DIFFUSION-WEIGHTED MRI CHARACTERIZATION OF SOLID LIVER LESIONS

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Abstract

MRI characterization of liver lesions is based on their morphology, behaviour in the different sequences, and with paramagnetic contrast. **Objective***:* to determine the usefulness of diffusion-weighted behaviour in various solid lesions, using ADC measurement. **Materials and methods**: between 2007 and 2008 we studied 51 hepatic solid focal lesions (26 patients) with MRI, using conventional sequences and diffusion-weighted imaging obtained with EPI technique with different b-values. Lesions corresponded to 20 haemangioma, 12 focal nodular hyperplasias (FNH), 5 hepatocellular carcinomas (HCC), and 14 metastases. **Results*:*** The statistical analysis allowed determining optimal cut-off level (ADC 1.28 $\times 10^{-3} mm^2/s$) to differentiate benign from malignant masses. ADC values of benign lesions were significantly higher than those of the malignant ones; the haemangioma was the solid lesion with higher ADC values, followed by FNH, HCC, and metastases, with lower values. Registered mean values were 1.68, 1.30, 1.08 and 1.03 ($\times 10^{-3} mm^2/s$), respectively. **Conclusions:** In our view, diffusion-weighted technique should be used as an additional sequence to supplement conventional MRI protocol studies for proper characterization of solid liver lesions.

Keywords: Diffusion, MRI, Solid liver lesions.

Introduction

Liver can present a wide variety of solid masses, both benign and malignant. The detection, characterization and accurate differentiation of these lesions have always been one of the goals of different imaging methods.

Focal nodular lesions characterization with Magnetic resonance imaging (MRI) is based on their morphology, signal intensity on different sequences (HASTE, T1)

and in their behaviour with paramagnetic contrast agents (Gadolinium). Specific contrast agents have also been used, but due to their high cost they are not commercially available in our country. However, even with regular protocol studies, including above-mentioned sequences, there are still solid lesions where an accurate differentiation between benign and malignant lesions is not always achieved,

MR diffusion-weighted technique, that not requires contrast agents, is widely applied in Central Nervous System lesions. However, its use in abdominal lesions was only described in 1994 when Muller et al [1] presented their first report in this area. From then onwards, multiple studies have been published on technical parameters [2-5] and characteristics of diffusion in different solid organs such as liver, spleen, kidney, and pancreas [6.7], including diffuse and focal disease of the liver [6, 8 -10]. In our country there are no reports on the use of this technique for the study of solid focal liver masses.

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Measuring the Apparent Diffusion Coefficient (ADC), which quantifies intravoxel incoherent motion, determined by, assesses diffusion characteristics of tissues:

a) Capillary perfusion

b) Brownian motion of free water particles or diffusion itself.

Diffusion-weighted MRI reflects tissue properties, such as amplitude of extracellular spaces, viscosity, cellularity, membrane integrity, etc.

Objective: The goal of this study was to assess the characteristics of diffusion-weighted imaging of different liver solid lesions, quantifying ADC values, to determine whether this technique is useful differentiating benign from malignant lesions.

Materials and Method

We retrospectively reviewed all liver MRI studies performed from August 1, 2007, to March 30, 2008, measuring ADC values of solid lesions found in the period.

Conventional and diffusion-weighted MRI studies were performed with a Siemens Avanto 1.5 Tesla scanner, using Spine Matrix antennas and Body Matrix Antennas.

All diffusion images were acquired with Echo Planar Imaging (EPI) with parallel acquisition technique in axial plane applying the following parameters: a) 12 to 18 images to cover the liver, b) repetition time (TR) 1800 ms, c) echo time (TE) 85 ms, d) matrix 192x192, e) field of view (FOV) of 350 mm, slice thickness 7 mm and 4 mm in small lesions, f) distance of 0 mm between slices, g) ascending diffusion b-factors, i.e., with different degrees of sensitiveness (50, 200, 400, 500, 700 and Seg/mm^2 850).

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Image acquisition was obtained with free-breathing using 4 shots, WITH an approximate total time of 2:15 minutes,. IPAT technique (Integrated Parallel Acquisition Technique) was applied in GRAPPA mode (Generalized Auto calibrating Partially Parallel Acquisition) with acceleration factor of 2 and measurement of dual mode antennas.

Conventional MRI studies were interpreted by an experienced radiologist specialized in gastrointestinal imaging. ADC measurements of all lesions were independently carried out by both, a radiologist and a technician, to be subsequently averaged. To avoid partial volume errors, only solid lesions equal to or larger than 1 cm diameter were selected; 3 measurements per lesion were performed with a sample area of 5 mm2, averaging them to get the final ADC of each lesion. In lesions with necrotic or fibrous core, measurement of this area was avoided (5 cases consisting of 1 haemangioma, 2 FNH, and 2 metastasis). In those patients with multiple solid lesions with similar characteristics, a maximum of 3 lesions was randomly selected.

Final diagnosis of the aetiology of lesions was determined by their characteristics in ultrasound imaging (U.S.), multislice computed tomography (MSCT), and MRI without or with iv contrast agent, in addition to follow up of benign cases (12-month follow-up period), history of known primary lesion, and follow up in metastases. Concerning HCC cases, the presence of cirrhosis plus one nodule with characteristics indicative of HCC in MRI, alpha-fetoprotein levels and/or biopsy were considered.

Statistics: Data analysis was performed with the R-software (http://www.r-project.org/); every decision was made with 95% confidence. ADC values according to final characterization of lesion were compared in accordance with Mann-Whitney procedure. A logistic regression model was adjusted to assess the

likelihood of having a malignant mass, being ADC value used as a predictive variable. With the modified model, optimal cut-off line was determined to achieve a good sensitivity and specificity.

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Results

Between August 1, 2007, and March 30, 2008, 97 patients with liver MRI were studied; 46 of them were diagnosed with one or more solid nodular liver lesions larger than 1 cm. From these 46 patients with, 20 of them were discarded: thirteen patients having no diffusion-weighted sequences, 1 patient whose final diagnosis was focal inflammatory process and received antibiotic treatment, 2 patients in whom nodule corresponded to a focal fat deposit, 1 patient with unconfirmed diagnosis of dysplastic nodule, and 3 patients with metastases who had received or were on chemotherapy or radiation treatment. Thus, the final group was composed of 26 patients with 51 solid nodular lesions: 11 men and 15 women, with an average age of 51.5 years and ages ranging from 30 to 73 years.

Final diagnoses of the 51 nodular lesions analyzed included 20 haemangioma, 12 FNH, 5 HCC and 14 metastases.

Measurement of ADC values for each type of lesion is shown in Table I and associated box plots are shown in Figure 1. Table I shows that the distribution of ADC values are in ascending order, showing a significant degree of overlap between them. Figure 1 evidence than in the FNH group there are 2 anomalous observations not following the normal behaviour of the group; this can be explained by the scarce number of observations and/or for inaccuracy of ADC measurement.

Table II shows statistical summaries of ADC measurements of the different types of lesions, grouped into benign or malignant masses. The mean ADC value obtained for benign lesions was 1.54 $\times 10^{-3} mm^2/s$, which differs significantly from the average for malignant lesions (1.04 $\times 10^{-3} mm^2/s$), according to the Mann-Whitney test ($p < 0.05$). Figure 2 shows box plots of ADC for measurements of the 51 lesions studied, showing that there is a high degree of overlap between the first and the last quartile of benign and malignant lesions, respectively.


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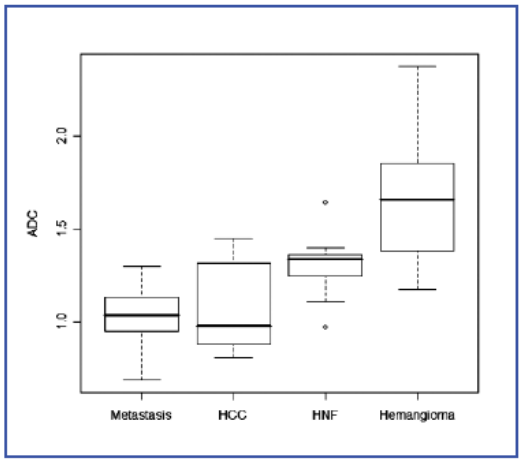

Figure 1. *Box Plots of ADC values in solid liver lesions.*

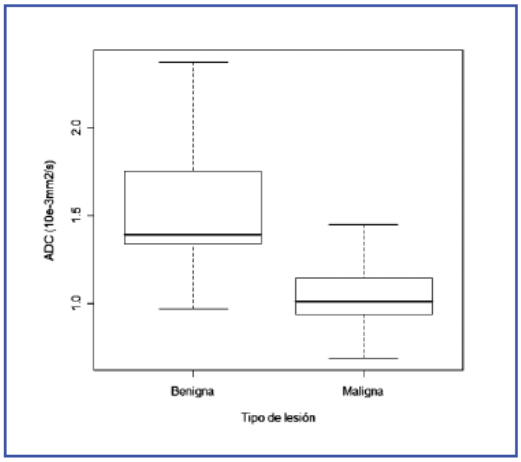

Figure 2. *Box Plot of ADC in benign and malignant liver lesions.*

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Table I. ADC values in solid liver lesions.

Type of lesion	Mean ADC	Deviation	Minimum	Maximum
Metástasis	1.03	0.17	0.69	1.30
HCC	1.08	0.28	0.81	1.44
HNF	1.30	0.16	0.97	1.64
Hemangiomas	1.68	0.34	1.17	2.37

Table II. ADC values in benign versus malignant liver lesions

Type of lesion	ADC	D.S.	Minimum	Maximum
Benig	1.54	0.34	0.97	2.37
Malignant	1.04	0.19	0.69	1.44

By adjusting the logistic regression model we sought the best decision rule (cut levels) based on the correct classification rate. ADC value obtained was 1.28 $\times 10^{-3} mm^2/s$.

Table III shows the relationship between benign and malignant liver lesions as well as the predictions of their nature, which was made based on a model with ADC cut-off level of 1.28 $\times 10^{-3} mm^2/s$. With this classification, sensitivity and specificity of 84% was obtained. Figure 3 shows the Box Plot of benign and malignant lesions and their relationship with the selected ADC cut-off level (1.28 $\times 10^{-3} mm^2/s$)

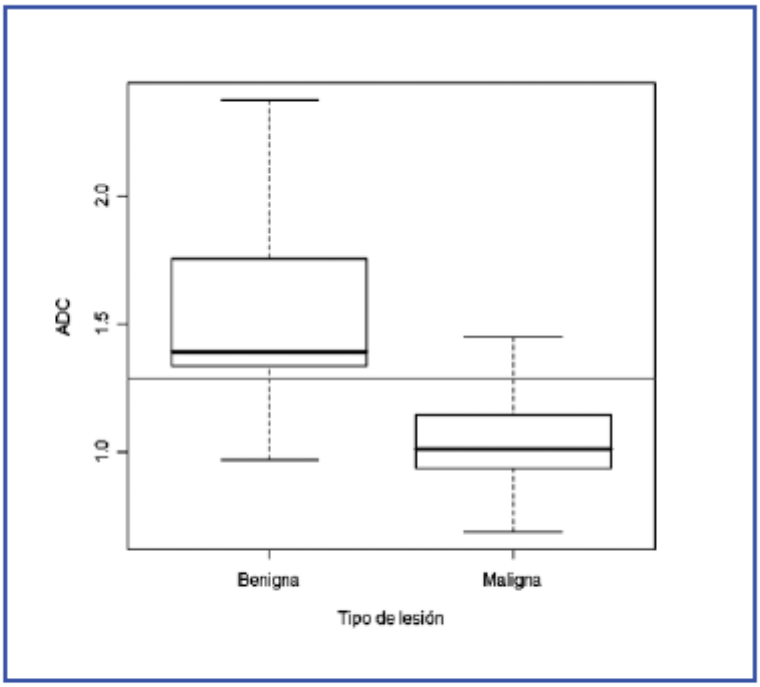

***Figure 3**. Box Plots of ADC values in benign and malignant lesions in relation to optimal cut-off level*

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Table IV shows the behaviour of different types of nodules, grouped according to used cut-off level (1.28 $\times 10^{-3} mm^2/s$). If we took values allowing 100% specificity as a ADC cut-off level, we would find that sensitivity would be very low. The 100% of lesions with ADC> 1.44 $\times 10^{-3} mm^2/s$ [14] corresponded to benign lesions (Figures 4 and 5) (13 out of 20 haemangioma and 1 out of 12 FNH) and 100% with ADC <0.97 $\times 10^{-3} mm^2/s$ % [7] accounted for malignant lesions (Figures 6 and 7) (2 out of 5 HCC, and 5 out of 14 metastasis). Between these two groups, we found overlapping values in 28 benign and malignant lesions (7 out of 20 haemangioma, 11 out of 12 FNH, 3 out of 5 HCC, and 9 out of 14 metastases).

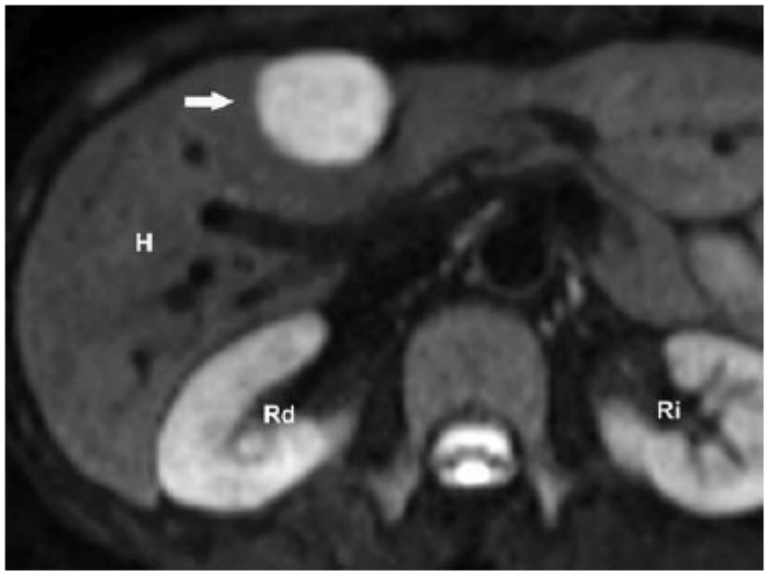

Figure 4. Diffusion-weighted study in patient with hemangioma. The image (arrow) is strongly hyperintense, indicative of high ADC, i.e., without significant restriction to molecular motion. H: liver, Rd and Ri, right and left kidney

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Table III. elationship between true nature and prediction of hepatic lesions.

		Type of Benign	Malignant
Predicted by the Model	Benign	27	5
	Malignant	3	16

Table IV. Distribution of hepatic lesions according to cutoff level.

ADC value	Hemangioma	HNF	HCC	**Metastasis**
> $1.28\times10^{-3}mm^2/s$	19	8	2	1
< $1.28\times10^{-3}mm^2/s$	1	4	3	13

Discussion

Previous publications have shown that ADC measurement has a good potential to characterize focal or diffuse [3,7,8,9,10] liver lesions, to detect focal lesions, and to control the response to treatment of primary and secondary liver tumours [12,13,14].

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In consonance with the existing literature, we have found that diffusion-weighted MR imaging technique using ADC value as an independent variable is useful in the study of solid liver lesions to differentiate between benign and malignant masses; it constitutes a statistically significant model which yields sensitivity and specificity of 84%. This value is limited by overlapping of values between both types of lesions, especially FNH and malignant masses (HCC and metastases).

Our findings on ADC values of the different types of lesions are similar to those found in the literature (values of haemangioma are higher than FNH values which in turn are higher than HCC and metastasis) but the absolute values are not similar, which is probably due to differences in techniques applied (b-value, breath measurement methods, and mathematical technique applied).

The limitations of this study lie in the number of lesions studied and in the absence of data on lesion location in the different liver segments. Some publications have shown a different ADC value of healthy liver parenchyma in some segments (e.g., segment VIII) which are susceptible to the influence of heart and diaphragm motion as well as to the lower signal-to-noise ratio in areas more distant from the antennas [15].

The fact of not having included necrotic or fibrotic areas (2 metastases, 2 FNH and 1 haemangioma) must also be taken into account when evaluating analysis outcomes, since these areas have a greater movement of free water and hence a higher ADC. This fact may have given rise to the differences reported by authors who included these areas in their measurement.

In conclusion, diffusion-weighted MRI is an easy-to-perform technique that requires no contrast agents, adds no significant time to exploration time and is able to differentiate benign from malignant solid liver lesions with high sensitivity and specificity (84%). However, diffusion-weighted MRI has not proved to be useful to differentiate between different types of benign solid lesions or distinguishing between different types of malignant lesions, because in this situation a significant

degree of overlap of ADC values is present.

In our opinion, diffusion-weighted technique should be used in the study of solid liver lesions to complement conventional MRI sequences, i.e. used as an additional sequence to the standard protocol study and not as a unique imaging series.

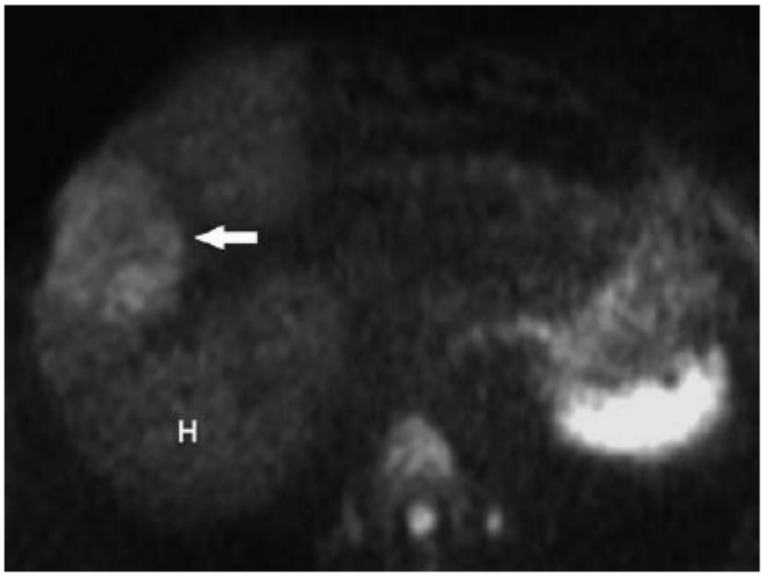

***Figure 5**. Study In patients with FNH (arrow). The image is less hyperintense as compared to Figure 4, which indicates a higher restriction to molecular motion and therefore a lower ADC. H: liver.*

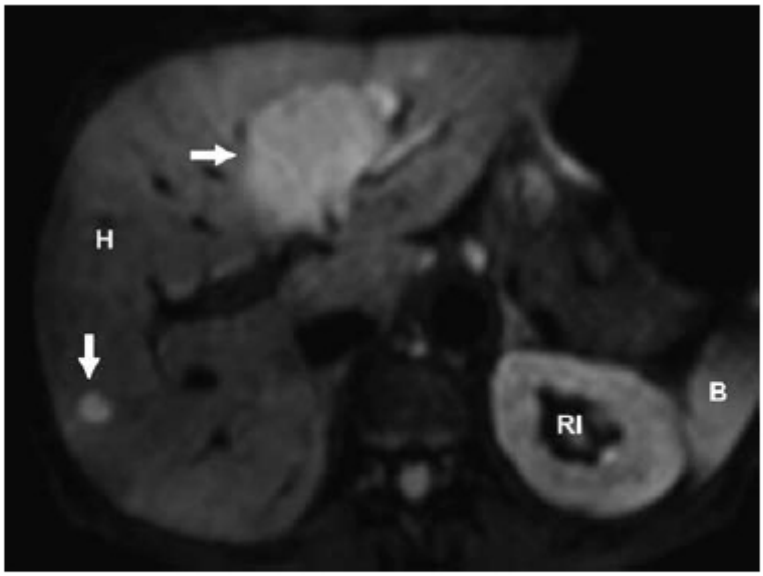

***Figure 6**. Diffusion-weighted study in patient with metastasis (Arrows). The restriction to molecular motion is slightly higher (lower ADC) than in benign lesions. H: liver, B: spleen, RI: left kidney.*

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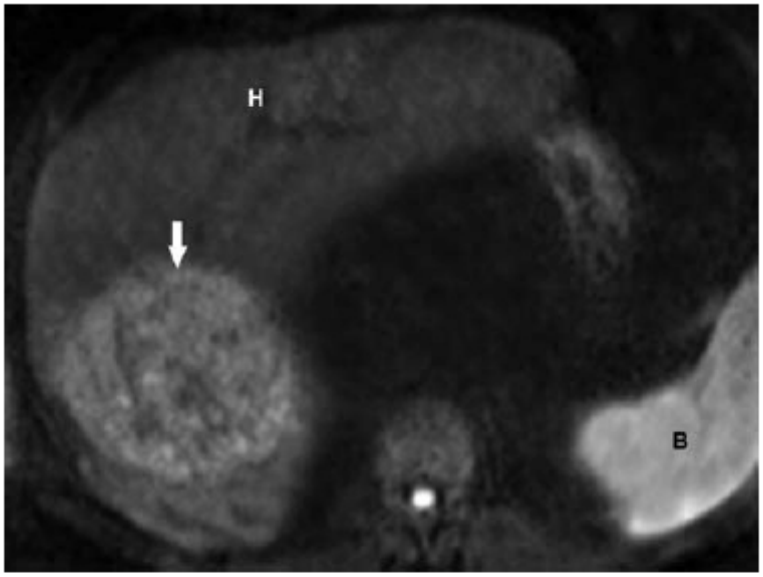

Figure 7. *Patient with HCC. Like Figure 5, the increased cellularity of the lesion restricts molecular motion, i.e. reduces ADC. H: liver, B: spleen.*

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