

Precontrast T1-Weighted Hyperintense Nodules in Patients with Liver Cirrhosis: The Utility of Dynamic and Hepatobiliary Phases with Gadoxetate-Enhanced MRI.

Jing Luo¹, Ka-kei Ngan¹, Michael Nalesnik², and Keyanoosh Hosseinzadeh¹

¹Radiology, University of Pittsburgh, Pittsburgh, PA, United States, ²Pathology, University of Pittsburgh, Pittsburgh, PA, United States

Target Audience: Radiologists with expertise in abdominal imaging.

Purpose: Current American Association for the Study of Liver Diseases (AASLD) guidelines stipulate that lesion hypervascularity with enhancement on the hepatic arterial (HA) phase and “washout” on the portal venous (PV) or delayed phases constitute a diagnosis of HCC [1]. Gadoxetate (Eovist®) is an IV contrast agent with 50% uptake and biliary excretion by functioning hepatocytes, producing an additional hepatobiliary (HB) phase on dynamic MRI. HCC and other non-functional lesions are typically hypointense on the HB phase. Hyperintense nodules on unenhanced T1-w MRI are diagnostically challenging because their intrinsic hyperintensity masks typical findings of HCC on post-contrast dynamic and HB phases [2]. We evaluate the utility of gadoxetate-enhanced MRI for detecting HCC in patients with liver cirrhosis who have incidentally discovered T1-weighted hyperintense lesions of varying size.

Methods: A retrospective chart review of patients with cirrhosis receiving gadoxetate-enhanced MRI from January 2008 to July 2011 was conducted. All patients with hyperintense lesions on precontrast T1-weighted imaging that had histological confirmation were included. Histopathology included: 12 well-differentiated HCC, 2 mod-differentiated HCC, 2 dysplastic nodules, and 15 regenerative nodules. Gadoxetic-enhanced MRI at 1.5T was performed. Dynamic and HB phase imaging was acquired after the administration of 0.1 mL/kg (0.25 mmol/mL) of gadoxetic acid at 1.5cc/sec. Post-processing included subtraction imaging of the HA phase to assess for enhancement. A coordinator not involved in the review process identified the histopathologic confirmed lesions on liver maps for the reviewers. Lesion size, location, unenhanced T1 and T2-w signal intensity, and signal intensity on contrast-enhanced dynamic and HB phases were recorded independently by two radiologists with experience in liver MRI who were blinded to both clinical information and final diagnosis. Each lesion was qualitatively classified as hyperintense, isointense or hypointense to background liver on each phase. A 4 point confidence scale was used to classify the nodules: 1=definitely benign, 2=probably benign, 3=probably malignant, and 4=definitely malignant. Conventional criteria for HCC included: arterial enhancement on HA phase followed by venous washout on PV and delayed phases; ancillary findings included hypointensity on the HB phase, and T2 hyperintensity. Each reviewer scored each nodule based on the precontrast and dynamic phase (“dynamic”), and the nodules were then reevaluated with the addition of the HB phase (“dynamic and HB”). Any discrepancies were then resolved by consensus. To calculate the diagnostic performance, scores 1 and 2 were grouped into “benign” and 3 and 4 as “malignant”. Using histology as the gold standard, diagnostic performance comparing “dynamic” phase, and “dynamic and HB” phase, were performed by calculating sensitivity, specificity, positive and negative predictive values (PPV and NPV). A bootstrap resampling technique was used to compare benign and malignant lesion sizes with statistical significance achieved if the 95% CI does not cross 0. Cohen’s kappa coefficients were calculated to quantify inter-observer agreement for each imaging phase and the final diagnosis with results classified as poor (<0.2), fair (0.21-0.4), moderate (0.41-0.6), good (0.61-0.8), and excellent (0.81). Fisher’s exact test was performed to evaluate the correlation between HB phase and histopathology.

Results: 31 histologically confirmed lesions in 9 patients (mean age 63 years, 6 M, 3 F) were included. Based on consensus data, combining dynamic and HB phase criteria did not change diagnostic performance compared to dynamic phase only (Table 1) with sensitivity and specificity of 0.71 and 0.94 respectively (Fig. 1). Cohen’s kappa coefficients showed that inter-observer agreement was moderate (0.54) for dynamic phase and good (0.65) for combined dynamic and HB phases, with the majority of disagreements occurring only within the benign (scores 1 and 2) and malignant groups (scores 3 and 4). 2/31 nodules showed disagreement between the two groups (Fig. 2). Cohen’s kappa coefficients showed that inter-observer agreement was moderate (0.59) for HA phase, good (0.628) for PV phase, good (0.735) for delayed phase, and good (0.651) for combined PV and delayed phases. Statistically significant correlation was noted between HB phase and histopathology (p<0.0004), detailed in Table 2. All lesions that were hypointense on the HB phase were found to be malignant (8/14 malignant nodules) and no benign nodules were hypointense on the HB phase. All 17 benign nodules were iso to hyperintense on HB phase. Malignant lesions had a mean size of 24.4 mm (range 6-83mm), and benign lesions had a mean size of 13.3 mm (4-22mm). Bootstrap resampling for difference in mean lesion size resulted in a 95% confidence interval of 0.1-23.7mm, which implies a statistically significant difference, although by a narrow margin.

	Sensitivity	Specificity	PPV	NPV
Dynamic	0.714	0.941	0.909	0.8
Dynamic & HB	0.714	0.941	0.909	0.8

Table 1: Diagnostic performance characteristics

HB phase	Histological results		
	Malignant	Benign	Total
Hypointense	8	0	8
Iso/hyperintense	6	17	23
Total	14	17	31

Table 2: Correlation between HB phase-only and histology results

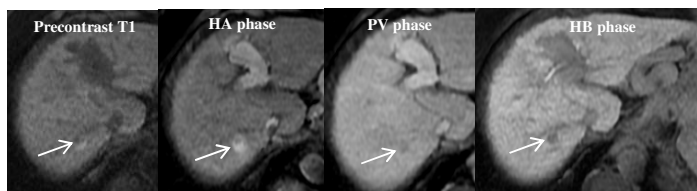


Fig. 1: Gadoxetate-enhanced MRI of a nodule in a 65-year-old female. 10 mm nodule (arrow) shows hypervascularity on HA phase with venous washout and hypointensity on HB phase. Surgical resection showed moderately differentiated HCC.

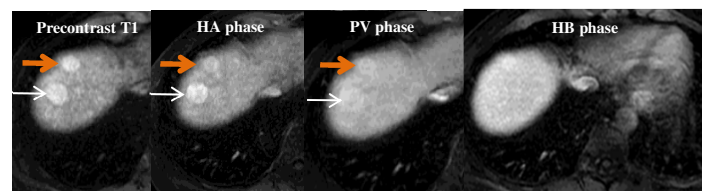


Fig. 2: Gadoxetate-enhanced MRI of 2 nodules in a 53-year-old female. 27mm segment 7 nodule (arrow) appears slightly hypervascular on HA phase without venous washout and isointense on HB phase. Initial scoring by reviewers raised both benign and malignant appearance. Segment 8 nodule (arrow) is considered benign by both reviewers. Resection of both showed low-grade dysplasia.

Conclusion: Sensitivity and specificity of 0.71 and 0.94 were noted with conventional dynamic MRI for T1-weighted hyperintense nodules, and there was no improvement in the diagnostic performance by the addition of HB phase. However, there is a strong correlation between a lesion’s HB phase appearance and its histopathology. Our data shows that nodules demonstrating both precontrast T1 hyperintensity and HB phase hypointensity are indeed malignant. Our results demonstrated a small statistical difference in mean size between benign and malignant lesions.

References: 1) Willatt J et al. *Radiology* 2008;247(2):311-30. 2) Chou C et al. *J Magn Reson Imaging* 2011;33(3):625-32.