Liver Tumor Imaging: Current Concepts

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Abstract. With the increasing availability of curative surgical techniques for primary and secondary hepatic neoplasms, the tasks for clinical imaging of liver cancer suspects have become more exacting. Detection of tumor, differential diagnosis of individual nodules, and mapping the anatomic extensions of malignant disease are now routinely required. Related and unrelated liver substrate abnormalities such as cavernous hemangioma and focal fatty deposits are often discovered in liver cancer suspects and must be differentiated from metastatic deposits. Moreover, modern imaging methods frequently display tiny subcentimeter nodules which often prove difficult to adequately characterize (micrometastases vs other). The most sensitive imaging techniques are CT after arterial portography and intraoperative ultrasound, but because of their invasiveness, these are reserved exclusively for staging. For primary screening MR imaging is increasingly preferred over CT because of its superiority in discriminating hemangiomas and cysts from metastases without the need for iodinated contrast material. (Keio J Med 40 (4): 194-205, December 1991)

Key words: cancer, CT, MR imaging

What issues will interest radiologists dealing with suspected liver tumor patients during the next decade? How will emerging new imaging technologies affect overall accuracy of radiologic diagnosis? Which techniques will flourish? Which will fade? What pathologic-radiologic insights will evolve? The answer will come, at least in part, from ongoing developments in several different areas.

First, recent advances in CT, sonography and MR imaging have vastly improved assessment of liver neoplasms just as they have benefited detection of abnormalities in other organs. Liver tumor nodules are now routinely discovered at small size thresholds (millimeters) and in most cases, mass lesions can be characterized with high reliability.

Second, hepatic surgeons now view the patient with primary liver cancer or metastases from colorectal carcinoma as a possible long term survivor not an end stage victim. In such cases, precise anatomic descriptions of the number and segmental location of neoplastic deposits are required. Hence, radiologic staging of malignant hepatic tumors has become a common clinical task.

Third, commercial manufacturers from the USA, Europe and Asia are introducing prototype imaging techniques and contrast agents with exceptional potential for liver applications. New CT and MR imaging systems can gather data in subsecond intervals, display regional organ perfusion and provide images formatted in multiple planes. Novel pharmaceuticals specifically targeted both to the hepatic reticuloendothelial system (RES) and to biliary excretion functions provide order of magnitude increases in tissue-tumor contrast.

The power and commitment of resources that is exemplified by these technical and clinical developments assures major further advances in clinical imaging of patients with suspected liver cancer. This article offers an overview and personal reflections on some of these trends.

Clinical Considerations

Surgical advances

In 1989, it was estimated that nearly 150,000 new cases of colorectal carcinoma would be diagnosed in the United States. Of these, some 40% or 60,000 patients will ultimately prove to have liver metastases. Worldwide, primary hepatocellular carcinoma (HCC) is an endemic disorder in many underdeveloped countries; in southeast Asia and sub-Saharan Africa, HCC accounts for one third of all malignant neoplasms. Considered globally, primary and secondary liver cancers affect...
literally millions of persons each year.

Among the most significant therapeutic advances in the management of HCC and colorectal liver metastases are the continued evolution of aggressive surgical techniques. Techniques for bloodless dissection through the hepatic parenchyma have diminished operative morbidity and mortality while serial carcinoembryonic antigen assays can lead to the discovery of silent deposits before they grow too large to resect. It is now estimated that as many as one fourth of all primary and secondary liver cancers are potentially resectable for cure. In the United States alone, approximately 7,000 patients a year with colorectal liver metastases are estimated to be potential candidates for hepatic resection. When resections have been carried out in patients with three or fewer colon deposits, 20–40% 5 year survival rates have been obtained in both single institution and cooperative studies. Similar favorable results have also been recorded with metastases from visceral sarcomas and endocrine tumors. Moreover, innovative nonoperative techniques for local tumor ablation such as intraoperative cryosurgery, transarterial chemoembolotherapy and fine needle intralesion alcohol sclerosis may improve these results further.

The hepatic substrate

Radiologic assessment of liver tumor suspects is commonly complicated by the coexistence of other abnormalities in the substrate of the liver parenchyma. These may be focal or diffuse, neoplastic or metabolic, and related or unrelated to the neoplasm being evaluated.

Cavernous hemangiomas are so often displayed on T2 weighted MR images as 5–10 mm bright dots as to become a serious confounding nuisance to clinical interpretation (Fig 1). Their prevalence has been traditionally estimated at 5–7%. However, a recent Finnish study of medicolegal autopsies in 95 men found cavernous hemangiomas in 20% of subjects, although the mean size was less than 1.0 cm. They are often multiple and may of course coexist with metastatic deposits. Thus, when multiple discrete masses occur, each must be characterized individually. Moreover, hemangiomas have been demonstrated to enlarge with time, and often develop a central fibrocollagenous scar when over 5.0 cm in diameter which may give atypical hypovascular filling patterns on CT, radionuclide blood pool scanning, and angiography.

Fatty metamorphosis of the liver appears commonly during the course of malignant disease and may occur as diffuse change or focal deposits. Both patterns cause diagnostic problems and often require correlation of several imaging techniques to resolve. Diffuse fatty liver lowers the attenuation of normal hepatic parenchyma on CT and may cause metastatic deposits to appear isodense and thus obscured. Alternatively focal areas of normal liver may be spared of fat and retain their normal higher CT density and thus simulate metastatic deposits. In both cases normal or hyperechoic texture on sonography and normal photon distribution on sulfur colloid scintigraphy are usually diagnostic. Focal deposits of fat may also appear as sharply defined low density areas simulating metastases on CT (Fig 2). These can enlarge on serial scans simulating disease progression.
Focal fatty deposits usually display geographic wedge or pyramidal shapes on CT and leave vessels intact, but again typical echogenic areas on sonograms and normal anatographic findings are confirmatory.12

Liver fat has not been a major interpretative problem on MR because conventional spin echo sequences are relatively insensitive to intrahepatic fat content. However, chemical shift proton spectroscopic imaging sequences are highly sensitive to fat-water proton differences and so called phase contrast techniques show both high contrast between tumor (bright) and fatty liver (dark), giving high cancer detection rates.13 Moreover, in occasional cases where focal fat deposits are suggested by short T1 bright signal areas, the presence of fat can be confirmed as the area becomes dark on a chemical shift sequence.13

Regenerating nodules occurring in hepatic cirrhosis may be difficult to differentiate from early or "minimal" hepatocellular carcinoma. They are usually small, 1–2 cm in diameter, multiple and appear hypoechoic on sonography and of high density on CT. Itai et al.14 found regenerating nodules particularly often shown by MR as numerous low intensity areas on T2 weighted images even when both sonography and CT findings were normal. They were readily differentiated from hepatomas which consistently appeared of high signal intensity. Recent pathologic studies of resected specimens have shown hemosiderin deposits in these nodules believed to account for the low MR signal due to magnetic susceptibility effects.15

Tasks of liver imaging

Imaging evaluation of liver cancer should be recognized as having several clinically distinct tasks. These are (1) Global patient detection — does the patient’s liver contain tumor deposits? (2) Individual lesion detection — how many lesions are there? (3) Individual lesion characterization — what is the nature of the masses seen? and (4) Staging for question of resectability — if cancerous, is the patient’s disease treatable by local measures?

In clinical practice, these functions are rarely confused, although they may not be necessarily performed in every case. In certain instances, a decision as to global status of the patient (cancerous liver or not?) suffices; in others more detailed lesion-by-lesion analysis is sought. Seltzer and Holman16 have thoughtfully discussed the increasingly important distinctions between global patient diagnosis and lesion-by-lesion diagnosis when comparing techniques. For example, hepatic imaging for staging breast cancer is quickly concluded when a typical positive scan is obtained, whereas patients with colorectal carcinoma often require more thorough assessment and differential diagnosis of individual lesions because of the possibility of curative surgical extirpation.

However, research papers on liver imaging sometimes blur these sequential tasks. Emphasis has often been directed toward the performance of a technique in terms of sensitivity for lesion detection, with all lesions displayed assumed to be cancerous. The magnitude and significance of the overlap error with incidental benign cysts and hemangiomas is rarely addressed. This will become a more widely recognized issue in the future.

Screening and Staging

In a 1982 review of hepatic metastasectomy for colon cancer, Marvin Adson, the pioneering liver surgeon from the Mayo Clinic, noted that among the major factors limiting success of surgical approaches was inadequate staging by radiologic imaging techniques.7 Failures occurred both because small lesions went undetected and because operative excision sometimes removed more tissue than was necessary. In the ensuing decade, fundamental advances in imaging technology have greatly improved the diagnosis of liver cancer largely answering Adson’s lament. In addition, even for patients with unresectable disease, more accurate assessments of tumor burden have improved efforts to monitor response to treatment.

Anatomy

Radiologic staging of liver cancer, either primary or metastatic, defines (1) extent and location of intrahepatic disease, (2) involvement of surgically critical areas ( porta hepatis, inferior vena cava, major bile ducts), and (3) presence of extrahepatic disease. In institutions where curative hepatic resections or other percutaneous loco-regional cancer therapy is available, staging assessments tend to become an automatic feature of most routine CT and MR interpretations.

The critical surgical anatomy of the liver is based not on external attachments or lobar landmarks but on the internal vascular skeleton of the liver.3–5 The French surgical anatomists Couinaud and Bismuth, popularized an eight segment partition based principally on the position of the three major hepatic veins (right, middle, left) (Fig 3).17,18 From these somewhat imaginary boundaries, simple and extended multi-segmental resections can be fashioned removing up to 80% of liver parenchyma.2–7 Thus in colorectal metastases, curative resections are feasible for up to four deposits provided they can be encompassed in a contiguous (multisegmental) en-bloc excision (Fig 4). Whenever possible, subsegmental or wedge excisions are employed even though liver parenchyma possesses considerable regenerative potential. By the same token, tumors located centrally with involvement of the portal vein or inferior vena cava are less likely to be resectable (Fig 5).
Further, there is the concept of “surgical” vs “medical” categories for therapy of liver metastases. This refers to the likelihood that hepatic secondary deposits from certain primary tumors such as adenocarcinoma of the colon and visceral sarcomas are often few in number, discretely marginated, and might be amenable to local surgical resection or other extirpative procedures, whereas metastases from primary sites such as the breast and pancreas are more often widespread throughout the liver and therefore are generally only amenable to medical management (Fig 6). In the latter group of patients, the...
only requirement of imaging in order to make treatment decisions in often a simple binary “liver positive” or “liver normal” choice.

Imaging techniques

At present some of the historical controversy about which of the many available techniques to use in what circumstance is abating. Table 1 shows the various techniques grouped according to their current roles in liver tumor imaging (i.e., screening, staging, and special situations).

Imaging techniques for screening must be generally noninvasive, quickly performed, show high sensitivity for lesion detection at low size thresholds, and have high accuracy in differentiating incidental benign masses from malignant neoplasms. Both CT and MR fulfill these criteria provided optimal examination techniques are used. Although CT has been the acknowledged gold standard for liver tumor imaging it must be performed with dynamic incremental bolus techniques to achieve superior results. For MR imaging, both heavily T1 and T2 weighted sequences are required to ensure high detection rates and accurate tissue characterization. Motion suppression techniques are generally required as well.

Conventional sonography often discloses hepatic tumor nodules during upper abdominal scanning for abdominal pain, palpable mass, or jaundice. However, its overall false negative rate for liver metastases exceeds 50%, images are not easily reproducible for comparative purposes, and differential diagnosis between benign and malignant nodules is often impossible. Thus, sonography is rarely used as a primary screening or surveillance technique in centers where CT and MR imaging are available.

Imaging the liver for the purposes of tumor staging involves more detailed delineation of the anatomic relation of neoplastic deposits to segmental anatomy and to critical anatomic structures such as portal and hepatic veins, inferior vena cava, and major bile ducts. Obtaining this degree of anatomic information frequently requires the greater detail of CT during arterial portography (CTAP) or intra-operative sonography (IOS). The likelihood of obtaining tumor free margins and relative risks of anatomic right and left lobe resection, segmental resection or multisegmentectomy can thus be weighed. On occasion, good quality MR images may provide sufficient information to make specific management decisions concerning surgical approaches. The principal question, however, is whether an apparently free segment of the right and left lobe is in fact uninvolved, permitting the obviously involved segments to be excised.

Scintigraphy and hepatic angiography now play only limited specialized roles. Scintigraphy is occasionally used to facilitate differential diagnosis of problematic suspected primary liver tumors. Hepatic angiography is generally reserved for problem cases where differential diagnosis remains in doubt or in patients in whom documentation of arterial anatomy is required for preoperative mapping of the vascular supply.

Invasiveness vs sensitivity

Clinical comparisons of imaging techniques must consider the degree of invasiveness. Intuitively, the most sensitive tests for detecting liver lesions are often the most invasive. A screening test applied to large populations, many of whom will have no disease, must be a less hazardous study than might be used for detailed anatomic tumor mapping before open hepatic resection. The two principal techniques used for staging, CTAP and IOS give high lesion detection rates but do involve some risk.

CTAP requires superior mesenteric artery catheterization for administration of contrast material immediately before CT scanning. Intense hepatic staining resulting from the high dose of iodine directly delivered to the liver and the recording of the highly sensitive CT attenuation values during the portal phase is an extremely accurate method for detecting small liver deposits. Using CTAP, Matsui et al. found 10/18 individual colon metastases less than 15 mm that were not shown by CT, sonography, or angiography (Fig 7). Heiken et al. showed more than twice as many metastatic deposits with CTAP (81% detected) than with standard CT (38% detected). Similar results were recorded by Nelson et al. The technique is therefore particularly useful to clear apparently “uninvolved” segments of the liver on screening CT or MR before surgical resection of obvious disease. Unfortunately, CTAP is marred by a high false positive rate due to laminar flow perfusion defects in up to 30–40% of cases. However, they can usually be recognized by a typical wedgelike shape and peripheral location. Moreover, the ability of CTAP to provide differential diagnostic information on newly discovered small nodules is uncertain.

IOS is an alternative method for staging that gives superb high resolution images of subcentimeter liver
Fig 7 High sensitivity of CT during arterial portography (CTAP) for lesion detection. (A) Screening MR image (T1-weighted) shows apparently solitary metastatic deposit replacing lateral portion of left lobe. No other lesions are apparent. (B) CTAP shows a single additional 0.6 cm deposit in peripheral portion of right lobe (arrow). Surgical excision showed a malignant focus (micrometastasis).

Lesion threshold: The subcentimeter nodule

An integral related issue is the question of the threshold size for the ability to both detect and discriminate the nature of liver mass lesions. Until recently, demonstration of metastatic lesions of 1.0 cm in diameter was the best that could be expected with conventional CT, and 30–50% of individual lesions went undetected.23–25 On the contrary, high quality MR techniques frequently display subcentimeter nodules, both benign and malignant, accounting for the greater sensitivity in lesion detection reported from several centers.21,36–38 Moreover, in several series CTAP has out performed conventional CT and MR by an order of magnitude for detection of lesions less than 1.0 cm.23–25,30

This higher sensitivity for detection of subcentimeter nodules has created the new and daunting problem of characterizing lesions that are usually too small to exhibit distinctive morphologic features. In fact, few authors have addressed the performance of any technique at distinguishing the nature of these tiny subcentimeter nodules (Fig 9). In the only specific study of this problem to date, Brick et al.31 using conventional CT, were not able to differentiate benign hepatic cysts from solid metastases accurately at the 1.0 cm level because of partial volume effects.31 The ultimate solution to assessing the nature of the millimeter size “dot” now so commonly seen on CT or MR liver scan remains to be found. For the present, only interval follow-up serial scanning is practical.
Several general comments on the CT vs MR issue are warranted at the outset. Opinions of the comparative merits of CT and MR for liver tumor imaging have spanned the full spectrum. Thus, various reports have concluded that CT remains the gold standard;32 that the results of the two methods are comparable;33-35 and that MR supercedes CT already.21,36-38 Experienced observers also recognize that the type of CT and MR equipment available, scanning methods used, and special expertise of the professionals involved greatly influence outcomes, and undoubtedly account for the divergent results.39 Moreover, multicenter clinical trials are often disappointing because grouped results often dilute the best efforts, and the usual long duration of such studies tends to lag technologic and interpretive refinements. It is also useful to acknowledge that a single liver imaging study may not yield a correct or complete diagnosis under the best of circumstances and it is often critical to integrate the results of multiple imaging studies.

CT vs MR

Notwithstanding these factors certain elements of current clinical experience with MR disclose real limitations of CT in terms of sensitivity for lesion detection, differential diagnosis and invasiveness. As previously noted several groups have recorded greater sensitivity for lesion detection by MR.21,36-38 This may be explained by the inherently greater image contrast in MR as well as the slice gap errors of CT when small nodules are present. Spin echo signal averaged MR techniques effectively cover the entire liver with high contrast even for subcentimeter nodules.21 Moreover, in two studies the specificity (false positive rate) was also more favorable with MR.21,38 This too is an important concern when imaging studies are used for screening. In the best reported CT series, Freeny et al.40 reported an 85% sensitivity for detecting the presence of liver metastases and 60% sensitivity when individual lesion detection was considered. However, the CT technique required to achieve these results is quite demanding, requiring dynamic bolus contrast media injection with power injectors and rapid table incrementation during infusion of contrast material. This allows images to be made during the first 2 min after contrast administration (perfusion phase of contrast distribution) in which there is high contrast differential between tumor tissue and normal liver. If images are obtained after equilibrium distribution of contrast into the interstitial compartment of the liver (2–5 min), lesions may become isointense with hepatic parenchymal and obscured.41 Moreover, in patients whose primary tumor tends to produce hypervascular liver metastases (islet cell, renal, melanoma), an unenhanced scan should be obtained because 25% of cases will be hypervascular and thus isointense, giving false negative results.42

Hemangioma is a particularly difficult problem for CT and no discussion of the two techniques can have clinical relevance unless assessments of metastases and hemangiomas are considered concurrently. Unfortunately, both metastases and hemangioma may be multiple, may coexist independently, and may be clinically occult (Fig 10). For proper treatment of patients it is often necessary to analyze each detected liver nodule individually.

In this context, there are three problems with CT in the evaluation of cavernous hemangioma. First, the criteria for differentiation from metastases are typical in no more than 55% of cases.22 Even when a typical pattern is present in a patient with a known primary neoplasm, the probability that it represents hemangioma is only 86%.43 Second, in many cases, delayed scanning up to 30 after administration of contrast material is required to confirm the typical peripheral centrifugal filling sequence. This can represent a throughput problem. Third, because of the temporal nature of the diagnostic filling pattern, it is often difficult to assess multiple lesions at different CT slice levels. Hence, other studies such as radionuclide blood pool scanning, percutaneous needle biopsy, or MR imaging are often required. MR imaging, obviously, shows multiple lesions at multiple slice levels with no need for additional or delayed imaging.

Conversely MR imaging has shown better than 85% accuracy in differentiating hemangiomas and metastases at various field strengths.22,38,44-45 Heavily T2 weighted spin echo images with TE's greater than 100 msec effectively display the long T2 bright signal typical of slowly flowing blood. A homogeneous “light bulb” pattern is seen morphologically, while quantitatively the re-
Fig 10  T2-weighted MR images show multiple cavernous hemangiomas, with a dominant lesion in left lobe and 6–7 smaller nodules scattered throughout right lobe. In patients with suspected metastatic disease and multiple lesions, each nodule must be analyzed individually for optimal patient care. This patient had a palpable liver and normal liver function tests. Based on results of imaging studies, which were considered typical for hemangioma, no further intervention was carried out.

Suiting high contrast/noise ratio accurately differentiates hemangiomas from metastases. More recently, fast MR imaging with gadolinium has effectively displayed the slow perfusion patterns of hemangioma analogous to contrast enhanced CT\textsuperscript{46–51} (Fig 11). Several different dynamic MR imaging techniques have been used including fast spin echo and gradient echo methods. All have succeeded in furthering the distinction between hemangiomas and primary and secondary malignant tumors and add a further criterion to the differential diagnosis for problem cases.

There is a final advantage of MR imaging over CT. The inherent dependence of CT on iodinated contrast material for lesion detection and characterization is an additional argument in favor of MR imaging. It is increasingly difficult to dismiss the risk (high osmolar) or cost (low osmolar) of iodinated contrast media when making judgments about the overall relative desirability of CT vs MR.\textsuperscript{52}

An important contrary balancing argument for CT has been its undisputed greater accuracy for displaying extrahepatic diseases such as pancreatic, adrenal, or retroperitoneal pathology.\textsuperscript{21} The prospect that MR bowel contrast agents might address this concern has yet to be fulfilled. However, no study has ever compared the clinical impact of trading off accuracy in diagnosing intrahepatic vs extrahepatic disease with either MR or CT. In the patient with colorectal carcinoma it may be justifiable to use MR and forego detail in the retroperitoneum to assure accuracy within the liver where

\begin{figure}[h]
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\includegraphics[width=\textwidth]{fig10.png}
\caption{T2-weighted MR images show multiple cavernous hemangiomas, with a dominant lesion in left lobe and 6–7 smaller nodules scattered throughout right lobe.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig11.png}
\caption{Dynamic Gd-DTPA perfusion study for cavernous hemangiomas. Two adjacent hemangiomas in right hepatic lobe surgically proven. Fast SE (225/13, two excitations) spin-echo MR images with IV injection of Gd-DTPA (0.1 \textmu mol/kg by body weight). (A) Before (B) 3 min after, and (C) 5 min after injection. Both lesions show marked and persistent signal enhancement. Dominant lesion shows an area of central scar formation.}
\end{figure}
there is greater risk of disease as well as a greater risk to the patient's welfare if a diagnostic error occurs. Given the new ultrafast CT and MR scanning methods and liver specific contrast agents under development for both, the debate as to which technique is best for liver tumor imaging will no doubt continue for years.

**Hepatocellular Carcinoma (HCC)**

Radiologic evaluation of HCC involves several further specific issues in addition to the general discussion of screening/staging liver cancer given above. HCC usually arises as a complication of liver cirrhosis, making initial recognition and differentiation from a regenerative nodule more difficult and limiting the number of patients who can tolerate surgical resection. Only patients with small (3–4 cm) encapsulated tumors and well compensated liver function became candidates for tumor excision. However, actuarial survival rates among such patients approach 90% at 3 years. Thus, recognition of the so-called “minimal” HCC is an important imaging challenge.

HCC tends also to be a highly aggressive tumor in terms of its local extension: invasion of veins and bile ducts; tendency for arterio-venous shunting and formation of daughter nodules are common occurrences. Most can be demonstrated radiologically and have obvious implications for setting boundaries of contemplated surgical resection.

Diagnostically, CT scanning following Lipiodol (an iodinated oil, Laboratoire Guerbet, France) injected via a catheter placed in the hepatic artery, can show subcentimeter HCC lesions, both primary and daughter nodules. However, this technique is presently used only in the Far East. Lipiodol gelatin sponge particles loaded with antitumor drugs have also proved an effective chemotherapeutic method for unresectable lesions.

MR imaging has also proven highly sensitive in detection, differential diagnosis and staging of HCC. It is able to recognize the frequent low signal intensity capsule, central fatty degeneration, vascular invasion, and daughter nodules that characterize this tumor (Fig 12). Unlike MR techniques for differentiating metastases from hemangiomas which rely on T2 weighted sequences, HCC is best characterized by T1 weighted sequences because they provide clear depiction of fat, capsule, and venous involvement. More recently, dynamic MR with gadolinium has been able to confirm the faster flow in HCC as opposed to the stagnant flow in hemangiomas adding another useful criterion for differential diagnosis.

As in the instance of metastatic liver disease, the powerful diagnostic capabilities of MR now allow it to rival or exceed CT as a primary liver imaging technique for hepatocellular carcinoma.

**Tissue Characterization**

As is evident from the foregoing, improved accuracy in differential diagnosis (tissue characterization) has been a dominant theme in development of clinical liver tumor imaging in recent years. As is well known, metastases, hemangiomas and hepatomas constitute the “big three” categories of liver masses. Whether CT or MR is used, the parameters for clinical differentiation are (1) signal intensity (contrast-noise) values, (2) morphologic architecture features, and (3) hemodynamic perfusion patterns. Although contrast enhanced CT has had an indisputable role, MR has contributed more by virtue of its inherently richer image contrast. Moreover, scintigraphy adds a unique special dimension for identification and characterization of primary liver tumors. Notwithstanding, tissue characterization of liver masses remains a complex challenge, and tissue sampling by needle or open surgical biopsy is frequently required.

MR signal intensity ratios have been widely utilized to differentiate hemangiomas from metastases. As initially described by Stark et al., high signal on late T2 weighted spin echo images typifies hemangiomas as opposed to...
metastases. For purposes of clinical interpretation, visual comparisons between lesion signal intensity and CSF are substituted for more onerous quantitative measurements.

The abundant morphologic architectural information displayed on both T1 and T2 weighted MR images also affords reliable differential diagnostic features. In addition to the typical bright “light bulb” appearance of hemangiomas, Wittenberg et al. also described bright peritumoral edema halo effects and central liquefaction necrosis associated with metastatic deposits. Rummeny et al. documented a high prevalence and diagnostic value of central scar formation as a specific sign of primary liver neoplasms (Fig 13). Ebara et al. described typical MR morphologic features of hepatocellular carcinoma to include a central high signal area due to steatosis, a low signal peripheral capsule, and daughter nodules. Hahn et al. drew attention to MR ring phenomena surrounding liver masses usually due to edema, hemorrhage or fibrosis.

Scintigraphy also plays a unique, albeit limited, role in liver tumor characterization, namely identification of specific primary liver neoplasms, i.e., hemangioma, focal nodular hyperplasia and hepatic adenoma/hepatoma. The condition suspected is confirmed by the scintigram scan specific for the entity as shown in Table 2.

For each condition, a positive photon uptake confirms the suspected diagnosis, although false negative results occur in all entities. However, use of scintigraphy for liver tumor characterization has declined as the superb capabilities of MR for liver tumor characterization have been defined.

An interesting new development involves the potential of a variety of different techniques to exploit hemokinetic data for differential diagnosis. RBC labelled scintigraphy displays the slowly flowing blood pool of hemangiomas and accurately distinguishes them from hepatomas and metastases. Color Doppler sonographic flow mapping has been found by Tanaka et al. to give a typical network vascular pattern in hepatomas as opposed to metastases (detour pattern) and hemangioma (dot pattern). MR contrast enhancement using fast scanning gadolinium has been described above. More recently, Hahn et al. found superparamagnetic iron oxide particles to show greater uptake and consequent greater signal loss in hemangiomas than in malignant tumors. Nearly all these methods will most likely undergo further refinement before their ultimate clinical role is clear, but useful information is already being provided.

**Table 2 Scintigraphic Techniques for Characterizing Primary Liver Tumors**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Radionuclide</th>
<th>Imaging Technique</th>
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<tbody>
<tr>
<td>Cavernous Hemangioma</td>
<td>Tc99m</td>
<td>RBC labelled blood pool scan sulfur colloid and/or HIDA scan citrate scan</td>
</tr>
<tr>
<td>Focal Nodular Hyperplasia</td>
<td>Tc99m</td>
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<td>Hepatic Adenoma/Hepatoma</td>
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**Future Directions**

What are likely developments in the next decade? The immediate future will be dominated by exploration of liver applications for fast and ultrafast CT (cine) as well as breathhold and millisecond “snapshot” MR techniques. Saini et al. obtained high resolution T2 weight MR images of the liver and abdomen in 1/25 sec working with a modified echo-planar technique at 2.0 T. In addition to the obvious potential for increased patient throughput and analysis of cardiac motion with such techniques, studies of organ and tumor perfusion kinetics will continue and command much attention. Many...
of these studies will involve novel MR contrast agents.

Certainly the entire field of tissue-specific liver contrast agent development will absorb vast amounts of research resources. The richness of the hepatic metabolic milieu will allow molecules to be specifically targeted to the reticuloendothelial system, biliary excretory pathways, and hepatocyte enzyme systems. Particulate superparamagnetic iron oxide (ferrite) particles have already been shown to give a threefold increase in MR lesion conspicuity and detection sensitivity in early clinical trials. Further reduction in lesion detection size thresholds from 10 mm to 2 mm has also been shown after ferrite in implanted rat tumor nodules. Particulate agents for CT such as perfluorooctylebromide (PFOB) have also been shown to give a threefold increase in MR lesion conspicuity and detection sensitivity in early clinical trials.

New relationships between contrast agents and imaging system hardware are also emerging in which the special physical effects of each are exploited and synchronized to optimize results. Thus magnetic susceptibility effects of ferrite particles are exaggerated by gradient echo techniques and may ultimately allow lower doses to be used. Other imaging hardware and software developments with liver applications already in clear view are ultra low-field MR systems (0.02 T), MR spectroscopy, multiplanar CT and MR (3-D) imaging, and color flow Doppler ultrasonography. Much has been accomplished, there is much to be done.

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