

Diagnostic Value of Enhancement Pattern Approach with Contrast-enhanced 3D Gradient-Echo MR Imaging in characterization Focal Liver Lesions

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Abstract

Objective: The purpose of this study was to assess standard dynamic liver MRI in characterization of focal liver lesions.

Material: We retrospectively study all liver MRI studies performed in imaging center of Imam Khomeini hospital between November 11, 2014 and October 10, 2016. Demographic data of patients and laboratory findings were recorded. 140 patients with 221 liver lesions (focal liver tumors) underwent 3-T MRI examination with TSE T2WI (TR = 2000 ms; TE = 100 ms); GE T1WI (TR = 176 ms; TE = 90 ms); Dynamic imaging using T1 THRIVE was performed after bolus injection of 0.1 mmol/kg body weight of Gd-DTPA at a rate of 2 ml/s, flushed with 20 ml of sterile 0.9% saline solution through the antecubital vein. The results were compared to laboratory, histopathology and other previous radiological (US &/or MSCT) findings done for all patients.

Results: Totally 221 hepatic lesions among 140 patients were assessed. Mean age of patients was 51.1 ± 12.4 years [18-86]. Among the patients, 72 were female [51.4%] and 68 were male [48.6%] (figure 25). 34 out of 221 lesions were found in cirrhotic liver [15%]. The analyzed lesions were hemangioma (n=81), cyst (n=24), FNH (n=9), adenoma (n=10), peliosis hepatis (n=4), HCC (n=33), metastasis (n=58), cholangiocarcinoma (n=1), epithelioid hemangioendothelioma (n=1). In our study Sensitivity, specificity, positive and negative predictive value and accuracy were respectively (98%, 97%, 96%, 98% and 98%).

Conclusion: We hope to use standard dynamic MRI we could get enough information regarding characteristics of liver lesions (malignant or benign) to reduce number of biopsies and cost.

Key Words: Magnetic Resonance Imaging, dynamic liver MRI, focal liver lesions.

Date of Submission: 03-07-2018

Date of acceptance: 21-07-2018

I. Introduction

Accurate detection and characterization of focal liver lesions (FLLs) are important for treatment planning for patients with liver neoplasms such as hepatocellular carcinoma (HCC) and metastases. The size and number of lesions can affect therapy, as patients with limited resectable metastatic lesions may benefit from curative resection. Patients with the more extensive disease should undergo trans-arterial chemoembolization, radiofrequency ablation, or systemic chemotherapy [1].

MR imaging has emerged as an important imaging modality for assessment of hepatic nodules, MR imaging is more useful than any other imaging modality currently available for accurate diagnosis and discrimination between benign and malignant hepatic masses. The state-of-the-art MR imaging technique includes single-shot fast spin-echo images with shorter and longer echo times, in phase and opposed-phase T1-weighted gradient echo images, T2-weighted fast spin-echo images with fat suppression. The T2-weighted fast spin-echo sequence with fat suppression is a very sensitive sequence for focal liver lesions. [2]. Contrast-Enhanced MR Sequences; Extracellular Agents are the most widely used, Extracellular fluid agents are composed of gadolinium (paramagnetic metal ion). Gadolinium shortens the longitudinal

relaxation time (T1). Timing of the Dynamic Acquisition Phases; the arterial phase (15-30 sec post injection); it is identified by marked enhancement of the hepatic arteries, pancreas, and spleen with early filling of the main portal vein branches but no enhancement of the hepatic veins. It is the most crucial phase. The portal phase; (30-60 sec post-injection); since most of the hepatic blood inflow (about 80%) arrives via the portal vein, parenchymal liver enhancement is maximum at this phase. The equilibrium phase; it occurs 1–3 minutes after injection; At this time enhancement of tissues with enlarged extracellular spaces such as hemangiomas is usually best seen in the equilibrium phase[3]. This study was conducted to assess the standard dynamic liver MRI in characterization of focal liver lesions.

II. Materials and methods

Study Population and study design

We retrospectively studied all liver MRI studies performed in imaging center of Imam Khomeini hospital between November 11, 2013, and October 10, 2016.

Ethical approval was obtained from Tehran University of Medical Sciences, International Campus (TUMS- IC, code number IR.TUMS.SPH.REC.1396.2297). Written informed consent was obtained from all participants after detailed description of the study method. Patient with focal hepatic lesions detected by US &/or MSCT were enrolled in this study.

All the patients sequentially enrolled in the study if they fulfill inclusion and exclusion criteria of the study. Demographic data of patients and laboratory findings were recorded. Abdominal MRI (pre- and post-contrast study) was performed in all participants. The results were compared to laboratory, histopathology and other previous radiological (US&/or MSCT) findings done for all patients.

MR Examination:

MR imaging was performed on high field system (3 Tesla) magnet unit (Siemens MAGNETOM TRIO) using a phased array coil to cover the whole liver. A gradient Strength 45 mT/m was used. MRI protocols included followings:

- T1 weighted (T1W) images: repetition time TR=10msec, echo time TE=4.58msec, matrix 179x320, slice thickness 7-8mm, slice gap 1-2 mm and FOV 355mm.
- T2 weighted (T2W) images (single shot free breathing): TR =2000msec, TE=221 msec, matrix 320x240, slice thickness 6.0mm, slice gap 1- 2mm and FOV 366.
- T2 SPAIR (Spectral Attenuated Inversion Recovery) fat suppression sequence: TR \geq 4000msec, TE=80msec, matrix 204x384, slice thickness 6.0mm, slice gap 1- 2mm and FOV 365.
- In phase and out phase gradient echo sequence (Dual/FFE): TR= 164msec, TE=4.6msec for in phase and 2.3msec for out phase, matrix 143x240, slice thickness 6.0mm, slice gap 0mm and FOV 360.

Dynamic study was performed after bolus injection of 0.1mmol/kg body weight of Gd- DTPA at a rate of 2ml/s, flushed with 20ml of sterile 0.9% saline solution through the antecubital vein. The injection of contrast media and saline solution was performed manually. Dynamic imaging using T1 THRIVE (High Resolution Isotropic Volume Examination) technique was performed in triphasic way [arterial phase (15-30 sec.), Porto-venous phase (30-60 sec.) and delayed equilibrium phase (1-3 min.)]

Statistical analysis:

Data entry was done by SPSS VERSION 18.Independent sample t test was used to compare quantitative variables. A dynamic liver MRI image was characterization for FLL detection and characterization by using a binary logistic regression model.

III. Results

Overall 221 hepatic lesions in 140 patients (72 females and 68 males) were included in this study. Mean age of patients was 51.1 \pm 12.4 years (18-86). No significant difference in the gender was noted between malignant and benign lesions (p value: 0.14). Out of 221 lesions, 93 were malignant (42.1%) and 128 were benign (57.9%). Charter 1 shows the detailed frequency of each lesion type. The final diagnosis in 106 lesions was proved by follow up [48%] and in 115 individuals was proved by biopsy (52%). Out of 93 malignant lesions, 90 were proved by biopsy [96.8%] (as three lesions were typical HCC and did not require biopsy for diagnosis) and out of 128 benign lesions, 103 were proved by follow up [80.5%] and only 25 were proved by biopsy (19.5%).

Dynamic contrast enhanced MRI was highly valuable in differentiation of benign and malignant lesions (p value< 0.001). Non-enhancing lesions were always benign in nature. The presence of arterial peripheral nodular enhancement with delayed centripetal fill in was always compatible with being nature of the lesion, as noted in 79 benign lesions. The presence of washout with central scar enhancement was also a

feature of being benign (as noted in 9 patients). In the other hand, the present of venous rim enhancement was compatible with malignancy. The presence of arterial wash in and venous washout highly favored malignant lesion, however an instance of overlap was occurred (Table 1 & 2).

IV. Discussion

Dedication and characterization of focal liver lesions is a big dilemma in every day practice of radiologists. Various imaging techniques exist for this purpose, however considerable overlaps exist. Standard dynamic liver MRI has been powerful in differentiation of a variety of benign and malignant lesions in various organs. Dynamic liver MRI makes qualitative evaluation of tissue. Several dynamic features were highly diagnostic for differentiation of benign and malignant lesions. The visualization of arterial peripheral nodular enhancement with delayed centripetal fill in pattern was always diagnostic for hemangioma. The presence of washout with central scar enhancement was also a feature of being benign. In the other hand, venous rim enhancement was compatible with malignancy. The presence of arterial wash in and venous washout highly favored malignant lesion, however an instance of overlap was occurred.

Ahn et al (24) investigated the utilization of heavily T2-weighted images gained before and after applying of gadoxetic acid in distinguishing hemangiomas from malignant solid hepatic lesions. In this study, Heavily T2-weighted images (TE ¼ 150 msec) were gained for 70 patients with 74 focal hepatic lesions 3 cm in diameter before and after gadoxetic acid enhanced dynamic magnetic resonance imaging (MRI).

In conclusion, we found when we considered rim or capsular enhancement or wash-in and wash-out pattern in dynamic study as the malignancy, we yielded the diagnostic indices of dynamic study as follows Sensitivity, specificity, positive and negative predictive value and accuracy were respectively (98%, 97%, 96%, 98% and 98%).

Benign Lesions Hemangioma:

Cavernous hepatic hemangiomas are the most the common type of benign, solid tumor in the liver[4]. They are composed of multiple vascular channels[4]. In these study 49 patients with 81 lesions. Giant hemangioma 6 patients with a scar and one patient sclerosing hemangioma (with cirrhosis). On MRI, the typical lesion is sharply defined with a geographic or rounded shape, hypo intense on T1WI, In/out phase no fat and markedly high on T2WI, no signal drop on T1 in-out phase. On contrast-enhanced images, hemangiomas demonstrate early peripheral nodular enhancement PNE with progressive centripetal enhancement on subsequent images, this comes in agreement with Bozgeyik et al. who reported that early phase images show peripheral enhancement which is typically nodular and discontinuous with centripetal filling during the portal venous and almost completely filled with contrast on the delayed images (figure1).

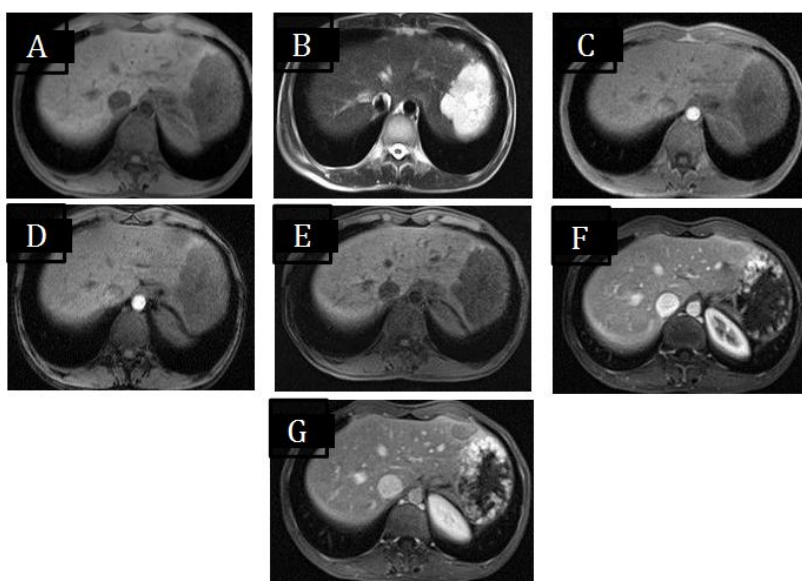


Figure (1). **Benign lesion giant hemangioma.**41year old female with 70×60 mm hemangioma. (A) Axial T1-weighted gradient-recalled echo three-dimensional image shows a well-delineated hypointense lesion. (B) Axial T2-weighted turbo spin-echo image, which appears as mild to moderate hyperintense with scar lesion. (C) (D) in and out phase no fat content (E) Gadolinium-enhanced axial T1-weighted image in the arterial phase showing it as peripheral nodular enhancement. (F) portal/venous phase as centripetal enhancement. (G) delayed phase showing centripetal filling.

(G)Equilibrium phase as centripetal with scar enhancement.

Focal Nodular Hyperplasia

FNHs are benign tumors thought to be due to a hyperplastic response to congenital vascular anomalies[4]. In these study 9 lesions with FNHs. on MRI, isointense on T1WI, no signal drop on In/out phase and mild to moderate hyperintense with a scar on T2WI images. On contrast-enhanced images, FNHs demonstrate washout with scar arterial enhancement that subsequently becomes isointense to background liver on portal venous and enhancement delayed phases. They can have a central scar is typically hypoenhancing in arterial phase, but may demonstrate enhancement on delayed phases (figure 2). This gets in agreement with (Ba-Ssalamah et al, 2010).

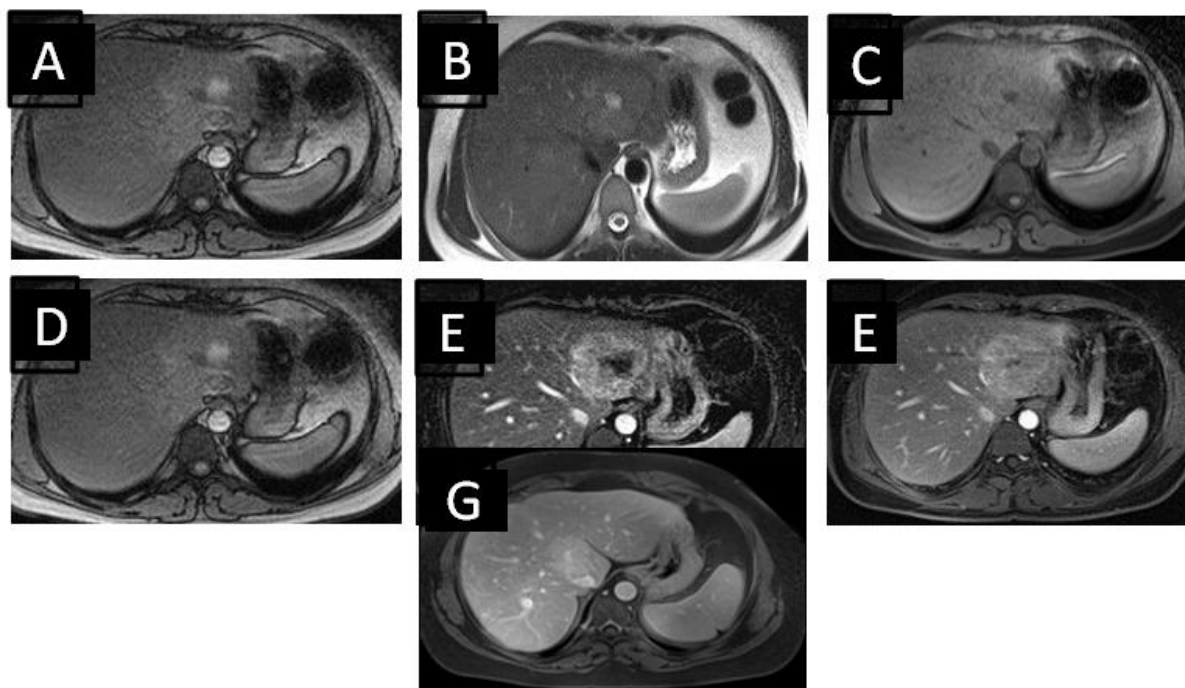


Figure. (2). **Focal Nodular Hyperplasia.** 33-year-old female with 62×52 mm Focal Nodular Hyperplasia (FNH). (A) Axial unenhanced T1-weighted isointense with a scar. (B) Axial T2-weighted image showing the FNH, which appears isointense with a scar. (C)(D)In and out phase no fat. (G) The gadolinium-enhanced axial T1-weighted image in the arterial phase showing it as a hyperintense instead of a central scar. (H) portal/venous phase relative wash out. (I)Equilibrium phase enhancement of center scare.

Adenoma

Hepatic adenomas are rare, benign tumors arising from hepatocytes[4]. In this study 10 lesions with adenoma. On MRI, isointense on T1WI, signal drop on In/out phase because of marked fat content with and isointense on T2WI images. On contrast-enhanced images, the hepatic adenoma is homogeneous on arterial phase and iso enhancing on portal and equilibrium phases. This comes in agreement with (Ba-Ssalamah et al., 2010).

Peliosis hepatis:

Peliosis is a rare benign disorder that is characterized by the presence of diffuse blood- filled cystic spaces and can occur in the liver. In this study 4 lesions with Peliosis hepatis 2 male (50%) and 2 female (50%). On MRI, hypointense on T1WI, no signal drop on In/out phase and hyperintense on T2WI images. On contrast-enhanced images, the peliosis hepatis is no enhancement on arterial phase and heterogeneous enhancement on portal and delayed phases. (Ba-Ssalamah et al., 2010).

Primary Malignant Lesions

Hepatocellular Carcinoma

HCC is a primary liver malignancy arising from hepatocytes[4]. In this study 33 lesions with HCC were evaluated (15) males and (18) females. Thirty-two cases were found in cirrhotic liver. On T1-weighted MR images, HCC is most often hypointense, signal drop on In/out phase because marked have fat, On T2-weighted images; HCC is generally mild to moderate hyperintense, although well-differentiated lesions that are

isointense relative to the liver parenchyma may be seen. Most HCCs show intense enhancement on arterial phase contrast-enhanced images with rapid wash in at the subsequent phases. On arterial phase dynamic gadolinium-enhanced images, most small HCCs show intense enhancement with rapid washout at the portal phase and capsule in some case in equilibrium phase This get in agreement with (Nasu et al., 2009)..

Cholangiocarcinoma (CCC)

Intrahepatic cholangiocarcinoma is a primary liver malignancy arising from bile ducts[4]. In this study 1 female patient with Cholangiocarcinoma. On MRI, hypointense on T1WI, In/out phase without signal drop and mild to moderate hyperintense on T2WI images with partial signal drop in heavy T2WI. On contrast-enhanced images, CCC demonstrate rim on arterial phase, on portal venous and delayed phases gradually fill-in enhancement. This gets in agreement with (Taouli and Koh et al., 2010).

Hepatic epithelioid hemangioendothelioma:

In this study 1 female patient with epithelioid hemangioendothelioma. Epithelioid hemangioendothelioma is an uncommon vascular tumor of intermediate malignant potential[4]. On MRI, hypointense on T1WI, no fat on In/out phase and heterogeneous mild to moderate on T2WI images with partial signal drop in heavy T2WI. On contrast- enhanced images, heterogeneous on arterial phase, portal and delayed phases.

Secondary Malignant Lesions:

Liver metastases are variable in their T1 and T2 signal intensities but are usually prolonged resulting in hypointense on T1-weighted MR images, fat on In/out phase and are mild to moderate hyperintense on T2WI. Hepatic metastases can be classified according to their enhancement pattern into two categories; Hypovascular Colon, lung, prostate, gastric, and transitional cell carcinomas; Hypervascular Islet cell tumors, breast cancer, melanoma, thyroid cancer, and carcinoid tumor. In our study, 58 metastatic lesions were evaluated in 30 patients.

Colorectal Metastases

Colorectal liver metastases are generally considered hypovascular metastases[5]. In our study was a primary tumor were colorectal carcinoma in 42 lesions. Dynamic liver MRI features of colorectal liver metastases with extracellular contrast agents include rim- enhancement on arterial phase, on portal/venous phase rim-enhancement on equilibrium phases show centripetal enhancement (figure 3).

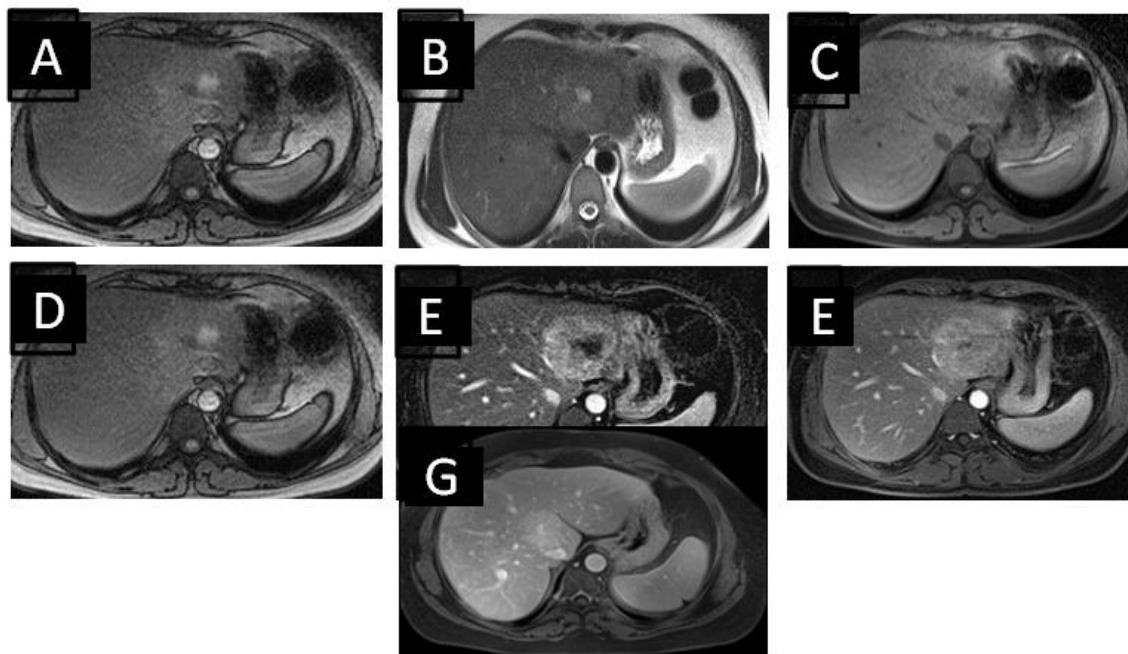


Figure (3) a 23-year-old man with a **history of RCC** cancer; with 50×47 liver metastasis mass. (A) Axial arterial phase contrast enhanced 3D GRE T1-weighted VIBE MR Image shows a rim enhancement. (B) Axial portal/venous gadolinium-enhanced T1FS GRE image shows of lesion with rim- enhancement. (C) On an

axial equilibrium phase show centripetal fill-in.

Breast Metastases

The vascularity of breast metastases can vary, although they are often considered to hypervascular metastases[6]. In our study was a primary tumor were breast carcinoma in 10 lesions, dynamic liver MRI features of breast liver metastases with extracellular contrast agents include rim-enhancement on arterial phase, on portal/venous phase wash out enhancement on equilibrium phases show wash out enhancement (figure 4).

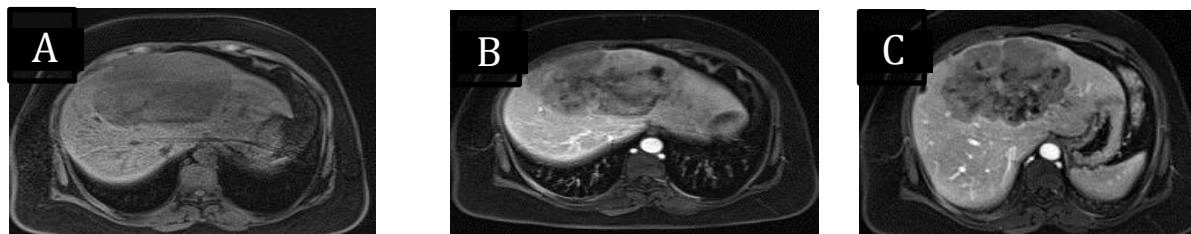


Figure (4) a 35-year-old female with a **history of Breast cancer**; with 124×85 liver metastasis mass. G) Axial arterial phase contrast enhanced 3D GRE T1-weighted VIBE MR Image shows a rim enhancement. (H) Axial portal/venous gadolinium-enhanced T1FS GRE image shows rim enhancement of lesion. (I) on an axial equilibrium phase contrast- enhanced 3D GRE T1-weighted VIBE MR Image shows a washout.

Neuroendocrine Metastases

Neuroendocrine liver metastases are hypervascular metastases[4].In our study was a primary tumor were Neuroendocrine carcinoma in 10 lesions, dynamic liver MRI features of breast liver metastases with extracellular contrast agents include rim-enhancement on arterial phase, on portal/venous phase wash out enhancement on equilibrium phases show wash out enhancement (figure 5).

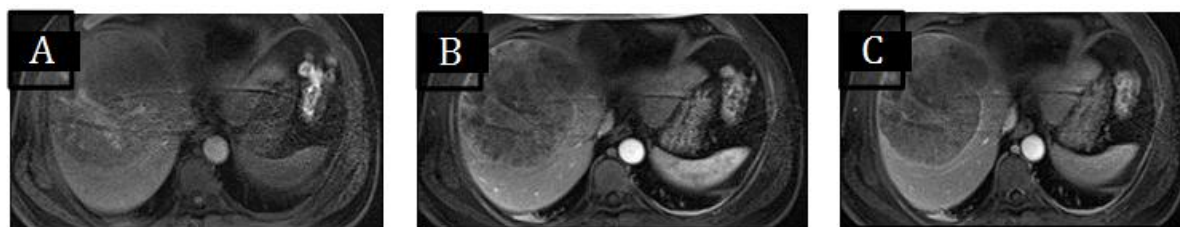


Figure (5) a 23-year-old man with a **history of neuroendocrine**; with 170*122 liver metastasis mass. A); B); C). Axial arterial; portal/venous and equilibrium phase contrast enhanced 3D GRE T1-weighted VIBE MR Image shows a hetero enhancement.

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Charter 1: The frequency of each type of hepatic mass lesion

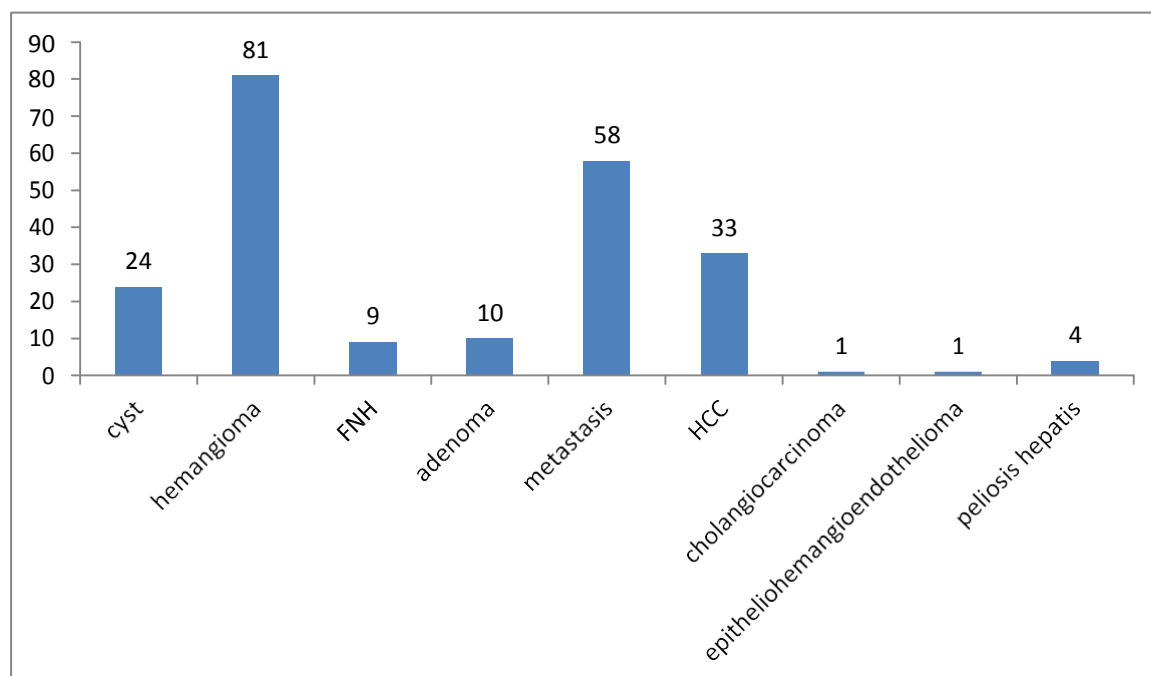


Table 1. Characterization of various hepatic lesions by dynamic contrast enhanced MRI

Dynamic enhancement	Final result		Total
	benign	malignant	
PNE+ centripetal fill-in Count % within dynamic enhancement	81 100.0%	0 .0%	81 100.0%
no enhancement Count % within dynamic enhancement	24 100.0%	0 .0%	24 100.0%
rim+ centripetal fill-in Count % within dynamic enhancement	0 .0%	27 100.0%	27 100.0%
heterogeneous Count % within dynamic enhancement	3 100.0%	0 .0%	3 100.0%
rim enhancement Count % within dynamic enhancement	0 .0%	29 100.0%	29 100.0%
iso+ arterial wash-in Count % within dynamic enhancement	0 .0%	2 100.0%	2 100.0%
homogeneous with iso-intense Count % within dynamic enhancement	10 100.0%	0 .0%	10 100.0%
heterogeneous enhancement Count % within dynamic enhancement	0 .0%	1 100.0%	1 100.0%
wash-in+ wash-out +capsular enhancement Count % within dynamic enhancement	0 .0%	21 100.0%	21 100.0%
wash-in and wash-out Count % within dynamic enhancement	1 7.1%	13 92.9%	14 100.0%
wash-in and iso scar enhancement Count % within dynamic enhancement	9 100.0%	0 .0%	9 100.0%
Total Count % within dynamic enhancement	128 57.9%	93 42.1%	221 100.0%

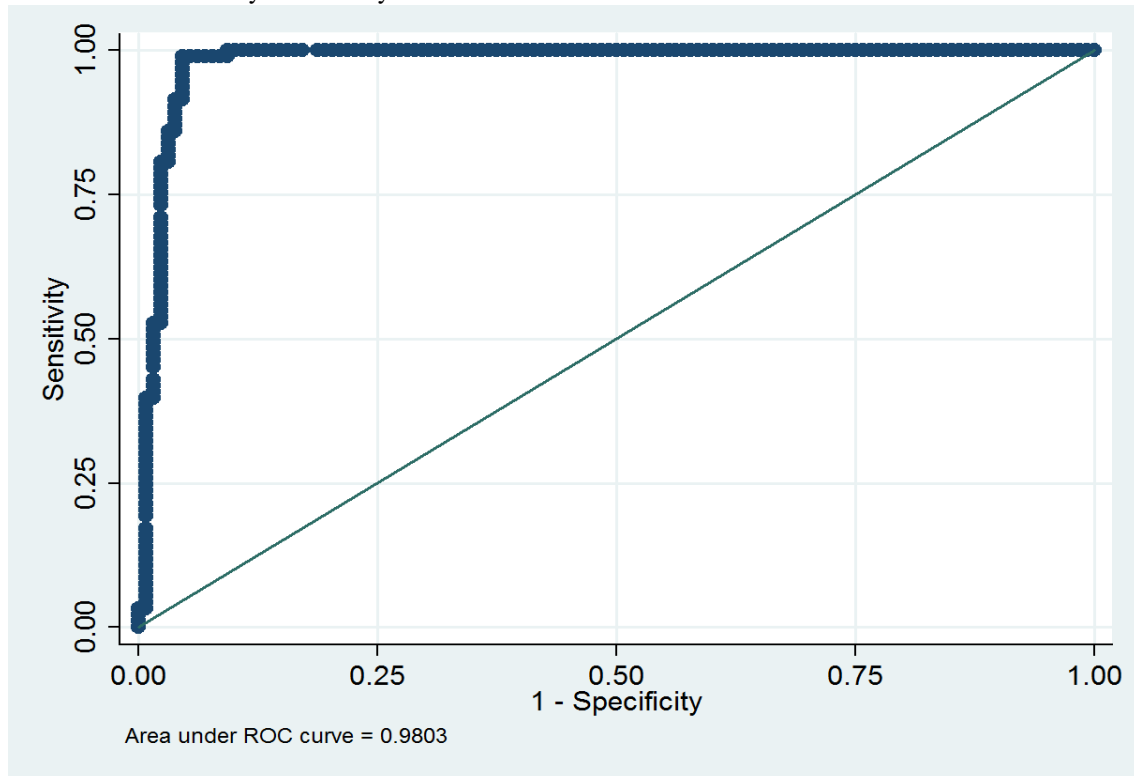
P-Value<0.001

Table 2: When we considered rim or capsular enhancement or wash-in and wash-out pattern in dynamic study as the malignancy, we yielded the diagnostic indices of dynamic study as follows:

Index	Symbol	Estimate	Lower 95% CI	Upper 95% CI
Sensitivity	SE	0/9890	0/9403	0/9997
Specificity	SP	0/9769	0/9340	0/9952
Efficiency (Correct classification rate)	EFF	0/9819	0/9543	0/9950
Predictive value of positive test	PVP	0/9677	0/9086	0/9933
Predictive value of negative test	PVN	0/9922	0/9572	0/9998
Likelihood ratio of positive test	LR+	42/8571	14/0021	131/1753
Likelihood ratio of negative test	LR-	88/9000	12/6565	624/4407

Odds ratio	OR	3810/0000	390/0042	37220/3696
Cohen's Kappa	□	0/9628	0/9266	0/9989

charter 2. ROC curve of dynamic study



Arvin Arian " Diagnostic Value of Enhancement Pattern Approach with Contrast-enhanced 3D Gradient-Echo MR Imaging in characterization Focal Liver Lesions.."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 7, 2018, pp 62-70.