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RESEARCH

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Comparison of magnetic resonance elastography and diffusion-weighted imaging for differentiating benign and malignant liver lesions

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Abstract

Background Imaging is a crucial diagnostic tool in focal liver lesions (FLLs) diagnosis. Without the need for an intravenous contrast agent, two such MRI methods that can distinguish between benign and malignant FLLs are diffusion-weighted imaging (DWI) and magnetic resonance elastography (MRE). The purpose of this study was to assess the utility of diffusion-weighted magnetic resonance imaging and magnetic resonance elastography in the identification and differentiation of benign and malignant hepatic focal lesions.

Methods This cross-sectional study was carried out on ninety patients (with mean age 52 years) with hepatic focal lesions (29 benign and 61 malignant). Both MRE and DWI were performed on the patients. A modified gradient-echo sequence was used for MRE, and respiratory-triggered fat-suppressed single-shot echoplanar DW imaging ($b = 0.800$) was used for DWI. Maps of the apparent diffusion coefficient (ADC) and stiffness were produced. Regions of interest were placed over the FLLs on stiffness and ADC maps to get FLL ADC values and mean stiffness. Receiver operating curve (ROC) analysis was used to compare the roles of MRE and DWI in the differentiation of benign and malignant FLL.

Results The ADC of FLLs and MRE stiffness exhibited strong negative correlation [(r: −0.559; $p < 0.001$)]. Compared to malignant FLLs, benign FLLs had much higher mean ADC values. However, compared to benign FLLs, malignant FLLs exhibited much greater mean stiffness. FNH has the lowest mean stiffness of all FLLs, at less than 2.22 kPa. Among FLLs, CCAs had the lowest mean ADC values and the highest mean stiffness. The results showed that the MRE and DWI cutoff values were > 4.23 and ≤ 1.43, respectively; the area under the curve (AUC) values were 0.991 and 0.894, and the sensitivity and specificity results were 96.7%, 93.1%, and 85.2%, 89.7%, respectively.

Conclusions MRE was found to be more sensitive method for identifying benign and malignant hepatic focal lesions than DWI.

Keywords Hepatic focal lesions, Benign hepatic lesion, Malignant hepatic lesion, MR elastography, Diffusion-weighted imaging

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Background

During abdominal examinations, Focal liver lesions (FLLs) are regarded as a serious issue. Globally, liver cancer ranks sixth for women and second for men in terms of cause of death [1]. A number of diagnostic imaging techniques can be used, such as computed tomography (CT), positron emission tomography (PET), magnetic resonance imaging (MRI), color Doppler, and ultrasound, and can be utilized to identify and characterize FLLs [2].

The gold standard for distinguishing benign from malignant tumors is a liver biopsy [3]. However, because of biopsy invasive nature, it is related to bleeding, pain complications, sampling error because of limited sample size, variation between inter- and intra-reader (pathologist), high cost, reluctance of the patient, heterogeneity of liver disease, and an extremely low risk of death [4].

MRI and CT depend on the proper utilization of contrast patterns and multiphasic investigations in order to assess characteristics enhancement which offer significant clues to different FLL types [5]. Nevertheless, the applying of contrast patterns can be costly, and in certain cases, it might not be appropriate for them [6].

Hepatic parenchyma stiffness can be evaluated using MRE, a low-cost noninvasive MRI-based technique, as a hepatic fibrosis indicator [7]. To image the propagation properties of mechanical waves produced by an external mechanical or pneumatic driver inside the liver, MRE employs a modified phase contrast technique [8].

Strain elastography has been shown in earlier studies to accurately differentiate between metastatic adenocarcinoma and hepatocellular carcinoma (HCC) as well as to be useful in differentiating between benign and malignant liver lesions [9, 10].

DWI is a functional imaging method that enables the qualitative and quantitative evaluation of different tissue types' diffusion properties. The importance of DWI in both oncologic and non-oncologic applications in the body has been confirmed by numerous research conducted over the last years [11, 12].

DWI provides quantitative and qualitative evaluation for both focal and diffuse hepatic parenchymal processes, which is a complement to routine liver MRI [13]. It increases the sensitivity of focal lesion detection, aids in the distinction of benign focal hepatic lesions from malignant also, enables the assessment of the response to both systemic and loco regional therapy for hepatic malignancies, including primary and secondary [14].

Few studies have examined the use of MRE for the assessment of FLLs, despite the fact that it is a reliable method for the identification and staging of liver fibrosis. Furthermore, there were not many published research that systematically compared DWI and MRE to distinguish FLLs [15].

Aim of the work

The purpose of this study was to assess the utility of diffusion-weighted magnetic resonance imaging and magnetic resonance elastography in the identification and differentiation of benign and malignant hepatic focal lesions.

Methods

This cross-sectional study was carried out on ninety patients (with mean age 52 years) with hepatic focal lesions (29 benign and 61 malignant). The study protocol was approved by the Research Review Committee of the Menoufia University Hospital, and informed consent from patients was taken before procedure from each subject.

Our study was performed from October 2020 to October 2023 at diagnostic medical imaging and intervention radiology department at National Liver Institute hospital, Menoufia University.

Inclusion criteria: patients diagnosed with single or multiple hepatic focal lesions.

Exclusion criteria: patients with cystic hepatic focal lesions, others that have contraindications to MRI machine as cardiac pacemaker, cochlear implant, aneurysm clip, deep brain stimulator and severe claustrophobia.

Some cases underwent biopsies (to verify whether metastases or HCC) and imaging, including MRI with DWI, and MRE was done for the subjects. The FLLs involved cholangiocarcinoma (CCA), hepatocellular adenoma (HCA), hemangioma (HEM), focal nodular hyperplasia (FNH), metastasis (MET), and hepatocellular carcinoma (HCC).

MRI examination

Optima MR450W GEM 1.5T Elite MRI machine (GE Healthcare, Milwaukee, WI, USA) was used to study all patients. A phased-array torso coil was used to perform liver imaging. The following procedures were performed: Conventional MRI, post-gadolinium-diethylenetriamine-penta-acetic acid (Gd-DTPA) dynamic MR imaging, DWI, and MRE. First according dynamic MRI features, assessment and identification of focal lesions were carried out then the diffusion images with ADC values and elastography image with stiffness values were examined.

MR protocol used

The pre-contrast axial T1 in-phase/out-of-phase imaging, DWI, T2 weighted, and dynamic contrast study were among the sequences included in the standard liver imaging protocol. Before starting the contrast study, DWI and MRE had been performed. Following bolus injection of 0.1 mmol/kg body weight of Gd-DTPA at a

rate of 3 ml/s, flushed with 10 ml of sterile saline solution via the antecubital vein dynamic study was carried out. The summary of parameters used in pre- and post-contrast sequences is summarized in Table 1.

Diffusion study

In order to increase cellular packing sensitivity, respiratory-triggered fat-suppressed single-shot echoplanar DW imaging was carried out in the transverse plane with tri-directional diffusion gradients using *b* values 0 and 800 s/mm^2. To improve quality of image, parallel imaging with generalized auto-calibrating partially parallel acquisition (GRAPPA) with an acceleration factor of two was performed. The other additional parameters were: matrix 128×256, 5-mm thickness, (TR/TE) = 1500–3000/91 ms, gap = 2 mm, scan time 3–4 min bandwidth = 1.5 kHz, number of excitations (NEX) = 5, matrix 256×256 with a field of view as small as possible with 52% rectangular field of view.

ADC calculation

A region of interest was drawn over each focal lesion to determine the mean ADC of each lesion. The ADC was measured twice, and the average of the two readings was calculated. The regions of interest were copied and pasted from DW images to ADC maps to assure that the same areas were examined.

MRE evaluation

A 19-cm diameter and 1.5-cm-thick cylindrical passive driver was used for MRE. It was placed over the right lower chest wall at level of right hepatic lobe, with center at xiphisternum. Via a flexible vinyl tube, a constant 60-Hz acoustic vibration was transferred from an active to a passive driver. The propagating shear waves were imaged with a modified phase contrast, gradient-echo sequence (MRE sequence) for collection of axial wave images sensitized along the through-plane direction of motion. The yielded images process indicating the waves of propagating in the liver. The dynamic MRI study was used to identify the tumors and the MRE slices drawn at hepatic FLL. MRE was done with gradient-echo sequence with breath-hold modified technique (matrix size, 95×256, with 6–10 mm slice thickness, TR/TE = 100/26 ms, bandwidth = 33 kHz, four phase offsets, NEX = 1). At the level of the FLL, four slices were obtained through the liver; if there were multiple FLLs, more slices were recommended. Two slices at least were confirmed to cut through the targeted FLL. An 11–16 s breath-hold was used to obtain each MRE slice, and the entire MRE sequence took two minutes to complete. Automatically elastograms were obtained through processing the acquired images of propagating shear waves to generate quantitative images, which showing tissue stiffness [16].

Image interpretation was carried out by two readers (an consultant radiologist with at least 15 years of experience in body imaging and experienced radiologist with more than 8 years of experience in abdomen MRI imaging). The final diagnostic and clinical data were concealed from the radiologists.

Manually round regions of interest (ROIs) were done, which measuring 15–30 mm^2 were drawn at targeted FLL on ADC map and the stiffness map at the same level. From ROIs drawn at FLL, the mean ADC values were obtained. Through MRE, two slices at least were present through the FLL. For each lesion, the values of mean ADC (10^{-3} mm2/s) and the values of mean stiffness in kilopascals (kPa) were derived and tabulated.

Table 1 Parameters used in the abdominal MRI scan protocol, TR/TE; Time of repetition/Time of Echo, FOV; field of view, ST; section thickness

Sequence	TR/TE (m s)	Matrix	FOV (mm)	ST (mm)	Others	
Cor T2 RTr Prop	2727/108	384×384	40	5		
Ax T2 RTr Prop	2857/86	320×320	40	5		
Ax T2 FS RTr Prop	4286/87	352×352	40	5		
Heavy T2 axial	1072/200	256×290	40	5		
Ax IN/Out phase	150/2.1,3.4	256×192	40	5		
Ax LAVA-Flex Multiphase		288×192	40	5	Delay time	Scan time
Ph1/Ax	06-Mar	288×192	40	5	24s	12s
Ph2/Ax	06-Mar	288×192	40	5	12s	12s
Ph3/Ax	06-Mar	288×192	40	5	25s	12s
Ph4/Ax	06-Mar	288×192	40	5	100s	12s
Axial LAVA delayed	06-Mar	288×192	40	5	5 min	

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test. A two tailed p value < 0.05 was considered statistically significant. To determine the area under curve (AUC) for diagnostic value of MRE and ADC for differentiation of benign and malignant lesions, we performed receiver operating characteristic (ROC) curve analysis. We selected sensitivity, specificity, negative predictive value, and positive predictive value for certain cutoff point according to highest sensitivity and specificity. Correlations were done using Pearson correlation coefficient.

Results

This study consisted of 90 FLLs included 61 malignant (CCA, MET and HCC) and 29 benign (FNH, HCA and HEM) FLL. We performed the final diagnoses with histopathological confirmation in 25 FLLs and with imaging characteristics features in the remaining 65 lesions (Table 2).

The values of mean ADC was significantly increased in benign FLLs than malignant FLLs (1.943 ± 0.44 vs. 1.198 ± 0.25 mm^2/s, $p = 0.000$), while the values of mean stiffness showed significantly increase in malignant FLLs than benign FLLs (9.318 ± 2.831 vs. 3.028 ± 1.01 kPa, $p = 0.000$) (Table 3).

A significant differences among lesions were observed by using one-way ANOVA analysis. The highest mean ADC among the FLLs was HEMs, which was increased than that of all malignant FLLs and of FNHs. There was a significant increase in the mean ADC of HCAs than that in all malignant tumors. There was a significant decreased in the mean ADC of FNHs than that of HEMs ($p < 0.05$). The mean ADC in all malignant tumors was significantly decreased than HCAs and HEMs. The values of mean ADC showed no difference between HEMs and HCAs or among malignant FLLs. Among all FLLs, mean stiffness was the lowest for FNH, at less than 2.22 kPa. Among the benign lesions, the highest stiffness was HCA. Also in our results, among FLLs, the lowest mean ADC values and the highest mean stiffness was CCAs. The mean stiffness was increased in HCC than MET and all benign FLLs (Table 4; Figs. 1 and 2).

The MRE and DWI were found to be effective in distinguishing benign FLLs from malignant FLLs ($p < 0.001$). MRE and DWI cutoff values were > 4.23, and ≤ 1.43, respectively; sensitivity and specificity results were 96.7%, 93.1% and 85.2%, 89.7%, and the area under the curve values were 0.991 and 0.894, respectively (Table 5; Fig. 3).

While, in comparison analysis of ROC curves showed that for differentiating malignant from benign FLLs, MRE was more diagnostic than DWI (Table 5; Fig. 3).

The ADC of FLLs and MRE stiffness exhibited strong negative correlation [(r: − 0.559;
$p < 0.001$)] (Table 6; Fig. 4).

Table 3 Mean stiffness and mean ADC of benign and malignant FLLs

	Benign group ($n = 29$)	Malignant group ($n = 61$)	p value
Mean stiffness (kPa)			
Mean ± SD	3.028 ± 1.01	9.318 ± 2.831	0.000
Range	1.87 – 5.7	4.1–16.23	
Mean ADC			
Mean ± SD	1.943 ± 0.44	1.198 ± 0.25	0.000
Range	0.95–2.51	0.85–2.1	

FLLs, focal liver lesions; Mean ADC, mean apparent diffusion coefficient

Table 2 Final diagnosis of FLLs

Lesion types	*n*	Histology	Imaging features (MRI)
HEM	21	0	21
HCA	3	1	2
FNH	5	3	2
HCC	32	3	29
CCA	14	7	7
MET	15	11	4
Total	90	25	65

FLLs, focal liver lesions; HCA, hepatocellular adenoma; HEM, hemangiomas; HCC, hepatocellular carcinoma; FNH, focal nodular hyperplasia; MET, metastases; CCA, cholangiocarcinoma

Table 4 Values of stiffness (kPa) and mean apparent diffusion coefficient (ADC) of different hepatic focal lesions

FLL	Number	DWI ADC ($\times 10^{-3}$ mm^2/s) Mean ± SD	MRE Stiffness (kPa) Mean ± SD
HEM	21	2.194 ± .21	3.088 ± .84
HCA	3	2.047 ± .26	3.217 ± .75
FNH	5	1.556 ± .23	2.224 ± .44
HCC	32	1.139 ± .18	9.017 ± 1.96
CCA	14	1.073 ± .15	12.557 ± 2.29
MET	15	1.193 ± .17	8.105 ± 2.08

FLLs, focal liver lesions; HCA, hepatocellular adenoma; HEM, hemangioma; HCC, hepatocellular carcinoma; FNH, focal nodular hyperplasia; MET, metastases; CCA, cholangiocarcinoma

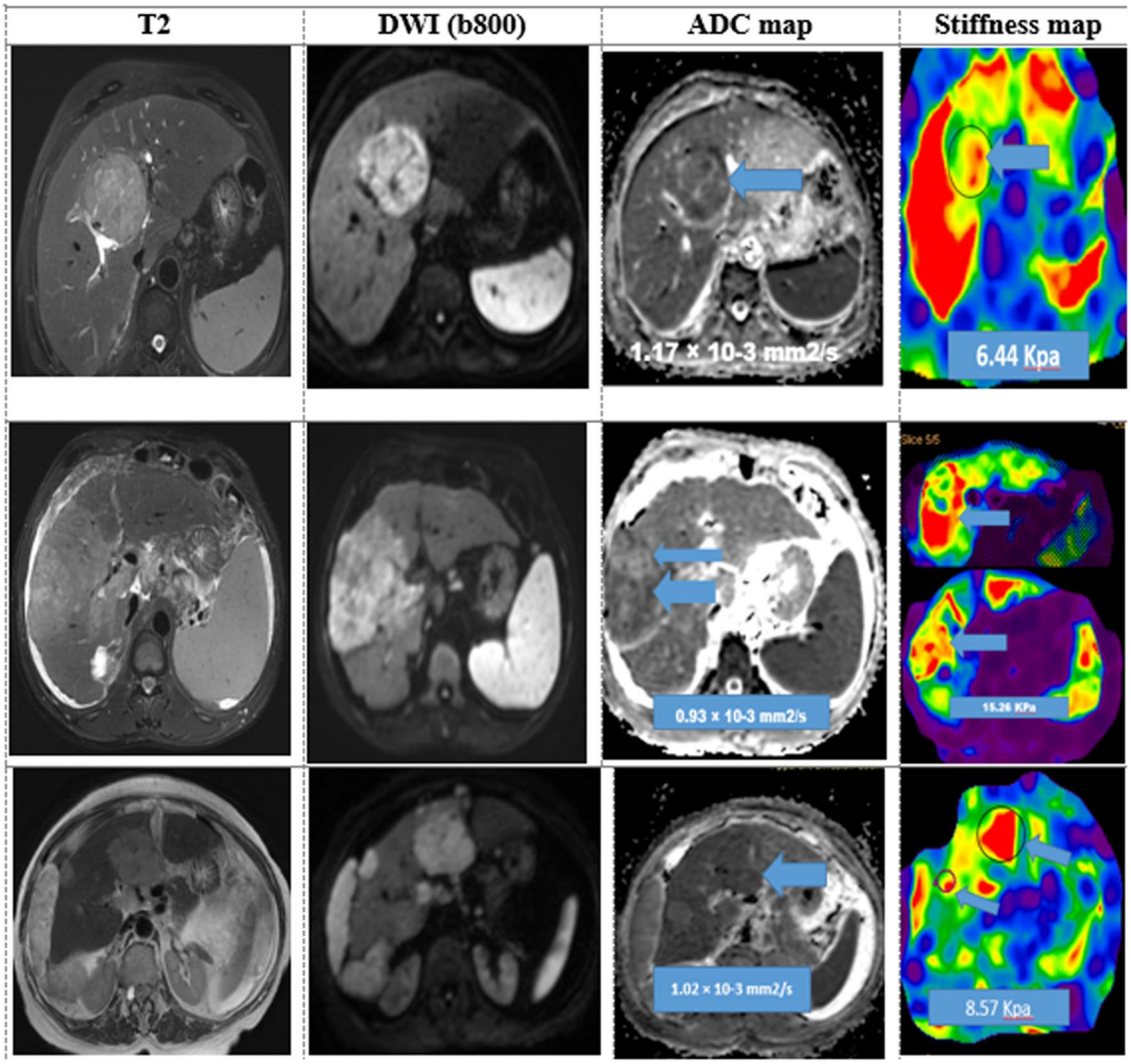

Fig. 1 DWI and MRE of malignant hepatic focal lesions. The top row was hepatocellular carcinoma (HCC), the second was cholangiocarcinoma, the third was metastatic cancer colon, first column was T2-WI images, second was DWI, third its corresponding ADC map and finally was MRE stiffness map. The mean values of focal lesions are represented numerically by the ADC and stiffness maps, (ADC 10^{-3} mm^2/s) and stiffness (kPa) values of the lesions. Arrows shown values of ADC and stiffness maps of each lesion

Discussion

Liver focal lesions are a frequently occurring accidental finding. With viral hepatitis being so common in Egypt, focal lesions may be benign or malignant, posing a diagnostic challenge [17]. To guarantee the best and most efficient treatment of hepatic focal lesions, an early diagnosis is necessary. Currently, depending on ultrasonography and computed tomography guidelines; Nowadays, by using a radiation-free technique and a safe contrast agent profile, MR is crucial to the liver lesions management (Matos et al.) [18].

In addition to being dependent on tissue cellularity, organization, and cell membrane integrity, diffusion imaging has been proven to be helpful for noninvasively assessing hepatic fibrosis.

MRE, a phase contrast-based magnetic resonance imaging technique, is a promising method for determining the stage of hepatic fibrosis. It allows for the direct visualization and quantitative measurement of propagating mechanical shear waves in biologic tissue, and it can be used to distinguish between fibrotic and normal liver with high accuracy [19]. These characteristics make them helpful in distinguishing benign hepatic focal lesions from malignant lesions [20].

The purpose of this study was to assess the utility of diffusion-weighted magnetic resonance imaging and

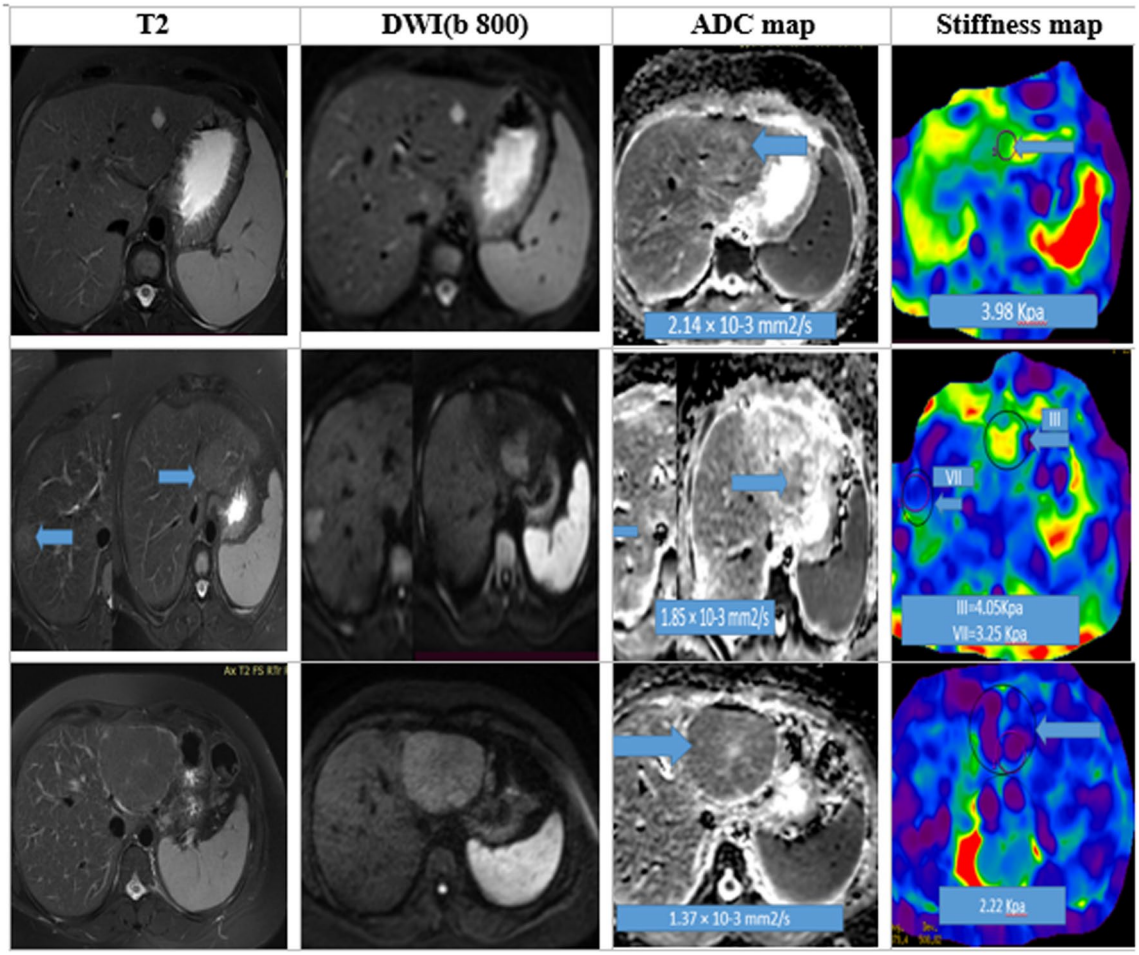

Fig. 2 DWI and MRE of benign types of hepatic focal lesions. The top row was hepatic hemangioma, the second was hepatocellular adenoma, the third was focal nodular hyperplasia, first column was T2-WI images, second was DWI, third its corresponding ADC map and finally was MRE stiffness map. The mean values of focal lesions are represented numerically by the ADC and stiffness maps, (ADC 10^{-3} mm^2/s) and stiffness (kPa) values of the lesions. Arrows shown values of ADC and stiffness maps of each lesion

Table 5 Role of MRE and DWI for differentiating benign and malignant FLLs

	Cutoff	Sensitivity	Specificity	PPV	NPV	AUC	*p* value
MRE	> 4.23	96.7%	93.1%	96.7%	93.1%	0.991	< 0.001 *
DWI	≤ 1.43	85.2%	89.7%	94.5%	74.3%	0.894	< 0.001 *

*Significant predictive value

PPV: positive predictive value, NPV: negative predictive value, AUC: area under the curve, MRE: magnetic resonance elastography, DWI: diffusion-weighted imaging

magnetic resonance elastography in the identification and differentiation of benign and malignant hepatic focal lesions.

Our study was performed on ninety patients (mean age 52 years) with hepatic focal lesions (29 benign and 61 malignant).

In our study, malignant FLLs showed significantly higher mean stiffness than benign FLLs so, the MRE was found to be effective in differentiating between benign and malignant focal liver lesions ($p < 0.001$) at cutoff value > 4.23, sensitivity and specificity results were 96.7%, 93.1%, and the area under the curve value was 0.991.

A study by Hennedige et al. [15] found that MRE is significantly distinguished between malignant and benign FLLs, the optimal cutoff was 4.54 kPa, AUC 0.986, sensitivity 96.3, specificity 95.5, PPV 97.5, and NPV 93.3. The cutoff stiffness value of > 5.45 kPa significantly identified all CCAs; on the other hand,

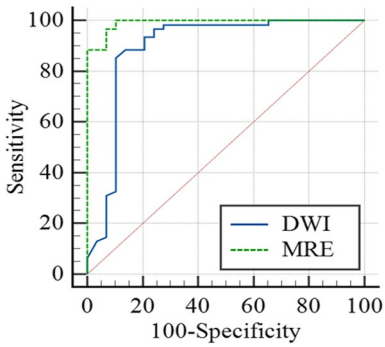

Fig. 3 A graph comparing the ROC curves for DWI and MRE in order to distinguish between malignant and benign localized liver lesions

Table 6 Correlation between mean values of ADC and mean stiffness of 90 FLLs

	Mean ADC	
	R	*p*
Mean stiffness	− .559	< 0.001*

* Significant as *p* value ≤ 0.05. r: Pearson Correlation.*Statistically significant at *p* ≤ 0.05, Mean ADC: mean apparent diffusion coefficient

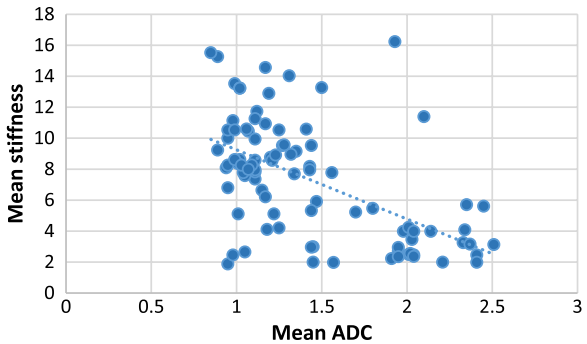

Fig. 4 Correlation between mean values of ADC and mean stiffness

specificity was less than 50%, indicating a stiffness overlap with other malignant FLLs.

The FLLs stiffness measured with MRE is not dependent on the surrounding liver stiffness. Consequently, in a cirrhotic or fibrotic liver, a benign lesion with decreased stiffness would appear as a focused area of lower stiffness set against a background of cirrhotic liver parenchyma higher stiffness. This result came in a line with Motosugi et al. [21] who reported that depending on the degree of fibrosis, a malignant liver lesion would manifest as a focal area of increased stiffness that would be either greater or lower than the surrounding fibrotic parenchyma. It is interesting to note that in one study, it was shown that elevated stiffness of the liver parenchyma surrounding the disease was associated with an increased risk of HCC development, In contrast, a different study by Anaparthy et al. [22] found no such relationship in the case of compensated cirrhosis.

Supporting our results, Venkatesh et al. [16] were the first who proven that malignant liver tumors had significantly increased mean shear stiffness (10.1 kPa; 95% CI 8.7 – 11.4) than benign tumors (2.7 kPa; 95% CI 2.4 – 3.0, $p = 0.001$). This study suggests that a cutoff value of 5.0 kPa may be very accurate (accuracy = 100%) for differentiating benign focal masses from malignant tumors. Our cutoff was lower, because of the greater number of benign lesions in our study and the variations in the demographics of the study group.

In agreement with the previous studies, Dominguez et al. [23] demonstrated that there was a significantly higher values of stiffness in malignant FLLs than benign FLLs, and they recorded that to provide 75 – 85% accuracy for differentiating these lesions, the optimal cutoff value was 5.8 kPa.

In our study, mean stiffness was the lowest for FNH, among all FLLs, at less than 2.22 kPa, although this overlapped with different types of benign FLLs (HEMs, HCA). Among the benign lesions, HCA showed the highest stiffness, but did not differ from HEMs or FNH. This MRE tendency of differentiation may be helpful for characterizing benign FLLs types; however, more research is required to confirm our study results.

Also in our results, among FLLs, the lowest mean ADC values and the highest mean stiffness were CCAs. CCAs have a higher quantity of fibrous stroma and are known to be scirrhous [16, 24], a characteristic that would be expected to restrict diffusion and increase stiffness to a greater extent than in predominantly cellular HCCs.

Similarly, Hennedige et al. [15] found that at less than 3.1 kPa, the lowest mean stiffness was HCAs, which overlapped with FNHs and HEMs. Among benign lesions, FNHs shown highest stiffness, yet didn't different from HCAs or HEMs. Among FLLs, the lowest mean ADC values and highest mean stiffness was CCAs.

Additionally, Garteiser et al. [25] enrolled ninety-four patients of 72 lesions with liver tumors > 1 cm who underwent MR elastography and observed higher absolute shear modulus and loss modulus in malignant versus benign tumors. They also observed a significant differences in loss modulus between FNHs and HCCs, HCAs and HEMs.

In the current study, the mean ADC values was significantly increased in benign FLLs than malignant FLLs. DWI was found to be effective in differentiating between benign and malignant focal liver lesions ($p < 0.001$) at cutoff value ≤ 1.43; sensitivity and specificity results were

85.2%, 89.7% and the area under the curve value was 0.894.

Our results were in the same line with El-Refaei et al. [26] prospectively scanned 31 patients with suspected liver focal lesion and demonstrated that there was a highly statistically significant difference in mean ADC between benign focal hepatic lesions such as hemangioma and malignant lesions such as metastases or HCC ($p=0.001$).

Also, Haradome et al. [27] retrospectively evaluated 166 patients with 269 FLLs (153 benign and 116 malignant) found that the diagnostic performance of DWI in the differentiation between solid benign tumors (adenoma and FNH) from malignant FLLs.

Additionally, Hennedige et al. [15] reported that with DWI, the mean ADC of the benign and malignant FLL groups differed significantly. Compared to all malignant FLLs, the mean ADC of HEMs and HCAs was substantially higher. Only the FNHs ADC values was significantly different from HEMs. Higher ADC was often seen in HCAs compared to FNHs, though the differences were not statistically significant.

Going with our results, Parikh et al. [28] reported that ADCs of malignant FLLs were significantly decreased than those of benign FLLs ($p<0.001$). By using a threshold ADC of less than 1.60×10^{-3} mm^2/s. The AUC for diagnosis of malignancy was 0.839, with specificity of 77.3%, sensitivity of 74.2%, negative predictive value of 62.3%, positive predictive value of 85.5%, and accuracy of 75.3%.

In our results, for differentiating benign from malignant FLLs, MRE was more diagnostic than DWI. The reason for MRE's higher performance is probably that it monitors the mechanical property of the tissue, while DWI measures diffusivity features of tissue, which is influenced by capillary microcirculation and vascular perfusion. It is unclear how vascular perfusion affects stiffness in FLLs, and more research is necessary to clarify this [15].

However, the low spatial resolution is the most significant limitation of MRE in differentiating liver tumor stiffness. Because of its 1 cm slice thickness, the traditional 2DGRE MRE is unable to quantify tiny tumors (less than 1 cm) correctly. By comparison, the spatial resolution of 3D MRE is substantially better than that of traditional 2D MRE reconstruction. The slice count of 3D MRE typically ranges from 32 to 40 slices. Recent study by Loomba et al. [29] has shown that for staging liver fibrosis, 3D MRE might be more accurate than 2DMRE. A greater vibration frequency may be appropriate to consider for smaller tumors since liver MREs utilizing a 60-Hz vibration frequency may be less effective in differentiating between small, hard HCC due to the long shear wavelength.

Our results showed that there was significant negative correlations between stiffness [i.e., stiffness (r: − 0.559; $p<0.001$)] and ADC. These results agreed with Hennedige et al. [15] who revealed a significant negative correlation ($r=-0.54$, $p<0.0001$, 95% CI −0.65 to −0.40) between ADC values of FLLS and stiffness.

Le Bihan et al. and Kromrey et al. [30, 31] reported a strong correlation between tissue elasticity in the liver and tissue water diffusivity. Specifically, in liver parenchyma, the shifted apparent diffusion coefficient (sADC) values (obtained from the *b* values of 200 and 1500 s/mm^2) were assured to be correlated strongly with the liver tissue elasticity obtained with MR elastography (MRE) in a small cohort ($n=15$) [30], and in a larger patient cohort ($n=74$) [31].

In both studies, tissue stiffness generated from sADC values was obtained, and was graded accurately depending on the stage of liver fibrosis. These results showed that DWI-based or intravoxel incoherent motion imaging (IVIM)-based virtual elastography (VMRE) [30] could serve as an alternative to MRE for the staging assessment of liver fibrosis. Additionally, tissue elasticity measurements are reportedly useful in the characterization of liver tumors [15, 16, 25]. Malignant tumors have more cellularity, and may result in increased stiffness that can be evaluated with MRE [15]. Thus, VMRE may also be useful for liver tumor characterization. However, the existence of a association between water diffusivity and tissue elasticity in other than liver parenchyma is remain unknown.

Supporting our results, Ota et al. [32] observed strong correlations between the sADC values and the MRE stiffness values not only in the liver parenchyma, but also in liver tumors.

Limitations and recommendations of the study

In limitations of our study, histological proof was not available for every FLL, yet could not avoided due to invasive pattern on biopsy, also preferable to obtain histological evidence when imaging criteria for benign or HCC are met. We only used two b values when doing DWI. Despite the suggestion that using more b values would lead to better outcomes. Lack of standard b values and inconsistent reproducibility between platforms are problems for DWI. Although MRE is a noninvasive methods for assessing focal lesion stiffness. They evaluate only a small portion of the lesion with a single parameter, which may yield substantial sampling error and incomplete information. MRE examinations may fail in patients with abnormal respiratory rate and cannot tolerate to hold breath movement during procedure.

We recommend future research that is necessary to verify our findings in order to ascertain the clinical

relevance of MRE, which offers a noninvasive quantitative measure that might be helpful in distinguishing between common benign and malignant FLLs.

Conclusions

Both MRE and DWI may provide new, quantitative tissue characterization parameters for differentiating benign and malignant liver tumors. However, MRE was better than DWI and shows great promise as a noninvasive method instead of invasive biopsy for the characterization nature of hepatic FLL, which benign or malignant types with cutoff values > 4.23 and ≤ 1.43, respectively; sensitivity and specificity results were 96.7%, 93.1% and 85.2%, 89.7%, and the area under the curve values were 0.991, and 0.894, respectively. There was significant negative correlations between stiffness and ADC.

Abbreviations

FLLs	Focal liver lesions
MRE	Magnetic resonance elastography
MRI	Magnetic resonance imaging
DWI	Diffusion-weighted imaging
ADC	Apparent diffusion coefficient
SPSS	Statistical package for social science
SD	Standard deviation
ROC	Receiver operating curve
AUC	Area under the curve
CT	Computed tomography
PET	Positron emission tomography
HCC	Hepatocellular carcinoma
HEM	Hemangioma
HCA	Hepatocellular adenoma
FNH	Focal nodular hyperplasia
CCA	Cholangiocarcinoma
MET	Metastasis
Gd-DTPA	Gadolinium-diethylenetriaminepenta-acetic acid
GRAPPA	Generalized auto-calibrating partially parallel acquisition
ROIs	Regions of interest
2D	Two dimension
3D	Three dimension

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Author contributions
All authors read and approved the final manuscript. OLE and MSA, MSK conceived and supervised the study; MEA and BAE were responsible for data collection. MEA and BAE analyzed and interpreted the data. All authors provided comments on the manuscript at various stages of development. Final paper writing, revision and editing were done by BAE (corresponding author).

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Availability of data and materials
Authors can confirm that all relevant data are included in the article and/or its supplementary information files.

Declarations

Ethics approval and consent to participate
All study techniques involving human subjects adhered to the ethical norms of the institution's research committee and the Declaration of Helsinki and its later revisions. Informed consent to participate in the study is obtained from participants.

Consent for publication
All patients included in this study give informed consent to publish the data contained within this study.

Competing interests
The authors declare no conflict of interest.

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