Use of Magnetic Resonance Imaging Contrast Agents in the Liver and Biliary Tract

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KEYWORDS

• Hepatobiliary-specific MRI contrast • Gadobenate dimeglumine • Multihance • Gadoxetic acid • Eovist/Primovist • Gd-DTPA • Magnevist

KEY POINTS

- Hepatobiliary-specific contrast agents can distinguish between hepatocyte- and non–hepatocyte-containing lesions. One important example is the ability of gadobenate dimeglumine and gadoxetic acid to differentiate focal nodular hyperplasia from hepatic adenoma, 2 benign lesions with different follow-up and treatment strategies.
- Hepatobiliary-specific agent use is controversial in hepatocellular carcinoma detection and characterization because they do not provide increased sensitivity with respect to the extracellular agents, their uptake may be compromised in the setting of abnormal liver function, and well-differentiated hepatocellular carcinoma may accumulate hepatobiliary-specific agents on delayed hepatocyte imaging, making them indistinguishable from benign hepatocyte-containing lesions.
- Contrast-enhanced magnetic resonance cholangiography has exciting potential uses, including troubleshooting abnormalities encountered at T2-weighted magnetic resonance cholangiography, preoperative biliary anatomy assessment, postoperative biliary tree complications such as bile leaks, and functional biliary tree imaging to aid in the diagnosis of choledocholithiasis and cholecystitis.

INTRODUCTION

Contrast agents have been used in magnetic resonance (MR) imaging since 1986.[1,2] Since the clinical approval of gadolinium (Gd) deglumine in 1988, the daily use of MR contrast agents became widespread. MR imaging contrast improves detection and characterization of liver lesions by increasing lesion-to-liver contrast as a result of decreased T1 relaxation times of liver parenchyma and enhancing lesions.

The major classes of MR contrast agents currently used for liver imaging include extracellular Gd chelates, hepatobiliary-specific agents (including hepatocyte-selective and combined agents), reticuloendothelial agents, and blood pool agents. In this article, the extracellular and hepatobiliary-specific agents will be discussed in detail, highlighting clinical indications, mechanism of action, imaging pitfalls, current clinical applications, and potential future uses.

EXTRACELLULAR CONTRAST AGENTS

Extracellular contrast agents, which are composed of Gd chelated to an organic compound, have been

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in clinical use the longest and remain the most frequently used MR contrast agents.[3,4] Several formulations of extracellular agents exist (**Table 1**); however, their pharmacologic and imaging characteristics are essentially identical.[4] Some of the benefits of the extracellular Gd chelates are that they are considered safe when given at clinically applicable doses in patients without renal failure, they demonstrate other abdominal organ lesions in addition to those of the liver, and they are the least expensive.

CLINICAL INDICATIONS

In the liver, indications for extracellular contrast agent use include lesion detection, lesion characterization, and liver vasculature assessment.[4] Furthermore, most of the "state-of-the-art" liver MR protocols include a dynamic series using an extracellular contrast agent.

MECHANISM OF ACTION

Extracellular contrast agents enter the liver via the hepatic artery and portal vein and freely redistribute from the intravascular to the interstitial space.[5] Liver lesion detection and characterization with extracellular agents rely on differential blood flow between the liver and the tumor.[6] Gd is highly paramagnetic and shortens the T1 (longitudinal) and T2 (transverse) relaxation times of adjacent water protons, causing T1-weighted signal enhancement and T2-weighted signal loss.[4,7] At clinical doses of the extracellular fluid agents, T1 shortening is observed in essentially all tissues.[4,5] Although iodinated contrast and Gd chelates have similar pharmacokinetics, Gd exhibits an amplification effect as a result of its paramagnetic properties, allowing for depiction of subtle areas of contrast accumulation that may not be seen on contrast-enhanced computed tomography (CT). Gd chelates offer better enhancement of the blood pool on equilibrium-phase images than iodinated contrast agents, enabling better delineation of blood vessels than on contrast-enhanced CT.[5,8]

DOSAGE AND ELIMINATION

The recommended dose of extracellular fluid agents is 0.1 mmol/kg, rendering a dose of 20 mL effective in most adults for liver imaging. Renal elimination predominates with the extracellular agents.[9] In patients with normal renal function, documented adverse effects of the extracellular contrast agents are mild and include headache, nausea, and vomiting. Anaphylaxis is exceedingly rare.[10,11] Patients with renal failure are at risk for nephrogenic systemic fibrosis after the administration of any Gd-based contrast agent; however, these risks can be minimized by adhering to restrictive Gd-based contrast agent administration guidelines.[12]

All extracellular fluid agents are labeled class C drugs by the Food and Drug Administration (FDA) with a teratogenic effect demonstrated in animal studies; however, no controlled human studies have been performed. Therefore, Gd chelates are typically avoided in pregnancy, particularly in the first trimester.[13] The effect of Gd excreted in breast milk is unknown, but studies have shown that the expected absorbed dose by the infant from ingesting breast milk is less than 0.05% of the recommended pediatric dose.[14]

IMAGING PROTOCOL

Three- (or more) phase dynamic postcontrast imaging with T1-weighted 2- or 3-dimensional (3D) spoiled gradient echo sequences with chemically selective fat suppression is of paramount importance with the extracellular fluid agents because lesion detection and characterization hinge on differential blood flow between the liver parenchyma and the characteristic enhancement

Table 1
Extracellular contrast agents used for liver MR imaging

Generic Name	Abbreviated Name	Trade Name	Manufacturer
Gadopentetate dimeglumine	Gd-DTPA	Magnevist	Bayer, Wayne, NJ
Gadodiamide	Gd-DTPA-BMA	Omniscan	Nycomed Amersham, Princeton, NJ
Gadoteridol	Gd-HP-DO3A	ProHance	Bracco, Princeton, NJ
Gadoversetamide	Gd-DTPA-BMEA	Optimark	Mallinckrodt Imaging, Hazelwood, MO
Gadoterate meglumine[a]	Gd-DOTA	Dotarem	Guerbet, Villepinte, France
Gadobuterol[a]	Gd-BT-DO3A	Gadovist	Bayer, Wayne, NJ

[a] Not approved by the FDA for use in the United States.