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Role of Diffusion Weighted Magnetic Resonance Imaging In Focal Liver Lesions

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ABSTRACT

To compare respiratory triggered diffusion-weighted single-shot echo planar imaging (RT DW-SS-EPI) and T2 weighted turbo spin echo imaging (T2W TSE). To determine apparent diffusion coefficients (ADCS) of focal liver lesions and normal liver parenchyma. The main sources of data for the study are patients from the following teaching Hospitals attached to Bapuji Education Association, J.J.M. Medical College, Davangere. 30 patients with focal liver lesions and additional 10 healthy volunteers (to know normal diffusion pattern and ADC values of liver) with no focal liver lesions were studied. Among the 30 included patients(with 85 lesions), there were 9 with 23 HCCs, 2 with 4 cholangiocelluar Carcinomas, 8 with 36 metastatic lesions, 11 with 22 benign lesions (6 hemangiomas in 4 patients, 9 cysts in 4 patients, 7 hydatid cysts in 3 patients). DWI was associated with significantly higher detection rate of FLLs when compared to T2WI. ($P < 0.001$). The number of malignant FLLs detected with DWI (62 out of 63-98.4%) was highly significant than that detected with T2 WI ($P<0.001$). There was no significant difference between the T2 weighted imaging and DWI for the detection of HCCs alone. The diffusion-weighted MRI sequence is a useful diagnostic tool with no need to use contrast media, and it can contribute to accurate diagnosis and discrimination between benign and malignant hepatic masses. The use of DWI was superior for the detection of malignant liver lesions than the use of T2 weighted imaging.

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Key Words
DW MRI liver, focal liver lesions, ADC of focal liver lesions

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INTRODUCTION

Liver diseases have been known to affect mankind since the dawn of civilization and have steadily gained recognition as a major health problem principally because of their world-wide distribution. The symptoms of liver disease such as jaundice, fever, abdominal enlargement and encephalopathy are striking phenomena that bring the patient to the physician. Clinical and biochemical examination provide information regarding liver size and functions but the assessment of the exact pathology is grossly inadequate.

Modern operative techniques and local therapies such as radio frequency (RF) ablation are effective methods to treat liver metastases or primary hepatic malignancies. Therefore, the determination of liver lesion count and the nature of the lesion are important.

With introduction of MRI contrast agents, MRI with contrast material enhancement has potential to become the leading imaging modality in evaluation of liver. Extracellular contrast agents have shown to be helpful in characterizing liver lesions. MRI is currently considered to be the most accurate noninvasive method in the evaluation of liver lesions .The utilization of tissue specific contrast agents such as SPIO or MnDPDP and the possibility to employ MR techniques that alter tissue contrast such as MT and the multiple slices SL render MRI an attractive tool for liver imaging.

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 examinations[1].

Stejskal and Tanner[2] were the first to describe an MR experiment that could be used to observe and measure water diffusion. They modified a standard T2-weighted imaging sequence by applying a symmetric pair of diffusion-sensitizing gradients on either side of the 180° refocusing pulse.

Diffusion coefficients in DWI are reflected in the apparent diffusion coefficient (ADC, expressed in mm2/s)[3].

Since the first brain diffusion imaging in 19864 and the widespread application for stroke detection in the early 1990s, diffusion-weighted (DW) magnetic resonance (MR) imaging has evolved into a mature functional MR imaging technique for many brain imaging applications. With recent advances in technology, DW MR imaging is reaching a potential for clinical use in the abdomen, particularly in the liver.

DW MR 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 nonenhanced 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[4].

The use of DWI in other parts of the body is relatively new, but very promising for the detection and differentiation of benign and malignant lesions, imaging for dissemination in oncological patients before treatment and for follow-up after treatment of liver tumors. Besides this, DWI is thought to be capable of predicting the response to therapy of malignant tumors[3].

Diffusion images should be interpreted in conjunction with conventional sequences. In patients who cannot receive gadolinium-based contrast agents, DW MR imaging has the potential to be a reasonable alternative technique to contrast-enhanced imaging[4].

Thus a study design to evaluate the contribution of imaging science towards the evaluation and diagnosis of focal liver lesions.

MATERIALS AND METHODS

The main sources of data for the study are patients from the following teaching Hospitals attached to Bapuji Education Association, J.J.M. Medical College, Davangere.

- Bapuji Hospital.
- Chigateri General Hospital.
- S.S. Institute of Medical Sciences and Research Centre.

Sample Size : 30 patients with focal liver lesions and additional 10 healthy volunteers with no focal liver lesion were studied to know to know normal ADC of liver.

Diagnosis on MRI was made with background of clinical context. Final diagnoses was reached in consensus with biopsy/FNAC, wherever applicable or clinical, laboratory, other imaging modality findings and follow up.

Method of Collection of Data (Including Sampling Procedure if Any):

- All patients referred to the department of Radio diagnosis Patients of all age groups referred to MRI clinically suspected of focal liver lesions. Patients with indeterminate lesions detected on USG or CT in a period of 1 year 2 months from October 2011 to November 2012 were subjected for the study.

Inclusion Criteria:
The Study Includes:

- All patients referred for MRI with clinically suspected focal liver lesions and patients with indeterminate liver lesions detected on USG or CT.
- Incidentally detected focal liver lesions.

Exclusion Criteria:
The Study will Exclude:

- All patients having cardiac pacemakers, prosthetic heart valves, cochlear implants or any metallic implants.
- Patient having history of claustrophobia.
- All patients who do not consent to be a part of the study.

Data Analysis: Results expressed as mean, standard deviation, number and percentages. One-way ANOVA was used for multiple group comparison and student unpaired 't' test for 2 group comparison. Categorical data was analyzed by chi-square test. P-value of 0.05 or less was considered for statistically significant.

Equipments: The studies were conducted on the Philips Achieva 1.5 TESLA.

MRI: A 16 channel phased array XL-TORSO coil was used.

MRI Protocol: T1WI, T2WI_TSE_FB, T2WI Spair in axial and coronal plane.
In- and out-of-phase T1-weighted GRE in axial plane.

Post Contrast Dynamic Study (Whenever Indicated):
E-Thrive- 3D T1W TFE.
Respiratory-triggered (with a navigator-echo technique) Fat-suppressed(SPIR-selective presaturation using inversion recovery) single-shot echo-planar DW imaging was performed in the transverse plane with tridirectional diffusion gradients by using three b values (0, 500 and 1000 sec/mm2) within the same acquisition, before contrast study.

The Other Parameters were as Follows: Repetition time msec/echo time msec, 2000-3000/67-82; matrix, 144 × 192; section thickness, 7 mm; intersection gap, 1.4 mm; field of view, 300-400 mm. Acquisition time was 6-8mins (dependent on respiratory rate).
All ADCs were calculated on a workstation with standard software (Diffusion Calculation, Philips Medical Systems). The signal intensities for ADC calculation were measured by using operator-defined region-of-interest (ROI).
In large lesions the mean value of 3 different ROI measurements on the same slice was calculated. In lesions with necrotic or fibrous core, measurement of this area was avoided. ADC of normal liver parenchyma was calculated in area away from focal liver lesions.

RESULTS AND DISCUSSIONS

In the present study maximum percentage of patients were in age range of 61-70 years (30%). Mean age of patients in the study was 55.6 years. There was male preponderance (63.3%), when compared to females (36.7%). Male: Female-1.7 : 1.

Table 1 : Distribution of Patients According to Diagnosis

Diagnosis	No. of patients	Percentage
HCC	9	30
METS	8	26.7
Cholangio Ca	2	6.7
Hemangioma	4	13.3
Simple hepatic cyst	4	13.3
Hydatid cyst	3	10.0
Total	**30**	**100**

In the present study, most common lesion was HCC (30%) and mets were (26.7%). In the present study 76.6% of patients had multiple focal hepatic lesions. In present study most of patients (50%) had involvement of both lobe involvement. 51 (60%). Out of 85 lesions were in the right lobe. In the present study out of 30, 19 (63.3%) were malignant and 11 (36.6%) were benign. 33% of patients were in the age group of 61-70 years. Most of the malignant lesions were seen in the age group of 51-70 years. Mean age of patients in the study was 55.6 years.
In the present study overall there were 19 males (63.3%) and 11 females (36.7%). Male: female=1.7 :1. All lesions were common in males HCC (88.9%), metastasis (62.5%), simple cysts (75%), hydatid (66.7%) except hemangiomas which is common in females. Cholangio carcinoma had equal sex distribution

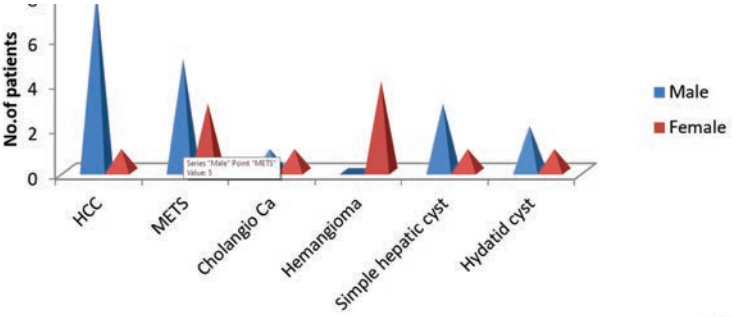

Fig.1: Sex Wise distribution of diagnosis of focal liver lesions

In the present study 19 (63.3%) were malignant and 11 (36.6%) were benign. Out of 85 FLLs seen in 30 patients 22 (25.9%) was benign and 63 (74.1%) were malignant lesions. Most common lesion was metastasis (42.4%).
In the present study, maximum 34 (40%) number of lesions were within <2 cm.
In the present study most of the HCC were between 2-5 cm, Metastasis, cholangio carcinoma and simple

hepatic cyst were <2 cm in sizes. Most of the malignant lesions (n=26) 26 OUT OF 85, 30.6% were less than 2 cm in size. Most of hemangiomas and hydatid cysts were more than 2 cm in size.
DWI was significantly better than T2W imaging in terms of detection for both lobes (RL-98% Vs 78%, LL-94.1% Vs 73.5% respectively). There was no significant difference for detection rate with DWI between right and left lobes (98% Vs 94.1%).

Table 2 : Detection Rate of Benign and Malignant FLLS in 30 Patients (85 lesions) with DW and T2 Weighted Imaging

Parameter	All lesions	Malignant	Benign
Total	85	63	22
T2WI	65 (76.51%)	44 (69.8%)	21 (95.5%)
DWI	82 (96.5%)	62 (98.4%)	20 (90.9%)
Z-value	3.99	4.77	0.61
P-value	<0.001 HS	<0.001 HS	0.54 NS

The number of malignant FLLs detected with DWI (62 out of 63-98.4%) was highly significant than that detected with T2 WI (P <0.001).
There was no significant difference noted between DWI and T2 WI in detection of benign FLLs may be due to most of benign lesions were more than 2cm in size and benign lesions consisted only cystic and hemangioma lesion and no solid benign lesions (FNH and adenoma) were studied.
The detection rate was stratified according to the lesion size. There was significant difference only for detection of FLLs with the diameter of less than 2 cm (p<0.001). No significant difference between DWI and T2WI for FLLs more than >2 cm.
In present study DWI was associated with significantly higher detection rate of metastatic (P<0.001)and cholangio carcinoma (P<.05) lesions when compared to T2WI. DWI MRI significantly improved the detection of metastases and cholangio carcinoma when compared to T2 WI. HCCs did not show significant detection rate, because most of HCCs were in more than >2cm in size.
In our study there was no significant difference in detection rate between DWI and T2W in FLLs more than 2 cm.
Total 20 lesions were missed by T2WI (HCC-3, metastasis-14, cholangio ca-2 and simple cyst-1), DWI missed 3 lesions (metastasis-1 and simple cysts-2).

Malignant Lesions: All HCCs and cholangio ca. detected on DWI were hyper in tense on DWI b=0, b=500, b=1000 and hypointense on ADC map.

Metastasis: All lesions were hyper on b=0. Most of the lesions were hyper (55.5%) and 41.6% were P. hyper on b=500 and b=1000. All these P. hyper lesions were more than 1 cm. Malignant lesions retained high signal intensity on high b values.

Benign Lesions: Hemangioma-DWI-on b=0 hyper and on high b=values (b=500 and b=1000) then was obvious signal intensity reduction. On ADC hemangiomas were Iso-hyper, or heterogeneously hyper. This may be due to T2 shine through effect.
Hydatid cysts - On low b-values (b=0) all lesions were hyper there was gradual decrease in signal on high b-values (b=500 moderate hyper and b=1000-Iso). On ADC map all lesions were hyper.

Simple Cysts: All detected lesions on DWI hyper on low b-values (b=0) and Iso – Hypo on high b-values (b=500, b=1000) on ADC all lesions were hyper intense.
There was no significant difference of mean ADC value of liver parenchyma between all three groups. Mean ADC value of normal liver parenchyma is 1.24±0.06 x $10^{[-3]}$ $mm^{[2]}$/s.
Simple cysts had high ADC value and malignant had lowest value. Among malignant, metastases had lowest

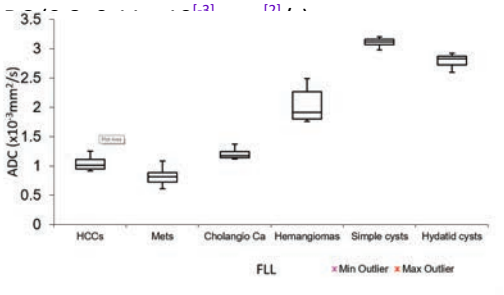

Fig.2: Box plots of the ADC values of 82 FLLS

Box plots of the ADC values of 82 FLLs (3 lesions were not detected on DWI).Boxes stretch across interquartile range (IR); median is shown as line across each bar; ADC values of metastases overlapped with ADC values of hepatocellular carcinomas (HCC).
In the present study the mean ADC values of malignant lesions were significantly lower than those of benign lesions (0.92 x $10^{[-3]}$ $mm^{[2]}$/sV/s 2.68 x $10^{[-3]}$ $mm^{[2]}$/s) (p<0.001).

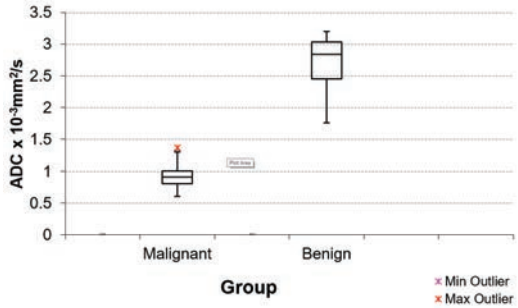

Fig.3: ADC of malignant and benign lesions

Box plot of ADC values calculated for 62 malignant lesions and 20 benign. With the optimal cutoff ADC value of 1.50×$10^{[-3]}$ $mm^{[2]}$/s to differentiate benign from malignant liver lesions. In the present study the difference between mean ADC values of simple cyst and hydatid cyst was significant. In the present study the difference between mean ADC values of cholangio carcinoma and metastasis was significant.

In the present study the difference between mean ADC values of HCC and metastasis was significant. Even with significant difference, there was lot of overlap of ADC values among HCCs and metastasis.

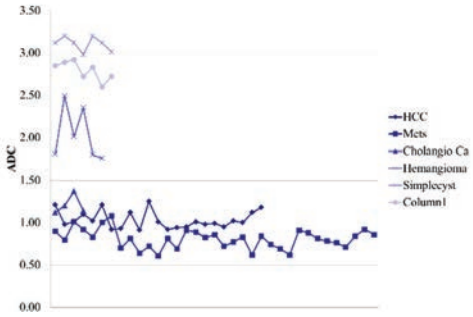

Fig.4: ADC CHART FLL

Out of 85 FLLs (30 patients) 82 (96.5%) were detected by DWI and 65 (76.5%) by T2WI. DWI was associated with significantly higher detection rate of all FLLs when compared to T2WI. (P<0.001). DWI MRI significantly improved the detection of FLLs when compared T2WI. These findings are comparable to Parikh[5] The number of malignant FLLs detected with DWI (62 out of 63-98.4%) was highly significant than that detected with T2 WI (P <0.001).

However, there was no significant difference between the T2 weighted imaging and DWI for the detection of HCCs alone. This result was different from a previous study [Parikh[5]].

In our study, 20 of 23 (87%) HCCs were detected on T2 weighted imaging and 23 of 23 (100%)on DWI. There was no significant difference p=0.064(p>.05). These findings where similar to Palmucci[6].

This may be explained by the different signal intensity observed in these lesions: in fact, in a recent study by Kim[7]. They were isointense or hyperintense to the liver. In a cirrhotic liver, HCCs may show the same signal intensity as the surrounding parenchyma, involved in a chronic fibrotic process and as a consequence the detection and characterization of HCCs may be difficult[7].

This may also be due to their sizes; most of these lesions were in the group of more than 2cms. In our study DWI detection rate was significant in lesions less than 2cms.

Vandecaveye[8] concluded that DWI provided higher sensitivity and positive predictive value for the detection of HCC<20 mm compared to conventional contrast enhanced MRI (sensitivity and specificity 91.2% and 82.9% vs 67.6% and 61.6%, positive predictive value 81.6% and 59.0%, respectively). DWI did not show significantly better results than conventional MRI in detecting HCC > 20 mm.

There was no difference determined between the use of T2 weighted imaging and DWI for the detection of benign hepatic lesions in our study. This result was different from a previous study [Parikh[5]].

In our study, 21 of 22 (95.5%) benign hepatic lesions were detected on T2 weighted images and 20 of 22(90.9%) on DWI. These findings were comparable to Yang[9].

However, in a study by Parikh[5], 83.3% of benign hepatic lesions were detected on T2 weighted images and 90% of benign hepatic lesions were detected on DWI.

Stratification by Lesion Location: DW imaging was significantly better than T2-weighted imaging in terms of detection for both lobes (RL-98% Vs 78%, LL- 94.1% Vs 73.5%). There was no significant difference for detection rate with DW imaging between right and left liver lobes (98% and 94.1%, respectively). These findings are comparable to Parikh[5].

Parikh[5] study showed that DW MR imaging significantly improved detection of small malignant lesions less than 2 cm when compared with breath hold T2-weighted imaging (78.5% vs.45.8%, P<.001).

Several publications have reported the use of DW MR imaging for liver lesion detection[10-5-11] Few of these studies have compared DW MR imaging and T2-weighted imaging in terms of lesion detection, generally showing improved detection with DW MR imaging[10] in terms of image quality, findings showed comparable image quality with that of DW MR imaging by using low b values[12]. Black-blood diffusion images (using low b values), in which background signal of vessels in the liver parenchyma is suppressed, allow for lesion detection[12] while images with higher b values give diffusion information that enable lesion characterization[5-13]. The improved lesion detection with DW MR imaging compared with T2-weighted imaging is explained by the improved image contrast with use of low b values and lack of blurring with single-shot SE echo-planar imaging, compared with T2-weighted fast SE or single-shot fast SE sequences[12] Coenegrachts[14] compared DW MR imaging (b values of 0, 20, 300 and 800 sec/mm2) and single-shot T2-weighted fast SE in 24 patients with focal liver lesions. They found that the best image quality was achieved with single-shot T2-weighted fast SE imaging and the best lesion conspicuity was achieved with single-shot T2-weighted fast SE imaging for cysts and with DW MR imaging (b=20 sec/mm2) for hemangiomas and metastases. DW MR imaging had the highest lesion-to-liver contrast-to-noise ratio for hemangiomas and metastases.

In another study, Bruegel[10] compared respiratory-triggered DW MR imaging to five different T2-weighted sequences (breath-hold fat-suppressed single shot T2-weighted fast SE, breath-hold fat-suppressed fast SE, respiratory-triggered fat-suppressed fast SE, breath-hold short inversion

Table 3 : Individual Case Detection Rate of FLLS in 30 Patients (85 Lesions) with DW and T2 Weighted Imaging

Parameters	HCC	METS	Cholangio Ca	Hemangiomas	Simple cyst	Hydatid	Total
Total	23	36	4	6	9	7	85
T2WI	20 (87%)	22 (61%)	2(50%)	6(100%)	8 (86.9%)	7(100%)	65 (76.5%)
DWI	23 (100%)	35 (97.2%)	4(100%)	6(100%)	7 (79.8%)	7 (100%)	82 (96.5%)
Z- value P-value	1.85 0.064 NS	4.21 <0.001 HS	2.00 <.05 Significant	0.00 1.00 NS	0.64 0.52 NS	0.00 1.00 NS	3.99 <0.001 HS

Table 4 : Lesion Chracterization on Diffusion Weighted Imaging

Malignant lesions		Diffusion			ADC
		0	500	1000	
HCC (n=23)	Hyper	23 (100%)	23 (100%)	23(100%)	
	Hypo	-	-	-	23 (100%)
	Hyper	35(97.22%)	20(97.22%)	20 (55.5%)	
METS (n=36)	Hypo				20(97.22%)
	P-hyper		15 (41.6%)	15 (41.6%)	
	P. hypo				15 (41.6%)
	ND	1 (2.77%)	1 (2.77%)	1 (2.77%)	1 (2.77%)
Cholangio Ca (n=4)	Hyper	4 (100%)	4 (100%)	4 (100%)	
	Hypo				4 (100%)

Benign Lesions

Benign lesions	0	Diffusion 500	1000	ADC
	Hyper 6 (100%)	Hyper - 5 (83.3%)	Mild hyper 5 (83.3%)	Iso-Hyper 5 (83.3%)
Hemangioma (n=6)		Hyper with central hypo 1 (16.6%)	Iso-Hyper with central hypo 1 (16.6%)	H-hyper 1 (16.6%)
	Hyper-7 (77.7%)	Iso-6 (66.6%)	Iso-6 (66.6%)	Hyper 7 (77.7%)
Simple cyst (n=9)		Hypo-1 (11.1%)	Hypo-1 (11.1%)	
	ND-2 (22.2%)	ND-2 (22.2%)	ND 2 (22.2%)	ND-2 (22.2%)
	Hyper-7 (100%)	Moderate hyper 7	Iso-7 (100%)	Iso Hyper 6 (83.3%)
Hydatid (n=7)		Iso – 0	Hyper-0	H-Hyper-1

time inversion recovery and respiratory-triggered short inversion time inversion recovery) for the diagnosis of hepatic metastases in 52 patients with 118 lesions at 1.5T. DW MR imaging demonstrated higher accuracy (0.91-0.92) compared with T2-weighted fast SE techniques (0.47-0.67). These differences were even more pronounced for small metastatic lesions (≤ 1 cm). Zech *et al* compared black-blood DW MR imaging (b=50 sec/mm2) with fat-suppressed T2-weighted imaging and observed significantly better image quality, fewer artifacts, and better sensitivity for lesion detection with DW MR imaging (83% versus 61%).

Malignant Lesions: These findings were similar to Scurr[15], who found that colorectal liver metastases showed rim high signal intensity, uniform high signal intensity or variegate high signal intensity at b value of 500 s/mm2 on DW-MRI. For metastases ≤1 cm in diameter, we found that the uniform pattern was most common, which may be difficult to distinguish from other solid liver lesions. However, for lesions >1 cm in diameter, the rim pattern was the most common

Benign Lesions:

Hemangioma: DWI-on low b values (b=0) hyper and on high b=values (b=500 and b=1000) there was obvious signal intensity reduction. Necrotic parts were hypointense on high b values.

On ADC lesions showed iso-hyper and H-hyper. Haemangiomas display high signal intensity on low b-values DW-MR images, but usually retain some of their high signal intensity at high b-value (b=1,000 s/mm2) DW-MRI. This may be due to T2 shine through effect[16-17].

On low b-values (b=0) all lesions were hyper and there was gradual decrease in signal on high b-values (b=500-mild hyper and b=1000-Iso). On ADC all lesions were hyper.

These findings where different from Inan[17] On trace DWI (b=1,000 s/mm2), most hydatid cysts were hyperintense, whereas most simple cysts (40/43, 93%) were isointense with the liver[16].

In our study all hydatid cyst were moderate hyperintense on b=500 and isointense on b=1000 DWI images.

On low b-value diffusion- weighted MR images, all masses were observed as hyperintense, whereas on high b-value images signals of cysts disappeared and signals of hemangiomas obviously decreased. In contrast, since there is a limitation of diffusion in solid tumors, they were also observed as hyperintense on high b-value diffusion weighted image and these results similar to those obtained by several others[16].

Evaluation of Normal Liver Parenchyma: Mean ADC values obtained from normal liver parenchyma in benign and malignant group 1.25±0.04 x 10-3 mm2/s and 1.23±0.06 x 10-3 mm2/s. respectively. Mean ADC values obtained from normal liver parenchyma in group with no FLL (healthy volunteers) 1.26±0.01 x 10-3 mm2/s. where not significantly different (ANOVA, F=1.66, P=0.20 NS).

Overall mean ADC of normal liver parenchyma in all 3 groups was 1.24± 0.05 x 10-3 mm2/s.

Despite significant differences in mean ADC of HCC and Metastasis FLLs on a group basis, characterization of FLLs by using ADCs showed overlap.

In the present study the difference between mean ADC values of simple cyst and hydatid cyst were significant. (3.11±0.08 V/s 2.79±0.12 x 10-3 mm2/s) These findings were comparable to Inan[17-18].

Benign hepatic lesions have generally higher ADC values compared with malignant lesions, with variable degree of overlap[13-16]. Different ADC cutoffs (1.4-1.6 × 10-3 mm2/sec) have been described in the literature, with a reported sensitivity of 74%-100% and specificity of 77%-100% for diagnosing malignant lesions. The ADCs of various benign and malignant hepatic lesions from selected published studies are summarized in table-30 given below.

CONCLUSION

No significant difference between DWI and T2WI for FLLS more than >2 cm. DW imaging was significantly better than T2-weighted imaging in terms of detection for both lobes ($p<0.001$). There was no significant difference for detection rate with DW imaging between right and left liver lobes (98% and 94.1%, respectively).

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