# The Value of Diffusion Weighted MRI in Differentiating Benign from Malignant Solid Focal Liver Lesions

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## ABSTRACT:

**BACKGROUND:**

Diffusion-weighted imaging (DWI) is increasingly used for the detection, characterization and diagnosis of various focal liver lesions (7-10).

**OBJECTIVE:**

to investigate the utility of (DWI) in evaluating solid focal liver lesions, and to measure the ADC values of these lesions trying to differentiate benign from malignant lesions.

**PATIENTS AND METHODS:**

A prospective study was conducted at MRI units of Al-Imamain Al-Kadhimain medical city and Baghdad teaching hospital between June 2014 to January 2015. Study included of 51 patients with 87 solid focal liver lesions more than 10mm in diameter. They underwent DWI using 1.5 tesla MR units .Mean apparent diffusion coefficient (ADC) values were measured and were correlated with histo-pathological results as well as follow-up imaging results.

**RESULTS:**

Of the 87 lesions, 50 (57.5%) were malignant and 37 (42.5%) were benign. The highest ADC value was for haemangioma with significant difference from other benign and malignant solid focal liver lesions. Mean ADC values for FNH and HA were close to each other with insignificant P value (0.903), but they were of significantly higher values than those of metastases and HCC. Mean ADC values for HCC and metastases were low and close to each other with insignificant P value (0.629). The mean ADC value of benign lesions was higher than that of malignant lesions with significant P value (0.0001). The mean size was 33.46±23.67mm for benign lesions and 40.04±41.81mm for malignant lesions, and this difference was statistically insignificant (P value 0.392).The mean age for malignant lesions (55.30±7.47 year) was higher than that of benign lesions (43.14±13.70year) and this difference was statistically significant (P value 0.0002).

**CONCLUSION:**

DWI is a good imaging modality for diagnosis and characterization of solid focal hepatic lesions, particularly in patients with renal impairment. In general ADC value of benign hepatic lesions was higher than the ADC value of malignant lesions.


**KEY WORDS:** Solid focal liver lesions, Magnetic Resonance Imaging, Diffusion weighted imaging.

## INTRODUCTION:

Liver masses are increasingly being identified due to the widespread use of imaging modalities such as ultrasonography (US), computed tomography (CT), and magnetic resonance imaging. The majority of these lesions are detected incidentally in asymptomatic patients. Accurate detection and characterisation of focal hepatic lesions is essential for adequate treatment planning [1, 2].

MRI is a well-established and widely used diagnostic modality for detecting and characterising focal hepatic lesions [3, 4]. T1 weighted, T2 weighted and gadolinium-enhanced T1 weighted imaging have been commonly utilised [5]. Recognition of nephrogenic systemic fibrosis (NSF) in patients with renal insufficiency who have been given intravenous gadolinium contrast has produced the need to develop novel Magnetic Resonance Imaging (MRI) techniques that do not require gadolinium. Diffusion-weighted imaging (DWI) is non-invasive, rapidly acquired, and does

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not require the administration of intravenous gadolinium [6].

Diffusion-weighted (DW) imaging is increasingly used for the detection, characterization and diagnosis of various focal liver lesions [7-10]. In theory, DW imaging measures the random motion of water molecules in biological tissues and reflects tissue properties, such as the size of the extracellular space, viscosity and cellularity [7, 11]. Diffusion is a marker of cellularity and its quantitative analysis can be obtained through the ADC. A high ADC implies that water can move freely, indicating low cellularity and a low ADC implies that water mobility is restricted, indicating high cellularity [7]. Malignant lesions, such as liver metastases, due to the large amount of cells usually found, frequently have low ADC values. On the other hand, benign lesions such as simple cysts and hemangiomas, due to the lower amount of cells usually found, frequently have high ADC values [12].

A review of the literature reveals that DWI is able to differentiate lesions with high water content (cysts and hemangiomas) from solid lesions. Apparent diffusion coefficient (ADC) provides quantitative characterization of liver lesions and Differences in apparent diffusion coefficients have been reported between benign and malignant focal liver lesions [13-15]. Several studies have characterised focal hepatic lesions by measurement of the lesion apparent diffusion coefficient (ADC) [7, 16] and have evaluated detection of focal hepatic lesion by use of diffusion-weighted imaging (DWI) [17, 18]. However, there is still controversy regarding the value of DWI for the characterisation of focal hepatic lesions as the ADC values of different types of lesions overlap [7, 16]. Furthermore, a limited number of studies have been performed using DWI for the detection of hepatic lesions [17, 18].

## AIM OF THE STUDY:

The objective of this study was to investigate the utility of diffusion-weighted imaging (DWI) in evaluating solid focal liver lesions, and to measure the ADC values of these lesions using diffusion weighted MRI trying to differentiate benign from malignant lesions.

## PATIENTS AND METHODS :

**Patients:** this prospective study was conducted at the MRI units of Al-Imamain Al-Kadhimain medical city and Baghdad teaching hospital in the period from June 2014 to the end of January 2015. A total of 51 patients with 87 solid focal hepatic lesions more than 10mm in diameter were included in this study. The patients were referred to the MRI unit on the basis of ultrasound findings of single or multiple solid hepatic lesions. The study sample included 28 women and 23 men, with an age range of 23-75 years (mean 50 years). The exclusion criteria were: patients with solid focal hepatic lesion less than 10mm in diameter, patients with presumed malignant solid focal hepatic lesion but no laboratory or pathologic results obtained for them, and patients whose images were of unsatisfactory to evaluate solid focal hepatic lesion on DWI. Verbal and written consents were obtained from all patients.

## METHODS:

MRI was performed with a 1.5 Tesla system (Achieva; Philips Medical Systems, the Netherlands) using a SENSE body coil. All patients were examined initially with a routine MRI protocol for the upper abdomen that included T2 weighted images, in- and opposed phaseT1 weighted images and dynamic T1 weighted images. Subsequently, diffusion-weighted images were obtained. All patients were examined in the supine position throughout the examination. Torbo spin echo (TSE) T2 weighted sequence (axial and coronal) was performed with the following parameters: repetition time (TR) ms/echo time (TE) ms= 601/80, matrix= 220x192, field of view (FOV) = 318x251mm, section thickness=5 mm, and section gap=1 mm. DualechoT1 weighted fast field-echo (FFE) sequence (axial) was performed with the following parameters: TR/TE=138/2.3 (opposed phase) and 138/4.6 (in phase), matrix= 288x177, field of view (FOV) =375x302mm, section thickness=5 mm; section gap=1 mm. Dynamic T1weighted MRI was obtained by using a spoiled gradient echo sequence (T1 weighted high-resolution isotropic volume examination, THRIVE) in axial section after injection of dimeglumine gadopentetate 469 mg(Magnevist Schering Pharma AG Germany) at a dose of 0.1 m.mol per kilogram of body weight. Arterial (30 s), portal (70 s) and delayed (3 min) phases of images were obtained. Acquisition parameters were as follows: TR/TE= 3.9/1.83, matrix=188x148, field of view (FOV) =375x295mm, section thickness=5 mm and no section gap.

**Diffusion-Weighted Imaging (DWI):** It was performed for all patients before injection of

contrast material. Diffusion-weighted images were obtained using a single shot echo planar imaging sequence EPI with the following parameters: (TR/TE=2467/59, matrix =124x100, FOV=375x302mm, section thickness=7mm, and section gap=1 mm) with diffusion sensitivities of b values = 0, 300, and 600 sec/mm2. ADC map was reconstructed. Scan time was < 4 min.

**Image Analysis**

a) Qualitative Assessment of DWI and ADC Map: all DW MR Images were analyzed. DW MR images were analyzed qualitatively by focusing on the signal intensity of the hepatic focal lesions in comparison with the signal intensity of adjacent normal hepatic parenchyma. The abnormal regions on DWI and ADC map were outlined by using the conventional images as a guide.

b) Quantitative Assessment of ADC: The ADC map was automatically generated for the b-value (600 s/mm2). Measurement of ADC value was made using an electronic cursor on the ADC map in different regions of interest (ROI) of the lesions. The region of interest with of approximately 50 mm2was positioned for the measurement of ADC value in each lesion avoiding necrotic or hemorrhagic components. Scar of FNH was avoided during placing ROI. The ADC values were expressed in mm2/sec. ROIs for each lesion were placed for three times to decrease inter-observer error and the mean ADC values for the lesions were calculated.

**Final diagnosis of the lesions:** Among the 51 included patients, all 15 cases of cavernous haemangiomas were confirmed by clinical manifestation, ultrasound, CT or/and MRI and follow up within 3 to 6 months; all 6 cases of FNH had typical imaging findings of rapid and strong arterial enhancement on arterial phase, and a central scar which shows high SI on T2WI (3 cases confirmed by core biopsy and the remaining 3 by FNAC); 3 cases of hepatic adenomas were confirmed by resection and one by core biopsy; all 6 cases of HCC had typical clinical, laboratory (an elevated a-fetoprotein level >400 ng/ml) and imaging findings (3cases confirmed by resection and the remaining 3 by core biopsy); and finally all 20 cases of hepatic metastases were confirmed pathologically(16 cases by FNAC and 4 cases by core biopsy).

**Statistical Analysis:** Statistical package for social science version 20 (SPSS 20) was used for both data entry and data analysis. Continuous variables were presented as mean ± SD and discrete variables presented as number (%). T test for independence used to test the significance of association of two continuous variables and one way ANOVA with post hoc test for more than two continuous variables. Chi-square test (or fisher exact test when appropriate) for discrete variable. P-value of < 0.05 was considered significant.

**RESULTS:**

Fifty one patients were included in this study; these patients had 87 solid focal hepatic lesions of more than 10mm in diameter. There were 28 women and 23 men with an age range (23-75 years) and a mean age of 50 ± 12 year.

Of the 87 lesions, 50 (57.5%) were malignant and 37 (42.5%) were benign. Metastases were the most common lesions 44 (50.6%), HA were the least 4 (4.6%) and the rest distributed between them as shown in table 1.

**Table 1: Distribution of lesions according to the final diagnosis (87 lesions).**

| Variables | | | Number of the lesions | Percent % | Total | |
|---|---|---|---|---|---|---|
| | | | | | No. | % |
| Final Diagnosis | Benign | Haemangioma | 27 | 31.0 | 37 | 42.5 |
| | | FNH | 6 | 6.9 | | |
| | | HA | 4 | 4.6 | | |
| | Malignant | Metastases | 44 | 50.6 | 50 | 57.5 |
| | | HCC | 6 | 6.9 | | |
| Total | | | 87 | 100. | 87 | 100 |

Regarding the mean ADC values of the lesions, it was 1.936±0.211 × $10^{-3}$ $mm^2$/sec for benign lesions and 1.065±0.135 × $10^{-3}$ $mm^2$/sec for malignant lesions, and this difference was statistically significant (P value 0.0001). The highest mean ADC value was for haemangioma (2.032± 0.131 × $10^{-3}$ $mm^2$/sec), whereas the lowest was for metastases (1.054±0.129 × $10^{-3}$ $mm^2$/sec) and the rest values were distributed between them as shown in table 2.

**Table 2: Mean ADC values for the hepatic lesions according to the final diagnoses.**

| Variables | | | ADC value(× $10^{-3}$ $mm^2$/sec) Mean ± SD | | Pvalue |
|---|---|---|---|---|---|
| Final Diagnosis | Benign | Haemangioma | 2.032± 0.131 | 1.936± 0.211 | 0.0001 |
| | | FNH | 1.711±0.128 | | |
| | | HA | 1.622±0.205 | | |
| | Malignant | Metastases | 1.054±0.129 | 1.065± 0.135 | |
| | | HCC | 1.149±0.160 | | |

Mean ADC value for haemangioma was significantly higher than those of FNH, HA, metastases and HCC and these findings were statistically significant (P values were 0.0001, 0.0004, 0.0001, and 0.0005 respectively). Mean ADC values for FNH and HA were close to each other and the difference was statistically insignificant (P value 0.903), but they were of higher values than those of metastases and HCC with statistically significant difference. Mean ADC values for metastases and HCC were close to each other and the difference was statistically insignificant (P value 0.629), but they were of lower values than those of haemangioma, FNH and HA with statistically significant difference as shown in table 3.

**Table 3: Difference of mean ADC value between each diagnosis and the other (Multiple Comparisons) in the 87 lesions included in the study.**

| Final Diagnosis | Haemangioma | FNH | HA | Metastases | HCC |
|---|---|---|---|---|---|
| Haemangioma | 1 | 0.0001 | 0.0004 | 0.0001 | 0.0005 |
| FNH | 0.0001 | 1 | 0.903 | 0.0001 | 0.0002 |
| HA | 0.0004 | 0.903 | 1 | 0.0001 | 0.0001 |
| Metastases | 0.0001 | 0.0001 | 0.0001 | 1 | 0.629 |
| HCC | 0.0005 | 0.0002 | 0.0001 | 0.629 | 1 |

Regarding the mean sizes of the lesions, it was33.46±23.67mm for benign lesions and 40.04±41.81mm for malignant lesions, and this difference was statistically insignificant (P value 0.392). The largest mean size (130.83±21.34mm) was for HCC, whereas the smallest mean size (18.50±3.10mm) was for HA as shown in table 4.

**Table 4: Distribution of final diagnoses of the lesions according to their mean sizes in mm in the 87 lesions included in the study.**

| Variables | | | Size of lesions/mm | | P - value |
|---|---|---|---|---|---|
| | | | Mean± SD | | |
| Final Diagnosis | Benign | Haemangioma | 26.67±13.01 | 33.46±23.67 | 0.392 |
| | | FNH | 74.00±27.39 | | |
| | | HA | 18.50±3.10 | | |
| | Malignant | Metastases | 27.66±25.13 | 40.04±41.81 | |
| | | HCC | 130.83±21.34 | | |

The mean age for malignant lesions (55.30±7.47 year) was higher than those of benign lesions (43.14±13.70year) and this difference was statistically significant (P value 0.0002). The oldest mean age was for HCC (58.00±10.29 year), whereas the youngest was for HA (33.25±4.27 year) as shown in table 5.

**Table 5: Distribution of final diagnoses of lesions according to their mean ages.**

| Variables | | | Age/year | | P - value |
|---|---|---|---|---|---|
| | | | Mean± SD | | |
| Final Diagnosis | Benign | Haemangioma | 46.07±13.8 | 43.14±13.70 | 0.0002 |
| | | FNH | 36.50±12.88 | | |
| | | HA | 33.25±4.27 | | |
| | Malignant | Metastases | 54.93±7.07 | 55.30±7.47 | |
| | | HCC | 58.00±10.29 | | |

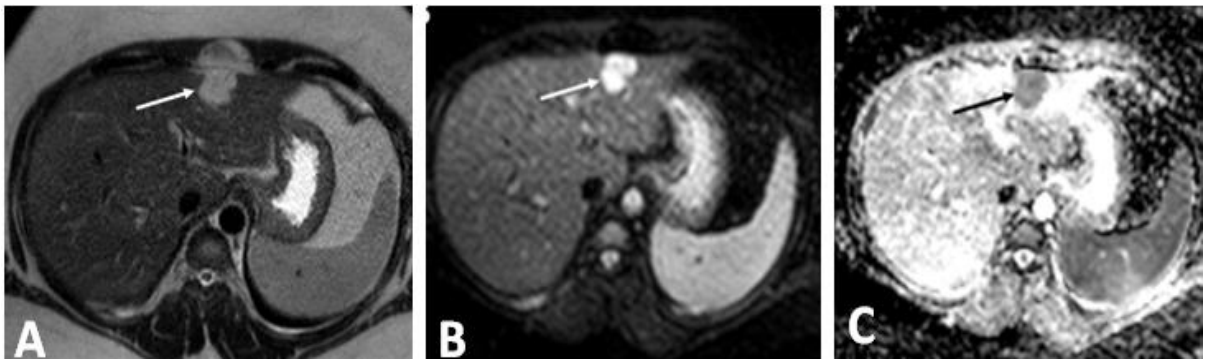


**Figure 1: Twenty three year-old woman with haemangioma. A: Axial turbo spin echo (TSE) T2 weighted image shows a high signal lesion (arrowed). B: Axial diffusion weighted image (b= 600 sec/mm$^2$) also shows a high signal lesion (arrowed). C: The lesion on ADC map (arrowed) shows low signal with ADC value 1.899 × 10$^{-3}$ mm$^2$/sec.**

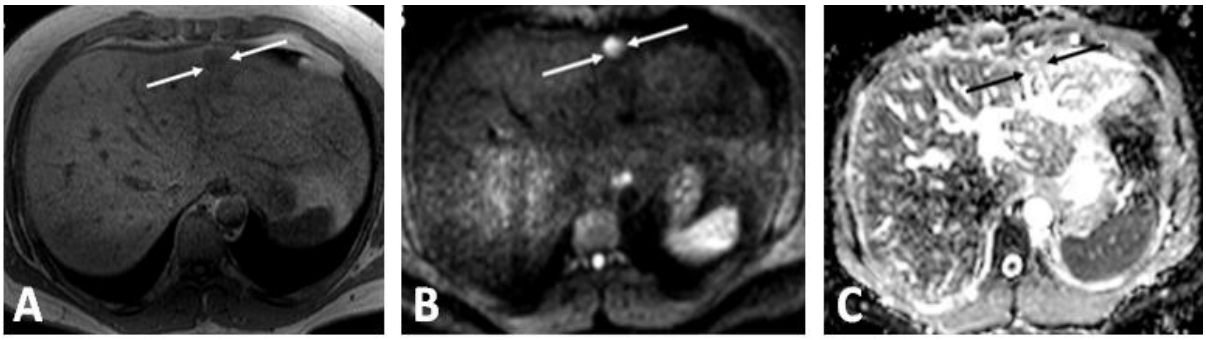


**Figure 2: Thirty two year-old man with hepatic adenoma. A: Non-contrast T1weighted image shows low signal focal lesion (arrowed). B: The lesion (arrowed) shows high signal on DWI (b value = 300 sec/mm$^2$). C: The lesion on ADC map shows intermediate signal (arrowed) with ADC value 1.690 × 10$^{-3}$ mm$^2$/sec.**

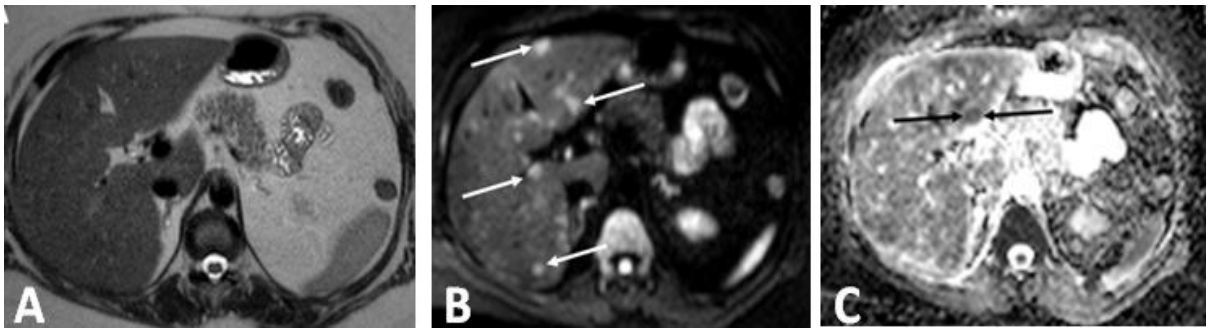


**Figure 3: Forty three year-old woman with breast carcinoma metastases. A: No lesion could be detected on this axial turbo spin echo (TSE) T2 weighted image. B: Axial diffusion weighted image (b= 600 sec/mm$^2$) shows at least 4 focal lesions (arrows) of high signal. C: One of these lesions (arrowed) on ADC map shows low signal with ADC value 0.967 × 10$^{-3}$ mm$^2$/sec.**

## DISCUSSION:

DWI technique yields qualitative and quantitative information that reflects changes at a cellular level and provides unique insights about tumor cellularity and the integrity of cell membranes [19-21]. DWI is an evolving technology with the potential to improve tissue characterization when findings are interpreted in conjunction with findings obtained with other conventional MR imaging sequences [22]. DWI is increasingly used for the evaluation of extra-cranial diseases. There is growing interest in the application of DWI for the evaluation of the patient with cancer [23]. DWI in the liver is a relative new and increasingly used imaging technique in addition to conventional contrast enhanced MRI [24]. Most prior studies have used DW imaging for focal liver lesion characterization through measurement of lesion apparent diffusion coefficient (ADC) [17, 25].

The ADC value is estimated to be lower in viable tumor tissue with densely packed diffusion-hindering obstacles, such as malignant tissue than in tissue with less densely packed obstacles, such as tumor necrosis and benign tissue [7]. This coincides with our results that showed high ADC value of benign hepatic lesions and low ADC value of malignant hepatic lesions.

The liver is the most common site of metastases from the gastrointestinal tract, pancreas, breast, and lung; and only 20% of liver metastases present as solitary lesions [26]. Benign liver lesions are found in more than 20% of the general population, including haemangioma (4%), focal nodular hyperplasia (FNH, 0.4%) and hepatic adenomas (0.004%) [27]. In our study malignant lesions (50 lesions) were more common than benign lesions (37 lesions) with the haemangioma (27 lesions) being the most common among the benign group

and the metastases (44 lesions) were the most common among the malignant one.

In our study the mean ADC value of haemangioma was 2.032 ± 0.131 × $10^{-3}$ $mm^2$/sec. This was close to the results previously reported by El-Badrawy et al.[28], Maksimović et al.[29], Türkbey et al. [30], Hernethet al. [31], and Moteki et al. [32]. But, it does not correlate with other studies reported by Quan et al. [33], and Goshima et al. [34]. This difference may be due to using different b value which was used in DW, or different pathological sub-types of haemangiomas. Mean ADC value of haemangioma was significantly higher than those of FNHs (P value 0.0001), HAs (P value 0.0004), metastases (P value 0.0001), and HCCs (P value0.0005). These results were similar to those reported by El-Badrawy et al. [28], Goshima et al. [34], Kele et al.[35], and Yoshikawa[36].

Mean ADC values for FNHs (1.711±0.128 × $10^{-3}$ $mm^2$/s) and HAs (1.622±0.205 × $10^{-3}$ $mm^2$/s) were close to each other with insignificant P value (0.903), but these values were significantly lower than that of haemangioma (P values 0.0001 and 0.0004 respectively). FNHs and HAs are of higher cellularity than haemangioma which is not a pure solid containing lesion. Our results were consistent with those previously reported by Miller et al.[37], El-Badrawy et al[28], Kele et al. [35], and Humphries et al. [38].

Mean ADC values for HCC (1.149±0.160 × $10^{-3}$ $mm^2$/s) and metastases (1.054±0.129 × $10^{-3}$ $mm^2$/s) were low and close to each other with insignificant P value (0.629) and they were significantly lower than those of benign lesions (P value 0.0001). Mean ADC values in cases with HCC were slightly higher than those of metastases. These results were similar to the findings of Taouli et al. [16] and Demir et al. [39], but were different from the findings of Sunet al. [40] and Ichikawa et al [41]. These two studies reported a significant difference of ADC value for HCC vs. metastases. However, their studies were limited by the use of only low b values (<55) where the perfusion and T2 effects predominate much more than diffusion properties.

The lesions were grouped into benign and malignant with mean ADC values of 1.936±0.211 × $10^{-3}$ $mm^2$/s and 1.065±0.135 × $10^{-3}$ $mm^2$/s for each group respectively with significant difference (P value 0.0001). These results are in agreement with those of O Kilickesmez et al.[42], Taouli et al.[16], Holzapfel et al.[24] and Demir et al. [39]; but our results were different from those of Miller et al. [37]. The difference might be attributed to the predominant inclusion of cases of haemangiomas and fewer cases of FNHs and HAs in our study.

Haemangiomas may reach up to 20 cm in size and FNHs may range from 1 to 20 cm [43, 44]. HAs may reach up to 10cm in size [26]. In our study malignant lesions were slightly larger in mean size than benign lesions but the difference was insignificant (P value0.392).

Haemangiomas, FNHs and HAs are more frequent in women of childbearing age. HAs are associated with oral contraceptive use and less frequently with anabolic androgens and type I glycogenosis [45, 46]. HCC in developed countries sits on a cirrhotic liver in more than 80% of cases[47]. In our study the mean age for malignant lesions (55.30±7.47 year) was higher than those of benign lesions (43.14±13.70year) and this difference was statistically significant (P value 0.0002). HCC was noticed in the oldest age (mean 58.00±10.29 year), whereas the HA was seen in the young age (mean 33.25±4.27 year).

DWI has the advantage that it is completely noninvasive, does not require exposure to ionizing radiation or administration of exogenous contrast medium and does not cause patient discomfort; so it can add great support to the conventional sequences for the differential diagnoses and discrimination of benign and malignant solid focal hepatic lesions.

We had several limitations to our study. First, avoiding susceptibility artifacts on DWI is rather difficult. Second, the patient population was relatively small, especially the cases of FNHs, HAs and HCC. Third, histopathological confirmation was not performed in cases of haemangiomas.

## CONCLUSION:

Diffusion weighted MR imaging is a new and good imaging modality for diagnosis and characterization of different benign and malignant solid focal hepatic lesions, particularly in patients with renal impairment. In general the ADC value of benign hepatic lesions was higher than the ADC value of malignant hepatic lesions. There is overlap in the ADC values of metastases and HCCs; and also FNHs and HAs.

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