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Contrast Enhanced Magnetic Resonance Imaging In Evaluation of Focal Liver Lesions

KEYWORDS: contrast enhanced MRI of liver, focal hepatic lesions, benign, malignant, characterization.

Madhuri Atluri	Tummala Nageswara Rao	Shyam Prasad Reddy Bitla
Associate Professor, Department of Radio-Diagnosis, NRI Medical College and General Hospital, Chinakakani, Mangalagiri Mandal, Guntur District, Andhra Pradesh, India.	Professor, Department of Radio-Diagnosis, NRI Medical College and General Hospital, Chinakakani, Mangalagiri Mandal, Guntur District, Andhra Pradesh, India.	Consultant Radiologist, Care Hospital, Hyderabad, Andhra Pradesh, India.

ABSTRACT *Purpose: To assess the value of contrast enhanced magnetic resonance imaging (MRI) for characterization of hepatocellular lesions.*

Materials and methods: MRI of patients was performed on a 1.5 T GE, Signa Exite General Electronics Medical System Milwaukee, USA, machine using T2 SSFSE, T1 FSPGR, Dual Echo FSPGR, 2D FIESTA before contrast and axial dual phase LAVA after injection of Magnavist (Bayer healthcare pharmaceuticals Inc, Wayne, NJ) 0.1mmol per kg body weight. Image evaluation is done by the size, number, intensity and enhancement properties of the lesions.

Results: For characterization of hepatocellular lesions Gadolinium enhanced imaging were significantly superior to non-enhanced imaging. Analysis of enhancement patterns aided in characterization and classification of hepatocellular tumors.

Conclusion: Administration of gadolinium based contrast agents improves the differentiation between benign and malignant tumors and in better characterization of various benign and malignant entities. The accuracy for arriving at a specific diagnosis is higher when unenhanced and Gadolinium enhanced images are considered together than for unenhanced MR images alone.

INTRODUCTION

Focal hepatic lesions constitute a common problem in the clinical setting. Benign focal liver lesions, including cysts, haemangiomas, biliary hamartomas, and focal nodular hyperplasia's may be found in up to 20% of the general population [1]. The liver is also a frequent site of primary and secondary malignant lesions. Hepatocellular carcinoma is the most common primary malignancy, although metastatic malignant liver lesions are more common. Most metastatic lesions originate from colorectal malignancies.

MR imaging is a useful and increasingly popular method for imaging the liver. Liver MR is most commonly used to evaluate an indeterminate focal hepatic lesion detected on other imaging studies and to image patients with contraindications to iodinated contrast material. Other clinical indications are also developing, especially now that it is clinically recognized that liver MR is more sensitive and accurate for detection and characterization of focal lesions than CT or US.

Accurate detection and characterization of focal hepatic lesions can be performed with MR imaging. Specific sequences, such as inversion recovery, are highly sensitive for the detection of lesions. Once detected, they can often be accurately characterized as malignant or benign, cyst or solid tumor, etc., based upon their appearance and relative signal intensity on T1- and T2- weighted sequences. Intravenous contrast material can increase MR´s sensitivity and specificity for detection and characterizing of focal hepatic lesions.

The need to characterize more accurately different histological types of liver lesions and to detect the full extent of malignant liver lesions has been the main reason for the use of contrast agent. The use of contrast agents potentially increases the sensitivity and specificity of liver MRI in numerous pathological conditions by improving morphological information and adding functional information.

Accurate evaluation of hepatic tumor involvement and possible extrahepatic disease constitutes the basis for appropriate selection and tailoring of treatment for cancer patients. In this process, imaging studies play a pivotal role. Liver cirrhosis and its complications, especially hepatocellular carcinoma, are major clinical problems that carry a considerable risk of disability and death [1]. Traditionally, liver cirrhosis has been diagnosed by liver biopsy. This invasive procedure in cirrhotic patients may run a risk of bleeding complications due to coexisting coagulopathy. Liver resection in cirrhotic patients also carries a high risk of operative mortality [2]. Non-invasive tools for the evaluation of liver parenchyma and the detection of tumors are therefore of the utmost importance.

MRI is used as the second method of choice for liver imaging. It is used after US in the characterization of solid focal liver lesions, and in the management of lesions in the cirrhotic liver. The MRI technique is also used after CT in metastatic patients, to further delineate the number and nature of the lesions, and always before computer tomography during arterial portography (CTAP). MRI provides versatile and unique soft tissue contrast, and is thus a powerful tool for evaluating a wide range of liver disorders. Over the past two decades MRI of the liver has experienced unprecedented growth due to advances in

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hardware and software. At present, MRI is considered to possess greater diagnostic accuracy than CTAP and helical CT [3,4,5,6]. However, the introduction of computer-assisted multidetector tomography (MDCT) challenges the superiority of MRI [7,8].

OBJECTIVES

1. The purpose of the study is to characterize all the liver lesions detected on ultrasound or clinical examination by using comprehensive MRI techniques and to compare them with histopathology studies obtained by image guided TRUCUT biopsy specimens or liver resection specimens.
2. To study enhancement patterns of various liver lesions.
3. To compare our results with existing studies.

MATERIALS AND METHODS

The study was conducted in the department of Radio-Diagnosis at NRI General Hospital, Chinnakakani, Mangalagiri, Guntur in 44 patients with Focal Liver lesions who were subjected for contrast enhanced MR Examination from October 2010 to September 2012. Patients of age group 10–70 years and of both genders, suspected to have a focal liver lesion on clinical examination or ultrasound were subjected to Contrast Enhanced MR examination. Patients with cardiac pace makers, metallic implants, renal insufficiency and uncooperative patients were excluded from the study.

Sequences done:

Precontrast: Axial T2-weighted SSFSE, Axial 2D FIESTA and Axial in phase and opposed phase 2D FSPGR sequences.

Post contrast: Dynamic Gd-enhanced MR imaging using the fat-suppressed Multiphase LAVA performed in the arterial, portal venous phases and equilibrium phases. (Magnavist, Bayer pharmaceuticals, 0.1 mmol/kg body weight; injection rate 2 ml/s. Liver-specific contrast agents were not used in our study.

Evaluation of images: On the basis of signal characteristics, enhancement patterns and morphology, the lesions were characterized. The size and number of liver lesions as well as the hepatic segments involved were recorded for the solid lesions. Couinaud's anatomical description of eight liver segments for lesion localization was used. Coexisting benign lesions such as hemangiomas and cysts were also noted. Benign or suspected malignant lymph nodes were scrutinized and the possibility of other extrahepatic involvement such as infiltration through the hepatic capsule or peritoneal metastases was considered.

Tissue diagnosis (Fine needle aspiration cytology/ trucut biopsy) is obtained in feasible cases. In patients with haemangiomas and simple cysts either follow up (average 1 year and one month) or post-surgical histopathology has been considered.

RESULTS AND OBSERVATIONS

There were a total of 44 patients in our study. Out of 44 cases, males outnumbered females with 27 as against 17. There is an equal distribution of cases in 4th, 5th and 6th decades (10, 10 and 10 cases respectively). There is a male predominance in all age groups except for 5th decade where females outnumbered males (4 males and 6 females). (Table 1).

"Table 1 about here".

Out of 44 cases studied, 22 cases were benign lesions. Out of the 22 benign lesions, hemangiomas (Fig 1) and hydatid cysts (Fig 2) of the liver constituted more than 50% of benign lesions (Table 2). Next were regenerative nodules followed by pyogenic liver abscess (Fig 3) and simple cyst (Fig 4).

"Table 2 about here". "Figures 1, 2, 3, 4 about here"

Out of 44 cases 22 cases were malignant (Table 3). Of these, hepatocellular carcinoma (Fig 5) constituted more than 50% of the malignant liver tumors, followed by metastasis (Fig 6). There was one case of cholangiocarcinoma (Fig 7).

"Table 3 about here". "Figures 5, 6, 7 about here"

On T1W imaging most of the lesions were hypointense except for regenerating liver nodules and focal nodular hyperplasia which were isointense and were not detectable on T1W images. On T2W images most of the lesions were hyperintense except for regenerating liver nodules which are hypointense and focal nodular hyperplasia which is isointense. This lesion was detected only on post gadolinium images where there is mild enhancement in the arterial phase. We reported this as focal nodular hyperplasia (FNH), biopsy was performed but proved to be a hepatocellular carcinoma. (Table 4).

"Table 4 about here"

Different patterns of enhancement are noted in our study. Characteristic puddling or nodular enhancement is noted in the arterial phase in case of hemangioma with gradual centripetal filling in the venous and delayed phases. In case of abscess, there is peripheral enhancement in all cases. Regenerating liver nodules showed a faint enhancement in the portal venous phase but were isointense in the equilibrium phases. Simple cysts and hydatid cysts did not show any enhancement on post contrast imaging. Hepatocellular carcinomas showed homogenous enhancement in the arterial phase with washout in the equilibrium phases. One case with a large lesion showed peripheral enhancement (pseudocapsule) with central unenhancing area, another case showed retained contrast with in the lesion even in the delayed phases. Metastasis showed complete ring enhancement except in one case with a large lesion which showed incomplete ring enhancement, washout of contrast noted in the equilibrium phase. Gadolinium enhanced images helped in picking up the lesions which were missed in the plain images. There was one case of intrahepatic cholangiocarcinoma. Post contrast images showed inhomogenous faint enhancement in the arterial phase with prominent delayed enhancement. (Table 5).

"Table 5 about here"

The single most effective sequence in our study for characterization of liver tumors is the dynamic gadolinium enhanced 3D gradient sequence, followed by dual echo sequence. T2W sequences were the least effective in our study. Detection and characterization of the lesions were most accurate when all the sequences were collectively evaluated. (Table 6).

"Table 6 about here"

All the cases were histopathologically proved except for hemangiomas and simple cysts. One patient with hemangioma underwent surgery and proved to be hemangioma. Rest of the five patients with hemangioma and patients with simple cysts are on follow up by serial ultrasound examinations of liver. All the 6 patients with hydatid cysts and 4 patients with regenerating nodules were proved histopathologically. Three cases of liver abscess are proved

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by percutaneous drainage and cytology. (Table 7).

"Table 7 about here"

Of the malignant lesions, cholangiocarcinoma diagnosed radiologically was proved histopathologically. Of all the seven cases of metastasis, six were proved histopathologically and the remaining one was proved to be HCC. Out of 9 cases of HCC, that were diagnosed radiologically. 9 were proved in histopathology. One case was diagnosed as Fibrolamellar HCC (Fig 8) but was proved to be well differentiated HCC at HPE. Out of 4 cases of multifocal HCC diagnosed radiologically, 2 were proved at HPE and 2 were proved to be metastasis at HPE. (Table 8).

"Table 8 about here". "Figure 8 about here"

DISCUSSION

Focal hepatic lesions are commonly discovered during routine radiological examinations, it is essential to distinguish a benign hepatic lesion from a malignant one because of their different clinical implications. Additionally, not only in detection of metastases, but also the determination of their number are important when cancer patients, especially those with colorectal malignancies, are evaluated. Current improvements in liver surgery and local invasive therapies with a curative potential put imaging into highlight when evaluating patients with liver metastases.

Liver tumor imaging beholds two equally important tasks: there is a need for effective lesion detection (high sensitivity), and a desire for accurate tumor characterization (high specificity). MRI is currently considered to be the most accurate noninvasive method in the evaluation of liver lesions [9,10].

Hepatic cysts with an incidence of 2–7% of the population, are common benign liver lesions. They may appear as isolated or multiple lesions and vary from a few millimeters to several centimetres in diameter. MRI shows the cysts to be hypointense in T1-weighted and hyperintense in T2-weighted images. Simple cysts do not enhance and have a homogeneous and well-defined appearance.

Hepatic hemangiomas are the most common benign solid liver tumors, with a reported incidence of up to 20%. Hemangiomas generally have moderately low signal intensity in T1-weighted images and high signal intensity in T2-weighted images with a homogeneous pattern. Hemangiomas have three basic enhancement patterns: uniform enhancement on arterial phase scans, typically seen in hemangiomas 1 cm in size or smaller, nodular peripheral enhancement with centripetal filling on sequential sequences, and nodular peripheral enhancement with centripetal filling in with persistence of a non-enhancing central scar.

In patients with cirrhosis, **regenerating nodules** are seen as lowsignal-intensity areas on both T1- and T2- weighted MR images, with minimal enhancement after contrast material administration.

Dysplastic nodules are generally hypointense or, more commonly, hyperintense on T1-weighted images and iso- or hypointense on T2-weighted images, without prominent arterial phase enhancement after contrast material administration.

Focal nodular hyperplasia - The signal intensity of both T1- and T2-weighted images may be close to that of normal liver parenchyma. If a central scar is present, it is hyperintense in T2-weighted images. With intravenous gadolinium injection, FNH displays a characteristic pattern of marked, uniform enhancement in arterial-phase images obtained immediately after the bolus administration. In the subsequent portal-venous phase, the lesion rapidly fades, becoming isointense or only mildly hyperintense relative to liver parenchyma.

Hepatic adenomas - The MR imaging appearance can be variable and nonspecific. Most have a heterogeneous appearance correlating with the amount of fat and hemorrhage. Adenomas often enhance strongly in arterial phase images.

Abscess usually appears as thick-walled lesion with homogeneous low signal intensity on T1W images, and homogeneous high signal intensity on T2W images. In addition to the enhancing abscess wall, contrast-enhanced MR imaging typically shows increased peripheral rim enhancement.

MR imaging of **hydatid cyst** clearly demonstrates the pericyst, the matrix, and daughter cysts. The pericyst is seen as a hypointense rim on both T1 and T2-weighted images. The hydatid sand appears hypointense on T1W images and markedly hyperintense on T2W images; when present, daughter cysts are more hypointense than the matrix on T2-weighted images.

The majority **of liver metastases** are hypovascular, usually originated from gastro-intestinal tract and from breast and lung carcinoma. Hypovascular metastases are best depicted in portal-venous phase image. Thus, in arterial phase images, hypervascular metastases will show marked enhancement against a background of minimally enhancing liver parenchyma. In T2-weighted MR images, metastases are usually mildly hyperintense relative to the liver.

Hepatocellular carcinoma (HCC) shows a highly variable appearance on both T1W and T2W images. Hyperintense regions within HCC in T1W images reflect the presence of fat, copper, or protein. On T2W images, HCCs are generally hyperintense (106), although well differentiated tumors may be isointense to liver parenchyma. A mosaic pattern is seen if the tumor is larger than 3 cm. HCCs are usually greatly enhanced in arterial dominant–phase images. The enhancement is often homogeneous in tumors less than 2 cm in diameter and heterogeneous in tumors larger than 2 cm.

In T1and T2 images, **cholangiocarcinoma** is hypo- and hyperintense, respectively. After injection of gadolinium, cholangiocarcinoma displays a characteristic pattern of slow, gradual enhancement. The delayed enhancement in equilibrium-phase images is considered to be a characteristic feature.

Our study group consisted of 44 patients. Hepatocellular carcinomas were the most common malignant lesions and Hemangioma and Hydatid cyst of liver were the most common benign lesion. The size of the lesions varied from 0.5 cm to 13 cm with an average of 6.6 cm for malignant lesions and 6.1 cm for benign lesions. The best individual sequence in distinguishing between malignant and benign liver lesions is the dynamic Gd-enhanced T1-weighted sequence. Several previous studies support this result as Gd-enhancement, particularly when used in a dynamic fashion in different phases of enhancement, has been considered to be highly important in liver tumor characterization

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[11,12]. As shown by the results of this study and by earlier investigations, the unenhanced T1- weighted sequence is of limited value in lesion characterization. The T1- weighted sequence is, however, useful for the evaluation of hemorrhagic lesions, tumors with a high fat or copper content such as hepatocellular carcinoma and hepatic adenoma and lesions that contain melanin such as melanoma metastases. The main value of T2-weighted MR imaging is in the diagnosis of hemangiomas. T2- weighted MRI has limited value in the characterization of malignant liver lesions because of the wide variety of lesion appearances (55,101). Reduced lesion conspicuity and the overlap in signal intensity characteristic of benign and malignant nodules diminished the diagnostic value of T2-weighted images in cases of cirrhotic liver. HCC can be difficult to detect on T2- weighted images because of heterogeneity of the cirrhotic liver, which obscures mildly hyperintense and isointense tumors. One of the useful distinguishing feature on MRI is that, whereas both malignancies and hemangiomas tend to have a high signal on conventional T2W images, the signal from malignancies tends to decrease as the TE is lengthened. Whereas the signal from hemangiomas tends to increase. Delayed T1-weighted SE sequence (performed at least 5 min after Gd-chelate injection) was the most accurate technique to identify metastases by showing hypo- or isointensity signal, whereas all hemangiomas are hyperintense.

In our study benign lesions were seen in 22 patients, of these were three simple cysts. All the cystic are hyperintense on T2 WI, Hypointense on T1W images and are non-enhancing on post contrast imaging.

Hydatid cysts were seen in 6 cases, they demonstrated a cystic lesion which are hypointense on T1 WI and hyperintense on T2 WI with hypointense pericyst on both T2 and T1 images. All the cysts were showing internal septations which are hypo on T2W images. Our findings are correlating with the study by Kalovidours et al and Severino et al [13,14] which showed thick wall with hypointense pericyst onboth T1 and T2 weighted imaging and T2 weighted sequences shows better delineation of cyst wall, pericyst, daughter cyst and membrane rupture.

There were only three cases of liver abscess and all are pyogenic liver abscess.

The lesions were hypointense on T1 W images and hyperintense on T2 W images. Minimal perilesional edema is seen in all of the cases, on post contrast images these lesions were showing rim enhancement on arterial, portal venous and equilibrium phases. No intralesional hemorrhage was identified in our patients. Our findings are correlating with the study by RJ Mendez et al which showed T2 hyperintense, T1 hypointense lesions, showed sharp or rim enhancement and 35% of cases showed perilesional edema.

We encountered six cases of hemangiomas in our study. All the hemangiomas had a high signal intensity on T2W images, hypointense on T1W images and on post contrast imaging puddling or peripheral nodular enhancement was noted in the arterial phase with centripetal filling in the portal venous phase and delayed phase.

We had an asymptomatic patient with evidence of homogenous lesion measuring 2.6cm which is hypointense on T1WI and isointense on T2WI. On contrast administration there is intense homogenous enhancement on arterial phase isointense to normal liver parenchyma on venous and delayed phases. No central scar could be visualized in unenhanced or enhanced images. Diagnosis of focal nodular hyperplasia was made and patient was biopsied, HPE came as HCC.

There were 4 cases of regenerative nodules in our study. All the patients showed multiple lesions that were isointense on T1 W images and Hypointense on T2 W images. On post contrast examination the lesions did not enhance in the arterial phase, faint enhancement noted in the venous phase and were isointense to the adjacent liver parenchyma in the equilibrium and delayed phases. One patient had HCC in the background of Cirrhosis and regenerative nodules.

Out of 22 malignant cases, HCC were seen in 14 cases. 10 cases showed solitary lesions, whereas 4 patients showed multiple nodules. All the lesions were hyperintense in T2 weighted images and Iso to hypointense on T1 weighted images. Two of the lesions showed central hyperintense signal on T2 weighted imaging corresponding to necrotic areas. These two cases were lesions of larger size (more than 7 cms). One case showed central hyperintense signal on both T1W and T2W images corresponding to hemorrhage. Of the 4 cases with multiple nodules, two were proved to be metastasis and two were reported as HCC on both biopsied specimens taken at the same time from different locations on HPE. Our results were correlated with studies done by Kelekes et al [15] which showed similar results as lesions with T2 hyperintense, T1 hypointense and diffuse heterogenous arterial enhancement with venous wash out. Small HCC are isointense on T1 and T2 weighted images and are detected only in arterial phase.

Our study consisted of seven cases of metastasis, of these one was solitary metastasis and rest were multiple. Right lobe was predominantly involved than the left lobe. The lesions were measuring 11mm to 65mm in diameter with an average of 36mm. All the lesions were hypointense on T1W images and iso to hyperintense on T2W images. On post contrast examination the lesions were showing continuous rim enhancement in 6 patients and lesions in one patient were showing incomplete ring enhancement. Recent sophisticated histologic investigations reveal that the peripheral rim enhancement is mainly at the extralesional area due to desmoplastic reaction, inflammation and vascular proliferation [16]. Imaging revealed the primary in 4 of the seven cases, the primary being transitional cell carcinoma, lower esophageal carcinoma, colon carcinoma and carcinoma gallbladder. The primary was unknown in the remaining three patients. Of the 7 cases that were biopsied 6 were proved to be metastatic deposits and one was proved to be HCC.

We encountered a case of intrahepatic cholangiocarcinoma. MR imaging showed irregular T1 hypointense, T2 hyperintense lesion with central radiating hypointensities in T2 W images. On post contrast images the lesion shows peripheral enhancement in the arterial phase and gradual centripetal filling in the equilibrium and delayed phases. The central hypointensities in the T2 W images were unenhancing suggesting central fibrosis. Our findings were correlating with the study done by Yoji Maetani et al [17] which showed similar findings on contrast enhanced MRI.

CONCLUSION

In my study 44 cases of focal liver lesions were evaluated by contrast enhanced MRI, 27 were male and 17 were fe-

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male. There was higher incidence of tumors in the 4thto 6th decade of life. Classification of liver lesions into malignant and benign categories can be accurately achieved by Contrast enhanced MRI. Histospecific diagnosis was most reliably achieved when all sequences were collectively evaluated. Most common malignant lesion encountered in our study was hepatocellular carcinoma and most common benign tumor was haemangioma. All the benign lesions could be accurately differentiated to cystic and solid lesions by utilization of various sequences. Hydatid cyst was the commonest cystic lesion encountered, this finding is plausible as most of our patient s hail from the endemic zone. Contrast enhanced liver MRI is able to differentiate between regenerative nodules and hepatocellular carcinoma in the cirrhotic liver with high degree of specificity. Three dimensional GRE imaging has several advantages over two-dimensional dynamic imaging, 3D images can be reformatted in any plane, high-quality thin-section images with no gaps can be obtained, and the detection and localization of small focal hepatic lesions is superior.

TABLES:

Table 1 – Age and gender distribution of patients

Age group (years)	Male	Female	Total
11-20	1	1	2
21-30	1	0	1
31-40	5	5	10
41-50	4	6	10
51-60	6	4	10
61-70	7	1	8
71-80	2	0	2
81 and above	1	0	
Total	27	17	44

Table 2 – Benign liver lesions

Benign liver lesion	No. of patients
Simple cyst	2
Hemangioma	6
Hydatid cyst	6
Liver abscess	3
FNH	1
Regenerating nodules	4

Table 3 – Malignant liver lesions

Malignant liver lesion	No. of patients
Hepatocellular carcinoma	14
Metastases	7
Cholangiocarcinoma	1

Table 4 – Signal intensity on T1W and T1W

Signal intensity	T1W	T2W
Isointense	4	0
Hypointense	40	4
Hyperintense	0	40

Table 5 - Enhancement patterns on gadolinium enhanced MRI

Type of enhancement	No. of lesions
Arterial phase enhancement	19
Delayed phase enhancement	8
Peripheral washout	3
Ring enhancement	4
Nodule within nodule enhancement	0
True central scar	0
Pseudocapsule	1

Table 6 - Characterization of lesions as benign and malignant by various sequences

	T2W	Dual echo	GD-T1W	Overall sequences
Benign	14	14	22	22
Malignant	16	16	22	22
Intermediate	14	14	0	0

Table 7 - Correlation between radiological and histopathological diagnosis of benign entity

Benign lesion	Radiological diagnosis	HPE diagnosis	Percentage (%)
Hemangioma	6	1 proved, 5 follow-up	100
Hydatid cyst	6	6	100
Abscess	3	3	100
Regenerating nodules	4	4	100
Simple cyst	2	2	100
FNH	1	0, proved to be HCC	-

Table 8 – Correlation between radiological and histopathological diagnosis of malignant entity

Malignant lesion	Radiological diagnosis	HPE diagnosis	Percentage (%)
HCC	9	9	100
Multifocal HCC	4	2	50
Fibrolamellar HCC	1	0	-
Metastases	7	6, one proved to be HCC	85
Cholangiocarcinoma	1	1	100

FIGURES

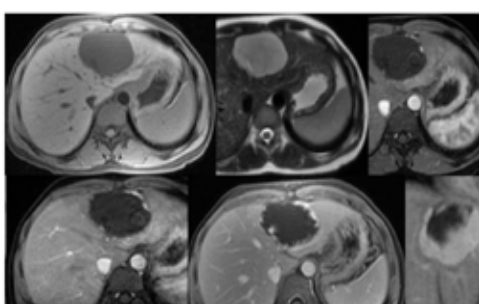

Figure 1: Hemangioma

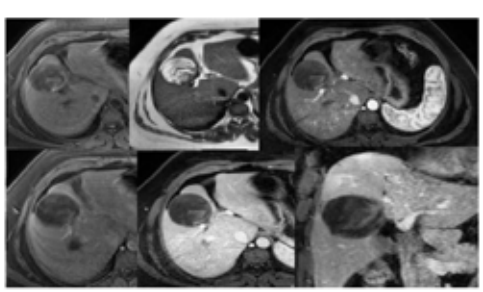

Figure 2: Hydatid Cyst

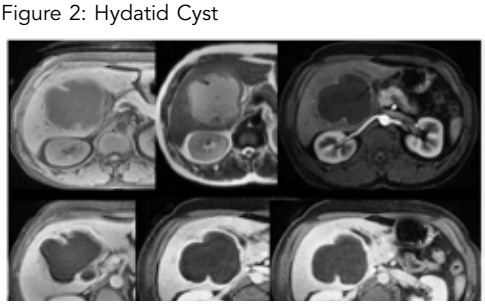

Figure 3: Liver Abscess

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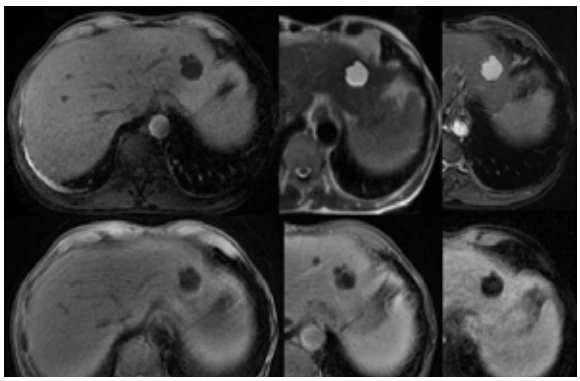

Figure 4: Simple Hepatic Cyst

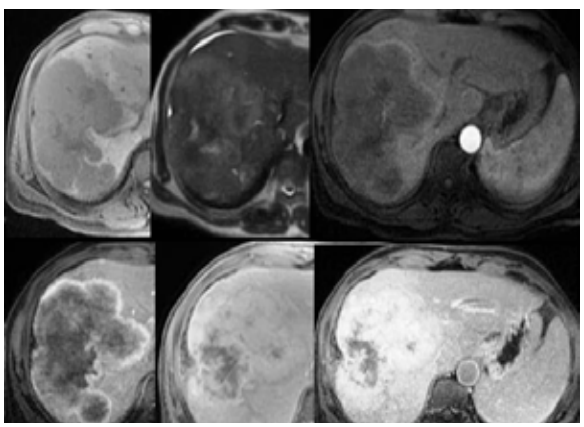

Figure 5: Hepatocellular Carcinoma

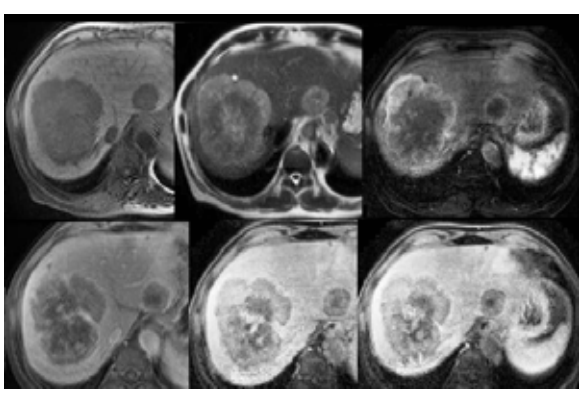

Figure 6: Metastasis

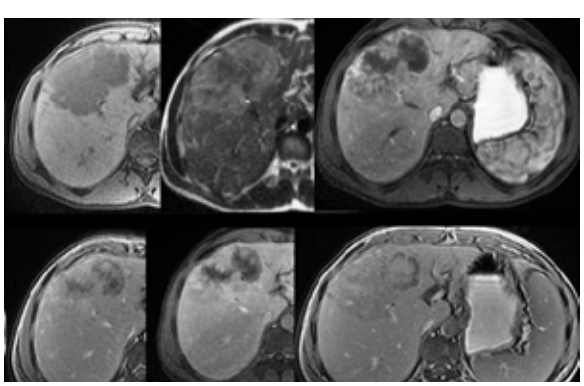

Figure 7: Cholangiocarcinoma

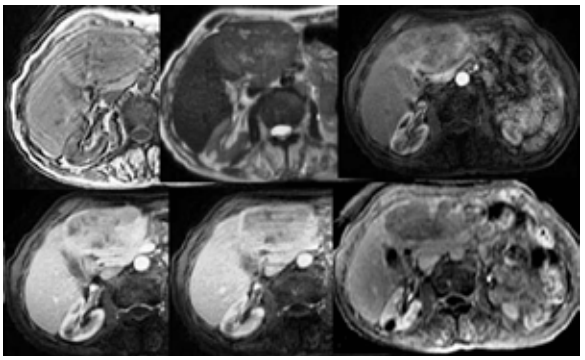

Figure 8: Fibrolamellar Carcinoma

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