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MRI of Liver: Techniques, Diseases and Contrast Agents

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LIVER

TECHNIQUE

The current standard MR examination of the liver includes a T1-weighted sequence, a T2-weighted sequence, and a contrast enhanced sequence.

The most comprehensive contrast administration approach is the use a nonspecific extracellular contrast agent, gadolinium chelate, as a rapid bolus injection with serial imaging using a spoiled gradient echo (SGE) sequence.

On high field MR systems, breath hold spoiled gradient echo performs well for T1-weighted imaging. The advantages of this sequence include fast data acquisition, robust sequence performance, avoidance of breathing artifact, complete coverage of the liver in one breath-hold, and good T1-weighting. Effective parameters for this sequence include relatively long TR (e.g.:100-150msec), which allows acquisition of sufficient sections in one breath-hold for complete liver coverage, and high signal-to-noise; lowest in-phase echo time (6msec at 1.0T, 4msec at 1.5T), which allows acquisition of multiple sections, high signal-to-noise and true T1-weighting; and a flip angle approximately 90° (range 60°-90°), the advantages of which are: good signal-to-noise and adequate T1-weighting.

One signal average and a matrix of 128 to 170 by 256 (phase encoding by frequency encoding) are also recommended. This sequence generates 14-22 sections in a 20 second breath-hold period. The other important use of SGE is for dynamic gadolinium chelate imaging [1-3]. It is usually advisable to use an in-phase echo time on SGE images for contrast enhanced studies in order to avoid 1) confusing variations in SI based on fatty infiltration of the liver and 2) black ring phase cancellation artifact which will mask capsular based disease.

T2-weighted imaging is most frequently performed as conventional spin-echo or as echo train spin-echo sequences (e.g.: fast spin-echo or turbo spin-echo sequences). Echo train techniques are currently employed more frequently on state-of-the-art MR systems due to the shorter sequence duration, which can be utilized to decrease data acquisition time, increase spatial resolution, or both. A variation of turbo spin-echo termed HAlf fourier Single shot Turbo spin Echo (HASTE) has been recently developed which acquires individual image sections in less than 1 second. Current implementations of this sequence result in robust, reproducible image quality which are breathing independent.

Chemically selective fat suppression is a useful addition to T2-weighted imaging as it reduces phase artifact, removes chemical shift artifact and improves the dynamic range of tissue signal intensities. The use of chemically selective fat suppression may be particularly important with echo train spin echo sequences. Fat is high in signal intensity on these sequences, and fatty liver will therefore be high in signal reducing the conspicuity of high signal intensity focal lesions.

Out-of-Phase imaging is an effective approach for the detection of fatty infiltration in the liver and is useful for characterizing focal lesions as focal fatty infiltration. It is reasonable to routinely include an out-of-phase sequence for liver examinations as the sequence is rapidly acquired in one breath hold, and fatty liver is a common entity which often has clinical implications. Out-of-phase imaging is best performed as an SGE technique with the lowest possible out-of-phase echo time (4msec at 1.0T and 2msec at 1.5T). This approach results in: good signal-to-noise and maximum number of sections per acquisition.

Contrast Enhancement

In current clinical practice, gadolinium chelates are frequently employed as liver contrast agents. These agents are nonspecific extracellular space agents.

Gadolinium chelates are distributed initially within the intravascular compartment and diffuse rapidly throughout the extracellular (vascular plus interstitial) space, in a distribution similar to water soluble iodinated contrast agents. These agents cause T1

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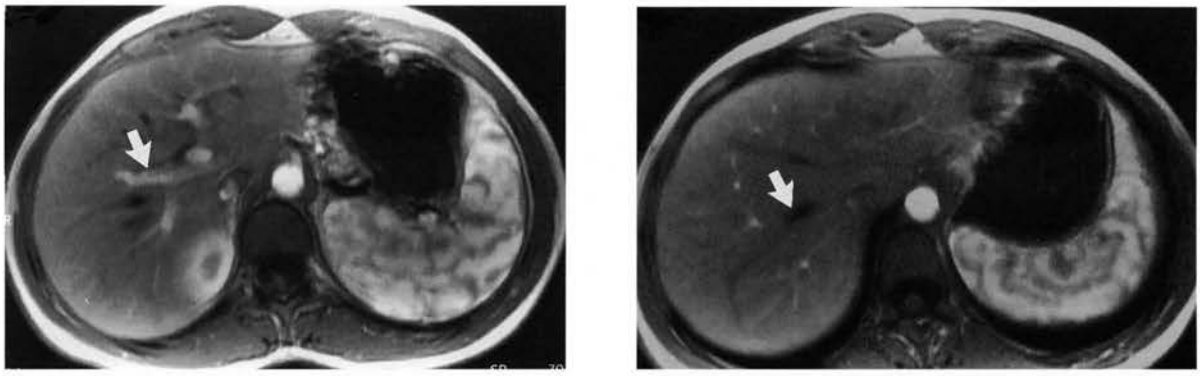

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Figure 1. Normal hepatic arterial dominant phase. Transverse spoiled gradient echo sections from more inferior (a) and superior (b) tomographic sections. Contrast is present in portal veins (arrow, a) and not yet present in hepatic veins (arrow, b) which denotes the optimal phase of hepatic arterial dominant enhancement.

shortening of adjacent water molecules, which results in tissue brightening on T1-weighted images. Gadolinium enhancement is visually similar to iodine contrast enhancement on CT images. This analogous appearance facilitates MR image interpretation for diagnosticians familiar with CT image interpretation.

Gadolinium chelates should be used with dynamic scanning techniques to maximize detection and characterization of liver lesions. The best results are achieved using SGE as a single breath hold with complete liver coverage.

The following phases of enhancement are important for lesion detection and characterization:

a. *Hepatic arterial dominant phase* images are especially important for detection of hypervascular malignancies such as hepatocellular carcinoma and metastases from hypervascular primary tumors (e.g. islet cell tumors, renal cancer, pheochromocytoma, carcinoid and leiomyosarcoma). These images are acquired immediately following a rapid bolus injection of gadolinium chelate, with the patient positioned in the magnet bore. Optimal timing of this sequence is demonstrated by the presence of contrast in hepatic arteries and in portal veins, but not within hepatic veins (**figure 1**). At this phase of enhancement the normal pancreas and renal cortex enhance intensely, renal medulla is minimally enhanced, and normal spleen has an arciform or serpiginous enhancement. Although gadolinium is present in portal veins, the majority of the gadolinium within the liver has been delivered by hepatic arteries at this early enhancement phase. Specific enhancement features of various hepatic lesions are best shown on these images as over time many focal lesions tend to enhance throughout their substance and approach the signal intensity of liver. Image acquisition timed approximately 6 seconds early demonstrates gadolinium present only in hepatic arteries. This phase is less ideal as the liver is essentially unenhanced and the blood supply of hepatic lesions is not visualized.

b. *Portal phase images* show maximal hepatic enhancement and maximal contrast between liver and hypovascular lesions. These images are acquired approximately one minute following contrast agent administration. All hepatic vessels are enhanced at this phase of enhancement and demonstration of vascular patency is usually well shown on these images.

c. *Equilibrium* (delayed, interstitial) images are acquired two or more minutes after injection of contrast material, by which time contrast material has diffused into the interstitium of non-CNS tissues. Delayed contrast enhancement is particularly prominent in edematous tissues such as in neoplasms, areas of inflammation, and within fibrosis . The concurrent use of frequency-selective fat suppression is useful to increase conspicuity of these types of disease processes on interstitial phase images. Images acquired between 5 to 10 minutes after injection permit sufficient time for many hemangiomas to fill in, which serves to increase observer confidence of lesion characterization.

New contrast agents which have tissue specific properties are currently under investigation.
These include agents which accumulate within hepatocytes (e.g.: Mn-DPDP Gd-EOB-DTPA, Gd-DTPA-BOPTA) [4,5], within reticuloendothelial cells (e.g.: superparamagnetic iron oxide particles) or within the

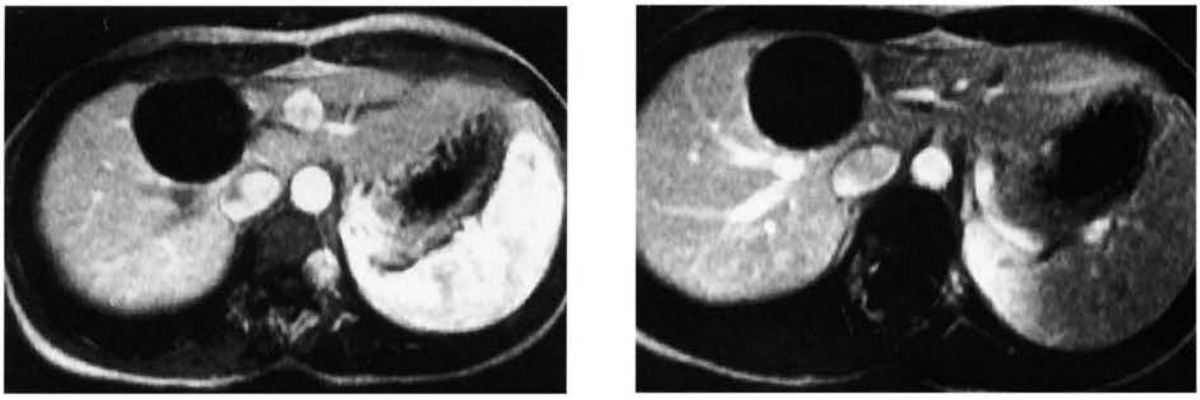

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Figure 2. Liver Cysts. Immediate (a) and 5 minute (b) post gadolinium spoiled gradient echo MR images demonstrate a well defined 6 cm lesion that is signal void on early (a) and later (b) post gadolinium images diagnostic for a liver cyst.

blood pool (e.g.: ultrasmall paramagnetic iron oxide particles) [6]. Other agents are targeted to cell membrane antigens.

DISEASE OF THE HEPATIC PARENCHYMA

MASS LESIONS

BENIGN

Cyst

Cysts are low signal on T1-weighted images and high signal on T2-weighted images and retain signal on longer TE (e.g. >120 msec) T2-weighted images. Cysts do not enhance with gadolinium on MR images. Delayed post gadolinium images (up to 5 minutes) may be useful to ensure that lesions are cysts and not poorly vascularized metastases which show gradual enhancement. An advantage of MRI over CT in the characterization of cysts is that on gadolinium enhanced MR images cysts are near signal void while cysts on contrast enhanced CT images are a light grey in attenuation. MRI is particularly valuable when lesions are small and the patient has a known primary malignancy. The vast majority of liver cysts are simple in type, and therefore the majority are low signal intensity on T1-weighted images and near signal void on post gadolinium images (**figure 2**).

Hemangioma

Hemangiomas have long T1 and T2 values so they are low in signal intensity on T1-weighted images, high in signal on T2-weighted images and maintain signal on longer TEs (e.g. >120 msec). Hemangiomas have well defined round or lobular borders. Small lesions typically appear round while larger lesions have a lobular margin. T2 measurements are however substantially shorter than that of cysts. Hemangiomas typically enhance in a peripheral nodular fashion on dynamic serial gadolinium enhanced MR images with slow progressive complete or nearly complete fill-in of the entire lesion by 10 minutes [7-11]. Serial gadolinium enhanced SGE images have been shown to be effective in distinguishing benign from malignant hepatic masses.

The MR appearances of small (<1.5 cm), medium (1.5-5.0 cm) and large (>5.0 cm) hemangiomas has been reported in a multi-institutional study [10]. Among the 154 hemangiomas in 66 patients, 81 lesions were small, 56 medium and 17 large. Hemangiomas were multiple in 68% of patients. All lesions were high in signal on T2 weighted images. Three types of enhancement patterns were observed: uniform high signal immediately following contrast (Type 1), peripheral nodular enhancement with centripetal progression to uniform high signal and peripheral nodular enhancement with centripetal progression with a persistent central scar (Type 3). Type 1 enhancement was observed only in small tumors. Type 2 and Type 3 enhancement were observed in all size categories. Type 3 enhancement was observed in 16/17 large tumors. In this study 68% of patients had multiple hemangiomas. A variation in the Type 2 enhancement pattern is that contrast enhancement may spread at a fairly rapid rate with complete enhancement at 1-2 minutes.

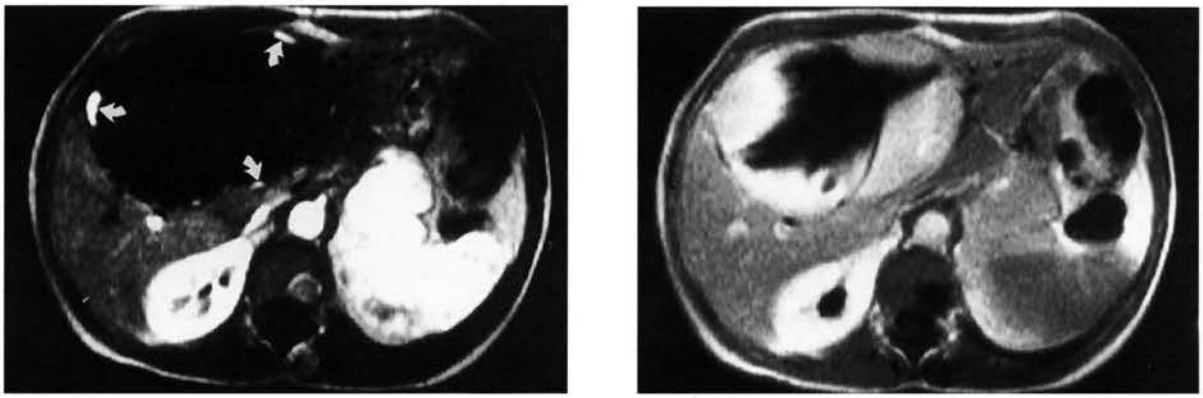

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Figure 3. Giant liver hemangioma. Immediate (a) and 10 minute (b) post gadolinium spoiled gradient echo images demonstrate nodular enhancement in a discontinuous ring initially (arrows, a) with coallescence of the nodules and centripedal progression on delayed images (b). Note the large near signal void center of the hemangioma consistent with a central scar which is invariably present in large hemangiomas.

Hemangiomas most commonly demonstrate Type 2 enhancement. The peripheral nodules of enhancement are typically very small. Type 1 enhancement is the next most common pattern. Type 3 enhancement is uncommonly observed in small hemangiomas. These lesions are difficult to distinguish from other types of liver lesions, specifically liver metastases, and MRI follow up is generally required.

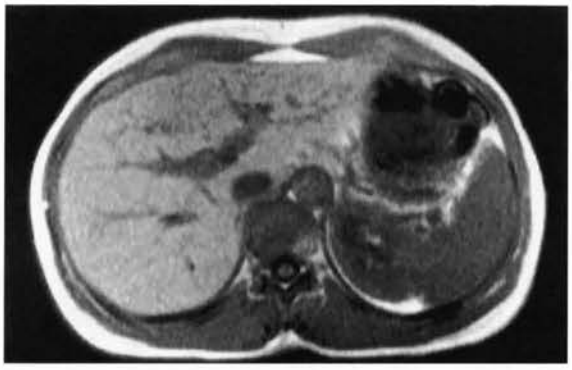
The great majority of medium-sized hemangiomas exhibit Type 2 enhancement, and these represent the "classical" hemangiomas. Type 3 enhancement is the next most common enhancement pattern.

The most distinctive imaging feature of hemangiomas is the demonstration of a discontinuous ring of nodules immediately following gadolinium administration. Nodular enhancement is most frequently eccentric in location however central enhancement may occur. Hemangiomas may fade in signal intensity over time, but will fade in a homogeneous fashion with no evidence of peripheral or heterogeneous washout. Hemangiomas may fade in signal to isointensity with liver, but will not fade to hypointensity. Small hemangiomas with Type 1 enhancement may be indistinguishable from hypervascular malignant liver lesions such as hepatocellulár carcinomas or leiomyosarcoma. Small hemangiomas are high in signal intensity on T2-weighted images, whereas small hepatocellular carcinomas are often near isointensity. Small hypervascular metastases may appear identical in appearance to small hemangioma on all sequences. Usually however a large lesion is also present which will exhibit the enhancement features of either a hemangioma or a metastases [12], so that the histology of the small lesions may be inferred.

Giant hemangiomas most frequently have a central scar; virtually all giant hemangiomas have Type 3 enhancement (**figure 3**).

Advantages of MRI over CT in the evaluation of hemangiomas include: 1) the ability to image the entire liver in the same phase of contrast enhancement, which is useful when multiple lesions are present, 2) greater lesion enhancement on contrast enhanced images such that lesions are comparatively brighter than background liver and 3) superior detection of small hemangiomas.

Reports have described that hemangiomas may be reliably distinguished from metastases on T2-weighted images based on the smooth lobular margins of hemangiomas and the higher calculated T2-values (mean 140 msec). Although this may be true in the majority of patients, cumulative experience from many centers has shown that T2-weighted images alone may not allow characterization of small tumors nor allow reliable distinction between hemangiomas and hypervascular malignant tumors (such as leiomyosarcoma and islet cell tumors) [8]. Therefore, the routine combination of T2-weighted information with serial gadolinium-enhanced SGE may be useful in order to increase observer confidence for establishing the correct diagnosis, and also to maximize evaluation of other hepatic and extrahepatic diseases.



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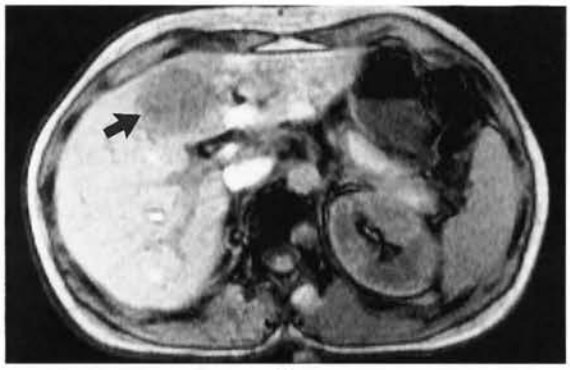

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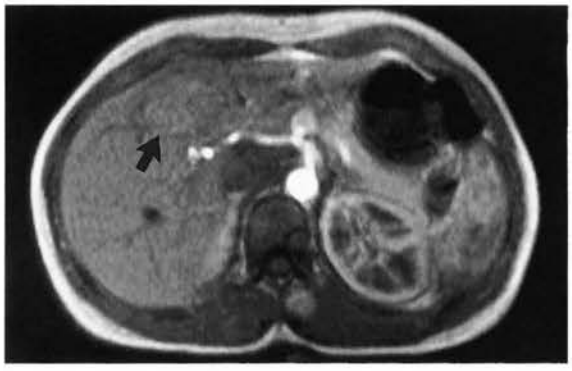

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Figure 4.
Hepatic adenoma. Precontrast (a) out-of-phase (b) and immediate and 90 sec (c) post gadolinium spoiled gradient echo images. A 4 cm hepatic adenoma is present in the medial segment of the left lobe which is near isointense on the precontrast in-phase image (a)and drops uniformly in signal intensity on the out-of-phase image (arrow, b). Uniform enhancement of the lesion greater than background liver on the immediate post gadolinium image (arrow, c) distinguishes the hepatic adenoma from focal fatty liver which would show isointense or mildly hypointense enhancement with background liver.

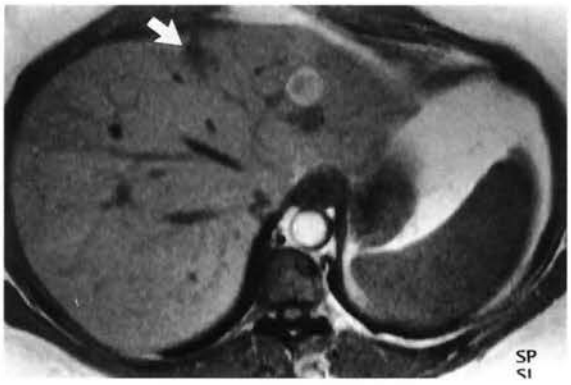
Adenoma

The typical MR appearance of an adenoma is a lesion which varies in signal intensity from mildly hypointense to moderately hyperintense on T1-weighted images, and is mildly hyperintense on T2-weighted images [13, 14]. The degree of high signal on T1-weighted images reflects the quantity of fat they contain. Tumors may decrease in signal on out-of-phase or fat suppressed images due to their fat content (**figure 4**). Lesions may be near isointense with liver on all imaging sequences reflecting similarity to liver parenchyma. Tumors may also have mixed high signal intensity on T1- and T2-weighted images due to the presence of hemorrhage. Characteristically tumors have a transient blush immediately following gadolinium chelate administration which fades by one minute. Coexistent fatty infiltration of the liver is not uncommon.

Focal nodular hyperplasia

The most common appearance on non contrast MR images is slight hypointensity on T1-weighted images and slight hyperintensity on T2-weighted images, although tumors may be near isointense on both these sequences. Unlike adenomas, FNH rarely has higher signal than liver on T1-weighted images. High signal intensity of the central scar on T2-weighted images is a characteristic feature of FNH but is observed in only 10-49% of patients. These lesions enhance with an intense uniform blush on immediate post gadolinium images and fade rapidly to near isointensity (typically at 1 minute post contrast) (**figure 5**) [15-18]. When observed, the central scar is low in signal on immediate post gadolinium images and gradually enhances to hyperintensity over time. This enhancement pattern is that of scar tissue independent of location. Fatty liver is not uncommon in the presence of FNH and the tumor may be mildly hypointense on in-phase T1-weighted images and hyperintense on out-of-phase images. Lesions that are isointense on all precontrast images may only be appreciated on the immediate post gadolinium SGE image as a mass which transiently enhances in a uniform homogeneous fashion.

Adenomas and FNH may be distinguished by the following features: the presence of a pseudocapsule, internal hemorrhage, or fat which are more typical for adenomas, and a central scar that shows delayed



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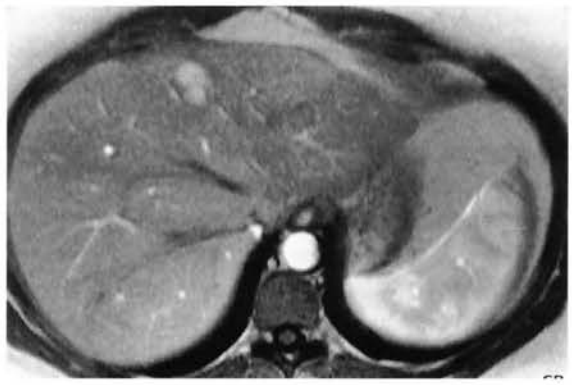

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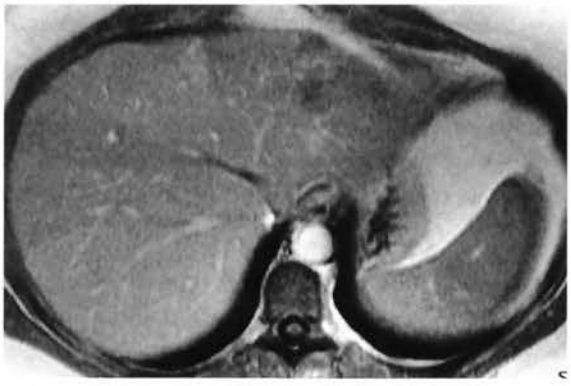

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Figure 5.
Hepatic focal nodular hyperplasia. Precontrast (a), immediate (b) and gradient echo images demonstrate a 2.5 cm lesion in the medial segment of the left lobe which is mildly hypointense precontrast (arrow, a) uniformly in the hepatic arterial dominant phase (b) and fadely rapidly to near-isointensity (c).

enhancement which is more typical for FNH . Both lesions have an early transient tumor blush on gadolinium enhanced images.

Malignant Tumors

Livers metastases

An imaging protocol including T1-weighted SGE, T2-weighted sequences and serial gadolinium enhanced SGE acquired with whole liver coverage per acquisition, achieves good lesion detection (T2-weighted images and immediate post gadolinium SGE images) [7] and characterization (T2-weighted images and serial post gadolinium SGE images). The use of fat suppression on T2-weighted sequences is advisable as it facilitates detection of subcapsular lesions. Fat suppression is especially important to apply on echo train spin echo sequences. Fat is high signal on echo train spin echo sequences, with the result that fatty liver is high in signal intensity and conspicuity of coexistent metastases is diminished. Fatty liver is not uncommon in the setting of liver metastases, which results from fatty metamorphosis as a response to the presence of metastases. On out-of-phase SGE images liver metastases may appear high in signal intensity, due to signal drop of background liver parenchyma. This may on occasion facilitate lesion detection, particularly if lesions are intrinsically high in signal intensity. The acquisition of at least one sequence in the coronal plane may be of value to evaluate the superior and inferior margins of the liver, particularly the infracardiac portion of the left lobe [19]. Breath-hold techniques such as SGE, HASTE, or both are useful for this purpose.

A previous study, which compared non-spiral dynamic contrast enhanced CT and MRI employing T2-weighted fat suppressed spin echo, SGE and dynamic serial post gadolinium SGE images in 73 patients with clinically suspected liver disease, demonstrated greater lesion detection and characterization by MRI [7]. Lesion detection was greatest with T2FS (272 lesions) and contrast enhanced SGE (244 lesions), which was statistically greater than with CT (220 lesions) and SGE (219) ($p<.03$). Lesion characterization was greatest with contrast enhanced SGE (236 lesions) ($p<.01$), followed by CT (199 lesions), SGE (164 lesions) and T2FS (144

lesions). A more recent comparison, between these MR sequences and dynamic non-spiral contrast enhanced CT, in 20 patients with solitary hepatic metastases detected by CT, demonstrated that MRI detected more than 1 lesion in 6/20 (30%) of patients [3].

Characterization of liver lesions is important as patients with known primary malignancies commonly have small hepatic lesions which are benign cysts or hemangiomas. A previous report described the detection of small (<15mm) lesions in 254 of 1454 patients who underwent CT examination. The majority of patients (82%) with liver lesions in this study had a known primary tumor and yet lesions in 51% of these patients were benign [20]. Another report described a large series of cancer patients, in whom 41.8% of detected focal liver lesions were benign [21]. Patients may have a variety of lesions which can be multiple and scattered throughout the liver, therefore the whole organ coverage per acquisition of SGE permits optimal evaluation of the entire liver in distinct phases of enhancement using serial image acquisition following gadolinium administration. In the presence of multiple liver lesions, the distinction of benign and malignant lesions is of critical importance and is well performed by MRI.

Comparison between spiral CT arterial portography (CTAP) and MRI employing these above described sequences for diagnostic accuracy, cost and effect on patient management has been recently reported involving a population of 26 patients referred for hepatic surgery with suspected limited malignant disease [22]. Regarding lesion detection CTAP and MR imaging showed 185 and 176 true-positive malignant lesions, 15 and 0 false-positive malignant lesions, 0 and 18 true-negative malignant lesions, and 13 and 22 false-negative malignant lesions, respectively. Regarding segmental involvement, CTAP and MR imaging showed 107 and 105 true-positive segments, 11 and 0 false -positive segments, 80 and 91 true-negative segments, and 4 and 6 false-negative segments, respectively. A significant difference in specificity of segmental involvement was observed between MRI (1.0 ± 0) and CTAP (0.88 ± 0.05), $p < 0.03$. Total procedural cost was $3,499 for CTAP and $1,224 for MRI. CTAP findings did not alter patient management over MRI in any patient, while MRI findings resulted in a change in patient management over CTAP findings in 7 patients, which was significant, $p = 0.015$. The results of this study showed that state-of-the-art MRI has higher diagnostic accuracy and greater effect on patient management than spiral CTAP, and is 64% less expensive. A major problem with CTAP is the frequent occurrence of perfusion defects which can resemble a focal mass. Perfusion defects are generally not problematic on MR images. Perfusion defects can also mask the presence of metastases on CTAP images.

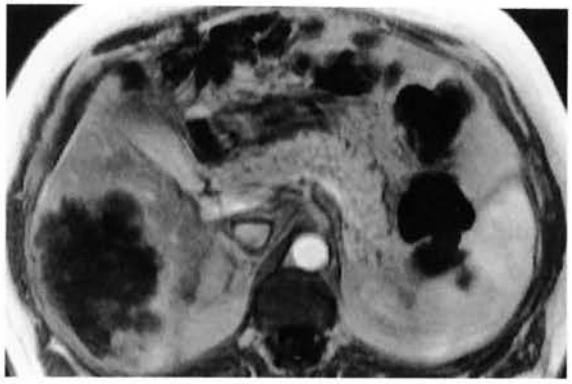


Figure 6.
Colon cancer liver metastasis. Immediate post gadolinium spoiled gradient echo image demonstrates a 7.5 cm mass lesion in the right lobe of the liver which has an irregular "cauliflower"shape, and peripheral ring enhancement with ill-defined perilesional enhancement. This is a common appearance for a colon cancer liver metastasis.

Metastases vary substantially in appearance on T1- and T2-weighted images. Borders are usually irregular but may be sharp. Lesion shape is frequently irregular but may be round or oval. Metastases generally are moderately low in signal on T1-weighted images and modestly high in signal on T2-weighted images. Some metastases, particularly vascular metastases from islet cell tumors, pheochromocytoma and renal cell cancer or necrotic metastases may be high in signal on T2-weighted images, rendering distinction from hemangiomas difficult.

Metastases do not have the classical enhancement patterns of benign lesions, i.e. no enhancement as seen with cysts, peripheral nodular enhancement as seen with hemangiomas, or, in metastases > 2 cm, transient immediate post-gadolinium homogenous blush as seen with FNH or adenomas. Transient tumor blush is however commonly observed in small (< 2 cm) hypervascular metastases. The most common enhancement feature of metastases is a peripheral ring of enhancement on immediate post gadolinium chelate SGE images (**figure 6**). This enhancement pattern reflects the underlying pathophysiology in which

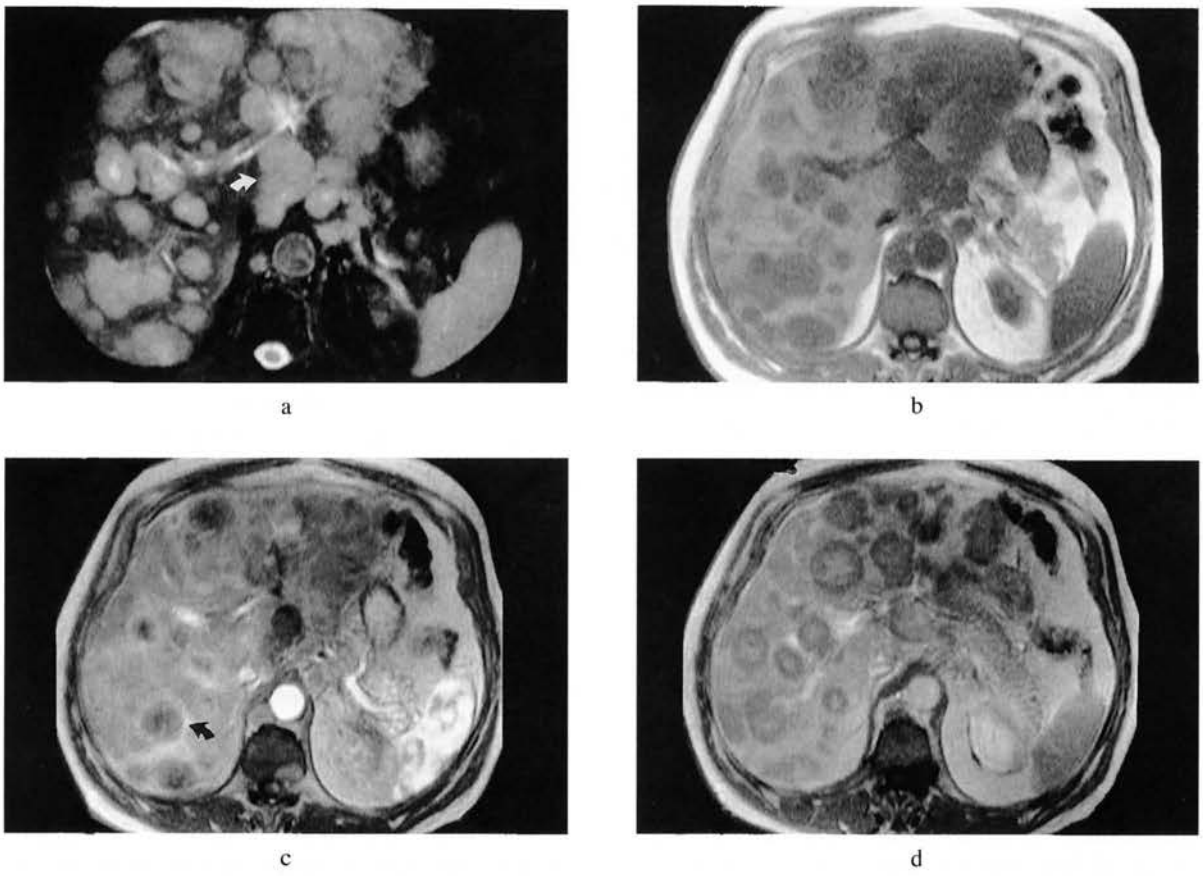


Figure 7. Hypervascular liver metastases. T2-weighted fat suppressed echo train spin echo (a), precontrast (b), immediate (c) and 5 minute (d) post contrast spoiled gradient echo images. Multiple liver lesions are scattered throughout the entire liver which are moderately high signal on T2-weighted images (a), moderately low signal intensity on T1-weighted images (b) and show intense ring enhancement on immediate post gadolinium images (arrow, c) that subsequently show peripheral wash out on delayed images. Intense rim enhancement on immediate post gadolinium images is characteristic for hypervascular metastases, and occasionally these lesions will exhibit peripheral washout. Additional note is made of enlarged lymph nodes in the porta hepatis which are well shown as moderately high signal structures in a background of suppressed fat and lower signal liver on fat suppressed T2-weighted images (arrow, a).

metastases parasitize surrounding hepatic arterial blood supply. Central progression of contrast enhancement is common. Irregular or peripheral contrast washout is also observed, and is common in hypervascular metastases [23, 24].

Hypovascular Metastases

Hypovascular metastases usually are low in signal on T1- and T2-weighted images, signal features comparable to muscle or fibrous tissue. They are hypointense relative to liver on T1-weighted images, and are often near isointense on T2-weighted images [25]. These tumors are usually most conspicuous on portal phase gadolinium enhanced SGE images. Hypovascular metastases may contain a large volume of extracellular fluid and mimic the appearance of cysts; that is: high signal intensity on T2-weighted images and near signal void immediately following gadolinium administration. Delayed post gadolinium images demonstrate that lesion borders become indistinct and lesions decrease in size due to peripheral enhancement.

Hypervascular Metastases

The malignancies which most commonly result in hypervascular liver metastases include: renal, carcinoid, islet cell, leiomyosarcoma, and melanoma. Malignancies which occasionally result in hypervascular liver metastases include bowel, breast and lung cancer. Hypervascular metastases are generally high in signal on T2-weighted images and possess an intense peripheral ring of enhancement immediately following gadolinium administration (**figure 7**). In many of these lesions, contrast will progress in a centripetal fashion. Dynamic serial gadolinium enhanced MR images are particularly important for lesion detection and characterization in patients with known vascular primary tumors. Vascular metastases from gastrinomas enhance with a uniform peripheral ring pattern on immediate post gadolinium images [23]. These metastases have a particular propensity to fade peripherally on more delayed images. Vascular metastases from renal cell cancer, bowel cancer, carcinoid, or nongastrinoma islet cell tumors tend to be irregular in size and shape and to enhance with a thick irregular rim, that may gradually fill in. Enhancement of hypervascular metastases is better shown on MR than CT images due to the higher sensitivity of MR for gadolinium chelates, the more compact bolus of contrast delivered to the hepatic parenchyma, and better temporal resolution for dynamic image acquisition.

Features which are more consistent with malignant lesions than hemangiomas are: 1) early intense peripheral ring, 2) uniformity of the thickness of the ring, 3) jagged or serrated internal margin of the ring rather than a lobular margin and 4) peripheral washout of the ring with presence of more central enhancement. Features which are more consistent with hemangiomas are: 1) discontinuous nodular ring of enhancement on immediate post gadolinium images and 2) progressively increased intensity of enhancement between immediate and 90 seconds following gadolinium administration.

Small hypervascular metastases frequently enhance in a uniform fashion and fade to near isointensity by one minute. Some small hemangiomas may enhance as rapidly, however hemangiomas tend to retain contrast and remain high in signal for a more prolonged period. Most often at least one lesion > 2 cm in diameter is present which possesses more typical enhancement of metastases or hemangiomas, which permits inference of the nature of the smaller lesions. The capillary phase of

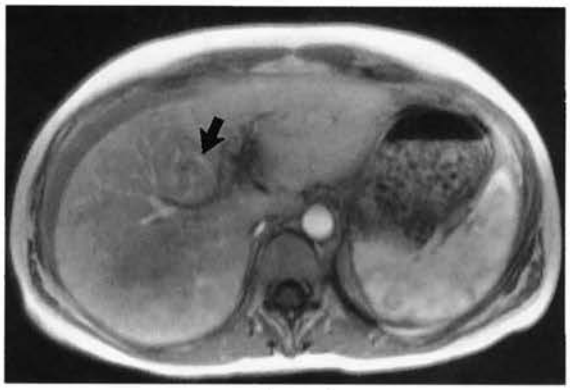


Figure 8.
Small hepatocellular carcinoma. Immediate post gadolinium spoiled gradient echo image demonstrates diffuse heterogeneous enhancement of a 2.5 cm hepatocellular carcinoma (arrow).

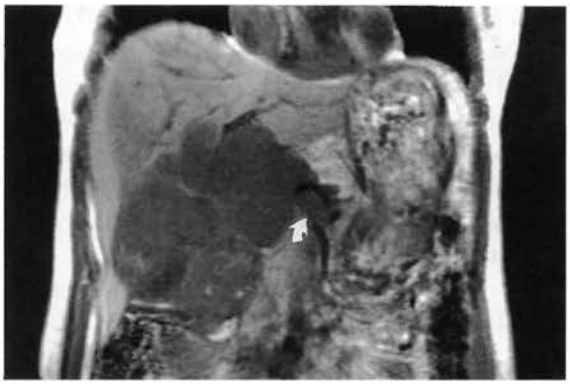
enhancement is the most important phase of image acquisition both for detection and characterization, and later phases assist with lesion characterization.

Lymphoma

Lesions are typically low in signal on T1-weighted images, but vary in signal intensity from low to moderately high on T2-weighted images. Enhancement on immediate post gadolinium images tends to parallel the signal intensity on T2-weighted images; lesions which are low in signal intensity on T2-weighted images tend to enhance in a diminished fashion while lesions which are high in signal intensity tend to enhance in a substantial fashion. As with liver metastases, enhancement on immediate post gadolinium images usually is predominantly peripheral, which reflects parasitization of surrounding hepatic parenchymal arterial blood supply.

Hepatocellular Carcinoma

On MR images, HCC's may have a variety of signal patterns on T1- and T2-weighted images. The most frequent appearance is minimally low signal on T1-weighted images and moderately high signal on T2-weighted images. HCC's may, however, range from hypo- to hyperintense on T1- and T2-weighted images [27-32]. Early HCC is frequently high in signal on T1-weighted images and isointense on T2-weighted images [28]. High signal on T1-weighted images on occasion is due to presence of fat, however, many of these tumors do



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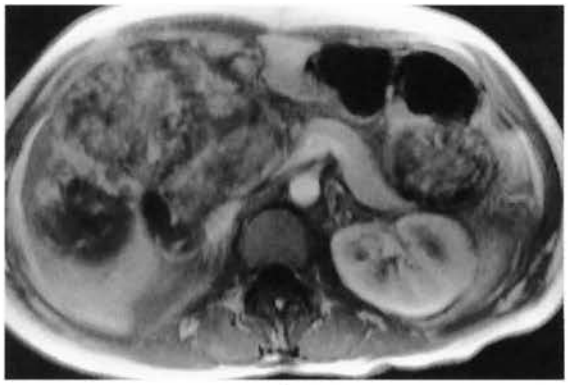

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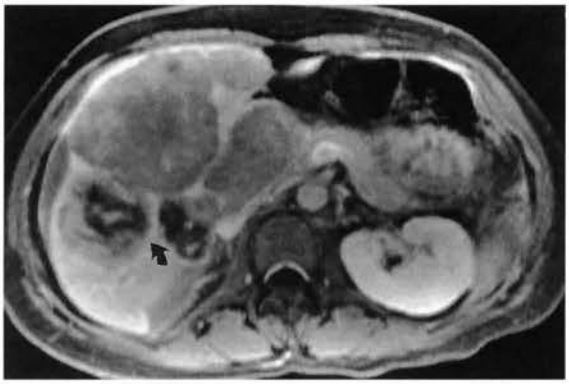


c

Figure 9.
Large hepatocellular carcinoma. Coronal spoiled gradient echo (a), and immediate (b) and 90 second fat suppressed (c) spoiled gradient echo images. A 12 cm hepatocellular carcinoma arises from the inferior aspect of the liver which is well shown on the coronal plane image. Tumor involvement of the celiac axis and superior mesenteric artery (arrow, a) is also shown. The mass exhibits diffuse heterogeneous enhancement immediately following contrast administration, with heterogeneous washout of contrast by 90 seconds and delayed capsular enhancement (arrow, c).

not contain fat or copper. Copper-binding protein or high protein content may be responsible for the high signal [31]. In early advanced hepatocellular carcinoma, low signal intensity nodule within a high signal intensity nodule (nodule within nodule) appearance has been described on T1-weighted images. This reflects the development of low signal high grade tumor within high signal low grade tumor. HCC's are commonly hypervascular and enhance in a diffuse heterogeneous fashion (**figures 8 & 9**). The appearance on hepatic arterial dominant phase gadolinium enhanced images often permits distinction of HCC from metastatic disease as HCC's typically demonstrate enhancing stroma throughout the entire tumor, whereas metastases have peripheral enhancement. The primary hepatic origin of HCC presumably results in a blood supply similar to and in continuity with background liver, explaining the early diffuse heterogeneous enhancement. The degree of vascularity of HCC's may vary substantially; many are hypervascular, however some neoplasms are very hypovascular. Hypovascular tumors are variable in signal on T1-weighted images but are near isointense on T2-weighted images, and these tumors are frequently well differentiated. Lesion size and number are best evaluated on combined T1- and T2-weighted images and immediate post gadolinium enhanced SGE images, as tumors vary in signal intensity on noncontrast images and this combination of sequences increases observer confidence. Small < 1.5 cm, tumors are often only apparent on immediate post gadolinium SGE images. Therefore detection of the presence of small satellite HCC's require the acquisition of hepatic arterial dominant phase SGE images. Margins in large tumors are usually best seen on T2-weighted images and less distinct on gadolinium enhanced MR images.

Diffuse infiltration with HCC may be difficult to recognize on imaging studies since the findings may be subtle or may simulate the appearance of scarring. The most common appearance of diffuse infiltrative hepatocellular carcinoma is mottled, punctate high intensity on T2-weighted images and mottled punctate intense enhancement on hepatic arterial dominant phase gadolinium enhanced images. The mottled liver texture is

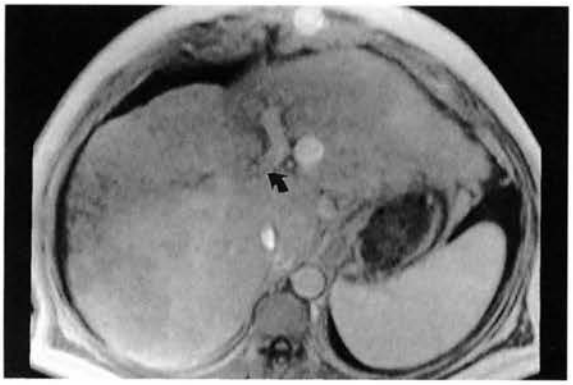


Figure 10.
Diffuse hepatocellular carcinoma. Immediate post gadolinium spoiled gradient echo image shows diffuse, heterogeneous, intense and mottled enhancement of much of the parenchyma of the right lobe consistent with diffuse hepatocellular carcinoma, associated with thrombus in the right portal vein (arrow).

more readily appreciated on hepatic arterial dominant phase images (**figure 10**). Diffuse infiltration may also appear as irregular linear strands which are hypo - to isointense on T1-weighted images, and iso- to moderately hyperintense on T2-weighted images. On immediate post gadolinium images these tumor strands tends to enhance less than adjacent liver although more intense enhancement also occurs. Late increased enhancement of the tumor strands may reflect fibrous composition.

A characteristic feature of HCC is tumor extension into the venous system. Tumor extension into portal veins occurs most frequently, but hepatic venous extension also occurs. This feature is observed in <50% of cases, but is common with large and advanced tumors. Diffusely infiltrative HCC very commonly has associated venous thrombosis. Pseudocapsules are not uncommonly observed in HCC, especially in early or well differentiated tumors. The typical signal intensity of a pseudocapsule is hypointensity on T1-weighted images, minimal hyperintensity on T2-weighted images, low signal on immediate post gadolinium images and increased enhancement on delayed images [34].

Fibrolamellar HCC

Fibrolamellar HCC are generally large, solitary tumors which are heterogeneous and low in signal intensity on T1-weighted images and heterogeneous and high in signal intensity on T2-weighted images. A central scar, which may have a radiating appearance, has large low signal components on T2-weighted images which do not enhance with gadolinium on delayed images. Enhancement of the tumor is diffuse heterogeneous and intense on immediate post gadolinium SGE images.

DIFFUSE LIVER PARENCHYMAL DISEASE

Cirrhosis

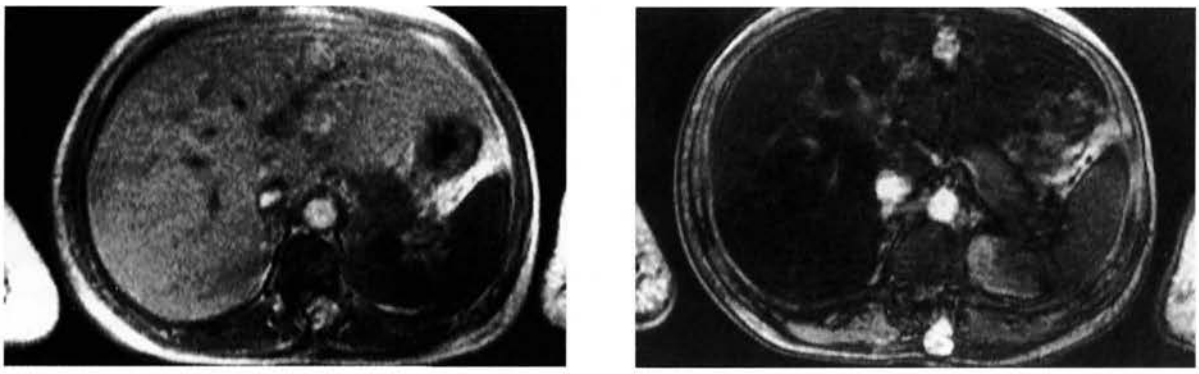
Fibrosis and occasionally mild iron deposition occur in cirrhotic livers, which decrease hepatic signal intensity on T1- and T2-weighted images. Many cirrhotic livers contain regions of low signal on T1-weighted images and high signal on T2-weighted images secondary to hepatocellular damage and/or inflammation.

MRI demonstrates regenerative nodules with greater conspicuity than they are shown by other imaging modalities. On T2-weighted images, regenerative nodules are low in signal intensity relative to high signal intensity inflammatory fibrous septa or damaged liver. Approximately 25% of regenerative nodules accumulate iron more than the surrounding hepatic parenchyma, facilitating their identification as low signal on T2-weighted SE images and T2*-weighted gradient echo images [35, 36]. Regenerative nodules are particularly well shown on early post gadolinium SGE images as low signal foci, since hepatic parenchyma enhances greater than iron containing nodules. Irregular linear high signal abnormalities may be observed on T2-weighted images in cirrhotic livers. These represent bands of fibrous tissue. They exhibit a characteristic enhancement pattern on serial post gadolinium SGE images, minimal enhancement on immediate post gadolinium images and delayed increased enhancement.

Atrophy of the right lobe and the medial segment of the left lobe is most severe in cirrhotic livers. Relative sparing of the caudate lobe and lateral segment of the left lobe are often present and these segments may undergo hypertrophy.

Fatty Infiltration

Fatty Infiltration is shown with a high degree of accuracy as hepatic parenchymal signal loss comparing



a b

Figure 11. Diffuse fatty infiltration of the liver. In-phase (a) and out-of-phase (b) spoiled gradient echo images show uniform drop in signal intensity of the liver between the two sequences diagnostic for diffuse fatty infiltration.

out-of-phase SGE to in-phase SGE (**figure 11**).

Iron Deposition

Idiopathic hemochromatosis

Idiopathic hemochromatosis results from increased gastrointestinal absorption and parenchymal deposition of dietary iron. Iron accumulates in the liver, pancreas, heart and other organs. Causes of death in these patients include cirrhosis, hepatocellular carcinoma, diabetes mellitus and congestive cardiomyopathy. Early in the disease process, iron accumulation is restricted to the liver. Disease detection at this stage, with institution of phlebotomy therapy, may result in a normal life expectancy. Over time, iron deposition progresses to involve other organs, primarily pancreas and heart. In advanced disease, decreased signal intensity occurs of the liver and pancreas, with normal signal intensity of the spleen, on T2-weighted and T2*-weighted images. Presence of iron deposition in the pancreas correlates with irreversible changes of cirrhosis in the liver [37].

Some patients who present with hepatocellular carcinoma (HCC) have previously unsuspected hemochromatosis. As tumor cells do not contain excess iron they are well shown as high signal intensity masses relative to iron-overloaded liver on MR images. Non-

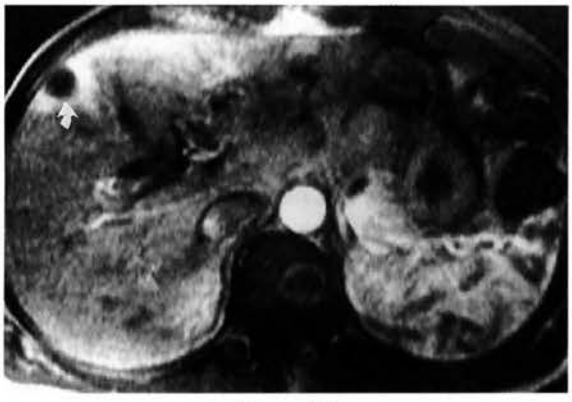


Figure 12.
Pyogenic hepatic abscess. Immediate post gadolinium spoiled gradient echo image demonstrates a 2 cm abscess (arrow) with intense perilesional enhancement that equilibrates with liver by one minute post contrast (not shown)

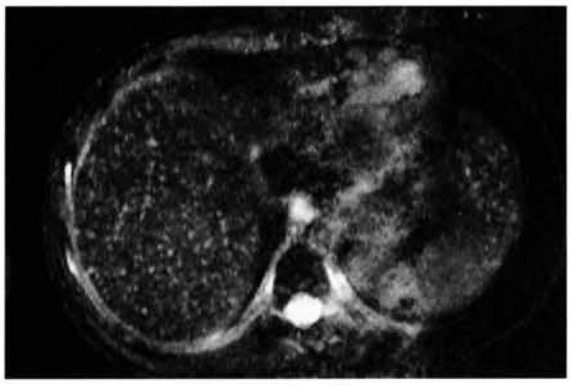


Figure 13.
Acute hepatosplenic candidiasis. T2-weighted fat suppressed echo train spin echo image demonstrates extensive <1 cm rounded high signal intensity foci in the liver diagnostic for acute hepatosplenic candidiasis in this patient with acute myelogenous leukemia.

siderotic nodules in a patient with hemochromatosis which are not hemangiomas or cysts, should be considered HCC, since regenerative nodules in these patients contain iron. Dysplastic nodules (adenomatous hyperplasia) in patients with increased hepatic iron may contain a differing concentration of iron than surrounding hepatic parenchyma.

Transfusional iron overload

Transfusional iron overload is the most common form of excess iron deposition in North America. Iron deposition in the reticuloendothelial system results in low signal intensity of the spleen, liver and bone marrow on MR images best shown on T2- or T2*-weighted images.

Infectious Diseases

Pyogenic abscesses

pyogenic abscesses may range in appearance on T2-weighted images from heterogeneous low signal intensity to uniform high in signal intensity. On serial post gadolinium spoiled gradient echo images abscesses typically exhibit transient ill-defined perilesional enhancement on initial post injection images (**figure 12**) in conjunction with intense persistent enhancement of abscess walls and internal septations. Unlike malignant tumors abscesses do not show progressive enhancement of internal stroma.

Abscesses

Fungal infection

Fungal microabscesses are observed as a complication of immunosuppression or an immunocompromised state. Patients on medical therapy for acute myelogenous leukemia (AML) are particularly susceptible to this infection. The most common infecting organism is *Candida albicans*, however other fungi may be found. Acute hepatosplenic fungal lesions are frequently < 1 cm in size and subcapsular in location. The small size and peripheral nature of these lesions make them difficult to detect with CT or standard spin echo MR sequences. Patients with AML undergo multiple blood transfusions so the liver and spleen are low in signal on T1-weighted and T2-weighted images. T2-weighted fat suppressed spin echo is effective at detecting these lesions because of the high conspicuity of this sequence for small lesions and the absence of chemical shift artifact which may mask small peripheral lesions [38]. MRI employing T2-weighted fat suppression and dynamic gadolinium enhanced SGE images has been shown to be more sensitive for the detection of hepatosplenic candidiasis than contrast enhanced CT. Acute lesions of fungal disease are abscesses and therefore are high signal intensity on T2-weighted images (**figure 13**). They may also be seen on gadolinium enhanced T1-weighted images as signal void foci with usually no appreciable abscess wall enhancement.

CONCLUSIONS

MRI is an excellent modality to evaluate diffuse liver disease and to detect and characterize focal liver masses. Although MRI may exceed spiral CT for many of these evaluations, due to the high cost of MRI it may be prudent to limit the use of MRI to circumstances in which the superiority of MRI may have a substantial impact on patient management. Among all focal liver lesions, MRI has the greatest impact on patient management over CT in the evaluation of hypervascular malignant lesions such as hepatocellular carcinoma or metastases from hypervascular primary tumors. MRI may be the most accurate nonoperative imaging modality to evaluate patients with suspected limited involvement of the liver with malignant disease who are considered candidates for partial hepatic resection. MRI is also the imaging modality of choice for the detection of hepatosplenic candidiasis. No other modality can exceed the accuracy of MRI for the evaluation of diffuse liver disease and therefore MR should be used to investigate patients with suspected iron deposition or fatty infiltration. In many settings however, MRI may be adequately employed as a problem-solving modality to characterize and determine the extent of focal liver lesions. It is also clear that patients who are not candidates for contrast-enhanced CT examination (e.g. patients with poor renal function or contrast allergy) should be studied with MRI.

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