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Targeted MRI contrast agents for pediatric hepatobiliary disease

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INTRODUCTION

Hepatobiliary specific contrast agents (HSA) for magnetic resonance imaging (MRI) have recently been approved for use in the United States. Originally developed to improve detection and characterization of liver lesions, these agents also provide exquisite detail of bile duct anatomy. HSA are injected intravenously, actively transported into hepatocytes, and excreted into bile ducts. This targeted imaging of the hepatobiliary system is advantageous when characterizing liver lesions and bile duct abnormalities. The test also obtains functional information.

Although originally described in adults,^{1–4} recent data support several promising pediatric applications for HSA.^{5,6} MRI with HSA may complement traditional imaging strategies and surmount several difficulties encountered when imaging the pediatric liver and biliary tract. This review describes the current state of the art for imaging the pediatric hepatobiliary system and suggests emerging applications for MRI in light of these new HSA.

CONVENTIONAL STRATEGIES FOR HEPATOBILIARY IMAGING

Unique challenges exist to non-invasively detect hepatobiliary disorders in the pediatric population. Overall, the ideal imaging test should be non-invasive, rapid to perform, and free of ionizing radiation, but still provide exquisite anatomic detail and perhaps functional information. Selection of the appropriate imaging test depends on a number of factors. First, children have smaller anatomic structures and require imaging strategies with higher resolution. For example, normal pediatric common bile duct measures between 1 and 3 mm in diameter⁷ and intrahepatic bile ducts are sub-millimeter in size,⁵ whereas normal adult common bile ducts approach 6 mm. Second, young children and older children with special needs may be unable to tolerate or hold still for an imaging test, so they may require sedation or anesthesia. Third, the use of imaging tests with ionizing radiation should be minimized given that children may be more sensitive to the long-term effects of radiation exposure than adults.

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CONFLICT OF INTEREST: None

Ultrasound

Ultrasound is the least costly and most widely used non-invasive method to evaluate the pediatric hepatobiliary system. Ultrasound is often the first imaging test of choice, because it offers quick, non-invasive evaluation of the liver parenchyma and bile ducts. The sonographic appearance of benign and malignant hepatic neoplasms may be difficult to differentiate by imaging alone, although significant information can be provided. The size and number of hepatic lesions, as well as the appearance of the underlying parenchyma, can be readily determined, aiding in narrowing of differential diagnoses.⁸

Common bile duct (CBD) dimensions as measured sonographically increase by age and demonstrate small changes in caliber during daily fluctuations in bile flow. In a study of sonographic CBD measurements in 173 healthy patients aged 1 day to 13 years, normal CBD diameters were 1.6mm for patients less than 1 year of age and 2.5–3.0 mm for children and early adolescents.⁷ Evaluation of the distal CBD by ultrasound can be limited due to overlying bowel gas, and no functional information is obtained.

Computed tomography

Contrast enhanced multidetector computed tomography (CT) provides better visualization of the distal CBD than ultrasound. Liver lesions and their involvement with adjacent structures may be depicted with excellent spatial resolution.⁹ Multiphase contrast-enhanced CT will further characterize liver lesions and improve diagnostic specificity, but at the expense of increased radiation exposure. Dual-phase helical CT is reported to have a sensitivity of 69% 71% and specificity of 86% 91% for characterizing benign and malignant hepatic lesions.¹⁰ The multiplanar display of CT images also gives improved anatomic localization and visualization of focal liver and biliary lesions. Shorter imaging times also decrease the need for sedation.^{11,12}

The intrahepatic bile ducts in normal, healthy pediatric patients are often barely perceptible by CT. Their assessment can be augmented with the use of hepatocyte specific contrast agents such as 52% iodipamide meglumine (Cholografin meglumine; Bracco Diagnostics, Princeton, New Jersey).^{4,5} Use of this agent, however, requires premedication due to its increased risk of allergic reactions as an ionic contrast agent. It is typically used for pre-operative assessment of adult living liver transplant donors and is not commonly employed in children because of its allergic potential and its use of ionizing radiation. An optimum balance between low-dose radiation and diagnostic quality imaging must be established at institutions performing CT in pediatric patients.

Magnetic resonance imaging (conventional)

MRI and magnetic resonance cholangiopancreatography (MRCP) affords comparable anatomic detail to CT without ionizing radiation. MRI is far superior in tissue contrast. Multiphase MRI using non-liver specific contrast agents has slightly improved ability to detect liver lesions compared to dual phase CT, but was significantly superior in lesion characterization.¹³ T1 and T2 weighted appearance and enhancement characteristics assist in narrowing diagnostic considerations in liver lesions. Since MRI is free of ionizing radiation, repeated imaging with multiple phases after the injection of contrast can be obtained. Limitations to MRI include longer imaging times and the need for sedation in younger patients. Improvements with faster sequences will likely lead to further reduction in sedation requirements.

Heavily T2-weighted 3D-MRCP sequences also provide exquisitely detailed imaging of the biliary system. T2-weighted MRI images allow creation of maximum intensity projections as well as three-dimensional reconstructed models of the biliary tract. Using this technique,

bile ducts as small as 1mm can be depicted.¹⁴ Obtaining such high-resolution duct anatomy requires excellent patient cooperation or anesthesia to limit motion. Moreover, no functional information is provided with this study.

Interventional

In cases where diagnostic confirmation or intervention is necessary, endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) may be performed. These tests involve the direct injection of contrast into the biliary system and allow for both diagnosis and intervention. The risks of this procedure which appear to have similar rates in adults and children^{15,16} must be balanced with the higher resolution and therapeutic options offered by ERCP over MRI with HSA.

PHARMACOKINETICS OF HEPATOBILIARY SPECIFIC AGENTS

MRI contrast agents for hepatobiliary imaging are injected intravenously (IV) and specifically target the liver. Both HSA and more routinely used non-HSA are designed with two basic components: gadolinium and a chelate for gadolinium. Gadolinium alters surrounding water hydrogen molecules, producing increased signal intensity on T1-weighted MR images.

The chelate prevents the escape of free gadolinium, and, more importantly, the outer coat of the chelate localizes the HSA to the liver. The outer surface of the chelate is recognized by hepatocytes for active transport into the liver and subsequent biliary excretion. Several transport mechanisms exist that allow transport from the hepatocytes to the biliary system. HSA are low in molecular weight so they will readily pass into interstitial spaces; contrast remaining in the blood pool will be rapidly excreted by the kidneys.

Several contrast agents have been tested for depiction of the biliary system. Gadoxetate disodium was FDA-approved for use in the U.S. in 2008 and marketed as Eovist® in the U.S. and Primovist® in Europe.^{17,18} Although imaging children with gadoxetate is currently off-label use, an ongoing, multi-center observational cohort study sponsored by the manufacturer is underway to examine the safety and efficacy of gadoxetate in pediatric patients.¹⁹

HSA initially follow similar blood distribution kinetics as other non-hepatobiliary specific contrast agents (non-HSA). Peak arterial enhancement typically occurs within 30 seconds and peak portal venous enhancement within 60 seconds. Peak enhancement varies depending on cardiac output and age of the child. Obtaining imaging during this early time will produce similar images as a routine contrast enhanced abdominal MRI (non-HSA), yielding excellent depiction of abdominal organs and masses.

Later than 60 seconds after the IV injection, the HSA show a very different biodistribution than non-HSA. The liver takes up approximately 50% of the HSA, with a noticeable decrease in hepatic venous enhancement and increase in liver enhancement (Figure 1). Approximately 50% of HSA contrast is excreted through the kidneys, compared with the majority of non-HSA contrast.

Over the next 20–40 minutes, the hepatocytes transport and excrete the HSA into the bile ducts. This accumulation of contrast material facilitates depiction of the biliary system.²⁰ Maximal biliary excretion, and thus optimal visualization of duct anatomy, occurs at approximately 20–60 minutes.

Since HSA relies on hepatocyte transport mechanisms, alterations in liver function alter the transport of HSA. Thus, liver function must be considered when interpreting these MRI

examinations.²¹ Patients with end-stage or decompensated cirrhosis will have substantially decreased liver uptake and biliary excretion, so liver lesions and bile ducts will be less well visualized in a cirrhotic liver.²² This is likely due to reduced number and function of OATP1 and cMOAT. Unfortunately, decreased liver uptake and excretion of HSA does not appear to correlate with serum markers of liver function.²³

Several other facets need to be considered when interpreting MRI with HSA in patients with liver dysfunction. Uptake and excretion times are similar to normal in patients with early or well-compensated cirrhosis.²¹ Alterations in the kinetics of HSA biodistribution in various forms of pediatric liver dysfunction have not been studied to date, but a safe assumption is that uptake is delayed. Cholestasis and cirrhosis are also associated with a longer plasma half-life but attenuated enhancement of the hepatic and portal veins. Renal insufficiency will further prolong blood vessel enhancement. As with non-HSA, HSA are contraindicated in patients with decreased glomerular filtration rates because of the associations among renal failure, intravenous gadolinium administration, and nephrogenic systemic fibrosis.

TECHNICAL CONSIDERATIONS FOR HEPATOBILIARY SPECIFIC MRI

Imaging of the hepatobiliary system has rapidly advanced over the past 5–6 years. High-resolution images of the biliary tree can now be routinely obtained in 20–30 seconds, well within the ability of most children to hold their breath. New hardware and pulse sequence design have enabled faster imaging with good signal-to-noise ratio (SNR).

High SNR is important to produce quality images with adequate image resolution and tissue contrast. These capabilities are found on MRI equipment developed by the major MRI manufacturers within the last 5–6 years. Increased field strength,^{24–26} fast gradients, and multichannel array coils^{27–29} give increased performance with higher SNR, better spatial resolution, and improved speed. This combination greatly improves body imaging and high-resolution images can be obtained in a single breath-hold.

The other critical component in both conventional MRI and MRI with HSA is the selection of pulse sequences. Pulse sequences drive MRI hardware to create images that emphasize different tissues based on T1 and T2-weighting. Pulse sequence design also allows wide flexibility in balancing image resolution and acquisition speed.

The strategy for imaging bile ducts with HSA is completely different than conventional MRCP. Conventional MRI/MRCP emphasizes structures that contain primarily water and employs heavily T2-weighted pulse sequences. Tissue contrast is decreased on T2-weighted imaging, such that structures containing water—like the lumens of the bile ducts, gallbladder, duodenum, and renal collecting system—are bright in signal intensity. Surrounding tissues that contain little water produce little signal, so the bile ducts stand out in contrast and are well depicted.

In MRI with HSA, two factors allow for increased visualization of ductal anatomy. First, rather than highlighting water contained in ducts, the T1-weighted pulse sequences highlight structures with gadolinium. Gadolinium increases the SNR for better visualization of duct anatomy.^{4,30} Second, the three-dimensional gradient echo T1-weighted imaging is performed in a single breath-hold, at a higher resolution, and can be transformed into three-dimensional images.²⁴ Ductal anatomy may be visualized in 1 mm slice thickness (Figure 2). This resolution is less than percutaneous or endoscopic cholangiography but MRCP provides extraluminal information, is less invasive, and radiation-free.

One important drawback of MRI with HSA should be mentioned. The time spent waiting for excretion of the contrast agent into the biliary system results in longer overall imaging times

than conventional T2-weighted MRCP. Although the extra 20–45 minutes the child spends in the MRI scanner are approximately 30 to 100% longer than conventional MRCP, select children will likely benefit from this study as illustrated by the cases below.

POTENTIAL APPLICATIONS FOR MRI WITH HEPATOBILIARY SPECIFIC AGENTS

Liver Lesions

Several clinical scenarios exist in which HSA provides information beyond other tests for the diagnosis and management of liver masses. Although liver masses are rare in children, proper classification is crucial for appropriate management. HSA identifies and helps distinguish between benign and malignant lesions and extends the capabilities of diagnostic imaging beyond other imaging modalities (CT/US/conventional MRI). Table 1 lists lesions where HSA might be useful to characterize liver lesions in children.

Focal nodular hyperplasia—MRI with HSA is an excellent diagnostic choice for characterizing focal nodular hyperplasia (FNH). The unique cellular composition of FNH, combined with the hepatocyte and biliary targeting properties of HSA, usually allow separation of FNH from other liver lesions on MRI. FNH contains normal hepatocytes which readily take-up HSA. Due to malformed bile ducts present in FNH the hepatocytes fail to excrete the HSA. Thus, FNH lesions readily enhance on the arterial phase of imaging and continue to enhance over an extended period of time (Figure 3).

FNH lesions remain high in signal intensity on MRI long after other liver lesions have washed out (lost signal intensity from clearance of the HSA) compared to surrounding normal liver parenchyma (Figure 3C). Separating FNH from metastasis and malignant tumors of liver origin is one of the primary advantages of HSA over US and conventional CT and MRI. Several studies have shown improved diagnostic capabilities for detecting FNH during the liver-specific phase of gadoxetate compared to non-contrast MR and spiral CT.^{31–33}

Hepatic adenoma—Similar to FNH, hepatic adenomas contain hepatocytes, though adenomas do not contain bile ducts. Adenomas are typically hyperintense to liver parenchyma on T1 weighted imaging (either secondary to intratumoral fat and/or hemorrhage), enhance on arterial phase imaging, and commonly show loss of signal on opposed phase sequences. Fat content is not specific for adenoma, however, as hepatocellular carcinoma can also contain fat.³⁴ Adenomas also tend to be solitary, round, or ovoid, contain a capsule, and often lack the central scar of FNH. Hepatic adenomas are rare in the pediatric population but are occasionally seen in adolescent girls, particularly those on oral contraceptives, or in children with glycogen storage disease type 1a, and in patients with Fanconi anemia.³⁵

Experience with other hepatocyte specific agents, specifically gadobenate dimeglumine, suggests the lack of bile ducts can be used to distinguish between adenomas and FNH. Adenomas are typically hypointense to liver parenchyma on hepatocyte phase imaging due to their lack of biliary canaliculi.³⁶ FNH, as described previously, often demonstrates hyperenhancement on hepatocyte phase imaging. There is, however, reported variability in the enhancement pattern of adenomas with gadoxetate and larger dedicated investigations are needed.²¹ Because the risk of hemorrhage, rupture, and malignant transformation associated with adenomas makes surgical resection the usual treatment, correct diagnosis is important and often possible with HSA.

Primary malignant liver lesions—Hepatoblastoma, hepatocellular carcinoma (HCC) and liver sarcomas are the primary malignant liver tumors in children and imaging may help distinguish these tumors from benign masses. Features atypical for FNH or hepatic adenoma on MRI with HSA should raise suspicion for a malignant tumor.

Hepatoblastoma is the most common primary malignant liver neoplasm in pediatric patients with the vast majority (>90%) of patients under the age of 5 at presentation.³⁷ An association exists between hepatoblastoma and certain syndromes, most notably Beckwith-Weideman. The majority (>80%) appear as large solitary lesions. These tumors contain differing amounts of epithelial and mesenchymal elements and thus can have a variable imaging appearance. Typical imaging appearance includes heterogeneous T2 hyperintensity, predominant T1 hypointensity, and heterogeneous enhancement with standard MRI contrast agents. With hepatobiliary specific agents hepatoblastoma has been described as hypointense to background liver parenchyma on all phases.³⁸

HCC contains hepatocytes dedifferentiated to varying degrees and HCC tends to show rapid arterial enhancement just as FNH. However, unlike FNH, HCC lesions will quickly washout and not show delayed enhancement (Figures 4 and 5). This washout of HSA should raise the possibility that a lesion is HCC.

Several caveats are important in interpreting imaging studies when HCC is suspected. HCC can be difficult to differentiate from regenerative nodules in the cirrhotic liver (Figure 3). Regenerative nodules contain functioning hepatocytes surrounded by fibrous septa. Thus, uptake of HSA in the hepatocyte phase should ideally match that of background liver tissue.²² There is, however, a spectrum of appearance in regenerative nodules which can be further complicated by underlying heterogeneous enhancement in a cirrhotic liver. Studies in adults suggest that HSA may be particularly useful in differentiating small HCC lesions from other hypervascular arterial enhancing pseudolesions because the former are usually hypointense in the hepatobiliary phase and the latter are typically isointense.³⁹ The appearance of HCC on hepatocyte phase imaging depends on the degree of differentiation.²¹ Moderate to poorly differentiated HCC appear hypointense relative to background liver parenchyma during the hepatocyte phase because they do not uptake HSA well, but well-differentiated HCC with functioning hepatocytes can mimic the uptake of benign tumors.

Liver lesions with no clearly established role for hepatobiliary specific agents

Hepatobiliary specific contrast agents would not be expected to provide additional information for liver lesions that lack hepatocytes (Table 1). For example, hepatoblastomas contain mainly incompletely differentiated hepatoblasts and mesenchymal cells.³⁵ Given the cellular constituents of this tumor, HSA is not likely to add significantly to standard contrast-enhanced MRI in its diagnosis since this lesion will likely have isointense signal intensity to background imaging on hepatocyte phase imaging.

Infection is usually readily separated from tumor on conventional imaging. MRI with HSA will provide similar information as non-HSA. Central enhancement is usually not seen in infection, since the lesions in focal liver infections tend to displace or replace hepatocytes. The lack of early or delayed enhancement of a liver lesion raises the possibility of infection.

Similarly, liver cysts are usually readily appreciated on conventional imaging. Liver hemangiomas are also characterized well by ultrasound and confirmed by multiphase MRI with non-HAS (Figure 8). Table 2 summarizes the imaging appearance of the commonly encountered pediatric liver lesions with HSA.

Biliary Duct Pathology

Magnetic resonance cholangiopancreatography (MRCP) with HSA can add additional information to the diagnosis and characterization of pediatric bile duct abnormalities. Several studies illustrate the utility of MRCP for defining bile duct abnormalities and pinpointing diagnosis in children^{40–42} MRCP with HSA will likely expand these capabilities. Furthermore, our initial experience with HSA suggests that this imaging tool is particularly useful in subtle or atypical biliary lesions as illustrated in the cases below.

Intrinsic bile duct obstruction—MRCP with HSA has several roles when evaluating children with known or suspected biliary stone disease. First, MRI with HSA provides radiation free evaluation of the intraluminal anatomy with exquisite resolution (Figure 6). Second, unlike ultrasound where bowel gas may obscure the distal common bile duct, MRCP with HSA can depict the majority of the biliary system and is less invasive than ERCP.

Although MRCP with HSA is usually not the first imaging test to consider when working up children for bile duct stones, moving to MRCP with HSA may be reasonable if ultrasound is uninformative. Furthermore, MRI may reveal unexpected findings outside the ducts. This may be helpful in patients with underlying chronic diseases who are susceptible to biliary stones as well as other abdominal pathologies, such as chronic hemolytic disease, cystic fibrosis, history of total parenteral nutrition or intestinal resection, familial hyperlipidemias, and cirrhosis or chronic cholestasis.⁴³ The utility of HSA is expected to increase due to the anticipated increase in prevalence of biliary obstruction in tandem with the obesity epidemic in the United States.⁴⁴

Extrinsic bile duct obstruction—The capability of MRCP with HSA to show extraluminal pathology also helps with the diagnosis of extraluminal bile duct stenosis. Extraluminal pathologies such as tumor are readily depicted on the abdominal imaging component of the examination and help distinguish between bile duct stenosis (Figure 6) and extrinsic compression from masses.

Aberrant and congenital variations in bile duct anatomy—MRI with HSA may have a role in mapping out the anatomy of choledochal cysts. Although cysts are readily seen on conventional MRI,⁴⁵ MRI with HSA can be particularly helpful in diagnosing very subtle dilations or stenoses of the biliary or pancreatic ducts or show communication between pancreatic and biliary systems (Figure 7). This may assist in surgical planning.

Subtle abnormalities of the ducts: primary sclerosing cholangitis—The high-resolution imaging provided by MRCP with HSA may show subtle lesions in early primary sclerosing cholangitis (PSC). The onset of PSC is usually insidious, with vague signs and symptoms.⁴⁶ Thus, diagnosis usually requires clinical suspicion and targeted imaging. Both MRCP and ERCP are helpful in diagnosis, with sensitivities estimated at 80–91% and specificity 80–96% in blinded studies of adult patients.^{47,48} Studies in pediatric specific population revealed sensitivity of 81%, specificity of 100%, negative predictive value of 62%, positive predictive value of 100%, and accuracy of 85% in the diagnosis of PSC in children.⁴⁹ Our experience suggests that the biliary excretion of HSA aids in the non-invasive identification of subtle PSC changes, particularly in the intrahepatic ducts.

FUTURE APPLICATIONS

The cases above illustrate applications specifically relevant for children with hepatobiliary disease and suggest the potential of HSA for additional diagnostic purposes. Given the

recent FDA approval of gadoxetate disodium for adults, its use in children has been guided by early experience with adults. The indications in childhood hepatobiliary disease rely on this adult experience. Specific roles for MRI with HSA are currently under-tested in children.

The excretion of gadoxetate disodium through the biliary ductal system may also be useful in delineating bile duct patency or perforations. One case report suggests HSA can detect active bile leak following laparoscopic cholecystectomy.⁵⁰ Bile duct injury and leaks occur in children after liver transplantation and choledochal cyst resections as well as more routine operations like cholecystectomy. HSA may provide a non-invasive method to delineate the extent and location of bile leaks. However, MRI does require sedation in younger children and does not provide therapeutic opportunities, as does ERCP or percutaneous transhepatic cholangiography. Use in the peri-transplant period should also be carefully considered depending on the patient's current and past renal function, given the risk for nephrogenic systemic sclerosis.

Although a role for HSA in children suspected of having biliary atresia has been proposed, the potential duct and liver dysfunction in these patients will likely alter the biliary excretion of HSA. Similar to hepatobiliary imino-diacetic acid (HIDA) scans, poor uptake and excretion prolongs imaging times and delivers less HSA into the liver and ducts, making it challenging to differentiate biliary atresia, Alagille syndrome, or neonatal hepatitis by using MRI with HSA. Liver uptake and excretion of HSA will be delayed, decreased, or absent within a reasonable timeframe for imaging in all three of these entities.

The small size of bile ducts in neonates and infants coupled with decreased biliary excretion will make visualization of ducts, when present, very challenging given the current resolution and tissue contrast capabilities of MRI with HSA. More importantly, as with HIDA scans, lack of visualization of the ducts does not rule in biliary atresia, so MRCP with HSA would not avoid need for intraoperative cholangiogram or liver biopsy in suspected biliary atresia. Despite these limitations, criteria and a role for MRCP with HSA might be developed to triage neonates suspected of having biliary atresia, especially when function tests are still relatively normal.

MRI with HSA may also be useful for identifying and delineating post-operative remnants of choledochal cysts. Cholangiocarcinoma is very rare in children, but is a major risk of retained choledochal cysts. It is also seen in children with sclerosing cholangitis and familial adenomatous polyposis. Preliminary studies in adults suggest that MRI with HSA may improve cholangiocarcinoma detection, as the abnormal epithelium shows irregular peripheral rim enhancement during the arterial phase followed by hypointensity relative to adjacent liver in the hepatocyte phase.²¹

CONCLUSION

MRI contrast agents targeted to the liver and bile ducts add a new dimension for diagnosis and patient management and will likely complement existing imaging techniques. Interpretation of MRI with hepatobiliary specific contrast agents utilizes the unique properties of the contrast agent for uptake into liver cells and subsequent excretion into the biliary system. These properties give functional information about liver masses and provide exquisite anatomic detail of the bile ducts. Although additional experience will be necessary to further establish roles for pediatric patients suspected of having liver lesions or bile duct disorders, MRI with hepatobiliary specific contrast agents will likely play an increasing role in clinical decision-making.

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Figure 1.

Typical kinetics of delivery, uptake, and excretion of the hepatobiliary specific agent gadoxetate. Arterial phase imaging at 30 seconds after intravenous injection of gadoxetate shows contrast material in the arteries and early filling of the portal vein and inferior vena cava (ivc). Portal venous phase at 70 seconds shows uniform filling of the arteries, veins, and hepatic parenchyma. At 20 minutes, contrast material has left the vessels, but retained in the liver parenchyma and also excreted in the bile ducts.

Figure 2.
Volume-rendered 3D image demonstrating dilated bile ducts and lumen of the common bile duct stent (s) depicted with gadoxetate, a hepatobiliary specific contrast agent. d=duodenum.

Figure 3.

Liver masses diagnosed as focal nodular hyperplasia by MRI after injection of a hepatobiliary-specific contrast agent (HSA). This 18 year-old patient has remote history of treated medulloblastoma (in remission) and found to have liver masses on ultrasound (not shown). (A) Dynamic imaging after the injection of the hepatobiliary agent shows rapid uptake into small (arrowhead) and large lesions (arrow) during the arterial phase 20 seconds after administration of HSA. (B) At 70 seconds after injection during the portal venous phase, the lesions are similar in intensity to the liver parenchyma and the smaller lesion is imperceptible. Delayed imaging at 14 minutes shows preferential retention into the disorganized hepatocytes of both lesions (C). Coronal imaging at 20 minutes (D) shows the dominant mass (*) adjacent to the eventual excretion of the HSA into the common bile duct (cbd), gallbladder (gb), duodenum (d) and jejunum (j).

Figure 4.

Hepatocellular carcinoma in a 16 year-old. (A) Portal venous phase 3D spoiled gradient echo images imaging with the hepatobiliary specific contrast agent shows early enhancement of the large mass. (A) On delayed imaging the hepatobiliary contrast material is excreted into the bile duct (arrow) and washes out of the mass relative to the liver. These features are typical of malignant tumors such as hepatocellular carcinoma and hepatoblastoma tumor, but atypical for focal nodular hyperplasia.

Figure 5.

Biopsy proven hepatocellular carcinoma in a 12 year-old with cirrhosis. The masses (arrows) rapidly enhanced on the arterial phase (A) and then wash out on delayed imaging (B). Similar to a regenerating nodule, hepatocellular carcinoma will show early enhancement and subsequent washout of contrast material. The wedge shaped area of arterial enhancement in the anterior right liver is a transient phenomenon. Ultrasound (C) and computed tomography (D) reveal the masses but do not provide the level of characterization as on MRI with dynamic contrast enhancement.

Figure 6. Stenosis of the common bile duct in a 4 year-old. Coronal T1-weighted fat suppressed image after orthotopic whole liver transplantation shows focal narrowing of the common bile duct (arrow head). The hepatobiliary targeted contrast material fills the lumen of the common bile duct (arrows). In addition, the liver is increased in signal intensity from residual hepatobiliary specific contrast agent that has yet to be excreted.

Figure 7.

Choledochol cyst in a 7 year-old. The hepatobiliary-specific contrast material helps determine the relationship of the cyst with the biliary and pancreatic ducts. (A) The mass located at the head of the pancreas (arrow) projects into the lumen of the duodenum on the T2-weighted fast spin echo fat suppressed image. (B) On the contrast enhanced maximum intensity image, the contrast material excreted by the liver fills the bile ducts and dilated and disorganized accessory ducts of the pancreas (ac) but not the cyst.

Figure 8.

Infantile hemangioma in an 18 month-old male. The dynamic phase imaging shows early peripheral enhancement during the arterial phase (A) and gradual peripheral filling towards the center during the portal venous phase (B). However, on the delayed hepatobiliary phase (C) the lesion is darker than the liver, thus, confirming hemangioma and excluding fibronodular hyperplasia. The complex pattern on ultrasound (D) lead to the need for further characterization with MRI.

Table 1

Conventional MRI/MRCP vs. MRI/MRCP with hepatobiliary specific contrast agents (HSA).

HSA provides additional information	HSA gives similar information
Focal nodular hyperplasia	Hepatocellular carcinoma
Hepatic adenoma	Regenerative nodules
Choledochal cysts	Hepatoblastoma
Bile duct obstruction (certain cases)	Hepatic sarcoma
Cholangiocarcinoma	Liver cyst
	Infection

Table 2
Characteristics of pediatric liver lesions on conventional MRI and MRI with hepatobiliary specific agents (HSA).

		T ₂ (fluid)	T ₁ before enhancement	T ₁ enhancement	T ₁ hepatocyte
Benign	Cyst	+++	===	---	---
	Hemangioma	+++	---	+++ (periphery)	+/-
	Focal Nodular Hyperplasia	-	--	++	+++
	Adenoma	+	--	++	--
	Regenerative Nodule	--	-	-	isointense to background
Malignant	Dysplastic Nodule	--	+/-	+/-	+
	Hepatoblastoma	++	--	--	--
	Hepatocellular carcinoma (HCC)	+	--	++	==
	Fibrolamellar HCC	++	--	++	--
	Metastases	++	--	--	--
	Undifferentiated Embryonal Cell	++	--	--	--

Increased (+), decreased (-), and iso-intense (=) signal intensity compared to background liver. T₁ = T₁-weighted pulse sequence depicts contrast enhancement. Note that the T₁ hepatocyte phase occurs approximately 20 minutes after IV injection of HSA. T₂=T₂-weighted pulse sequence depicts fluid.