

Diffusion-Weighted MR Imaging of the Benign Hepatic Focal Lesions

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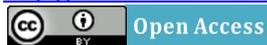
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Abstract

Purpose: To determine the role of diffusion weighted MR imaging and apparent diffusion coefficient (ADC) in benign hepatic focal lesions. **Method and Materials:** This study included 47 patients (29 M, 18 F with mean age of 43 years) with benign hepatic focal lesions. They were cyst (n = 8), hemangioma (n = 23), abscess (n = 5), adenoma (n = 5), focal nodular hyperplasia (n = 4) and nodular regenerative hyperplasia (n = 2). They underwent routine MR imaging and diffusion MR weighted imaging using 1.5 tesla MR unit (Symphony-Siemens). Diffusion MR imaging was done using spin echo type of single shot echo planar imaging (EPI) with b value of 0, 500 & 1000 sec/mm². The apparent diffusion coefficient (ADC) map was reconstructed and ADC value was measured. The mean ADC values correlated with histo-pathological results as well as follow-up imaging results. **Results:** Adequate ADC maps were obtained in 47 patients. The mean ADC values were $3.4 \pm 0.12 \times 10^{-3}$ mm²/sec in cystic lesion, $2.23 \pm 0.08 \times 10^{-3}$ mm²/sec in hemangioma, $1.94 \pm 0.05 \times 10^{-3}$ mm²/sec in abscess, $1.72 \pm 0.07 \times 10^{-3}$ in focal nodular hyperplasia, $1.65 \pm 0.06 \times 10^{-3}$ mm²/sec in adenoma, $1.62 \pm 0.07 \times 10^{-3}$ mm²/sec in nodular regenerative hyperplasia. The mean ADC values were significantly different within benign hepatic focal lesions (P < 0.001). The differences between the mean ADC values of FNH, adenoma and NRH were not statistically significant (P < 0.23). **Conclusion:** Diffusion weighted MR imaging is a new imaging modality for diagnosis and characterization of different benign hepatic focal lesions, particularly in patient with renal dysfunction.

Keywords

Diffusion; MR Imaging; Apparent Diffusion Coefficient; Benign Hepatic Focal Lesion

1. Introduction

Diffusion-weighted (DW) MR imaging can now be applied to liver imaging with improved image quality. DW MR imaging enables qualitative and quantitative assessment of tissue diffusivity (apparent diffusion coefficient) without the use of gadolinium chelates, particularly in patients with severe renal dysfunction at risk for nephrogenic systemic fibrosis [1]. DWI 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. Recent advances enable the technique to be widely applied for tumor evaluation in the abdomen and pelvis and have led to the development of whole-body DWI [2]. DWI is a simple and sensitive method for screening focal hepatic lesions and is useful for differential diagnosis [2]-[4]. The purpose of this study was to determine the role of diffusion weighted MR imaging and apparent diffusion coefficient (ADC) in benign hepatic focal lesions.

2. Materials and Methods

2.1. Patients

Our study received institutional review board approval, and all patients provided informed consent. This is retrospective study of confirmed benign hepatic focal lesions. This study included 47 patients (29 M, 18 F with mean age of 43 years) with benign hepatic focal lesions. Patients with diffuse liver disease like cirrhosis or steatosis were excluded. Thirty-two patients underwent triphasic CT scanning using 64 MDCT scanner (Brilliance 64, Philips). Pathological confirmation was on the basis of tru-cut biopsy (n = 10), fine needle aspiration cytology (n = 11), characteristic triphasic CT and dynamic MRI findings (n = 26). Follow up was done of more than 1 year. The methods of examination were fully explained to patient before imaging to obtain his consent. They were instructed to remove ferromagnetic materials.

2.2. MRI Techniques

All patients underwent MR examinations using a 1.5 tesla superconducting unit (Symphony; Siemens AG Medical systems, Forchheim, Germany) using body phased-array coil. The machine was equipped with a self-shielding gradient set (23 mT/m maximum gradient strength and 120 mT/m/s slew rate). All patients were examined in the supine position throughout the examination.

- All patients underwent diffusion MRI in addition to routine MR protocol. It included true FISP axial and coronal imaging (4.3/2.1 TR/TE, 80° flip angle, 4mm slice thickness, 350 × 350 FOV, 220 × 256 matrix size and 0.9 mm inter-slice gap), in phase (160/2.4 TR/TE, 78° flip angle, 4 mm slice thickness, 350 × 350 FOV, 256 × 256 matrix size and 0.9 mm inter-slice gap), and out phase (160/4.8 TR/TE, 78° flip angle, 4 mm slice thickness, 350 × 350 FOV, 256 × 256 matrix size and 0.9 mm inter-slice gap), axial FLASH (128/ 4.8 TR/TE, 70° flip angle, 4 mm slice thickness, 350 × 350 FOV, 256 × 256 matrix size and 0.9 mm inter-slice gap), heavy T2 10000/260 TR/TE, 150° flip angle, 4 mm slice thickness, 350 × 350 FOV, 256 × 256 matrix size and 0.9 mm inter-slice gap). A multiphase (arterial, portal and delayed phases), dynamic gadolinium-enhanced examination was performed for 37 patients. After injection of 20 mL of gadopentetate dimeglumine (Magnevist; Bayer HealthCare Pharmaceuticals, Wayne, NJ, USA) at a rate of 2 mL/sec. Sequential axial spoiled gradient echo MR images were obtained through the lesion at 25, 60 and 120 - 200 seconds after start of injection. The following parameters were used (3.3/1.4 TR/TE, 15° flip angle, 3 mm slice thickness, 350 × 350 FOV, 220 × 256 matrix size and no inter-slice gap). Then a 20 mL saline flush was delivered into the antecubital vein.

2.2.1. Diffusion-Weighted Imaging

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 (5200/139 ms TR/TE, 5 mm slice thickness, 1 mm slice

interval, 350×350 mm FOV, 256×512 matrix) with diffusion sensitivities of b values = 0, 500, 1000 sec/mm². The diffusion gradient was applied sequentially in the three orthogonal directions. ADC map were reconstructed. Scan time was <2 min.

2.2.2. Image Analysis

- *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, which was classified by using visual assessment of hypointensity, hyperintensity or mixed signal 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. Signal intensity of ADC map assessed visually.

- *Quantitative Assessment of ADC*

The ADC map was automatically calculated by commercially available software (Leonardo, version 2.0; Siemens AG Medical systems, Forchheim, Germany).

Measurement of ADC was made using an electronic cursor on the ADC map in different regions of interest (ROI) of the lesions. The region of interest with a diameter of approximately 1.0 cm was positioned for the measurement of ADC in each mass avoiding necrotic or hemorrhagic components. Scar of FNH was avoided during placing ROI. The ADC values were expressed in 10^{-3} mm²/sec. ROI for each lesion was placed not less than three times. Then the mean ADC value for the lesions was calculated.

2.3. Statistical Analysis

The statistical analysis of data was done using SPSS program [statistical package for social science version 10]. The mean \pm SD was used for data description. One way ANOVA test was used when compared more than two groups, independent sample t-test when compare two groups. A P value is considered significant if ≤ 0.05 at confidence interval 95%.

3. Results

The final diagnoses of benign hepatic focal lesions were: cyst/cysts (n = 8), hemangioma (n = 23), abscess (n = 5), adenoma (n = 5), focal nodular hyperplasia (n = 4) and nodular regenerative hyperplasia (n = 2). The mean ADC values were $3.4 \pm 0.12 \times 10^{-3}$ mm²/sec in cystic lesion (**Figure 1**), $2.23 \pm 0.08 \times 10^{-3}$ mm²/sec in hemangioma (**Figure 2**), $1.94 \pm 0.05 \times 10^{-3}$ mm²/sec in abscess, $1.72 \pm 0.07 \times 10^{-3}$ in focal nodular hyperplasia, $1.65 \pm 0.06 \times 10^{-3}$ mm²/sec in adenoma, $1.62 \pm 0.07 \times 10^{-3}$ mm²/sec in nodular regenerative hyperplasia (**Figure 3**) (**Tables 1** and **2**). The mean ADC values were significantly different within benign hepatic focal lesions (P < 0.001). The difference between the mean ADC values of FNH, adenoma and NRH were not statistically significant (P < 0.23) (**Table 3**).

4. 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 [2] [5] [6]. 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 [7]. DWI is increasingly used for the evaluation of extracranial diseases. There is growing interest in the application of DWI for the evaluation of the patient with cancer [1].

The ADC value is estimated to be lower in viable tumor tissue with densely packed diffusion-hindering obstacles than in tissue with less densely packed obstacles, such as tumor necrosis and benign tissue [8]. This coincides with our results that showed high ADC value of benign hepatic lesions.

DWI in the liver is a relative new and increasingly used imaging technique in addition to conventional unenhanced and contrast enhanced MRI [9]. Most prior studies [10]-[15] have used DW imaging for focal liver lesion characterization by enabling measurement of lesion apparent diffusion coefficient (ADC).

Sun et al., (2005) measured ADC in four sets (0, 100, 500, 1000) and stated that ADC values had higher stabilization with higher b value [16]. In the current study we measured ADC from high b value (b1000) to avoid false measurements related to T2 shine through effect or perfusion.

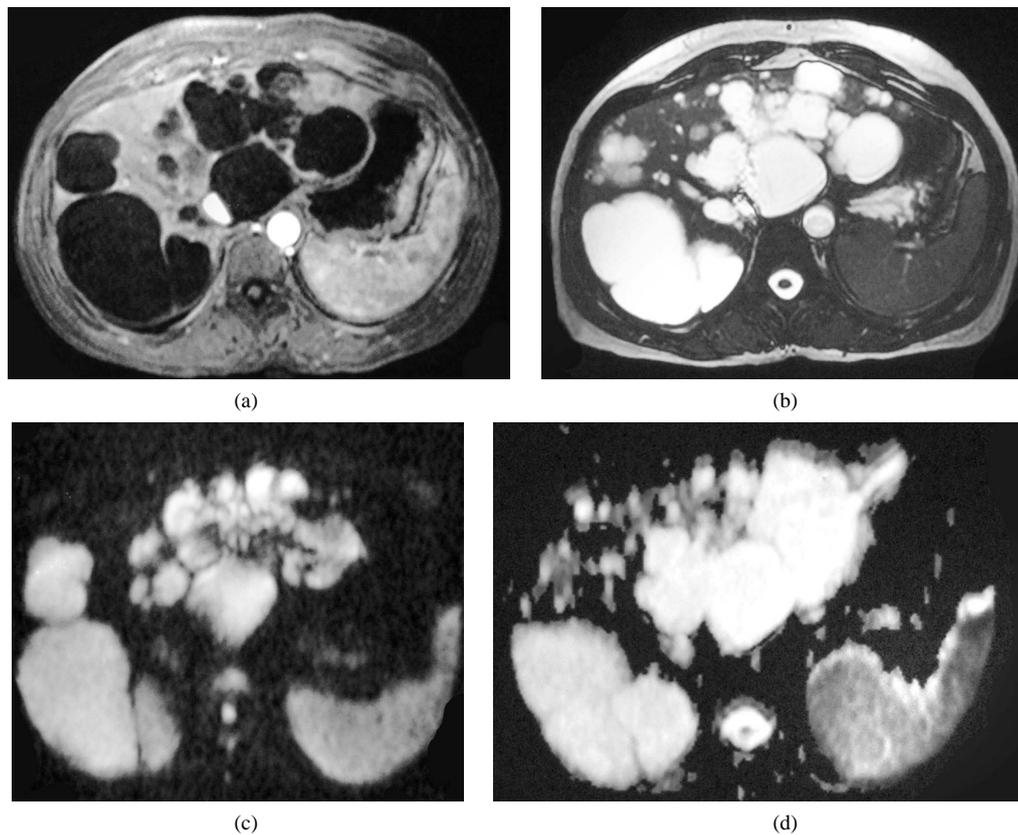


Figure 1. 40-year-old women presented with multiple hepatic cysts. (a) Post-contrast T1 WI and (b) T2 FISP show multiple non-enhanced cysts. (c) Cysts show high signal on DWI (b vale = 0 s/mm²). (d) ADC map shows high signal with ADC value is $3.4 \pm 0.12 \times 10^{-3} \text{ mm}^2/\text{sec}$.

Table 1. Mean ADC value of 47 benign hepatic lesions.

Pathology	Mean ADCs value ($\times 10^{-3} \text{ mm}^2/\text{sec}$)
Cyst	3.4 ± 0.12
Haemangioma	2.23 ± 0.8
Abscess	1.94 ± 0.05
FNH	1.72 ± 0.07
Adenoma	1.65 ± 0.06
NRH	1.62 ± 0.07

FNH: Focal nodular hyperplasia; NRH: Nodular regenerative hyperplasia.

Table 2. Mean ADC value of benign hepatic lesions in this study and those previous reports.

Parameter	Kandpal <i>et al.</i> [5]	Gourtsoyianni <i>et al.</i> [6]	Oner <i>et al.</i> [7]	Bruegel <i>et al.</i> [8]	Holzappel <i>et al.</i> [9]	Parikh <i>et al.</i> [10]	Taouli <i>et al.</i> [11]	Miller <i>et al.</i> [12]	Current study
N.	31	22	8	111	98	75	28	382	47
Hemangioma	2.22	1.9	1.72	1.92	1.69	2.04	2.95	2.26	2.23
Cyst	2.66	2.55	2.34	3.02	2.61	2.54	3.63	3.4	3.4
Abscess	1.21	N.A.	N.A.	N.A.	N.A.	1.64	N.A.	1.97	1.94
FNH	2.03	N.A.	N.A.	1.40	1.43	1.49	1.75	1.79	1.72
Adenoma	N.A.	N.A.	N.A.	N.A.	1.43	1.49	1.75	1.49	1.65
NRH	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	1.62

N.: Number of patients; FNH: Focal nodular hyperplasia; NRH: Nodular regenerative hyperplasia; N.A.: Not applicable.

Table 3. Statistical results.

Pathology	P value
Within this benign group	<0.001
Cyst vs haemangioma	<0.001
Cyst vs abscess	<0.001
FNH vs adenoma	<0.14
Adenoma vs NRH	<0.58
FNH vs NRH	<0.17
Within FNH, Adenoma and NRH	<0.23

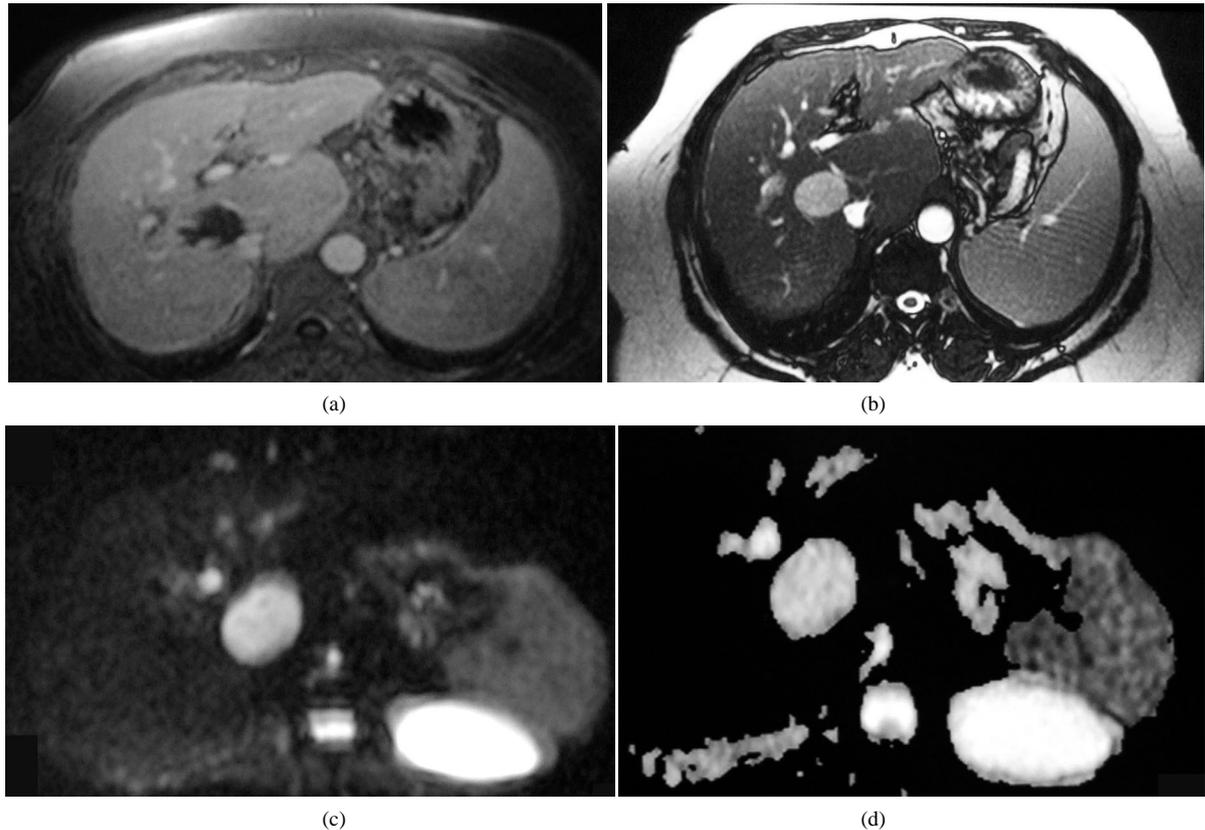


Figure 2. 55-year-old man presented with hepatic focal lesion imaging characteristic of haemangioma. (a) Post-contrast T1 WI shows peripheral nodular enhancement. (b) T2 FISP shows high signal. (c) The lesion shows high signal on DWI (b value = 500 s/mm²). (d) ADC map shows high signal with ADC value is $2.23 \pm 0.08 \times 10^{-3} \text{ mm}^2/\text{sec}$.

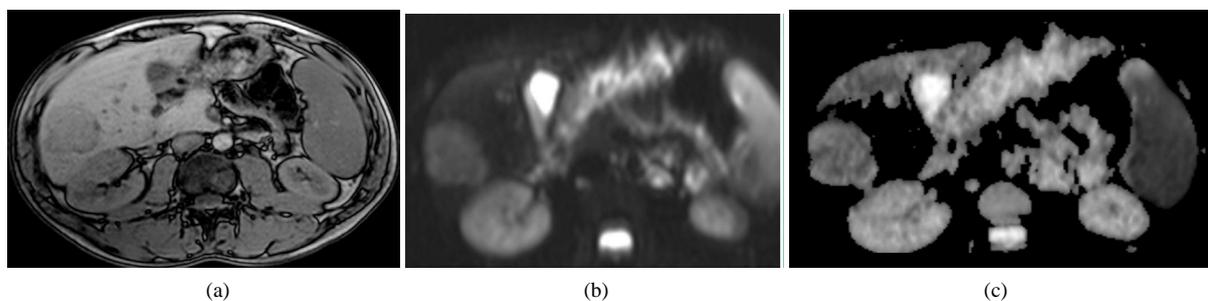


Figure 3. 24-year-old man presented with pathologically proved NRH. (a) Non-contrast T1WI shows low signal focal lesion. (b) The lesion shows high signal on DWI (b value = 0 s/mm²). (c) ADC map shows intermediate signal with ADC value is $1.62 + 0.07 \times 10^{-3} \text{ mm}^2/\text{sec}$.

ADC value of haemangioma in our study was $2.23 \pm 0.08 \times 10^{-3} \text{ mm}^2/\text{sec}$ in hemangioma. This coincides with previous results [4] [14] [17]-[21]. But, it does not correlate with other studies [22]-[24]. The difference may be due to using different b value, different technique either breath-hold or respiratory triggered, or different pathological types of haemangiomas.

Our results shows cyst has the highest ADC value. This is in agreement with previous studies [4] [19]-[22]. There is difference in ADC value of cyst from other study [3] [18] [19] [23]. This variability in ADC values is probably due to imaging parameters, b value combination or different technique either breath-hold or respiratory triggered.

Mean ADC value of cyst was significantly higher than haemangioma. Mean ADC values of cyst and haemangioma were significantly higher than other benign hepatic focal lesions. This coincides with other studies [18] [20] [24].

Restricted diffusion within abscess cavities is assumed to be due to the presence of viscous fluid containing bacteria, inflammatory cells, mucoid proteins, and cellular debris [25]. An inverse correlation between ADC and cell density has been described in animal models [26]. During the process of abscess maturation, the central parts liquefy, and T2 shine-through gradually replaces the true restriction of diffusion with increasing signal intensity on low-b-value DW images and an increasing ADC [27]. Our results are in agreement with Miller *et al.*, (2010) [12]. The difference between our results and other studies [18] [19] may be attributing to stage of abscess, type of abscess or under therapy.

On DW MR Images, FNHs and HCAs often show findings that suggest restricted diffusion. The mean ADC value of FNHs was significantly higher than that of HCAs ($P < 0.001$) [28]. Adenoma, FNH and NRH are high cellularity. So, they exhibit low ADC value in relation to other benign hepatic focal lesions. Our results are coincide with previous studies [18] [29]. But, variability in ADC values is probably due to tumor type, imaging parameters, b value combination, and region of interest placement (whether or not the solid part was included).

Our study results strongly suggest that there is an inverse relationship between lesion cellularity and ADC. Lesions with high cellularity as adenoma, FNH and NRH have low ADC values. Lesions with low cellularity as cyst and haemangiomas have high ADC values. This in agreement with previous study [29].

The advantage of DWI is that it is completely noninvasive, does not require exposure to ionizing radiation or administration of exogenous contrast medium and does not cause patient discomfort. In this study, we found that the P value within benign hepatic focal lesion was <0.001 . The differences in ADC values might reflect differences in histopathologic features: adenoma, FNH and NRH had high cellularity, so its ADC values tended to be lower in our study. Therefore, it is feasible to use DWI to distinguish cyst, haemangioma and abscess from adenoma, FNH and NRH and this technique would be of great benefit to radiologist for differential diagnosis of benign hepatic focal lesions.

Our study has several technical limitations. The main limitation was that the echo-planar sequence used with a higher b value had a lower SNR, resulting in greater image distortion. Second, avoiding susceptibility artifacts on DWI is rather difficult. Although we use phase array coil with cardiac gating and respiratory compensation techniques to improve image quality and speed, artifacts associated with echo-planar imaging sequences and macroscopic movement still existed which resulted in image distortion. Fortunately, these artifacts were not very severe and the images could fulfill the requirements needed to make the diagnosis. Lastly, FNH, adenoma and NRH were small in number.

5. Conclusion

Diffusion weighted MR imaging is a new imaging modality for diagnosis and characterization of different benign hepatic focal lesions, particularly in patient with renal dysfunction. Further studies are recommended to differentiate between FNH, adenoma and NRH using diffusion-weighted MRI.

Conflict of Interest

No financial disclosure.

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Abbreviations

DWI: diffusion-weighted imaging
 ADC: apparent diffusion coefficient
 FNH: focal nodular hyperplasia
 NRH: nodular regenerative hyperplasia
 MDCT: multi-detector computed tomography
 HCAs: hepatocellular adenomas
 SNR: signal-to-noise ratio