of expressed organic ion transporters in dysplastic nodules decreased, which reduced their ability to take up gadolinium acid<sup>(12)</sup>. Therefore, some

dysplastic nodules (especially high-grade) showed hypointense on hepatobiliary phase, as shown in many previous studies<sup>(18,19)</sup>.

The study had several limitations. First, all lesions were not pathologically confirmed. Only six nodules underwent surgical resection. Most of HCC nodules were diagnosed by angiography with evidence of lipiodol staining on follow-up post-TACE images. If any lesion showed no lipiodol staining on follow-up images and no characteristic of typical hypervascular HCC, the lesion was classified in benign group. Furthermore, all benign cirrhotic nodules in the present study were not pathologically proved, but were diagnosed by follow-up imaging at least 1 year. A small HCC may take a long time to increase in size<sup>(20)</sup>, it might be too early to evaluate the true nature of these nodules. Second, relatively small sample size was seen, which may cause no statistical significance in some of our results. Finally, the heterogeneous in MR imaging techniques and parameters may due to using either a 1.5 or 3.0 Tesla system.

## Conclusion

Gadoxetic acid-enhanced MR imaging has an excellent diagnostic performance for diagnosis of more than 2 cm-HCCs in cirrhotic liver, but still limited in small HCCs. Added hepatobiliary phase images in dynamic Gadoxetic acid-enhanced MR imaging improve detection of small HCCs. However, due to relatively low specificity, interpretation of non-uptake gadoxetic acid lesion in hepatobiliary phase should be caution.

## What is already known on this topic?

Non-invasive diagnosis is organized when the HCC radiological hallmarks (arterial hypervascularity and venous/late phase washout) are shown. However, several previous studies found that the detection and diagnosis of small HCC (2 cm or smaller) was still problematic by using multiphasic MDCT and dynamic contrast enhanced MR imaging. Poor and variable sensitivities of both imaging examinations were seen, ranging from 30 to 65% for multiphasic MDCT and 35 to 66% for dynamic contrast enhanced MR imaging. Atypical imaging appearances are frequently seen in small HCC and well-differentiated HCC. The previous investigators found that 87% of well-differentiated HCCs and 41 to 62% of small HCCs showed either absence of arterial hypervascularity, venous washout, or both. Whenever, the diagnosis is based on vascular enhancement pattern alone, it may lead to under-detection

and under-diagnosis of small or well-differentiated HCC.

## What this study adds?

A new combined extracellular-hepatobiliary contrast agent has been developed, Gd-EOB-DTPA, also known as gadoxetate disodium or gadoxetic acid (Primovist®, Bayer Schering Pharma, Germany). This contrast agent combines the properties of a conventional extracellular contrast agent that evaluating tissue vascularity, and a hepatobiliary agent that assessing hepatocyte function. Accordingly, it may overcome some of the limitations of pure extracellular agents for detection and diagnosis of HCC with atypical enhancement pattern.

From the present study, Gadoxetic acid-enhanced MR imaging has an excellent diagnostic performance for diagnosis of more than 2 cm-HCCs in cirrhotic liver, but still limited in small HCCs. Added hepatobiliary phase images in dynamic Gadoxetic acid-enhanced MR imaging improves detection of small HCCs. However, due to relatively low specificity, interpretation of non-uptake gadoxetic acid lesion in hepatobiliary phase should be caution.

## Potential conflicts of interest

None.

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การศึกษาประสิทธิภาพของการตรวจด้วยเครื่องสร้างภาพสะท้อนในสนามแม่เหล็กโดยใช้สารจำแนกความแตกต่างชนิด gadoxetic acid ในการตรวจวินิจฉัยมะเร็งระดับชนิดhepatocellular carcinoma ในผู้ป่วยที่มีภาวะตับแข็ง

วรรณวรางค์ ตีรสมิทธิ์, รณิษฐา ทองดี, จิรวดี ยอดยิ่ง

**วัตถุประสงค์:** เพื่อศึกษาประสิทธิภาพของการตรวจด้วยเครื่องสร้างภาพสะท้อนในสนามแม่เหล็กโดยใช้สารจำแนกความแตกต่างชนิด gadoxetic acid และประโยชน์ที่ได้เพิ่มขึ้นจากภาพในช่วง hepatobiliary ในการวินิจฉัยมะเร็งระดับชนิด hepatocellular carcinoma ในผู้ป่วยที่มีภาวะตับแข็ง

**วัสดุและวิธีการ:** เป็นการศึกษาย้อนหลังโดยเก็บข้อมูลตั้งแต่เดือนกรกฎาคม พ.ศ. 2554 ถึง ตุลาคม พ.ศ. 2555 ในกลุ่มผู้ป่วยโรคตับแข็งจำนวน 14 ราย ซึ่งมีก้อนในตับรวมกัน 34 ก้อน รังสีแพทย์ 2 คน ร่วมกันแปลผลภาพการตรวจด้วยเครื่องสร้างภาพสะท้อนในสนามแม่เหล็กโดยใช้สารจำแนกความแตกต่างชนิด gadoxetic acid โดยแยกการแปลผลภาพเป็น 2 กลุ่ม คือ กลุ่มที่ 1 เป็นภาพก่อนฉีด และในช่วง dynamic ภายหลังฉีดสารจำแนกความแตกต่างชนิด gadoxetic acid และกลุ่มที่ 2 เป็นภาพก่อนฉีด ช่วง dynamic ภายหลังฉีดสารจำแนกความแตกต่างชนิด gadoxetic acid และเพิ่มภาพในช่วง hepatobiliary เข้าไปด้วย หลังจากนั้นจะทำการวิเคราะห์ผลทางสถิติถึงประสิทธิภาพของการแปลผลภาพจาก 2 กลุ่มดังกล่าว รวมถึงประสิทธิภาพเมื่อจำแนกตามขนาดของก้อนอีกด้วย

**ผลการศึกษา:** พบว่ามีค่าความไวและค่าพยากรณ์ลบที่ดีขึ้นในกลุ่มที่ 2 ซึ่งเป็นกลุ่มที่เพิ่มการแปลผลภาพในช่วง hepatobiliary โดยเพิ่มจาก 75% เป็น 95% สำหรับค่าความไว และ 68.8% เป็น 87.5% สำหรับค่าพยากรณ์ลบ อย่างไรก็ตามความแม่นยำในทั้งสองกลุ่มไม่แตกต่างกัน (76.5%) ประสิทธิภาพทั้งในแง่ความไว ความจำเพาะและความแม่นยำของการตรวจด้วยเครื่องสร้างภาพสะท้อนในสนามแม่เหล็กโดยใช้สารจำแนกความแตกต่างชนิด gadoxetic acid ในการวินิจฉัยก้อนเนื้องอกที่มีขนาดใหญ่กว่า 2 เซนติเมตร ได้ผลดีมากในทั้งสองกลุ่ม (100%) นอกจากนี้ยังพบว่าค่าความไวจะดีขึ้นจาก 58.3% เป็น 91.7% ในกลุ่มของก้อนเนื้องอกที่มีขนาดเล็กกว่า 2 เซนติเมตร เมื่อเพิ่มการแปลผลภาพในช่วง hepatobiliary เข้าไปด้วย

**สรุป:** การตรวจด้วยเครื่องสร้างภาพสะท้อนในสนามแม่เหล็กโดยใช้สารจำแนกความแตกต่างชนิด gadoxetic acid มีประสิทธิภาพดีมากในการวินิจฉัยมะเร็งระดับชนิด hepatocellular carcinoma ในผู้ป่วยที่มีภาวะตับแข็งที่มีขนาดใหญ่กว่า 2 เซนติเมตร แต่ยังคงมีข้อจำกัดในก้อนเนื้องอกที่มีขนาดเล็ก การเพิ่มการแปลผลภาพในช่วง hepatobiliary จะช่วยเพิ่มความสามารถในการค้นหาก้อนที่มีขนาดเล็กเหล่านี้ได้มากขึ้น

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