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## Diffusion-weighted MRI: Role in diagnosing hepatic focal lesions

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# Diffusion-weighted MRI: Role in diagnosing hepatic focal lesions

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## Abstract

### Objective

The objective of this study was to highlight the role of quantitative and qualitative diffusion-weighted MRI (DW-MRI) in differentiating benign and malignant hepatic focal lesions, thus increasing the efficacy of conventional hepatic MRI, in addition to evaluating the effect of using different *b*-values.

### Patients and methods

This study was carried out from January to November 2016. We prospectively scanned patients with suspected liver focal lesion referred from Hepatology Unit by high-field 1.5 T MRI. The data were tabulated and manipulated using SPSS, version 14, with the level of significance set at less than 0.05.

### Results

The study revealed that benign lesions such as simple hepatic cysts and hemangiomas showed facilitated diffusion [high signal intensity (SI) on diffusion-weighted imaging and also high SI on apparent diffusion coefficient (ADC) map], whereas malignant solid tumors such as hepatocellular carcinoma (HCC) and metastases demonstrated restricted diffusion (high SI on diffusion-weighted imaging and low SI on ADC map). Regarding the quantitative results, the mean ADC of non-neoplastic liver parenchyma, simple liver cyst, hepatic hemangioma, liver metastases, and HCC measured  $1.08 \pm 0.22$ ,  $2.83 \pm 0.19$ ,  $2.11 \pm 0.18$ ,  $1.34 \pm 0.27$ , and  $1.07 \pm 0.21 \times 10^{-3}$  mm<sup>2</sup>/s, respectively. There was a highly statistically significant difference in mean ADC between benign focal hepatic lesions such as hemangioma and malignant lesions such as metastases or HCC ( $P = 0.001$ ).

### Conclusion

DW-MRI is a very useful additive to conventional MRI sequences in categorizing focal hepatic lesions, thus increasing the confidence of differentiating benign and malignant lesions, particularly if there is a contraindication for contrast injection or for better detection of minute lesions adjacent to vessels.

**Keywords:** Apparent diffusion coefficient, diffusion-weighted MRI, focal liver lesions

## INTRODUCTION

Imaging is an important decision-making tool in the diagnosis of focal liver lesions (FLLs), as it can accurately differentiate benign from malignant lesions in most of the cases. Most FLLs have a characteristic imaging aspect, allowing a confident final diagnosis. In atypical FLLs, follow-up and/or biopsy might be required. In this kind of FLLs, the usage of an additional imaging tool to differentiate benign from malignant lesions would be helpful [1]. Nowadays, focal masses are primarily

detected via ultrasonography scanning and/or computed tomography (CT) scanning. However, MRI is used if more characterization of these focal lesions is required [2].

Triphasic CT has traditionally been considered the optimal diagnostic tool of FLLs. However, many limitations have been reported concerning triphasic CT study such as renal

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impairment, radiation dose, and inability to confirm the specific tissue properties of focal lesions in some cases, leading to indeterminate diagnosis. So, there is a necessity for another diagnostic means that reveals high contrast and spatial resolution with accurate capability for acquiring criteria for lesion characterization without the need for contrast agent administration or ionizing radiation and also can make up for invasive techniques used for obtaining tissue biopsy [2].

Diffusion-weighted imaging (DWI) has been reported to be beneficial for the early detection of small focal hepatic lesions, in addition to its capability of characterizing lesions without the need of depending on contrast-enhanced study by quantifying diffusion effects via apparent diffusion coefficient (ADC) measurements, providing better accurate results compared with those of conventional MR techniques alone [3]. DWI can characterize specific tissue properties without any harm to patients, especially for those who are at risk for complications of a biopsy procedure [4]. More importantly, lack of ionizing radiation, high contrast, and spatial resolution have made DWI a promising diagnostic tool of benign and malignant tumors of various organs [4].

The aim of this study was to highlight the role of quantitative and qualitative diffusion-weighted MRI (DW-MRI) in differentiating benign and malignant hepatic focal lesions as well as evaluating the effect of using different *b*-values in the final diagnosis.

## PATIENTS AND METHODS

### Patients

The study included 31 patients, with 32 different FLLs lesions (one patient has double pathology). All patients were referred to the MRI Unit from Hepatology Unit from January 2016 to November 2016.

### Ethical considerations

Hospital review board permission was obtained for assessment of imaging and clinical data. All patients and normal personal who shared in this study signed out an informed consent, in which a simple explanation of the imaging study was included.

### MRI protocol

MRI as performed on high-field superconducting unit Achieva 1.5 T (Philips Medical Systems, Best, The Netherlands)

- (1) Precontrast MRI included the following:
  - (a) T1-weighted image (WI): repetition time TR = 10 ms, echo time TE = 4.58 ms, matrix  $\times 179 \times 320$ , slice thickness 7–8 mm, slice gap 1–2 mm, and FOV = 355 mm.
  - (b) T2-WI: TR  $\geq 445$  ms, TE = 26–28 ms, matrix (180–200)  $\times 240$ , slice thickness 7–8 mm, slice gap 1–2 mm, and FOV = 365 mm.
  - (c) T2-Spectral Attenuated Inversion Recovery fat-suppression sequence: TR  $\geq 400$  ms, TE = 80 ms, matrix  $\times 204 \times 384$ , slice thickness 7–8 mm, slice gap 1–2 mm, and FOV = 365 mm.

- (2) Dynamic MRI study:

Dynamic study 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. Dynamic imaging was performed in triphasic way [arterial phase (16–20 s), portovenous phase (45–60 s) and delayed equilibrium phase (3–5 min)] after administration of the contrast medium.

- (3) Diffusion-weighted study:

Respiratory-triggered fat-suppressed single-shot echoplanar DWI was performed in the transverse plane with tridirectional diffusion gradients by using different *b*-values (16 cases at *b*-values = 0, 300, and 600; eight cases at *b*-value = 0, 400, and 800; and finally, eight cases at *b*-value = 0, 200, and 750).

### Image analysis

The morphological features of each lesion that were considered for characterization of focal lesions include size, shape, margin, signal characteristics, pattern of enhancement in the dynamic study as well as number and site of the detected focal lesions.

Correlation between conventional MRI and DWI findings was considered throughout all cases of our study to ensure confidence of diagnosis and assess specific and additive diagnostic findings of DWI besides conventional MRI.

In some cases, we correlated dynamic contrast-enhancing MRI finding with both conventional MRI and DWI findings, but unfortunately, not all cases were subjected to dynamic contrast-enhancing MR scanning because of concerns of renal impairment of some patients and patients' concern in other situation.

Using a commercial workstation (view forum workstation; Phillips Dicom, Philips Center, 1070 MX Amsterdam, The Netherlands), ADC maps were formed automatically and then a single observer placed a circular region of interest (ROI) over more than 50% of the focal lesion, taking in consideration avoiding areas of artifact, gallbladder, and vessels. Another ROI was placed on approximately the same area of the non-neoplastic liver parenchyma at the same slice.

In cases of necrotic FLLs [metastases or hepatocellular carcinoma (HCC)], ROI was placed on the solid part, trying to avoid inclusion of any necrotic part.

Then qualitative and quantitative assessments of the lesions were done at each *b*-value.

### The statistical methods

IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp. was used for statistical computations. ADCs of FLLs were compared with Student's *t*-test. Mean ADCs of FLLs and non-neoplastic liver were compared between patients using Student's *t*-test. Differences in mean ADC values were considered to be statistically significant when *P* value was less than 0.05.

## RESULTS

This study included 31 patients with suspected FLLs, comprising 20 males and 11 females, with age ranging from

47 to 67 years and mean age of 56.5 years, which means that hepatic focal lesions were more predominant after the age of 50 years.

Qualitative assessment of DWIs was a helpful means for lesion detection and characterization by observing the differential signal intensity (SI) between different tissues. Cellular tissues, such as tumors or abscesses, demonstrated restricted diffusion (high SI on DWI and low signal on ADC maps) using high *b*-value images. In contrast, cystic or necrotic tissues showed a greater degree of signal attenuation on high *b*-value diffusion images and returned higher ADC values.

Quantitative assessment was generated through calculating the ADC values and displayed as a parametric map. Depending on quantitative analysis of ADC values of liver focal lesions, differentiation between benign and malignant lesions was done, where the results demonstrated statistically significant differences between higher mean ADC values of benign lesions and lower mean ADC values of malignant tumors.

Six types of focal lesions of the liver have been included in this study, which was revealed to represent both benign and malignant natures. Patients with HCC represented 31.3% of the study group, patients with hepatic metastases represented 25%, hemangioma 21.9%, simple cyst 15.6%, and lastly, abscess and adult polycystic kidney disease each represents 3.1% of the study group (Table 1).

By using *t*-test, this study revealed that there was a highly statistically significant difference ( $P = 0.001$ ) in mean ADC of different types of lesions, with high level of mean ADC in simple cyst and hemangioma more than that of metastasis and HCC, with highly statistically significant difference ( $P = 0.001$ ) in mean ADC between benign and malignant lesions. However, no significant difference ( $P = 0.08$ ) could be assessed between different malignant lesions such as HCC and metastasis (Tables 2 and 3).

Another finding of *t*-test of comparing mean ADC of non-neoplastic hepatic parenchyma revealed that there was no statistically significant difference ( $P = 0.08$ ) in mean ADC of different non-neoplastic hepatic parenchyma in different members of the study group (Table 4).

On the basis of paired *t*-test results, there was a significant difference between non-neoplastic and neoplastic segments, as there was a highly statistically significant difference ( $P = 0.001$ ) in mean ADC between non-neoplastic and diseased segments in hemangioma cases as well as statistically significant difference in mean ADC between non-neoplastic and neoplastic segments in metastatic cases ( $P = 0.04$ ). In contrast, there was little difference ( $P = 0.8$ ) between mean ADC of HCC lesions and non-neoplastic segments in patients with HCC (Table 5).

The evaluation of effect of alteration of *b*-values was one of the targets of this study and was proven to have considerable effect on diagnostic ability, especially with the utility of multiple different *b*-values. There was a highly statistically significant difference using *t*-test in mean ADC between benign and malignant diseases using different *b*-values, with the highest

**Table 1: Frequency of different types of focal liver lesions in the studied group**

Type of lesions	Frequency (n=32) [n (%)]
Abscess	1 (3.1)
Adult polycystic kidney disease	1 (3.1)
Hemangioma	7 (21.9)
Hepatocellular carcinoma	10 (31.3)
Metastasis	8 (25)

**Table 2: Mean apparent diffusion coefficient of focal liver lesions in the studied group**

Variables	ADC [mean±SD (range)]	t-Test	P
Hemangioma	2.11±0.18×10 <sup>-3</sup> (1.77-2.32)	48.2	0.001**
HCC	1.07±0.21×10 <sup>-3</sup> (0.98-1.25)		
Metastasis	1.34±0.27×10 <sup>-3</sup> (1.02-1.78)		
Simple cyst	2.83±0.19×10 <sup>-3</sup> (2.76-3.15)		

The study involved only one patient with hepatic abscess having mean ADC of 1.429×10<sup>-3</sup>. ADC, apparent diffusion coefficient; HCC, hepatocellular carcinoma. \*\* $P \leq 0.001$ , statistically highly significant difference.

**Table 3: Comparison between different focal liver lesions in the studied group using mean apparent diffusion coefficient**

Different FLLs of the studied group	P
Hemangioma versus HCC	0.001**
Hemangioma versus metastases	0.001**
HCC versus metastases	0.08

FLL, focal liver lesion; HCC, hepatocellular carcinoma. \*\* $P \leq 0.001$ , statistically highly significant difference.

**Table 4: Mean apparent diffusion coefficient value of non-neoplastic hepatic parenchyma in the studied group**

Variables	ADC [mean±SD (range)]	t-Test	P
Patient with hemangioma	1.12±0.32×10 <sup>-3</sup> (0.91-1.86)	1.2	0.08
Patient with HCC	1.08±0.1×10 <sup>-3</sup> (0.64-1.46)		
Patient with metastasis	1±0.25×10 <sup>-3</sup> (0.74-1.5)		

ADC, apparent diffusion coefficient; HCC, hepatocellular carcinoma.

difference ( $P = 0.0001$ ) found with applying *b*-values of 0, 400, and 800 followed by the group of *b*-values of 0, 300, and 600 ( $P = 0.002$ ), whereas the least was that group of *b*-values of 0, 200, and 750 ( $P = 0.006$ ) (Table 6).

## DISCUSSION

DWI provides tissue characterization based on the diffusion properties of water molecules in tissue, without injecting any contrast agents. Its principle is based upon measuring the random motion of water into a voxel of tissue. It provides quantitative information about tissue cellularity, distinguishing between normal parenchyma and malignant tissues [1,5].

A review of the literature reveals that DWI is able to differentiate lesions with high water content (cysts and

hemangiomas) from solid lesions. Differences in ADCs have been reported between benign and malignant FLLs [5].

In our study, we depended on both quantitative and qualitative analyses of DWI and ADC maps in correlation with imaging findings of conventional MRI that played a reliable role in final diagnoses of some of our cases.

Conventional MRI findings of our study almost always coped with the well-known findings in literature. Conventional MRI findings of hemangioma were strongly hyperintense on a T2-WI with centripetal enhancement in triphasic MRI study [1] (Fig. 1), whereas simple hepatic cyst showed hypointensity in T1-WI and hyperintensity in T2-WI, with no enhancement in CE-MRI. Those findings were consistent with what was stated by Hussain and Sorrell [6] who stated that typical simple cyst at MRI is not difficult to be diagnosed and can be confidently differentiated from other cystic lesions. On delayed postcontrast images, simple cysts appear as unenhanced lesions, and this finding can ensure that lesions are cysts and not poorly vascularized gradually enhancing metastases.

Metastases are usually multiple and hypovascular (but can also be hypervascular) with an enhancing peripheral ring, which rapidly washes out. In cirrhotic liver, focal lesions with arterial hyperenhancement and portovenous or late washout is considered hepatoma until proved otherwise. Hepatoma also demonstrated high SI in T2-WI [1] (Fig. 2).

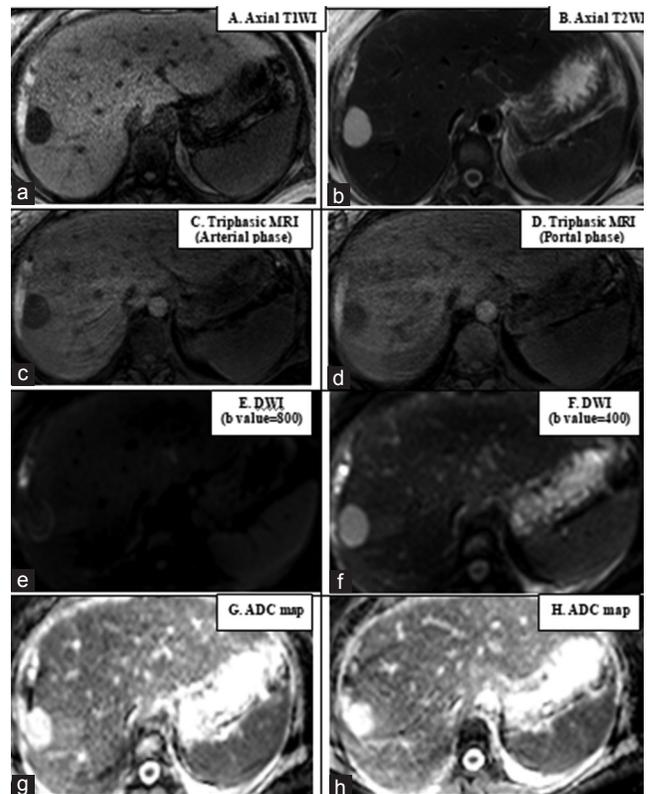
**Table 5: Comparison between mean apparent diffusion coefficient of non-neoplastic hepatic parenchyma and focal liver lesions in the same patient of the studied group**

Variables	ADC (mean±SD)	Paired t-test	P
Number of patients with hemangioma (n=7)			
Non-neoplastic segment	1±0.25×10 <sup>-3</sup>	7.8	0.001**
Diseased segment	2.11±0.18×10 <sup>-3</sup>		
Number of patients with HCC (n=10)			
Non-neoplastic segment	1.08±0.01×10 <sup>-3</sup>	0.2	0.8
Diseased segment	1.07±0.21×10 <sup>-3</sup>		
Number of patients with metastasis (n=8)			
Non-neoplastic segment	1.12±0.3×10 <sup>-3</sup>	2.4	0.04*
Diseased segment	1.35±0.25×10 <sup>-3</sup>		

ADC, apparent diffusion coefficient; HCC, hepatocellular carcinoma. \*P≤0.05, statistically significant difference. \*\*P≤0.001, statistically highly significant difference.

In our study, we attempted to highlight the usefulness of using diffusion-weighted sequence in differentiating different focal lesions of the liver, using both quantitative and qualitative findings as well as evaluating the effect of using different b-values.

Throughout our study, we used different high b-values, and then categorized the involved patients into groups, with each group scanned using a pair of different b-values (0, 400, and 800 vs. 0, 300, and 600 vs. 0, 200, and 750 s/mm<sup>2</sup>),



**Figure 1:** (a–h) A 40-year-old female patient with known cancer of the ovary with total abdominal hysterectomy with bilateral salpingo-oophorectomy. Liver shows average size with homogenous parenchyma with a well-defined segment VII focal lesion measuring 3.5 × 2.5 cm demonstrating low signal intensity (SI) in T1-weighted image (WI) with high SI in T2-WI. Contrast-enhanced MRI revealed peripheral nodular discontinuous enhancement with centripetal filling. Localized peritoneal fluid collection could be seen related to hepatic surface with peritoneal thickening. Diffusion-weighted images (DWIs) at b-values of 400 and 800 s/mm<sup>2</sup> revealed that the focal lesion demonstrated free diffusion [high SI in DWI with high SI in apparent diffusion coefficient (ADC) map], with mean ADC value of 2.43 × 10<sup>-3</sup> mm<sup>2</sup>/s. MRI diagnosis hepatic hemangioma.

**Table 6: Comparison of the effect of different groups of b-values in differentiating benign and malignant focal liver lesions in the studied group**

Variable (b-value groups)	Benign ADC (mean±SD)	Malignant ADC (mean±SD)	t-Test	P
Group A (0, 400, and 800)	2.2±0.02×10 <sup>-3</sup>	1.13±0.15×10 <sup>-3</sup>	9.5	0.0001**
Group B (0, 200, and 750)	2±0.39×10 <sup>-3</sup>	1.14±0.18×10 <sup>-3</sup>	4.6	0.006*
Group C (0, 300, and 600)	2.1±0.07×10 <sup>-3</sup>	1.29±0.27×10 <sup>-3</sup>	4.9	0.002*

ADC, apparent diffusion coefficient. \*P≤0.05, statistically significant difference. \*\*P≤0.001, statistically highly significant difference.

so as to evaluate the possible effect of altering *b*-values on characterization of the detected focal lesions.

The advantage of using both low and high *b*-values is aimed to acquire better images, as lower *b*-values can null the signal of intrahepatic vasculature, producing black-blood images ameliorating detection of FLLs, whereas high *b*-values usually cause better signal detection of cellular tumors that have higher cellularity compared with the normal liver. Moreover, the differential contrast between malignant and benign lesions gets better with high *b*-values [7,8].

The choice of the *b*-values in this study matched other previous studies, where Cariani *et al.* [9], used two *b*-values (400 and 800 s/mm<sup>2</sup>) that cope with ‘group A’ patients in this study, whereas Testa *et al.* [10] and Tokgoz *et al.* [11] chose a single *b*-value (600 s/mm<sup>2</sup>), which we used in ‘group C’ in our study in addition to another lower *b*-value (300 s/mm<sup>2</sup>) to increase the efficacy. Another two *b*-values (200 and 750 s/mm<sup>2</sup>) were applied in our study in ‘group B’ patients to check for the effect of *b*-value alteration on the ability of focal lesion characterization.

In this study, cysts and hemangiomata showed facilitated diffusion, whereas solid lesions showed restricted diffusion.

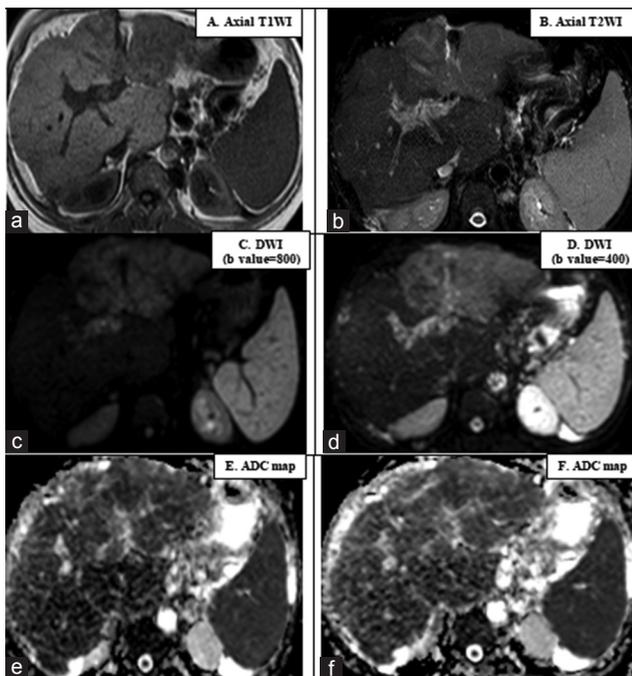
Those findings are similar to that present in literature stating that benign fluid FLLs (i.e. hemangiomas and biliary cysts) demonstrated high SI in both DWI and ADC map [9–11] (Fig. 1), whereas malignant solid tumors (i.e. HCC and metastases) demonstrated restricted diffusion (high SI in DWI and low SI on the ADC map) [1,12–14] (Figs. 2 and 3).

A new dimension in our research was comparing the mean ADC values of non-neoplastic liver parenchyma with different focal lesions, including benign FLLs such as simple cyst and hepatic hemangioma, as well as malignant focal lesions such as liver metastases and HCC, where they measured  $1.08 \pm 0.22$ ,  $2.83 \pm 0.19$ ,  $2.11 \pm 0.18$ ,  $1.34 \pm 0.27$ , and  $1.07 \pm 0.21 \times 10^{-3}$  mm<sup>2</sup>/s, respectively.

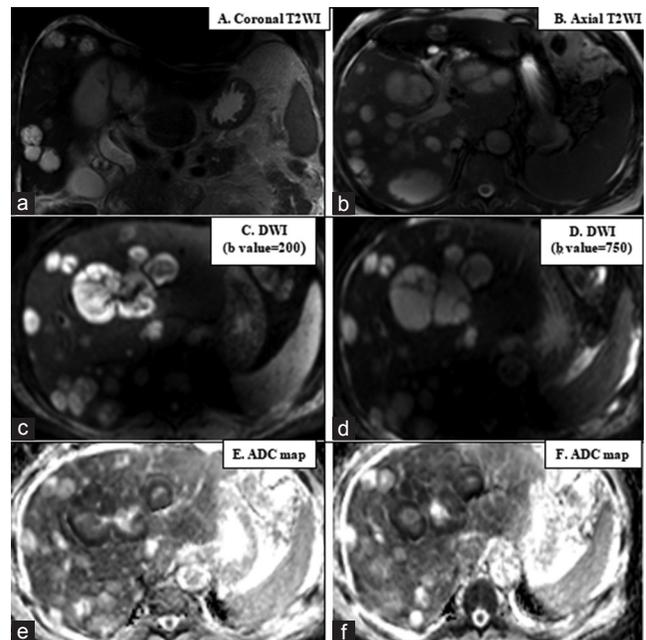
Regarding the value of mean hepatic ADC values, our results cope with those of Vermoolen *et al.* [15] who stated that according to fourteen previous studies, the mean ADC values of benign liver lesions ranged from  $1.94$  to  $2.86 \times 10^{-3}$  mm<sup>2</sup>/s and mean ADC values of malignant tumors ranged from  $0.86 \pm 0.11$  to  $1.52 \pm 0.55 \times 10^{-3}$  mm<sup>2</sup>/s.

Our results were also compared to those stated by Muhi and Ichikawa [16] (Table 7), which elucidated results of different previous studies using different parameters and *b*-values.

Our study revealed no cutoff value for ADC values in normal parenchyma, benign lesions, and malignant lesions. This could



**Figure 2:** (a–f) A 53-year-old female patient with history of liver cirrhosis presented with Right upper quadrant abdominal pain and swelling and high level of  $\alpha$ -fetoprotein (865 ng/ml). MRI study revealed liver cirrhosis with infiltrative focal lesion of the whole left lobe, demonstrating low signal intensity (SI) in T1-weighted image (WI) with high SI in T2-WI. Portal vein is dilated with hypointense T1 but hyperintense T2 thrombus. Diffusion-weighted images (DWIs) at *b*-values of 400 and 800 s/mm<sup>2</sup> showed restricted diffusion of the focal lesion [high SI in DWI with low SI in apparent diffusion coefficient (ADC) map] and also of the portal vein, with mean ADC value of  $1.15 \times 10^{-3}$  mm<sup>2</sup>/s of the detected left lobe infiltrative focal lesion. MRI diagnosis: hepatocellular carcinoma.



**Figure 3:** (a–f) A 55-year-old male patient with known colonic carcinoma. MRI study revealed multiple variable-sized focal liver lesions within both hepatic lobes (largest one measures  $5.7 \times 5$  cm size), demonstrating hypointense T1-weighted image (WI) signal and hyperintense T2-WI signal intensity (SI), whereas diffusion-weighted images (DWIs) revealed restricted diffusion at *b*-values of 200 and 750 s/mm<sup>2</sup> [high SI in DWI with low SI of apparent diffusion coefficient (ADC) map], with mean ADC values of the three largest lesions of  $1.33 \times 10^{-3}$ ,  $1.49 \times 10^{-3}$ , and  $1.41 \times 10^{-3}$  mm<sup>2</sup>/s. MRI diagnosis: hepatic metastases.

**Table 7: Mean apparent diffusion coefficient values of normal liver and hepatic focal liver lesions [16]**

DW-MRI technique	ADC values of focal liver lesions (mean±SD) ( $\times 10^{-3}$ mm <sup>2</sup> /s)						
	Namimoto <i>et al.</i> (1997a, b)[17]	Ichikawa <i>et al.</i> (1997)[18]	Kim <i>et al.</i> (1999a, b)[19]	Taouli <i>et al.</i> (2003)[20]	Bruegel <i>et al.</i> (2008)[21]	Gourtsoyianni <i>et al.</i> (2008)[22]	Parikh <i>et al.</i> (2008)[23]
	Breath-hold	Breath-hold	Breath-hold	Respiratory triggered	Respiratory triggered	Respiratory triggered	Respiratory triggered
<i>b</i> -values (s/mm <sup>2</sup> )	30, 1, and 200	1.6, 16, and 55	≤850	0-500	50,300, and 600	0, 50, 500, and 1000	0, 50, and 500
Normal liver	0.69±0.31	2.28±1.23	1.02±0.25	1.83	1.24±0.15	1.25-1.31	-
Metastases	1.15	2.85±0.59	1.06±0.50	0.94±0.60	1.22±0.31	0.99±0.07	1.50±0.42
HCC	0.99	3.84±0.92	0.97±0.31	1.33±0.13	1.05±0.09	1.38±0.59	1.31±0.33
Cholangiocarcinoma	-	-	1.51	-	-	-	-
Cyst	3.05	-	2.91±1.51	3.63±0.56	3.02±0.31	2.55±0.14	2.54±0.67
Hemangioma	1.95	5.39±1.23	2.04±1.01	2.95±0.67	1.92±0.34	1.90±0.19	2.04±0.42
FNH and/or adenoma	-	-	-	1.75±0.46	1.40±0.15	-	1.49±0.49
Angiomyolipoma	-	-	0.77	-	-	-	-
Liver abscess	-	-	-	-	-	-	1.64±0.05
ADC cutoff for malignant lesions	-	-	1.60	1.50	1.63	1.47	1.60

ADC, apparent diffusion coefficient; DW-MRI, diffusion-weighted MRI; FNH, focal nodular hyperplasia; HCC, hepatocellular carcinoma.

be attributed to differences in *b*-values that can be considered the main cause of non-equivocal results as well as differences in other scanning parameters [12].

This study revealed that there is no overlap between simple hepatic cyst and the rest of detected hepatic focal lesions like abscess, hemangioma, metastases, or HCC, as simple hepatic cyst has the highest mean ADC ( $2.83 \pm 0.19 \times 10^{-3}$  mm<sup>2</sup>/s) besides its signal characteristic in conventional MRI.

Concerning hepatic abscess, only one case was involved in this study, where mean ADC measured was  $1.43 \times 10^{-3}$  mm<sup>2</sup>/s. This was consistent with the study done by Park *et al.* [24], revealing mean ADC of  $1.47 \times 10^{-3} \pm 0.36$  mm<sup>2</sup>/s for liver abscess (Fig. 4).

Comparing the mean ADC of different FLLs, there was a highly statistically significant difference in mean ADC between hemangioma and metastases or HCC ( $P = 0.001$ ); however, a less significant difference between mean ADC of metastases and HCC was reported ( $P = 0.08$ ). This matches with what was stated by Cosmin and colleagues [1,9] and Testa *et al.* [10] and also matches with Vermoolen *et al.* [15] who stated that among 14 different studies describing ADC values of benign and malignant liver lesions, 11 studies showed a statistically significant difference between benign and malignant FLLs.

This study revealed a highly statistically significant difference ( $P = 0.001$ ) in mean ADC between hemangioma ( $2.11 \pm 0.18 \times 10^{-3}$ ) and the surrounding non-neoplastic hepatic parenchyma ( $1 \pm 0.25 \times 10^{-3}$ ) and to a lesser extent ( $P = 0.04$ ) between metastasis ( $1.35 \pm 0.25 \times 10^{-3}$ ) and the surrounding non-neoplastic hepatic parenchyma ( $1.12 \pm 0.3 \times 10^{-3}$ ), but there is little difference ( $P = 0.8$ ) between mean ADC of HCC ( $1.07 \pm 0.21 \times 10^{-3}$ ) and the surrounding non-neoplastic hepatic parenchyma ( $1.08 \pm 0.01 \times 10^{-3}$ ). This could be attributed to the nature of the surrounding parenchyma, as HCC develops on top of cirrhotic parenchyma but

hemangioma – which is considered a congenital entity by many authors – almost always develops on noncirrhotic parenchyma, whereas metastases can develop on both. To our cognizance, no previous study has discussed this finding.

The assessment of the mean ADC of non-neoplastic liver parenchyma in all cases of our study revealed no statistically significant difference in mean ADC of nontumorous segments of liver ( $P = 0.08$ ).

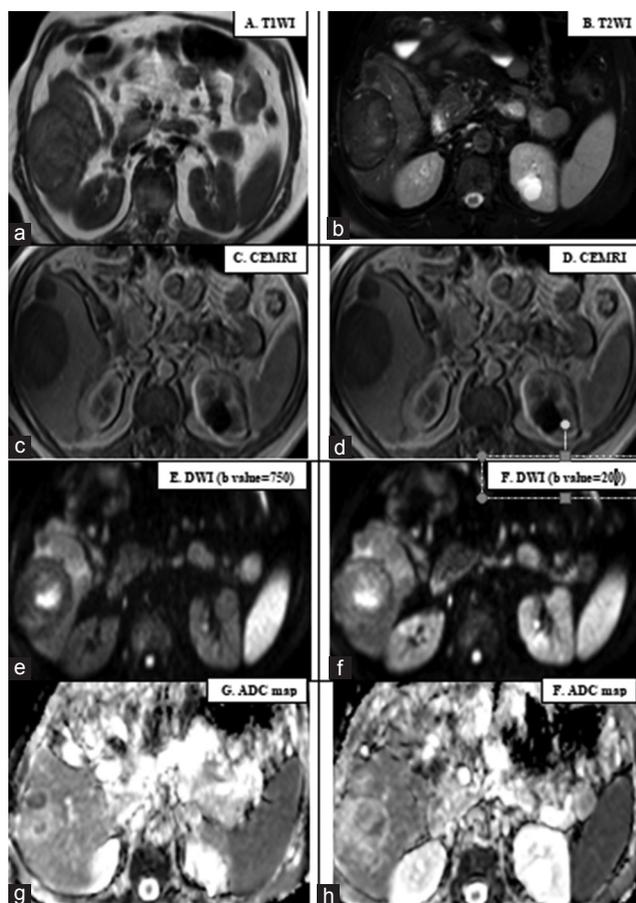
Finally, this study revealed that there can be a highly statistically significant difference in mean ADC between benign and malignant diseases using different *b*-values and that there can be an improvement in differentiation between malignant and benign FLLs.

Utility of *b*-values of 0, 400, and 800 demonstrated highest statistical significance, with mean ADC of benign lesions of  $2.2 \pm 0.02 \times 10^{-3}$  mm<sup>2</sup>/s and of malignant lesions of  $1.13 \pm 0.15 \times 10^{-3}$  mm<sup>2</sup>/s, with *P* value of 0.0001; followed by *b*-values of 0, 300, and 600, with mean ADC of benign lesions of  $2 \pm 0.39 \times 10^{-3}$  mm<sup>2</sup>/s and of malignant lesions of  $1.14 \pm 0.18 \times 10^{-3}$  mm<sup>2</sup>/s, with *P* value of 0.002; and finally, *b*-values of 0, 200, and 750, with mean ADC of benign lesions of  $2.1 \pm 0.07 \times 10^{-3}$  mm<sup>2</sup>/s and of malignant lesions of  $1.29 \pm 0.27 \times 10^{-3}$  mm<sup>2</sup>/s, with *P* value of 0.006.

#### Limitations of our study

First, the DW data set included was only respiratory-triggered images that have superiority over breath-hold DWI for lesion detection, yet there were some limitations of the respiratory-triggered technique, like cardiac motion artifacts and noise contamination, which may distort ADC values to a certain degree. Additional pulse triggering may overcome cardiac motion-related artifacts.

Second, some of the lesions were not presented in the study, especially the benign solid hepatocellular lesions (e.g. hepatic



**Figure 4:** (a–h) A 60-year-old male patient with right upper quadrant abdominal pain and fever. MRI study showed a well-defined right lobe peripheral subcapsular round focal lesion within segment VI measuring  $7.5 \times 5.5$  cm, demonstrating heterogeneous low signal intensity (SI) in T1-weighted image (WI) with heterogeneous intermediate to high SI in T2-WI. Contrast-enhanced MRI revealed peripheral ring enhancement with no enhancement of the center of the lesion. Another smaller focal lesion ( $2.2 \times 1.8$  cm) could be detected anterior to the previously described focal lesion within segment V, revealing similar signal characteristics. Diffusion-weighted images (DWIs) at  $b$ -values of 200 and  $750$  s/mm<sup>2</sup> depict restricted diffusion (high SI in DWI with low SI in ADC map), with mean ADC value of  $1.43 \cdot 10^{-3}$  mm<sup>2</sup>/s. MRI diagnosis: hepatic abscess.

adenoma and focal nodular hyperplasia), thus making the comparison between solid benign and malignant masses limited, besides involvement of only one cases of hepatic abscess.

Third, pathologic diagnosis was not available for some patients. However, these lesions showed specific diagnostic imaging findings unchanged on serial imaging. Clinical and radiological evaluation of these lesions did not require histopathological confirmation.

Another limitation was the ability to perform a contrast-enhanced study for only 10 patients owing to considerations of renal impairment and patient's consent. Moreover, the diagnosis of those patients was carried out depending on conventional MRI sequences, as well as clinical and laboratory evaluation.

Finally, we assume there is need for a uniformly applicable scanning protocol to eliminate discrepancies in ADC values caused by different scanning parameters and  $b$ -values.

## CONCLUSION

DW-MRI is a very useful test to differentiate FLLs in conjunction with the conventional MRI sequences to increase the confidence of distinguishing malignant from benign hepatic focal lesions especially if intravenous contrast administration is to be avoided or for small lesions near blood vessels. This is very helpful in the setting of poor renal functions or history of allergic reaction to contrast.

Using the combination of  $b$ -values of 0, 400, and 800 yielded the most effective results, with significant discrimination between benign and malignant liver focal lesions.

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## Conflicts of interest

There are no conflicts of interest.

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