The detection and discrimination of malignant and benign focal hepatic lesions: T_2 weighted vs diffusion-weighted MRI

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Objective: The purpose of this study was to evaluate the use of diffusion-weighted imaging (DWI) for the detection and characterisation of focal hepatic lesions compared with the use of T_2 weighted imaging.

Method: 45 patients with 97 hepatic lesions (51 malignant lesions and 46 benign lesions) were included in this retrospective study. Malignant hepatic lesions included 12 hepatocellular carcinomas, 26 metastases and 13 intrahepatic cholangiocarcinomas. Benign hepatic lesions included 19 haemangiomas and 27 cysts. The MRI protocol for the upper abdomen included T_2 weighted images, in- and opposed-phase T_1 weighted images and dynamic T_1 weighted images. Breath-hold fat-suppressed single-shot echo planar DWI was performed with the following parameters: 1338/66; b factors, 0, 50 and 800 s mm⁻². Two independent observers reviewed the T_2 weighted images and the DWI to detect and to characterise the hepatic lesions.

Results: For detection of malignant hepatic lesions, the use of DWI showed a significantly higher detection rate than the use of T_2 weighted images ($p < 0.05$). However, there was no significant difference between the use of DWI and T_2 weighted images for benign hepatic lesions. For the differentiation between malignant and benign hepatic lesions, there was no significant difference in sensitivity, specificity and accuracy between the use of T_2 weighted images and the use of DWI.

Conclusion: The use of DWI was better for the detection of malignant hepatic lesions than the use of T_2 weighted images. However, for detection of benign hepatic lesions and characterisation of hepatic lesions, the use of DWI was equivalent to the use of T_2 weighted images.

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Accurate detection and characterisation of focal hepatic lesions is important for treatment planning in patients with hepatic tumours. For the detection and characterisation of hepatic lesions, CT and MRI are usually employed [1, 2]. MRI, T_1 weighted, T_2 weighted and gadolinium-enhanced T_1 weighted imaging have been commonly utilised [3, 4].

With rapid progress of the use of parallel imaging techniques such as sensitivity encoding (SENSE), the quality of diffusion weighted single-shot echo-planar imaging has improved [5]. Diffusion-weighted MRI of the abdomen has become possible by the use of this technique, which reduces acquisition time, minimises echo-planar imaging artefacts and improves the quality of images [5].

Several studies have characterised focal hepatic lesions by measurement of the lesion apparent diffusion coefficient (ADC) [6–11] and have evaluated detection of focal hepatic lesion by use of diffusion-weighted imaging (DWI) [12–16]. 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 [6–11]. Furthermore, a limited number

of studies have been performed using DWI for the detection of hepatic lesions [12–16].

The purpose of this study was to evaluate the use of DWI for the detection and characterisation of focal hepatic lesions compared with the use of T_2 weighted imaging.

Methods and materials

Patients

Our institutional review board approved this retrospective study and waived informed patient consent. We performed a review of clinical records of abdominal MRI examinations from 1 January 2008 to 30 August 2008 that demonstrated the presence of focal hepatic lesions. The criteria for inclusion in the study were pathological, radiological and/or clinical confirmation of the nature of the lesions, the presence of a focal hepatic lesion ≥ 5 mm and the availability of both T_2 weighted images and diffusion-weighted images. The retrospective analysis included 45 patients (age range, 31–75 years; mean age 56 years; 15 women, 30 men). A total of 51 malignant lesions were diagnosed in 18 patients (12 hepatocellular carcinomas (HCCs) in 9 patients, 26 metastases in 7 patients and 13 intrahepatic cholangiocarcinomas in 2 patients).

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Liver metastases arose from a gastric carcinoma (two patients), pancreatic carcinoma (two patients), colon carcinoma (one patient), gall bladder carcinoma (one patient) and a cervix carcinoma (one patient). 27 patients had benign lesions, including haemangioma ($n=19$) and cyst ($n=22$). 4 of the 18 patients with malignant hepatic lesions had 5 coexistent cysts. Therefore, a total of 46 benign lesions were diagnosed (19 haemangiomas and 27 cysts) (Figure 1).

A diagnosis of an HCC was based on the histopathological findings of the lesions after surgery (two patients) or typical clinical, laboratory (an elevated α -fetoprotein level >400 ng ml $^{-1}$) and imaging findings (seven patients). In seven patients with metastases, diagnoses were based on the histopathological findings of the primary tumours with lesion growth on serial cross-sectional radiological images obtained over a period of 6 months or less ($n=7$). Two patients with intrahepatic cholangiocarcinomas were confirmed by histopathological findings after a percutaneous biopsy. Diagnosis of haemangiomas was established with a classic contrast enhancement pattern at MRI and/or CT (peripheral nodular enhancement at the early phase and persistent enhancement with fill-in at the delayed phase) (15 patients), and homogeneous enhancement at early and delayed-phase contrast-enhanced MR and/or CT with no change in the size of the lesions for 6 months or more at serial CT (2 patients). Diagnosis of cysts were made by means of no enhancement at contrast-enhanced MR and/or CT and characteristic appearance (echo-free) at sonography (15 patients; 4 patients with malignant lesions and 3 patients with haemangiomas), and no enhancement at contrast-enhanced MR and/or CT with unchanged imaging findings at least 6 months later (2 patients).

One of the investigators without knowledge of the clinical findings performed all of the measurements. The diameter of the lesions ranged from 0.5 cm to 5.5 cm (mean 1.6 cm). The diameter of the malignant lesions ranged from 0.5 cm to 5.5 cm (mean 1.76 cm) and the diameter of the benign lesions ranged from 0.5 cm to 4.6 cm (mean 1.44 cm).

MRI techniques

MRI was performed with a 1.5 Tesla system (Achieva; Philips Medical Systems, Best, the Netherlands) and a SENSE body coil. All patients were examined initially with a routine MRI protocol for the upper abdomen that included T_2 weighted images, in- and opposed-phase T_1 weighted images and dynamic T_1 weighted images. Subsequently, diffusion-weighted images were obtained.

Breath-hold, fat-suppressed T_2 weighted fast spin-echo (SE) MRI was performed with the following parameters: repetition time ms/echo time ms, 441/90; matrix, 256×183 ; field of view, 36×28 cm; acquisition of two signals; section thickness, 6 mm; section gap, 1 mm. Dual-echo T_1 weighted fast field-echo (FFE) MRI was performed with the following parameters: 187/2.3 (opposed phase), 4.6 (in phase); flip angle, 80° ; matrix, 256×256 ; field of view, 36×28 cm; acquisition of one signal; section thickness, 6 mm; section gap, 1 mm. Dynamic T_1 weighted MRI was obtained by using a spoiled gradient-echo sequence (T_1 weighted high-resolution isotropic volume examination, THRIVE) before and after injection of gadopentetate dimeglumine (Magnevist, Schering, Berlin, Germany) at a dose of 0.1 mmol per kilogram of body weight followed by a 20 ml saline flush with a power injector. Arterial (10 s), portal (40 s) and delayed (2 min) phases of images were obtained. Acquisition parameters were as follows: 4.8/2.4; flip angle, 15° ; matrix, 352×256 ; field of view, 36×28 cm; acquisition of two signals; section thickness, 6 mm; no section gap.

Breath-hold fat-suppressed single-shot echo planar DWI was performed prior to performing dynamic T_1 weighted imaging with the following parameters: 1338/66; b factors, 0, 50 and 800 s mm $^{-2}$; matrix, 112×88 ; field of view, 36×28 cm; acquisition of two signals; section thickness, 6 mm; section gap, 1 mm; receiver bandwidth, 2627 Hz; transverse plane with three directional diffusion gradients; SENSE parallel imaging factor, 2; acquisition time, less than 25 s for breath-hold acquisition.

Figure 1. Flow diagram of the study group. HCC, hepatocellular carcinoma; pts, patients. Asterisk: three patients had malignant and benign lesions.

Table 1. Detection rate of focal hepatic lesions with T_2 weighted imaging and diffusion weighted (DW) imaging

Image	All lesions (n=97) (%)			Malignant lesions (n=51) (%)			Benign lesions (n=46) (%)		
	Observer 1	Observer 2	Mean	Observer 1	Observer 2	Mean	Observer 1	Observer 2	Mean
T_2	79.4	75.3	77.3	62.7	54.9	58.8	97.8	95.7	96.7
DW	91.8	87.6	89.7	86.3	80.4	83.3	97.8	95.7	96.7
p-value	0.023	0.041	0.032	0.012	0.011	0.009	>0.05	>0.05	>0.05

Image analysis

Analysis of all MR images was performed with a picture archiving and communications system (PACS) workstation monitor. Two experienced radiologists, with more than 5 years of experience in the practice and interpretation of abdominal MR, evaluated all of the MR images independently. The observers were blinded to the pathological results and clinical MRI reports.

Images were reviewed to determine if differences in lesion detection were seen between the T_2 weighted images and DWI using a b-value of 0 s mm^{-2} and 50 s mm^{-2} . Each reader indicated with arrows the presence of detected lesions and saved the digital images on the workstation. We recorded detected lesions on a data sheet on which lesion location, lesion size and image number were noted. T_2 weighted images and DWI were randomly analysed in two different sessions separated by at least 4 weeks to minimise recalling bias.

4 weeks later, images were reviewed to determine if differences in lesion characterisation were seen on T_2 weighted images and DWI using a b-value of 0 s mm^{-2} and 800 s mm^{-2} . Two observers reviewed the T_2 weighted images using a five-point scale (a score of 1 indicated a definitely benign lesion; a score of 2 indicated a probable benign lesion; a score of 3 indicated an indeterminate lesion; a score of 4 indicated a probably malignant lesion; a score of 5 indicated a definitely malignant lesion). Next, two observers reviewed the DWI using the same five-point scale. As seen on T_2 weighted images, if the lesion had a sharp margin and a round shape and was homogeneously hyperintense, it was considered as benign. If the lesion had an indistinct margin and an irregular shape and was slightly hyperintense as seen on T_2 weighted images, it was considered as malignant. On DWI, if the lesion was hyperintense on $b=0 \text{ s mm}^{-2}$ images and showed decreased signal intensity or a decreased size of the lesion on $b=800 \text{ s mm}^{-2}$ images, it was considered as benign. If the lesion had the same or increased signal intensity or an increased size on $b=800 \text{ s mm}^{-2}$ images rather than on $b=0 \text{ s mm}^{-2}$ images, it was considered as malignant. To reduce recall bias, the two observers had a 4 week interval for analysing T_2 weighted images and DWI.

Confidence level ratings of the images were used to calculate the sensitivity, specificity and accuracy of an observer for the diagnosis of malignant or benign hepatic lesions. A score 1 and 2 indicated a reading for a benign lesion. Score 3 was considered an incorrect reading. Scores 4 and 5 indicated a reading for a malignant lesion. Sensitivity, specificity and accuracy were calculated as follows: sensitivity = (number of malignant lesions with correct diagnosis/number of confirmed malignant lesions) $\times 100$; specificity = (number of benign lesions with correct

diagnosis/number of confirmed benign lesions) $\times 100$; accuracy = (number of malignant and benign lesions with correct diagnosis/number of confirmed malignant and benign lesions) $\times 100$. The sensitivity, specificity and accuracy for T_2 weighted images were compared with the sensitivity, specificity and accuracy for DWI.

The standard of reference for detection and characterisation of hepatic lesions was determined based on a consensus reading of the two observers. The standard of reference included typical MRI findings including T_1 weighted images, T_2 weighted images and gadolinium enhancement images, pathological findings and relevant clinical history.

Statistical analysis

Statistical analysis was performed to compare the use of T_2 weighted images and DWI for the detection and characterisation of the hepatic lesions using the χ^2 test. Probability values less than 0.05 were considered as statistically significant. Data were analysed using a statistical software package (SPSS, version 12, Chicago, IL).

Weighted κ statistics was calculated to assess inter-observer agreement for lesion detection and characterisation. The level of agreement was defined as follows: κ values of 0.00–0.40 indicated poor agreement; κ values of 0.41–0.75 indicated good agreement; κ values of 0.76–1.00 represented excellent agreement.

Results

The detection rates of the hepatic lesions with T_2 weighted images and DWI are listed in Tables 1. For malignant hepatic lesions, Observer 1 detected 32 of 51 (62.7%) lesions on T_2 weighted images and 44 of 51 (86.3%) lesions on DWI. Observer 2 detected 28 of 51 (54.9%) lesions on T_2 weighted images and 41 of 51 (80.4%) lesions on DWI. For both observers, the use of DWI had a significantly higher detection rate for malignant hepatic lesions and all hepatic lesions than the use of T_2 weighted images ($p < 0.05$) (Figures 2 and 3).

However, for the detection of benign hepatic lesions, there was no significant difference between the use of T_2 weighted images (Observer 1, 45 of 46 (97.8%) lesions; Observer 2, 44 of 46 (95.7%) lesions) and DWI (Observer 1, 45 of 46 (97.8%) lesions; Observer 2, 44 of 46 (95.7%) lesions) ($p > 0.05$).

On T_2 weighted images, 19 malignant lesions (2 hepatocellular carcinomas, 11 metastases and 6 cholangiocarcinomas) and 1 benign lesion (haemangioma) were not detected by Observer 1 and 23 malignant lesions (3 hepatocellular carcinomas, 14 metastases and 6 cholangiocarcinomas) and 2 benign lesions (2 haemangiomas) were

Figure 2. A 52-year-old man with hepatic metastases from a stomach cancer. (a, b) T_2 weighted image and diffusion-weighted image obtained at $b=50 \text{ s mm}^{-2}$ show a hyperintense mass (arrow) in the left hepatic lobe (segment IV). (c), On T_1 weighted post-contrast image (c), the mass is hypovascular. A diffusion-weighted image (B) and T_1 weighted post-contrast image (C) show two additional small lesions (thin arrows) in the right hepatic lobe (segment VIII) that are not seen on a T_2 weighted image.

not detected by Observer 2. On DWI, 7 malignant lesions (1 hepatocellular carcinoma, 2 metastases and 4 cholangiocarcinomas) were not detected by Observer 1 and 10

malignant lesions (2 hepatocellular carcinomas, 4 metastases and 4 cholangiocarcinomas) and 4 benign lesions (2 haemangiomas) were not detected by Observer 2.

Figure 3. A 65-year-old man with hepatic metastases from a stomach cancer. (a) Diffusion-weighted image obtained at $b=50 \text{ s mm}^{-2}$ shows a hyperintense mass (arrow) in the right hepatic lobe. (b) On T_1 weighted post-contrast image, the mass is hypovascular. However, the mass is not seen on a T_2 weighted image (c).

Table 2. Differentiation of malignant hepatic lesions and benign hepatic lesions on T_2 weighted imaging and diffusions weighted (DW) imaging

Image	Observer 1		Observer 2		Mean	
T_2						
Sensitivity	95.7	(85.2–99.5)	97.8	(88.5–99.9)	96.7	(90.8–99.3)
Specificity	82.2	(68–92)	88.9	(76–96.3)	85.6	(76.6–92.1)
Accuracy	89.0		93.4		91.2	
DW						
Sensitivity	95.7	(85.2–99.5)	97.8	(88.5–99.9)	96.7	(90.8–99.3)
Specificity	88.9	(76–96.3)	86.7	(73.2–95)	87.8	(79.2–93.7)
Accuracy	92.3		89.0		90.7	

Data in parentheses are 95% confidence intervals.

On T_2 weighted images, four false-positive interpretations were recorded by Observer 1 and five false-positive interpretations were recorded by Observer 2. On DWI, four false-positive interpretations were recorded by Observer 1 and six false-positive interpretations were recorded by Observer 2. On T_2 weighted images, all pseudolesions were attributed to vessels ($n=6$), artefacts ($n=3$) and partial volume effect from colon ($n=1$).

The sensitivity, specificity and accuracy for the differentiation of malignant and benign hepatic lesions on T_2 weighted images and DWI are listed in Tables 2. The mean sensitivity, specificity and accuracy for the two observers were 96.7%, 85.6% and 91.2%, respectively, for the use of T_2 weighted images; the corresponding values were 96.7%, 87.8% and 90.7%, respectively, for the use of DWI. There was no significant difference in the sensitivity, specificity and accuracy between the results

obtained with the use of T_2 weighted images and DWI ($p>0.05$) (Figures 4 and 5).

Weighted κ values indicated excellent agreement between the two observers for detection of focal hepatic lesions on T_2 weighted images ($\kappa=0.856$). The weighted κ values indicated good agreement between the two observers for the detection of focal hepatic lesions on DWI ($\kappa=0.667$) and for the characterisation of focal hepatic lesions on T_2 weighted images ($\kappa=0.456$) and on DWI ($\kappa=0.691$).

Discussion

In this study, the use of DWI with small b-values (0 s mm^{-2} and 50 s mm^{-2}) had a high detection rate for malignant hepatic lesions compared with the use of T_2 weighted images. This finding was similar to findings

Figure 4. A 62-year-old man with a hepatocellular carcinoma. (a) T_2 weighted image shows a slightly hyperintense mass (arrow) in the left hepatic lobe (segment IV). (b, c) Although the centre of the lesion shows greater signal attenuation compared with the peripheral portion on the high b-value image ($b=800 \text{ s mm}^{-2}$), this mass is diagnosed as a malignant mass because the signal intensity of the peripheral portion of the mass (arrow) prominently increases for the image obtained at $b=800 \text{ s mm}^{-2}$ rather than for the image obtained at $b=0 \text{ s mm}^{-2}$. (d) On T_1 weighted post-contrast image, the mass (arrow) is hypervascular.

Figure 5. A 49-year-old man with a hepatic haemangioma and hepatic cyst. (a) T_2 weighted image shows a slightly hyperintense mass (thin arrow) in the right hepatic lobe (segment VII) and shows a hyperintense mass (arrow) in the left hepatic lobe (segment IV). As seen on diffusion weighted images obtained at $b=0 \text{ s mm}^{-2}$ (b) and obtained at $b=800 \text{ s mm}^{-2}$ (c) the signal intensity of the masses (arrow) prominently decrease for the image obtained at $b=800 \text{ s mm}^{-2}$ rather than for the image obtained at $b=0 \text{ s mm}^{-2}$. (d) On T_1 weighted post-contrast image, the right hepatic mass (thin arrow, haemangioma) is homogeneously enhanced and the left hepatic mass (arrow, cyst) is not enhanced.

of previous studies [11, 15, 16]. The reason for a high detection rate of focal hepatic lesions on DWI is attributed to the better contrast-to-noise ratio and better lesion conspicuity by suppression of background vessels [15]. Furthermore, the solid tumours tended to appear larger on DWI than on T_2 weighted images [5]. This phenomenon may contribute to the high detection rate of small solid tumours on DWI [5, 15].

Although the use of T_2 weighted images is helpful for the detection of the focal hepatic lesions [17, 18], lesion detectability is suppressed by low lesion-to-liver contrast and the interfering high signal intensity from intrahepatic vessels [16]. Intrahepatic vessels may be seen as false-positive lesions on T_2 weighted images.

However, there was no difference determined between the use of T_2 weighted images and DWI for the detection of benign hepatic lesions in our study. This result was different from a previous study [15]. In our study, 44.5 of 46 (96.7%) benign hepatic lesions were detected on both T_2 weighted images and DWI. However, in a study by Parikh et al [15] 83.3% of benign hepatic lesions were detected on T_2 weighted images and 90% of benign hepatic lesions were detected on DWI. We think that this difference is due to a different lesion distribution between the two studies. All of the benign lesions in our study were cystic lesions including haemangiomas and cysts. Conversely, benign hepatic lesions in the study by Parikh et al [15] were composed of both solid and cystic lesions including haemangiomas, cysts, adenomas, liver abscesses, focal nodular hyperplasia and intrahepatic haematomas. Haemangiomas and cysts are

usually detected on T_2 weighted images [19]. However, a small benign solid tumour might not be detected on T_2 weighted images because of less conspicuity of the solid lesions by the magnetisation transfer effect [19].

DWI can aid in the characterisation of focal hepatic lesions by measurement of the lesion ADC [6–11]. Malignant hepatic lesions have demonstrated a significantly lower ADC than benign hepatic lesions, but the ADC of some individual lesions such as a metastasis and a haemangioma may have overlap [11]. In our study, for the differentiation of benign and malignant hepatic lesions on DWI, we evaluated the signal intensity change between DWI using a b-value of 0 s mm^{-2} and a high b-value (800 s mm^{-2}). With high b-value DWI, although a suboptimal signal-to-noise ratio and artefacts may hinder detection of the focal hepatic lesions, it facilitates differentiation of metastatic lesions from haemangiomas and cysts: metastatic lesions show high signal intensity because of restricted diffusion of extracellular water molecules. In contrast, cystic lesions such as haemangiomas and cysts show decreased signal intensity at increasing b-values owing to a high fluid content [16]. In our study, malignant lesions such as hepatocellular carcinomas and metastases showed less signal attenuation on DWI using a high b-value (800 s mm^{-2}) rather than a b-value of 0 s mm^{-2} . Conversely, benign lesions including haemangiomas and cysts showed less signal intensity on DWI using a high b-value (800 s mm^{-2}) than a b-value of 0 s mm^{-2} .

In our study, the overall accuracy for the differentiation between malignant and benign hepatic lesions was 91%

on T_2 weighted images and 90.7% on DWI. For both observers, there was no significant difference in sensitivity, specificity and accuracy between the use of T_2 weighted images and DWI ($p>0.05$). This finding was similar to a previously reported result [15]. Interestingly, in our study, some haemangiomas showed increased signal intensity on DWI using $b=800 \text{ s mm}^{-2}$ rather than $b=0 \text{ s mm}^{-2}$. Increased signal intensity of haemangiomas as the b -value increases is possibly due to a fibrous tissue content, which is typically seen in hyalinised haemangiomas [20]. Hyalinised haemangiomas are usually seen with only slightly high signal intensity on T_2 weighted images [20].

Although measurement of the hepatic lesion ADC is helpful for the characterisation of hepatic lesions, we obtained a good result (90.7%) for the differentiation of benign and malignant hepatic lesions by evaluation of the signal intensity change between the use of DWI with a b -value of 0 s mm^{-2} and a high b -value (800 s mm^{-2}) without measurement of the hepatic lesion ADC. Nasu et al [5] have described that the visual evaluation of signal intensity change between two sequences relies on intuitive interpretation of the ADC. The measurement of ADC values is controversial as the ADC values of different types of hepatic lesions show a broad overlap [21]. We believe that the signal intensity change between DWI using a b -value of 0 s mm^{-2} and high b -value (800 s mm^{-2}) can be used for the differentiation between malignant and benign hepatic lesions without ADC measurement. However, DWI is influenced by both T_2 relaxation time and tissue diffusivity, the ADC map is at least independent of any T_2 effects, and can help to clarify the degree of T_2 shine through, which can be substantial in some liver lesions.

A number of limitations in this study should be considered. First, the patient population was small and all of the benign lesions were cystic lesions, including haemangiomas and cysts. We did not encounter solid benign lesions such as adenomas and focal nodular hyperplasia during the study. With a large number of solid benign masses, which can mimic a malignant tumour as depicted on T_2 weighted images and DWI, the detection rate of lesions might have been lower and characterisation may have varied for the differentiation between malignant lesions and benign lesions. Second, our study had a relatively small number of lesions with pathological confirmation. However, two experienced observers carefully reviewed all of the MR sequences and follow-up cross-sectional imaging was performed, so we believe that the probability of misclassification of a lesion is low. Third, one of the problems of using qualitative signal intensity on DWI to evaluate hepatic lesions is that the perception of the degree to which a lesion is deemed to be hyperintense depends on the window and width level setting of the image display. This is set automatically on most commercial MR systems, the degree of signal attenuation with increasing b -values may differ from study to study. Fourth, we used a relatively short echo time (90 ms) T_2 weighted imaging sequence to compare DWI. For the characterisation of the hepatic lesions, it is widely acknowledged that T_2 weighted images acquired using a shorter and longer echo time (more than 160 ms) is more helpful for lesion characterisation. If we had used T_2 weighted images with

longer echo time in our study, the results might have been higher. Further studies may be necessary. Fifth, the receiver operating characteristic (ROC) curve has many advantages over single measurement of sensitivity, specificity and accuracy. However, we did not obtain the ROC curve for lesion characterisation. Finally, comparing T_2 weighted imaging (single echo time) and DWI in isolation without using any of the unenhanced MR images is a limitation of our study.

Conclusion

The use of DWI was superior for the detection of malignant hepatic lesions than the use of T_2 weighted images. Our findings indicate that the DWI may provide useful information in patients with suspected malignant hepatic lesions. However, in our populations, no significant difference was observed between DWI and T_2 weighted imaging for the detection of benign hepatic lesions, which included only cysts and haemangiomas and characterisation of hepatic lesions.

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