Clinical Imaging 39 (2015) 278–284

Contents lists available at ScienceDirect

Clinical Imaging

journal homepage: http://www.clinicalimaging.org

Assessment of diffusion-weighted imaging for characterizing focal liver lesions

Arman Parsai [a,*], Imene Zerizer [b], Oran Roche [a], Panos Gkoutzios [c], Marc E. Miquel [a]

[a] Barts Health NHS Trust
[b] Royal Marsden NHS Trust
[c] Guy's and St Thomas NHS Trust

ARTICLE INFO

Article history:
Received 29 January 2014
Received in revised form 31 August 2014
Accepted 19 September 2014

Keywords:
Diffusion-weighted imaging (DWI)
Focal liver lesions
MRI
Malignant
Benign

ABSTRACT

In 150 patients, 153 hepatic lesions (39 metastases, 27 hemangiomas, 26 hepatocellular carcinomas, 25 cysts, 15 adenomas, 8 focal nodular hyperplasias, 5 abscesses, 4 hamartomas, and 4 cholangiocarcinomas) were evaluated during a 24-month period. Apparent diffusion coefficient (ADC) values of benign lesions (1.994×10^{-3}mm^2 s^{-1}) were significantly higher than ADC values of malignant lesions (1.070×10^{-3}mm^2 s^{-1}). Mean ADC value for solid benign lesions (1.143×10^{-3}mm^2 s$^{-1}\pm0.214\times10^{-3}$mm^2 s^{-1}) was not significantly different from malignant lesions. ADC values did not allow differentiating malignant from benign solid lesions (area under the curve=0.61). ADC cutoff value threshold of 1.6×10^{-3}mm^2 s^{-1} yielded higher accuracy for differentiating benign from malignant lesions.

1. Introduction

Accurate detection and characterization of focal liver lesions is important for treatment planning and patients' management. This is especially true for patients with background liver cirrhosis in whom early detection and treatment of hepatocellular carcinoma (HCC) will modify management and increase survival. Currently, ultrasound (US) and computed tomography (CT) scan in conjunction with magnetic resonance imaging (MRI) with gadolinium or small particulate iron oxides are used to better detect and characterize focal liver lesions. More recently, diffusion-weighted imaging (DWI) has been reported to be useful for the detection and characterization of focal liver lesions [1–8]. DWI is a noninvasive, rapidly acquired imaging technique, which does not require the administration of intravenous gadolinium. This technique is related to the molecular mobility of water molecules (Brownian motion) and reflects different tissue properties such as cellularity, viscosity, and the extracellular space [9–15]. It can therefore provide information independent of the T1 or T2 relaxation times of the tissue via the apparent diffusion coefficient (ADC) measurement. Malignant tumors have lower ADC values due to a combination of higher cellularity, tissue disorganization, and increased extracellular space tortuosity, all contributing to reduced motion of water [16]. Due to short scanning times, DWI can be easily added to standard MRI sequences and can therefore provide functional information for assessing liver pathology. However, only a limited number of studies have evaluated the value of ADC to characterize and differentiate malignant from benign focal liver lesions [3,4]. The results are conflicting with some studies finding statistically significant differences in ADC between malignant and benign lesions while others dismiss the use of DWI due to significant overlap of ADC values. The purpose of this study is to (1) compare ADC values for benign and malignant hepatic lesions in a large cohort with a wide variety of focal liver lesions and (2) to determine the cutoff ADC value with the highest sensitivity and specificity for differentiating benign from malignant lesions.

2. Material and methods

2.1. Study population

We retrospectively reviewed liver MRI imaging with DWI performed in 224 patients with liver lesions during a 24-month period (from July 2010 to July 2012). These lesions were detected on either US or CT scan and referred subsequently to MRI for further characterization. Only a small proportion of patients ($n=19$) were referred from hepatitis B/C screening programs after the screening US scan detected a lesion. All the images were reviewed on the institutional picture archiving and communication system. A waiver consent form was obtained in all patients. Of these, 74 were excluded from the study. Exclusion criteria were lesions less than 1cm in diameter, suboptimal DWI/ADC images, and prior chemotherapy treatment, which could have altered imaging characteristics of the lesions and patients without definitive diagnosis.

The diagnosis of all hepatic lesions was confirmed histopathologically ($n=39$) (resection or biopsy), using typical MRI characteristics ($n=93$) or follow-up imaging over at least 6months time (CT, US, or MRI)

* Corresponding author. Barts Health NHS Trust, Whitechapel Road, Whitechapel, London, E1 1BB, United Kingdom.
E-mail address: armanparsai@hotmail.com (A. Parsai).

http://dx.doi.org/10.1016/j.clinimag.2014.09.016
0899-7071/

(n=21). Of the 150 patients included in the study, 74 were female and 76 male; mean age was 52years (range, 27–77years old).

2.2. Magnetic resonance imaging

Scans were performed on a 1.5-T Achieva system (Philips Healthcare, Best, The Netherlands) in conjunction with an 8-element body coil array.

Our institutional abdominal MRI protocol for imaging the liver included coronal T2-weighted turbo spin-echo (TSE), axial T2-weighted TSE with fat suppression (SPAIR), diffusion-weighted images, T1-weighted in and opposed phase, and unenhanced and dynamic gadolinium-enhanced breathhold T1-weighted images (THRIVE).

Diffusion images were obtained using a free-breathing multislice spin-echo echo-planar imaging (EPI) sequence: repetition time, 5300–5800ms; echo time, 62ms; EPI factor, 60; three averages; field of view (FOV), 400–450mm; rectangular FOV, 75%; matrix, 112×256; 20–28 slices in order to cover the liver; slice thickness, 5mm; slice gap, 1mm. Six motion probing gradients with b-values of 0, 100, 200, 500, 750, and 1000s mm^{-2} were applied in three orthogonal directions and trace images were synthesized for each b-value using the mean of three orthogonal directions. ADC maps were calculated on a pixel-by-pixel basis using a monoexponential fit, and b=0 was excluded from the calculation in order to eliminate perfusion effects.

2.3. ADC measurements

Two experienced hepatobiliary radiologists reviewed all the MRI images independently (8 and 10years of experience). Both were blinded to the clinical history, pathological results, MRI reports, and reports of other imaging studies. Lesions were assigned to the following types: HCC, metastases, cholangiocarcinoma, adenoma, cysts, focal nodular hyperplasia (FNH), hemangiomas, hamartomas, and abscess. Most benign and malignant lesions with typical imaging characteristics or increase in size on follow-up were not biopsied. However, histopathological confirmation was warranted in 12 HCCs, 4 cholangiocarcinomas, 20 metastases, 1 hamartoma, and 2 hemangiomas. For lesion analysis, these were grouped into the following classes: "malignant—all" (HCC, metastasis, cholangiocarcinoma), "benign—all" (adenoma, cyst, FNH, hemangioma, hamartoma, and abscess), "benign—solid" (adenoma, FNH), and "begin—cystic" (hemangioma, liver cyst, hamartoma, and abscess). The ADC values were measured on the ADC maps created by DWI. ADC maps were calculated on a pixel-by-pixel basis using a monoexponential fit, and b=0 was excluded from the calculation in order to eliminate perfusion effects. The mean ADC value for each lesion was measured by drawing a region of interest (ROI) (minimum diameter=1cm) on the focal liver lesion. If the lesion was heterogeneous, the ROI was made as large as possible to be representative of the whole lesion. In patients with multiple lesions of different types, each lesion was assessed independently. In cases with multiple lesions of the same type, ADC values were assessed on the two largest most representative lesions.

2.4. Statistical analysis

Interobserver and intraobserver agreement was calculated for the entire cohort using a one-way analysis of variance. Mean and median ADC values for each liver lesion type were determined. Mean ADC values were compared between malignant and nonmalignant lesions, malignant and benign solid lesions (adenomas, FNH), as well as malignant and benign cystic lesions (cysts, hemangiomas, hamartomas, and abscesses) using a Student's t test. The mean ADC value of benign solid lesions and benign cystic lesions was also compared. Significant difference was considered at a level of P<.05.

The accuracy of using the ADC value to differentiate the different subgroups of focal liver lesions was assessed using a receiver operating characteristic (ROC) curve. ROC curve was fitted to differentiate malignant compared to benign lesions, solid lesions versus cystic lesions, malignant compared to solid benign lesions, and malignant compared to cystic lesions. A threshold cutoff value to differentiate malignant lesions from benign lesions was then derived.

3. Results

3.1. Lesion types

A total of 153 lesions were reviewed in this study in 150 patients, with 84 found to be benign and 69 found to be malignant. Details of the type and number of lesions found are summarized in Table 1. Out of the 84 benign lesions, 23 were solid lesions (FNH and adenoma) and 61 were cystic (hemangioma, liver cyst, hamartoma, abscess). The mean and median lesion size was 1.5cm (range, 1–10cm) and 2.5cm, respectively. A box-and-whisker plot of the lesion sizes for the different groups is given in Fig. 1. The number of patients with these lesions was as follows: cyst (n=18), hamartoma (n=4), hemangiomas (n=16), abscess (n=5), FNH (n=7), adenoma (n=12), cholangiocarcinoma (n=4), HCC (n=19), and metastases (n=23). Metastases were found in 23 patients with the following primaries: colorectal (n=13), breast (n=3), gynecological (n=2), melanoma (n=1), and lung (n=5). One patient had 2 primaries (colorectal and lung cancer).

Multiple liver lesions were found in 29 out of the 150 patients in the study; among these, 18 had more than one type of lesion and 11 had several lesions of the same type. An example of a patient with a hemangioma, a cyst, and liver metastasis is given in Figs. 2–4.

3.2. ADC measurements

There was an excellent agreement between the two readers with an intraclass correlation of 0.98 for intraobserver and 0.97 for interobserver. There was no significant difference between ADC values for the two readers (P=.37 for a paired t test). Both readers detected the same number of lesions and the measurements were made in 96% of cases on the same slice on the ADC map and in 4% in an adjacent slice.

The mean ADC values of the different liver lesions in our cohort are summarized in Table 2 and are comparable with other published data [1,4,8,17–20]. The box-and-whisker plots of the ADC values of individual lesion types are shown in Fig. 5 and by groups of lesions in Fig. 6.

The ADC values of benign hepatic lesions ($1.994\times10^{-3}mm^2\ s^{-1}\pm0.63810^{-3}\times10^{-3}mm^2\ s^{-1}$) were significantly higher than the ADC values of malignant hepatic lesions ($1.070\times10^{-3}mm^2\ s^{-1}\pm0.237\times10^{-3}mm^2\ s^{-1}$) ($P$<.0001, CI [$-0.923\times10^{-3}$, -0.585×10^{-3}]) [confidence interval (CI)]. The mean ADC value of benign cystic liver lesions ($2.080\times10^{-3}mm^2\ s^{-1}\pm0.605\times10^{-3}mm^2\ s^{-1}$) was significantly higher compared to malignant liver lesions (P<.0001, CI [-1.167×10^{-3}, 0.854×10^{-3}]). In addition, the mean ADC value for cysts (P<.0001, CI [-923×10^{-3}, -585×10^{-3}]), hamartomas (P<.0001, CI [-1.165×10^{-3}, -0.684×10^{-3}]), abscesses (P<.001, CI [-0.883×10^{-3}, -0.443×10^{-3}]), and hemangiomas (P<.0001, CI [-0.670×10^{-3}, -0.430×10^{-3}]) was significantly higher than malignant lesions.

Table 1
ADC values by lesion type

Lesion type	Mean ADC ($10^{-3}mm^2\ s^{-1}$)	Standard deviation ($10^{-3}mm^2\ s^{-1}$)	Sample size (n)
HCC	1.07	0.25	26
Adenoma	1.12	0.19	15
Cyst	2.66	0.41	25
Metastases	1.04	0.20	39
FNH	1.19	0.25	8
Hemangioma	1.62	0.33	27
Cholangiocarcinoma	1.43	0.15	4
Hamartoma	1.99	0.13	4
Abscess	1.73	0.26	5