Editor's note: The protocols described below represent the in-house imaging recommendations of the indicated radiology departments and are suggestions only. These protocols are designed for use at 1.5 T and may include off-label uses of contrast media. Further information may be available from your imaging equipment and contrast media vendors.

wo types of commercially available contrast media are useful when imaging the liver. One type is composed of purely extracellular agents. The other is composed of hepatobiliary agents, which have properties of extracellular agents but are also taken up differentially by functioning hepatocytes.

Extracellular agents are suited to liver imaging applications that require:

- information obtained during the dynamic contrast-enhanced phase, or
- excellent vascular visualization.

With their ability to visualize vascular perfusion, extracellular agents such as gadobutrol (Gadavist[™] [US], Gadovist[®] [EU], Bayer) and gadoversetamide (Optimark[™], Covidien [Mallinckrodt]) can be used to detect and characterize focal liver lesions.

Hepatobiliary agents are suited to applications focusing primarily on:

- biliary visualization, and
- distinguishing between hepatocytes and lesions not containing hepatocytes.

Liver-specific agents such as gadoxetate disodium (Eovist® [US], Primovist® [EU], Bayer) and gadobenate dimeglumine (MultiHance®, Bracco) have extracellular properties but also have an affinity for hepatocytes.

The European Union has approved liver imaging indications for Gadovist, Optimark, Primovist, and MultiHance. The US Food and Drug Administration (FDA) has approved Eovist and Optimark for liver imaging. MultiHance is widely used off-label in the United States for liver imaging.

The pharmacokinetic differences between extracellular agents are insignificant, according to Dr. Scott B. Reeder, Chief of Cardiovascular, Chest and Abdominal Imaging at the University of Wisconsin-Madison. Consequently, the choice of an extracellular contrast medium is based primarily on differences in local preference, safety profile, and cost considerations.^[1]

In regard to hepatobiliary agents, UW-Madison guidelines^[1] recommend:

- Eovist for bile duct imaging and lesion characterization using delayed imaging (*Note: Eovist should not be used for nonhepatobiliary applications*)
- MultiHance for vascular imaging and characterization of lesions using dynamic imaging

GENERAL APPLICATIONS/INDICATIONS

The following protocols are described in UW-Madison guidelines.^[1]

MULTIHANCE

- Cirrhotic liver (hepatocellular carcinoma screening/evaluation; complications of portal hypertension)
- Metastatic disease with no prior liver imaging (known malignancy; no known metastatic disease -- rule out liver metastases)
- Pre-liver transplantation (evaluate liver anatomy; unsuspected pathology)
- Complications of liver transplantation

 vascular complications (hepatic arterial or portal venous stenosis/occlusion/thrombosis)
 - Biliary and vascular complication suspected (biliary leak/stenosis, vascular complication)
- Characterization of liver lesion (incompletely characterized focal liver lesion/unlikely to be focal nodular hyperplasia (FNH) or hepatic adenoma)
- Evaluation of nonhepatic abdominal pathology or symptomatic patient with no prior imaging/relevant history

EOVIST

- Metastatic disease with prior imaging with MRI, CT, and/or ultrasound (follow known metastatic disease; improve characterization of extent of disease seen on other imaging; liver segment volume measurements prior to resection)
- Complications of liver transplantation with biliary complications such as biliary leak; anastomotic stenosis
- Living related liver donor (liver and vascular anatomy; liver segment volumes, if CT is contraindicated) (Note: Eovist is indicated if MR angiography is not needed. Otherwise, consider giving Eovist after dynamic phase imaging with MultiHance to provide MR angiography.)
- Biliary disease
 - primary sclerosing cholangitis (PSC) (evaluate for complications of PSC, including strictures, biliary obstruction, stones, cholangiocarcinoma)
 - other biliary disease (intrahepatic biliary stones, bile leak [eg, trauma], choledochal cyst/Caroli disease)
 - Characterization of FNH vs adenoma (incompletely characterized focal liver lesion with high suspicion for FNH or hepatic adenoma (Note: Prior imaging with CT or ultrasound required.)

OPTIMIZED PROTOCOLS

EXTRACELLULAR CONTRAST MEDIA

Radiologists at Duke University Medical School in Durham, North Carolina, apply the following protocols when using extracellular gadolinium contrast agents and MultiHance to enhance the liver.

Field Strength: 1.5 T

PRECONTRAST PULSE SEQUENCES

- Multiplanar localizer
- 2D coronal T2-weighted single-shot fast spin echo (FSE)
- 3D axial fat-suppressed T1-weighted in- and out-ofphase gradient echo (GRE) with 2-point fat only and water only Dixon reconstructions
- Diffusion-weighted imaging (axial)
- T2-weighted imaging: 2D axial T2-weighted FSE

INJECTION

- **Dose**: 0.1 mmol/kg body weight
- Injection Rate: 2 mL/sec followed by 20 mL of saline chaser injected at 2 mL/sec
- Data Acquisition Start: delay in data acquisition depending on the patient's age of 15 seconds in patients younger than 60 years and 20 seconds in patients older than 60 years

CONTRAST PULSE SEQUENCES BY PHASE

- Arterial: 3D axial fat-suppressed T1-weighted GRE triple arterial phase
 - acquire 3 consecutive phases (triple-arterial) at 2 mL/sec injection rate
 - acquire single phase (single-arterial) at 2 mL/sec injection rate with bolus triggering
- Portal Venous: 3D axial fat-suppressed T1-weighted GRE
- 3D coronal heavily T2-weighted FSE respiratorytriggered MR cholangiopancreatography (MRCP) at high resolution
- Delayed: 3D axial fat-suppressed T1-weighted GRE

HEPATOBILIARY CONTRAST MEDIA

Hepatobiliary agents are taken up by functioning hepatocytes. This behavior can be exploited on delayed T1weighted imaging for liver lesion characterization and imaging of the bile ducts.

MultiHance

Off-label, but widely used in liver imaging because of high relaxivity and contrast enhancement; main disadvantage is the hepatobiliary phase peak approximately 1-2 hours after contrast injection, which requires a short interval follow-up study.

Field Strength: 1.5 T

PRECONTRAST PULSE SEQUENCES

- Multiplanar localizer
- 2D coronal T2-weighted single-shot FSE
- 3D axial fat-suppressed T1-weighted in- and out-ofphase GRE with 2-point fat only and water only Dixon reconstructions
- Diffusion-weighted imaging (axial)
- 2D axial T2-weighted imaging

INJECTION

- Dose: 0.1 mmol/kg body weight
- Injection Rate: 2 mL/sec followed by 20 mL of saline chaser injected at 2 mL/sec
- Data Acquisition Start: delay in data acquisition depending on the patient's age of 15 seconds in patients younger than 60 years and 20 seconds in patients older than 60 years

CONTRAST PULSE SEQUENCES BY PHASE

- Arterial: 3D axial fat-suppressed T1-weighted GRE triple arterial phase
 - acquire 3 consecutive phases (triple-arterial) at 2 mL/sec injection rate
 - acquire single phase (single-arterial) at 2 mL/sec injection rate with bolus triggering
- Portal Venous: 3D axial fat-suppressed T1-weighted GRE
- 3D coronal heavily T2-weighted FSE respiratorytriggered MRCP at high resolution
- Delayed: 3D axial fat-suppressed T1-weighted GRE
- Hepatobiliary (acquisition 1-2 hours after contrast injection; consider increased flip angle approximately 20-30 degrees to improve signal-to-noise ratio and contrast-to-noise ratio)
 - o Sequential 3D axial fat-suppressed T1-weighted GRE
 - o 3D coronal T1-weighted GRE (last acquisition to look at biliary ductal system)

EOVIST/PRIMOVIST (BAYER) FOR NONCIRRHOTIC AND CIRRHOTIC LIVER

Radiologists at Duke University Medical School in Durham, North Carolina, apply the following protocol when doing Eovist-enhanced studies of the liver. The protocol was developed in collaboration with colleagues at Hannover Medical School in Hannover, Germany, and the University of California in San Diego for imaging the noncirrhotic^[2] and cirrhotic liver.^[3]

Field Strength: 1.5 T

PRECONTRAST PULSE SEQUENCES

- Multiplanar localizer
- 2D coronal T2-weighted single-shot FSE
- 3D axial fat-suppressed T1-weighted in- and out-ofphase GRE with 2-point fat only and water only Dixon reconstructions
- 3D coronal heavily T2-weighted FSE respiratorytriggered MRCP at high resolution

INJECTION

- Dose: 0.025 mmol/kg body weight (FDA approved dosage); Duke/Hannover/UCSD often use nondiluted dose of either 10 mL or 20 mL, depending on patient weight (rounded to nearest bottle) for patients with normal renal function. Doses are administered without rounding for those with an estimated glomerular filtration rate less than 60 mL/min.
- **Injection Rate**: 1-2 mL/sec followed by 20 mL of saline chaser injected at 2 mL/sec
- Data Acquisition Start: delay in data acquisition depending on the patient's age of 15 seconds in patients younger than 60 years and 20 seconds in patients older than 60 years, if a triple arterial phase approach is used (2 mL/sec injection rate); the use of bolus triggering is recommended if using a single arterial phase approach (1 mL/sec injection rate)

CONTRAST PULSE SEQUENCES BY PHASE

- Arterial: 3D axial fat-suppressed T1-weighted GRE triple arterial phase (acquire 3 consecutive phases [triple-arterial] or single arterial phase with higher spatial resolution)
- Portal Venous: 3D axial fat-suppressed T1-weighted GRE
- Late Dynamic: 3D axial fat-suppressed T1-weighted GRE
- Diffusion-weighted imaging (axial) (performed after contrast injection to boost workflow; contrast does not change apparent diffusion coefficient values)
- T2-weighted imaging: 2D axial T2-weighted FSE (performed after contrast injection to increase contrastto-noise ratio and to optimize workflow)

- Hepatobiliary (acquisition no sooner than 10 minutes after contrast injection; consider increased flip angle; consider T1-weighted respiratory triggering)
 - Sequential 3D axial fat-suppressed T1-weighted GRE (performed until major bile ducts enhance intensely with contrast agent or until at least 30 minutes after contrast injection, whichever is sooner)
 - 3D coronal T1-weighted GRE (last acquisition to look at biliary ductal system)

References

- Reeder SB. Contrast media for liver MRI: which one to choose? Program and abstracts of ISMRM 2011; May 7-13, 2011; Montreal, Quebec, Canada.
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