Gadoxetic Acid (Eovist) and Hepatobiliary MR Imaging

- Gadoxetic acid (Eovist) is a new hepatobiliary MR contrast agent that was approved for clinical use in the USA in 2008
- Gadoxetic acid is specifically taken up by hepatocytes and therefore provides increased lesion-liver contrast compared to standard extracellular contrast agents
- At Massachusetts General Hospital, contrast enhanced MR imaging with gadoxetic acid is approved for examinations for:
  - Liver metastases
  - Suspected focal nodular hyperplasias (FNH)

Gadoxetic acid (Eovist®) is a new hepatobiliary MR contrast agent that was approved for clinical use in the USA in 2008. Gadoxetic acid is specifically taken up by hepatocytes using the same molecular mechanism as bile acid. It is eliminated from the body in equal quantities by the biliary and urinary systems. Unlike the standard extracellular gadolinium contrast agents, gadoxetic acid binds weakly to plasma proteins. As a result, T1 relaxivity is greater and enhancement is more intense. For this reason, the dose of gadoxetic acid (0.025 mmol/kg body weight) is one fourth that of conventional MR contrast agents. Gadoxetic acid is well tolerated, and drug-related adverse events are uncommon and mild or moderate in severity. However, there is a small risk of developing nephrogenic systemic fibrosis (NSF) in patients with poor kidney function (see Radiology Rounds, June 2007). Therefore, all patients must have kidney function tests prior to imaging.

Gadoxetic acid can be used for dynamic imaging in the same way as standard extracellular agents as well as during the prolonged hepatobiliary phase. Imaging does not have to be as precisely timed as when standard extracellular imaging agents are used. This allows the acquisition of high-resolution images over multiple breath holds and the possibility of imaging for longer periods to study bile leak. Contrast enhancement in the dynamic phase is similar to that of standard extracellular agents. However, during the hepatobiliary phase, lesions that contain hepatocytes take up gadoxetic acid and may appear hyperintense compared to liver. On the other hand, cancerous lesions and necrotic tissue do not take up gadoxetic acid, appear hypointense, and are visualized more easily than with standard extracellular agents.

The MGH Pharmacy Committee has approved the use of gadoxetic acid for the detection of metastases in patients with colorectal cancer as well as other cancers in which metastases are confined to the liver and resection is being considered. In addition, gadoxetic acid has been approved for the accurate diagnosis of patients who are suspected of having focal nodular hyperplasia (FNH).

Detection of Liver Metastases

Resection of liver metastases in patients with colorectal cancer has the potential to cure and is associated with longer survival compared to other treatments for this disease. Because of the significant risk of partial hepatectomy, it is essential that lesion detection is both sensitive and specific and that lesions are accurately located in relation to the vasculature and the biliary ducts for surgical planning.
Figure 1. Liver Metastases from Colon Cancer: Portal venous phase of contrast after Eovist injection shows ill defined hypodense metastatic lesions (arrows). On the delayed hepatobiliary phase of contrast, the normal liver parenchyma is enhanced whereas the metastases show no contrast uptake and are hence better delineated.

Eovist can provide information from both dynamic and hepatobiliary phase imaging to aid detection of metastases (Figure 1). During dynamic imaging, Eovist has a similar distribution in the extracellular compartments as the more commonly used contrast agents. Therefore, metastases are enhanced because of the vascular abnormalities of metastatic tissue. However, because metastases do not contain hepatocytes, there is no specific uptake of Eovist and metastases appear hypointense compared to the liver parenchyma in the hepatobiliary phase. As a result, contrast-enhanced MR imaging with a hepatobiliary-specific agent depicts more colorectal metastatic lesions in the liver than contrast enhanced MR imaging with an extracellular contrast agent, thereby adding diagnostic information and confidence. This may be particularly useful after neoadjuvant chemotherapy, which often renders known metastases difficult to depict on either contrast enhanced CT or MR imaging, presumably because of changes in tumor vascularity and steatosis in the liver parenchyma.

Focal Nodular Hyperplasia

Focal nodular hyperplasia (FNH) is the second most prevalent tumor of the liver. Eighty to 95% of FNH cases are found in women, most commonly in their third or fourth decade of life. Most are found incidentally after patients have undergone cross sectional imaging for unrelated symptoms. FNH is comprised of normal components of liver but in an abnormally organized pattern with blind ductules that do not lead to larger bile ducts. In 60-70% of cases a central stellate scar and fibrous septa are present. FNH is benign with no malignant potential and rarely grows or bleeds. However, FNH lesions are often resected because of the difficulty of distinguishing them from other lesions such as hepatic adenomas.

Dynamic contrast MR imaging using a standard extracellular contrast agent such as Gd-DTPA (Magnevist) has an estimated sensitivity of 70% and specificity of 98% diagnosing FNH. FNH lesions appear iso-intense with liver parenchyma in T2 images, with a higher signal from the central scar. On dynamic contrast MR imaging using standard extracellular agents (such as gadopentate), FNH is strongly enhanced during the arterial phase and, during the portal phase, becomes isointense with liver parenchyma while the central scar is enhanced. In comparison, hepatocellular adenomas show less enhancement and typically lack a central scar. However, the presence of a central scar is not diagnostic for FNH because such scars can found in some patients with fibrolamellar hepatocellular carcinoma, hepatic adenoma, or intrahepatic cholangiocarcinoma. Therefore, although dynamic contrast MR imaging can be used to diagnose FNH with a high degree of confidence, follow-up imaging after 6-12 months is recommended to confirm the diagnosis.

MR imaging using gadoxetic acid increases the degree of confidence in an FNH diagnosis, especially in atypical cases that can be hard to differentiate from hepatocellular adenoma, hepatocellular carcinoma, fibrolamellar carcinoma, or hypervascular metastases. Because FNH lesions contain hepatocytes, they take up Gd-EOB-DTPA but, because of their structure, biliary excretion is slow compared to normal liver parenchyma. Therefore, FNH lesions are hyperintense in hepatobiliary phase imaging, 10-60 minutes after injection of Gd-EOB-DTPA (Figure 2). This hyperintensity confirms the diagnosis of FNH, and the patient can be managed conservatively without follow-up imaging.
**Figure 2.** Hepatic Focal Nodular Hyperplasia (FNH): Arterial phase of contrast after Eovist injection shows brisk enhancement of the lesion (arrow). On the delayed hepatobiliary phase of contrast, the lesion shows contrast uptake and is hyperintense when compared to background liver parenchyma, which is a specific sign for liver FNH.

**Scheduling**

MR imaging examinations are performed on the main Mass General campus, Mass General West Imaging – Waltham and Mass General Imaging - Chelsea. They may be scheduled online through Radiology Order Entry (http://mghroe) or by calling 617-724-9729 (4-XRAY).

**Further Information**

For further questions on the use of Eovist (gadoxetic acid, please contact Mukesh Harisinghani, MD, Abdominal Imaging and Intervention, Department of Radiology, Massachusetts General Hospital at 617-726-8396.

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**References**


