# Optimal Timing and Diagnostic Adequacy of Hepatocyte Phase Imaging with Gadoxetate-Enhanced Liver MRI

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**Rationale and Objectives:** To evaluate clinical and imaging features associated with adequacy of the hepatocyte phase (HP) in gadoxetate disodium–enhanced liver magnetic resonance imaging (MRI) in patients without chronic liver disease (CLD).

**Materials and Methods:** This was a retrospective institutional review board–approved study of 97 patients who underwent liver MRI examinations with gadoxetate disodium and had no history of CLD. Available late dynamic and HP sequences (3–20 minutes postinjection) were independently analyzed by four radiologists for perceived image adequacy and level of biliary enhancement. Signal intensity ratios (SIRs) of liver/inferior vena cava (IVC), liver/spleen, and liver/muscle were measured. The Spearman $\rho$ and receiver operating characteristic analyses were performed correlating various factors with HP adequacy. A rule for predicting HP adequacy was also derived and tested to determine whether overall examination time could be shortened.

**Results:** A visually adequate HP was observed in 12% of subjects by 10 minutes, 80% by 15 minutes, and 93% by 20 minutes. An $SIR_{liver/IVC} > 1.8$ was the imaging feature that had the strongest correlation with an adequate HP ($\rho = 0.813$, $P < .001$), and was more predictive of adequacy of the HP than the time postinjection ($\rho = 0.5$, $P < .001$). The time at which an adequate HP was first observed did not correlate with any tested demographic or laboratory values. Stopping imaging when an $SIR_{liver/IVC} > 1.8$ would have successfully reduced mean postcontrast time to 15:39 $\pm$ 4:02 from 20:00 ($P < .001$), although maintaining HP adequacy.

**Conclusions:** Most patients without CLD undergoing gadoxetate-enhanced liver MRI achieve adequate HP at 20 minutes. However, a shorter postcontrast stopping time can be used in most patients.

**Key Words:** Gadoxetate disodium; gadoxetic acid; hepatocyte phase; hepatobiliary.



Gadoxetate disodium is becoming a well-established contrast agent for contrast-enhanced magnetic resonance imaging (MRI) of the noncirrhotic liver for the detection of metastatic disease and the evaluation of focal lesions (1–8). In particular, hepatocyte phase (HP) imaging with this agent along with an optimized imaging protocol has been shown to provide high-resolution imaging with strong liver-to-lesion contrast and lesion conspicuity (9–12). At many centers, gadoxetate-enhanced MRI has become the study of choice for the detection of hepatic metastases from a variety of primary tumors.

Although most publications describe the performance of the HP performed at 20 minutes postinjection, there remains debate as to whether shorter imaging times can be used for the delayed phase without compromising image quality (13–15). In particular, the use of 10-minute postinjection HP image sets has been described, with excellent performance for the detection of focal lesions (14,16). Thus the ideal timing of the HP is unclear.

Importantly, the rapidity and strength of hepatic gadoxetate uptake is strongly dependent on the functional status of the liver, although definitive laboratory and clinical predictors of uptake are lacking. In addition, MRI examinations using gadoxetate often require more time than those obtained with other gadolinium-based contrast agents, and the total examination time depends partly on the delay for HP imaging. For this reason, a prediction rule for stopping a gadoxetate-

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enhanced MRI before the 20-minute postinjection time point may be helpful.

The purpose of this study was to evaluate clinical and imaging features associated with adequacy of the HP in gadoxetate disodium–enhanced liver MRI in patients without chronic liver disease (CLD).

## MATERIALS AND METHODS

This was an Health Insurance Portability and Accountability Act (HIPAA)-compliant retrospective study, approved by our institutional review board. The requirement for informed consent was waived by the institutional review board.

A search of the electronic medical record at a single institution was performed for all consecutive patients who underwent gadoxetate-enhanced liver MRI at our institution between February 28, 2012 and August 21, 2012. Imaging protocols included postcontrast three-dimensional T1-weighted sequences obtained 3–6 minutes postcontrast injection, at 6–15 minutes postinjection, and 15–25 minutes postinjection. Precise timing and number of postcontrast sequences were variables because of the variability of acquisition time for T2-weighted and diffusion-weighted sequences obtained between T1-weighted acquisitions, as well as patient and technologist factors. Additional inclusion criteria included at least one postcontrast T1-weighted acquisition obtained at 3–15 minutes and at least one at 15–25 minutes after contrast media injection, and T1-weighted image data set obtained using identical protocols on identical MRI systems (detailed subsequently). Patients with a history of CLD, including cirrhosis, viral hepatitis, nonalcoholic steatohepatitis, primary sclerosing cholangitis, or primary biliary cirrhosis were excluded ($n$ = 28). Patients without a documented history of CLD but with imaging findings of CLD or portal hypertension were also excluded, in particular liver contour nodularity ($n$ = 1) and gastroesophageal varices ($n$ = 1). Ultimately, 97 patients with 240 corresponding HP data sets comprised the study population. Patient demographics and laboratory values obtained within 4 weeks of imaging were collected.

All included image data sets were obtained on a 3 T MRI system (Skyra; Siemens Healthcare, Erlangen, Germany) using a three-dimensional T1-weighted dual-echo acquisition, postprocessed with a Dixon water–fat separation algorithm (17,18). Only the water-only image sets were reviewed. Additional parameters included repetition time 3.9–4.2 milliseconds, source in/opposed phase echo times 1.2/2.5 milliseconds, flip angle 9°, acquisition matrix 288 × 230–288 × 72 slices, section thickness 4 mm, field of view 38–40 × 27–40 cm, receiver bandwidth 1020 Hz/pixel, and number of signal averages 1. All patients received a standard dose of 10 mL of gadoxetate disodium (Eovist; Bayer Healthcare, Wayne, NJ) intravenously at 2 mL/seconds followed by a 20 mL saline chaser also injected at 2 mL/seconds. Nonweight-based dosing was used clinically as this has been shown to increase the average amount of contrast enhancement compared to weight-based dosing of 0.025 mmol/kg (15,19). The time between data set acquisition and contrast media administration was calculated using Digital Imaging and Communications in Medicine (DICOM) header data.

Image sets were randomized so that data sets from the same examinations were reviewed nonconsecutively, and were also randomized with respect to timing of acquisition. In addition to anonymization, all information regarding image set timing was removed. Four fellowship-trained abdominal radiologists who were faculty at four different academic institutions, each with 3–8 years of postfellowship experience with abdominal MRI, independently evaluated HP data sets meeting the previously mentioned criteria in a fully blinded manner. All radiologists had at least 3 years experience interpreting gadoxetate-enhanced MRI.

Readers were asked to grade each data set according to the following features: (1) Adequacy of HP/timing for the specific task of evaluation for focal liver lesions (Grade 0, nondiagnostic; Grade 1, suboptimal; Grade 2, diagnostic; and Grade 3, ideal), (2) The presence and delayed phase intensity of any focal liver lesions (Grade 0, no lesion; Grade 1, hypointense lesion(s); Grade 2, isointense lesion(s); Grade 3, hyperintense lesion(s); and Grade 4, combination of lesion types). (3) The presence of contrast material in the biliary system (Grade 0, no excretion; Grade 1, intrahepatic ducts; Grade 2, common duct; and Grade 3, duodenum).

One board-certified abdominal imaging fellow performed region of interest (ROI)-based measurements as follows. For each image set, three ROIs were placed over the hepatic parenchyma in the region of the inferior vena cava (IVC), taking care to avoid large vessels and areas of artifact. Three ROIs were also placed on each of the intrahepatic IVC, right paraspinous muscles, and spleen (when possible; $n$ = 88) on the same image as the liver ROIs. Signal intensity ratios (SIRs) were calculated as follows: $SIR_{LV}$ = mean $SI_{liver}$/mean $SI_{IVC}$; $SIR_{LM}$ = mean $SI_{liver}$/mean $SI_{muscle}$; and $SIR_{LS}$ = mean $SI_{liver}$/mean $SI_{spleen}$. Severity of hepatic steatosis was calculated as an estimated signal fat fraction ($FF_{est}$) from the precontrast in/opposed phase acquisition as $FF_{est} = (k_{in} \times SI_{in} - k_{out} \times SI_{out})/(k_{in} \times SI_{in} + k_{out} \times SI_{out})$, where $k_{in}$ and $k_{out}$ are correction factors for the spectral complexity of fat, derived from previous publications (20).

### Statistical Analysis

"Mean phase adequacy" was calculated for each image set as the average of reader grades of each phase adequacy. "Overall phase adequacy" was determined for each image set if at least three readers assigned it a phase adequacy grade of 2 or greater. Using these scores, "time to adequacy" was determined as the postcontrast acquisition time of the first image set to achieve overall phase adequacy by the previously mentioned definition.

Intraclass correlation coefficients (ICCs) were calculated to determine reader agreement for phase adequacy, presence/