Revisiting arterial enhancement of small (1-2 cm) hepatic nodules on dynamic MRI in patients at high risk for hepatocellular carcinoma

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Introduction: Arterial enhancement, major diagnostic criteria for hepatocellular carcinoma (HCC), has been defined as "hyperintense compared to the surrounding liver parenchyma on arterial phase". With this definition, however, we often encounter false positive or false negative results in daily practice. Subtraction of pre-contrast from arterial phase images has been used more and more, with the technical development of registration correction. Therefore, the purpose of our study is to revisit the definition of arterial enhancement by comparing the diagnostic accuracy of enhancement determined on arterial phase image alone, on arterial phase with pre-contrast images, and on subtraction images in addition to arterial phase with pre-contrast images for the diagnosis of HCC in patients with surgically confirmed small hepatic nodules.

Methods: This retrospective study was approved by the institutional review board, and informed consent was waived. Thirty-eight patients with 62 small (1-2 cm) hepatic nodules (37 malignant, 25 non-malignant) underwent dynamic MRI within 60 days before curative liver resection or transplantation for suspected HCC. MRI was performed with a 3.0-T MR system (MAGNETOM Trio a Tim; Syngo MR B15; Siemens Medical Solutions, Erlangen, Germany) and subtraction of multi-phasic contrast enhanced dynamic series was automatically acquired. Two abdominal radiologists independently determined arterial enhancement of each hepatic nodules with the following three methods: assessing (1) arterial phase alone, (2) pre-contrast and arterial phase together, and (3) subtraction images of pre-contrast from arterial phase images as well as pre-contrast and arterial phase images. For each of the three methods, accuracy, sensitivity and specificity were calculated for the diagnosis of HCC. McNemar test was used to compare accuracy, sensitivity, and specificity. To evaluate interobserver agreement, kappa statistics were used.

Results: Compared to assessing enhancement on only arterial phase images, assessing both pre-contrast and arterial phase images improved specificity (from 88% to 96%) but decreased sensitivity (from 73% to 62%) and accuracy (from 79% to 76%) for the diagnosis of HCC, without statistical significance ($p > .05$). Diagnostic performance was highest when subtraction images were reviewed in addition to pre-contrast and arterial phase images (sensitivity, 76%; specificity, 96%; accuracy, 84%), without statistical significance ($p > .05$) (**Table 1**). Interobserver agreements between the two reviewers were excellent for all three methods of evaluating arterial enhancement (mean $\kappa = 0.92$ for arterial phase alone, 0.89 for arterial phase with pre-contrast images, and 0.92 for subtraction images).

Table 1: Diagnostic Performance of Arterial Enhancement on Three Sets of Images for Diagnosis of HCC

	Accuracy	Sensitivity	Specificity	PPV	NPV
Enhancement determined on	(TP+TN)/total	TP/(TP+FN)	TN/(TN+FP)	TP/(TP+FP)	TN/(TN+FN)
Arterial phase alone	79% (49/62)	73% (27/37)	88% (22/25)	90% (27/30)	68.8% (22/32)
Arterial phase with precontrast	75.8% (47/62)	62% (23/37)	96% (24/25)	95.8% (23/24)	63.2% (24/38)
Subtraction images with arterial phase and precontrast	83.9% (52/62)	75.7% (28/37)	96% (24/25)	96.6% (28/29)	72.7% (24/33)

Note.- TP = true-positive, TN = true-negative, FP = false-positive, FN = false-negative, PPV = Positive predictive value, NPV = Negative predictive value

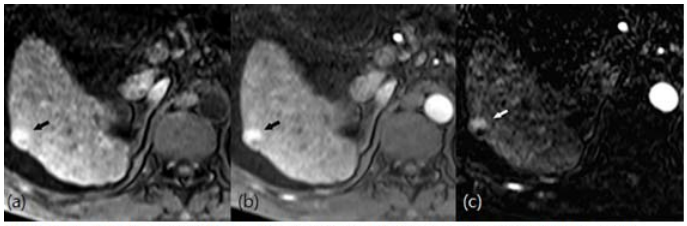

Figure 1. A pathologically confirmed small HCC in a 58 year old male. This mass shows high signal intensity on both **(a)** pre-contrast and **(b)** arterial phase images of Gd-enhanced T1-weighted MRI, and was determined to be hypervascular by assessing arterial phase alone but hypovascular by visually comparing pre-contrast and arterial phase images. **(c)** Dynamic subtraction of pre-contrast from arterial phase images allows easy determination of arterial enhancement.

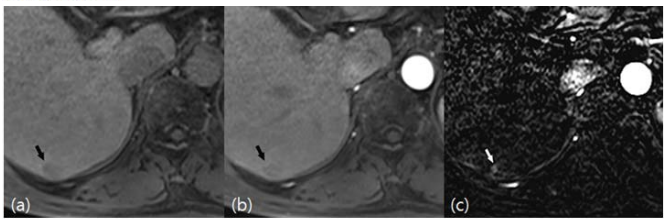

Figure 2. A pathologically confirmed small HCC in a 52 year old male. Both reviewers reported that this mass had low signal intensity on both **(a)** pre-contrast and **(b)** arterial phase images of Gd-enhanced T1-weighted MRI. **(c)** However, dynamic subtraction of pre-contrast from arterial phase images shows a focal area of arterial enhancement, which is difficult to detect by visually comparing pre-contrast and arterial phase images.

Discussion: Visually assessing both pre-contrast and arterial phase images to determine arterial enhancement of a hepatic nodule can increase specificity but decrease sensitivity, compared to assessing only arterial phase images. Additional review of subtraction images can improve both sensitivity and specificity mainly because it enables more accurate evaluation of a hepatic lesion showing no signal intensity change from pre-contrast to arterial phase (**Figure 1, 2**).

Conclusions: For better diagnosis of small HCC, arterial enhancement on dynamic MRI should be defined as an increase in signal intensity relative to the surrounding liver from pre-contrast to arterial phase. For this purpose, subtraction imaging should be used as it can more accurately demonstrate arterial enhancement than visual comparison of the two phases.

References

1. Bruix J, Sherman M, Llovet JM, et al. Clinical management of hepatocellular carcinoma. Conclusions of the Barcelona-2000 EASL conference. European Association for the Study of the Liver. Journal of Hepatology 2001;35(3):421-430.
2. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. Hepatology 2011;53(3):1020-1022.