ROLE OF DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN DIFFERENTIATING BETWEEN MALIGNANT AND BENIGN LIVER LESIONS

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ABSTRACT

Objectives: To evaluate role of Diffusion weighted Magnetic Resonance Imaging in differentiating between Malignant and Benign Liver lesions based on ADC values and its correlation with Multidetector CT scan findings.

Methodology: This one year cross sectional study was conducted in the Department of Radiodiagnosis in a tertiary hospital in Davangere. A total of 30 patients were studied. Focal hepatic lesions diagnosed on MDCT, were evaluated prospectively. Diffusion weighted imaging was performed with b values of 50, 400 and 800 mm²/s, ADC were calculated and results were analyzed.

Results: Out of the 30 lesions, 19 lesions had features of malignancy on MDCT. All the 19 malignant FHLs (11 HCC and 9 Metastatic FHLs) showed restricted diffusion. Out of 11 benign FHLs diagnosed on CT, there were 5 hemangiomas, 3 abscesses, 2 simple hepatic cysts and 1 FNH. 8 of these lesions showed no area of restricted diffusion on DWI and ADC map. While 3 benign lesions which showed typical imaging findings of abscess on MDCT, showed restricted diffusion. The mean ADC values of the 11 benign lesions was 1.372 ± 0.308 x 10⁻³ mm²/s, (Range 0.790 x 10⁻³ to 2.176 x 10⁻³ mm²/s) and mean ADC of 19 malignant lesions was 0.878 ± 0.147 x 10⁻³ mm²/s with range from 0.591 x 10⁻³ to 1.047 x 10⁻³ mm²/s. The values are comparable to the published data.

Conclusion: All the focal hepatic lesions (FHLs) which were malignant, whether biopsy proven or with CT features of malignancy, showed true restricted diffusion on DWI and had lower ADC value than that of benign FHLs. Using threshold value of 1.077 x 10⁻³ mm²/s for mean ADC we can differentiate maximum number of benign from malignant FHLs.

INTRODUCTION

MR imaging has emerged as an important imaging modality for assessing and characterising focal hepatic lesions. The introduction of faster sequences has allowed high quality imaging of the entire liver with high intrinsic soft tissue contrast. Because of lack of ionizing radiation, routine and gadolinium enhanced multiphasic imaging with high temporal and spatial resolution and fat suppression can be performed.

Although dynamic contrast enhanced examinations have become a routine component of abdominal imaging, the high cost/benefit ratio and risk of contrast media side effects remain an issue. Moreover, sometimes it is not possible to distinguish between highly vascular metastases and hemangiomas, even using dynamic examination1. DW MR imaging is an MR imaging technique that derives its image contrast on the basis of differences in the mobility of protons (primarily associated with water) between tissues. In tissues that are highly cellular (eg, tumour tissues), the tortuosity of the extracellular space and the higher density of hydrophobic cellular membranes restrict the apparent diffusion of water protons2. Apparent diffusion coefficient (ADC) is a quantitative parameter calculated from DWI and is a measure of diffusion in biological system. Diffusion weighted (DWI) MR imaging, combined with apparent diffusion coefficient (ADC) measurement is an important method for in-vivo quantification of the combined effects of capillary perfusion and diffusion3. Focal masses are diagnosed using ultrasonography (USG) and/or computed tomography (CT). Additionally, magnetic resonance imaging (MRI) is preferred when further characterization of these masses is needed. MRI has many advantages (e.g., high contrast resolution, the ability to obtain images in any plane, lack of ionizing radiation, and the safety of using particulate contrast media rather than those containing iodine) that make it a favoured modality.

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Diffusion Weighted imaging (DWI) is reaching a potential for clinical use in the abdomen, particularly in the liver. DW imaging is an attractive technique for multiple reasons: it can potentially add useful qualitative and quantitative information to conventional imaging sequences; it is quick (performed within a breath hold) and can be easily incorporated to existing protocols; and it is a non-enhanced technique (performed without the use of gadolinium-based contrast media), thus easy to repeat, and useful in patients with severe renal dysfunction at risk for nephrogenic systemic fibrosis\(^5,6\).

**AIMS AND OBJECTIVES**

1. To determine the role of diffusion weighted MR imaging in differentiating between benign and malignant hepatic lesions by calculating apparent diffusion coefficient (ADC) values.
2. To correlate Apparent Diffusion Coefficient (ADC) values with results obtained on Contrast Enhanced CT scan (CECT) and histopathology or other laboratory investigations in patients attending JJM MEDICAL COLLEGE.

**Study Design**

The study design was a one year cross-sectional study.

**Source of data:** Patients diagnosed with liver lesions on Contrast Enhanced CT abdomen for a period of one year at a tertiary medical college, Davangere.

**Sample size**

A total of 30 patients fulfilling the selection criteria were studied.

**Sampling Procedure**

A minimum sample of 30 patients who fulfil the selection criteria during the study period were planned.

**Selection criteria**

**Inclusion criteria**

All the patients who are diagnosed with liver lesion on contrast enhanced CT abdomen will be undergoing T1, T2 and Diffusion Weighted MR Imaging and scans will be reviewed in the department of radio-diagnosis.

**Exclusion criteria**

1. Patients with hepatic neoplasm’s who have undergone chemotherapy or radiation therapy.
2. Patients with history of trauma.
3. Post-Operative patients.
4. General contraindication to MRI examination such as pacemaker, metallic implants, metallic foreign body etc.

**Ethical clearance**

Prior to the commencement, the ethical clearance was obtained from Institutional Ethics Committee.

**Informed consent**

Patients fulfilling the selection criteria were briefed about the nature of the study and a written consent was obtained.

**Data collection**

Once a patient fulfilled the inclusion criteria for this study he/she was administered the predesigned/pretested proforma. Demographic characteristics of the study population such as age, sex were obtained through an interview.

The patients were then briefed about the procedure i.e. about the noise of the gradient coils and need to control the body movements for successful image acquisition.

**Imaging**

Patients diagnosed with liver lesions on CECT abdomen will undergo Diffusion weighted MR imaging using 1.5 T MRI of Siemens Magnetom Symphony.

**Scan protocol**

The tests were performed using following parameters.

- FOV – 350 to 400 (in adult) and 180 to 200 (in paediatrics)
- Slice thickness – 4 to 5 mm
- Matrix size – 512 x 512
- The following sequences were obtained: Spin-echo T1 weighted (axial/sagittal), Spin-echo T2 weighted (axial/coronal), Single shot echo-planar imaging (axial) [DWI].
- Diffusion MR imaging will be done using single shot Echo Planar imaging (EPI) with b-value of 50, 400 & 800 sec/mm\(^2\). The Apparent Diffusion Coefficient (ADC) values will be calculated by marking three regions of interest (ROI).
- The mean ADC values will be calculated and correlated with results obtained on contrast enhanced CT scan and Histopathology or other laboratory investigations.

**Statistical Analysis**

The data obtained was coded and entered into Microsoft Excel Worksheet. The categorical data was expressed as rates, ratios, proportions and percentages. The continuous data was expressed as mean ± standard deviation.

All tests will be considered significant if p value equals or less than 0.05.

**DISCUSSION**

This one year cross sectional study of characterization of focal hepatic lesions using diffusion weighted MR imaging included a total of 30 patients, who had undergone CT scan abdomen pain and contrast, from January 2017 to December 2017 at the department of Radio-diagnosis. In the present study, most of the patients were males constituting 63.3% of all cases, while 36.67% were females with male to female ratio being 1.7:1.

In this study, the age ranged between 24 to 89 years. The commonest age group was between 51 to 60 years which comprised 43.33 % of patients. The next common age group was more than or equal to 61 years with 33.33 % of patients. Around 23.33 % of all the patients were aged less than or equal to 50 years.
The mean age was 56.7 ±13.53 years.

In our study, all the 19 patients with features of malignancy on MDCT, showed early enhancement on arterial phase (appearing hyperdense) with a p-value of 0.0010 (<0.05) suggesting a significant relation. While 18 out of the 19 lesions showed washout of contrast on delayed phase, appearing isodense or hypodense. Out of these 19 lesions, 11 lesions underwent biopsy. All of these cases came out to be positive for malignancy.

The diagnosis was established on classical radiological imaging findings and/or follow up imaging or HPE/ cytology. The lesions were:

1. **Benign hepatic lesions (n =11):** simple cyst (n=2), Hemangioma (n=5), FNH (n=1), and abscess (n=3).

2. **Malignant lesions (n=19):** Hepatocellular carcinoma (HCC) (n=11) and metastasis (n = 8).

### Table 1

<table>
<thead>
<tr>
<th>Lesion type</th>
<th>Lesion Subtype</th>
<th>No. of lesions evaluated</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign FHLs</td>
<td>Hemangioma</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abscess</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Simple cyst</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>FNH</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Malignant FHLs</td>
<td>Hepatocellular carcinoma</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metastasis</td>
<td>8</td>
<td>19</td>
</tr>
</tbody>
</table>

A total of 11 patients were diagnosed with HCC. All of the 11 lesions were established on typical imaging findings of arterially enhancing lesions with early wash out on venous phase. HPE/ cytology were available in 7 patients except in 4 patients with small lesion where biopsy was not done, however imaging features were classical of HCC and AFP was significantly high.

The diagnosis of metastatic FHL’s were established on basis of HPE/imaging findings/clinical background and follow up.(Table -3)

### Table 2 Basis of final diagnosis of FHL’s

<table>
<thead>
<tr>
<th>FHL Subtype</th>
<th>Basis of Final Diagnosis</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatocellular</td>
<td>CF+HC</td>
<td>11</td>
</tr>
<tr>
<td>carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastasis</td>
<td>CF+HC</td>
<td>8</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>CF</td>
<td>5</td>
</tr>
<tr>
<td>Abscess</td>
<td>CF+HC</td>
<td>3</td>
</tr>
<tr>
<td>Simple cyst</td>
<td>CF</td>
<td>2</td>
</tr>
<tr>
<td>FNH</td>
<td>CF</td>
<td>1</td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th>Final Diagnosis</th>
<th>Mean ADC (x10^3 sq mm/s) ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEPATOCELLULAR CARCINOMA (n=11)</td>
<td>0.868 ± 0.168</td>
</tr>
<tr>
<td>METASTASIS (n=8)</td>
<td>0.888 ± 0.127</td>
</tr>
<tr>
<td>Mean ADC for Malignant lesions (n=19)</td>
<td>0.878 ± 0.147</td>
</tr>
<tr>
<td>HEMANGIOMA (n=5)</td>
<td>1.650 ± 0.316</td>
</tr>
</tbody>
</table>

### Diffusion Restriction in Benign Vs Malignant Lesions

All the 19 malignant FHLs (11 HCC and 8 Metastatic FHLs) showed restriction of diffusion on DWI and ADC map. In cases with FHLs showing necrosis within them, restriction of diffusion was noted along the non necrotic part of the lesions. Some of the malignant lesions were heterogeneous in appearance, with only some part of tumour showing restricted diffusion. In these patients ADC was calculated over the region showing restricted diffusion. There were no malignant FHL that showed absence of restricted diffusion on DWI and ADC map.

Out of 11 benign cases with FHLs, 8 lesions showed no area of restricted diffusion on DWI and ADC map. These included 5 hemangiomas, 2 benign simple hepatic cysts and 1 FNH. 3 lesions revealed restricted diffusion, these being cases of hepatic abscesses.

### Table 4 Restriction of Diffusion in Benign Vs Malignant Lesions

<table>
<thead>
<tr>
<th></th>
<th>Total no of lesions</th>
<th>Lesions with true restriction on DWI</th>
<th>Lesions with no true restriction on DWI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>30</td>
<td>19</td>
<td>11</td>
</tr>
</tbody>
</table>

For the differentiation of benign and malignant hepatic lesions on DWI, in our study we evaluated the signal intensity change between DWI using a b-value of 50 s/ mm², 400 s/ mm² and a high b value (800 s/ mm²). Although suboptimal signal-to-noise ratio and artefacts may hinder detection of the focal hepatic lesions with high b-value DWI, it facilitates differentiation of malignant FHLs from haemangioma and cysts: malignant lesions showed high signal intensity because of restricted diffusion of extracellular water molecules. In contrast, cystic lesions such as Hemangiomas and cysts showed decreased signal intensity at increasing b-values owing to a high fluid content. However some hemangiomas show persistence of high signal in some part of the lesion.

Also in our study, 3 benign cases of hepatic abscesses showed restricted diffusion. Two of these cases were proven infective (abscess). While the third case had the CT findings and clinical history of abscess.

Malignant lesions such as Hepatocellular carcinomas and metastases showed high signal attenuation on DWI using a high b-value (800 sec/sq mm) rather than at b-value of 50 sec/sq mm. Conversely, benign lesions including Hemangiomas and cysts showed less signal intensity on DWI using a high b-value (1000 sec/sq mm) than at b-value of 50 sec/sq mm.

So out of 30 patients with focal hepatic lesions studied, we could differentiate 27 FHL’s in to benign and malignant lesions by visual assessment with DWI and ADC value assessment. The 3 that could not be differentiated were cases of abscess.
When ADC values were taken into consideration the benign lesions showed higher ADC values in comparison to the malignant FHLs. Benign lesions, such as liver cysts and hemangiomas showed higher ADCs than malignant lesions, such as Hepatocellular carcinomas and metastases. Though, ADC values are often variable from a study to another, partially related to different equipment and different b-values. ADCs tend to be larger when using small b-values, because the signal attenuation due to diffusion plays only a minor role in that case, and ADC values are contaminated by micro-perfusion. When higher b-values are used, ADCs tend to decrease, in relation with less perfusion contamination.

Using a threshold mean ADC value of $1.077 \times 10^{-3}$ sq mm/sec we were able to differentiate benign from malignant lesions.

**CONCLUSIONS**

**Based upon these outcomes following Conclusion could be reached**

a. Malignant FHLs shows true restriction of diffusion on DWI and have low ADC value than that of benign FHLs.

b. The diffusion-weighted MRI sequence is a useful diagnostic tool since it can be obtained in free breathing, there is no need to use contrast media, and it can contribute to accurate diagnosis for discrimination of benign and malignant hepatic masses.

c. This study recommends threshold value of $1.077 \times 10^{-3}$ sq mm/s for mean ADC to differentiate maximum number of benign and malignant FHLs.

d. Hence, DWI combined with ADC can be used as screening tool for detecting FHLs and as diagnostic tool for characterising them as benign or malignant.

e. DWI must be done both at low and high b values for high sensitivity in detection of FHLs.

**Summary**

To summarise, in our set of 30 patients with focal hepatic lesions that we screened using DWI, we got following outcomes:

1. All malignant FHLs (n= 19) showed true restriction of diffusion on DWI and ADC map.
2. Out of 11 benign FHLs, 8 FHLs showed absent restricted diffusion on DWI and ADC map, while 3 FHLs showed areas of restricted diffusion on DWI and ADC map.
3. 11 out of the 19 lesions which were labelled as malignant based on imaging findings using MDCT underwent biopsy, all of which came out to be positive.
4. The malignant FHLs showed low ADC values than that of benign FHLs. The mean ADCs of benign and malignant lesions were $1.372 \pm 0.38 \times 10^{-3}$ sq mm/s and $0.878 \pm 0.147 \times 10^{-3}$ sq mm/s, respectively.
5. Using a threshold value of $1.077 \times 10^{-3}$ sq mm/s for ADC we could differentiate maximum number of malignant from benign FHLs.
6. The three benign cases which showed restricted diffusion were abscesses. They cannot be differentiated from malignant lesions based on ADC value. CT findings and clinical history are essential for their diagnosis.

**References**


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