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## Role of ADC Mapping in the Assessment of Therapeutic Response of Hepatocellular Carcinoma in Patients with Post-trans-catheter Arterial Chemoembolization

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### ABSTRACT

**Background:** Hepatocellular carcinoma (HCC) is more common in persons with chronic liver disease and cirrhosis. The apparent diffusion coefficient (ADC) has the ability to detect tumour response to treatment weeks before morphological alterations are evident.

**Aim of The Work:** To compare the response to therapy of HCC cases after trans-arterial chemoembolization using the ADC mapping MRI approach to the dynamic contrast study (DCE MRI).

**Patients and Methods:** The current study involved 30 patients who underwent dynamic MRI with ADC mapping technique before and after TACE. All patients had been subjected to clinical assessment, laboratory investigations (AFP, liver functions, serum albumin bilirubin, coagulation profile, CBC) and ultrasound to exclude ascites. All cases underwent baseline and follow-up MR imaging.

**Results:** DCE-MRI and DWI/ADC assessments regarding active lesions showed; comparable sensitivity, specificity, PPV, NPV and accuracy in HCC patients; without significance ( $p > 0.05$ ) (Table 3). Table (4) shows a good agreement between dynamic-MRI and DWI/ADC evaluation of reactivity between HCC cases. DWI/ADC value at a cutoff point ( $\leq 2.17$ ) can identify cases with remnant active pathology, with good (83.3%) accuracy, sensitivity= 87.5% and specificity= 81.8% ( $p < 0.001$ ).

**Conclusion:** Authors conclude that dynamic MRI is useful and the standard in identifying relapsed pathology but, this value is enhanced by DWI/ ADC protocol which will significantly be of great value in increasing the confidence in our diagnosis.

**Keywords:** Axillary lymph node US; elastography; Breast US.

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**Authorship:** All authors have a substantial contribution to the article.

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### INTRODUCTION

Hepatocellular carcinoma (HCC) is more frequent in individuals with chronic liver diseases and cirrhosis.<sup>1</sup> HCC is currently the third major etiology of cancer mortality globally, with over 500,000 persons suffering.<sup>2</sup>

As regard to the Milan criteria, liver transplantation is still the best choice for individuals with HCC. However, there is a shortage of high-quality dead donor organs. As a result, different therapies such as resection, radiofrequency ablation (RFA), and may be systemic treatment are required.<sup>3</sup>

Transcatheter arterial chemoembolization (TACE) is the most often used treatment. TACE is done by cannulation of the tumor's feeding artery and gives high local dosage of chemotherapy such as doxorubicin, cisplatin, or mitomycin C. To avoid systemic toxicity, the feeding artery is blocked with gel foam or coils.<sup>4</sup>

Dynamic contrast-enhanced MRI (DCE MRI) has the potential to be a valuable radiological indicator,

particularly in the identification of active tumour cells the distinction of necrosis from active tumour, and prediction of therapeutic efficacy.<sup>5</sup>

Diffusion-weighted imaging (DWI) is the primary method for determining tumour cells and cell membrane stability. As a result, it may be susceptible to differences in the tumour microenvironment after therapy. Also, it may be assessed quantitatively by computation of the apparent diffusion coefficient (ADC).<sup>6</sup>

ADC may be useful in predicting tumour response to therapy weeks earlier to morphological alteration. It assesses the movement of water inside tissues. Active tumours have a high cellularity, and intact cell membrane, which inhibits water molecule movement and leads in a relatively reduction of ADC. However, cellular necrosis enhances membrane permeability, allowing water molecules to flow easily and resulting in a relative rise in ADC. It has emerged as an intriguing indicator of tumour response to treatment.<sup>7</sup>

Our rationale was to evaluate the response to therapy of HCC cases after trans-arterial chemoembolization

using the ADC mapping MRI approach to the dynamic contrast study (DCE MRI).

### PATIENTS AND METHODS

A prospective study carried out at El Maadi Armed Forces Hospital, Radiology Department during the period from 1 May 2020 to 1 October 2021. The current study involved 30 patients who underwent dynamic MRI with ADC mapping technique before and after TACE. The study was accepted by Al-Azhar University's Ethics Board, and each subject signed an informed written permission form.

Patients with unresectable hepatic tumor, its size <50% of total liver size, patent portal vein, serum bilirubin < 1.7, INR <1.5 and serum albumin >2.8 were enrolled in this study. However, subjects with any contraindication to contrast media, e.g. kidney failure and allergy, contraindication to MRI, e.g. claustrophobia, heart prosthesis and pacemakers and metallic implants and plates, extra hepatic metastases, tumor size > 50% of total liver size, portal vein thrombosis and poor liver function were excluded from the study.

Clinical evaluations had been performed to all participants, laboratory investigations (AFP, liver functions, serum albumin bilirubin, coagulation profile, CBC) and ultrasound to exclude ascites.

All participants underwent an initial and follow-up MRI using 3 Tesla (GE Discovery 750) MRI machine. Abdominal coil was used with respiratory triggering. The imaging protocol included the following:

Pre contrast MR imaging before the diffusion weighted examination:

T1-weighted image was done with the following parameters: (TR = 400ms, TE = 20ms, 385 x 385mm field of view (FOV), 256 x 256 matrix, section thickness 5-7mm).

T2-weighted image with the following parameters (TR = 3000ms, TE = 90, 385 x 385mm FOV, 256 x 256 matrix and section thickness: 5-7mm).

STIR (short time inversion recovery) was done using the following parameters: (TR = 418ms, TE = 80, TI = 140ms, 385 x 385 FOV, 256 x 256 matrix and section thickness 5-7mm).

Dynamic study: A bolus injection of 0.05mmol of gadobenate dimeglumine per kilogram of body weight followed by 20ml of saline flush at a rate of 2mL/s by using a power injector.

Three consecutive post-contrast imaging were obtained employing a dual (early and late) hepatic arterial phase, followed by portal and delayed phases. Early and late arterial phases were done without interruption, with a set delay of 15 seconds following the start of contrast material injection and within a breath hold of 20 seconds. The portal venous phase was obtained 30 seconds after the late arterial phase ended, and the delayed phase was obtained 175 seconds after the contrast material was administered.

Diffusion weighted images: Functional DWI was performed using single-shot spin-echo-planar imaging during one or more

breath holds with two b-values (500, 800mm<sup>2</sup>/s) applied in the z direction. These b-values were chosen to overcome the effect of capillary perfusion and water diffusion in extracellular extra vascular space. ADC maps were reconstructed from each set of DWIs acquired at each slice position.

Statistical analysis:

All data analyzed using statistical package for social sciences (SPSS) version 22 (SPSS Inc, Chicago, USA). For qualitative data, frequency and percent distributions was calculated. For quantitative data, mean, standard deviation (SD) was calculated. Significance was defined as P value < 0.05. The following tests were used; Student T test, Mann-Whitney U test, Chi-Square test and McNemar's test.

### RESULTS

This study involved 30 participants with HCCs who subjected to trans-catheter arterial chemoembolization. Their mean age was 65.57 ± 6.21 years and ranged from 41 to 74 years. 25 (83.3%) patients were more than 60 years while 5 (16.7%) were less than 60 years. Male predominance was noticed in our study as male represented 96.7% cases while there was one female (3.3%). Eighteen (60%) patients live in rural region while 12 (40%) patients live in urban region. Concerning tumor size, the size ranged from 1.3\*1.2 cm to 10.0\*7.6 cm with mean ±SD was 4.01\*3.07 ± (2.32\*1.71) cm. The AFP ranged from 2.70 to 8299 with mean ±SD was 421.41 ± 281.96.

Regarding dynamic MRI, there was 10 (33.3%) cases showed positive changes while 20 (66.7%) cases showed negative changes. As regards to DWI/ADC, there was 8 (26.7%) cases showed positive changes while 22 (73.3%) cases showed negative changes. The mean (± SD) ADC value was 2.15 ± 0.124 × 10<sup>-3</sup> mm<sup>2</sup>/s. 2 (6.7%) cases had mean ADC value < 1.2 × 10<sup>-3</sup> mm<sup>2</sup>/s while 28 (93.3%) cases had mean ADC value > 1.2 × 10<sup>-3</sup> mm<sup>2</sup>/s (Table 1). The patients were classified according to active lesions into 2 independent groups; active group (10 patients) and inactive group (20 patients). ADC value in active group was lower than inactive group with high significance (p < 0.001) (Table 2).

DCE-MRI and DWI/ADC assessments regarding active lesions showed; comparable sensitivity, specificity, PPV, NPV and accuracy in HCC patients; with no significance (p > 0.05) (Table 3). Table (4) shows a good agreement between dynamic-MRI and DWI/ADC evaluation of reactivity between HCC cases (kappa = 0.684).

By using ROC-curve analysis, Dynamic-MRI can detect cases with residual active pathology, with excellent (96.7%) accuracy, sensitivity = 100% and specificity = 95% (p < 0.001). DWI/ADC value at a cutoff point (≤ 2.17) can detect cases with residual active pathology, with good (83.3%) accuracy, sensitivity = 87.5% and specificity = 81.8% (p < 0.001) (Figure 1).

	HCC patients (n=30)	
	No.	%
<b>Activity by dynamic MRI</b>		
Negative	20	66.7%
Positive	10	33.3%
<b>Activity by DWI/ADC</b>		
Negative	22	73.3%
Positive	8	26.7%
<b>ADC value:</b>		
Mean± SD	2.15± 0.124	
Median (IQR)	2.44 (1.42- 2.82)	
Range	1.12- 2.96	
< 1.2 × 10 <sup>-3</sup> mm <sup>2</sup> /s	2	6.7%
≥ 1.2 × 10 <sup>-3</sup> mm <sup>2</sup> /s	28	93.3%

SD: standard deviation, IQR: Interquartile range, MRI: magnetic resonance imaging. ADC: apparent diffusion coefficient. DWI: Diffusion-weighted imaging.

**Table 1:** dynamic MRI, DWI/ADC characteristics in the studied HCC patients:

		Inactive group (n = 20)		Active group (n = 10)		P-value
		n	%	n	%	
ADC value (x 10 <sup>-3</sup> mm <sup>2</sup> /s)	Mean± SD	2.48± 0.57		1.50± 0.33		<0.001**
	Median (IQR)	2.73 (2.44 – 2.85)		1.42 (1.31 – 1.80)		
	Range	1.38 – 2.96		1.12 – 2.17		

p≤0.01 is high significant, SD= standard deviation, IQR= Interquartile range,

\*\*Mann-Whitney U test

**Table 2:** Comparison between the two groups as per ADC value

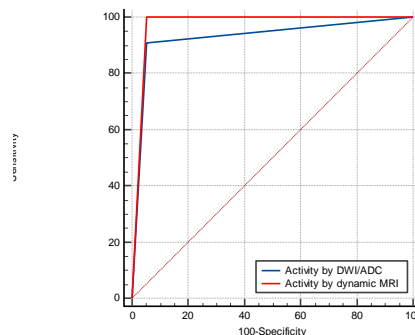
Variables	Dynamic -MRI assessment	DWI/ADC assessment	P value
Sensitivity (TPR) (true positive rate)	100.0 %	87.50 %	0.156
Specificity (TNR) (true negative rate)	95.0 %	81.82 %	0.235
Positive predictive value (PPV)	90.91 %	63.64 %	0.089
Negative predictive value (NPV)	100.0 %	94.74 %	0.235
Accuracy (AUC)	96.67 %	83.33 %	0.423

\* McNemar's test.

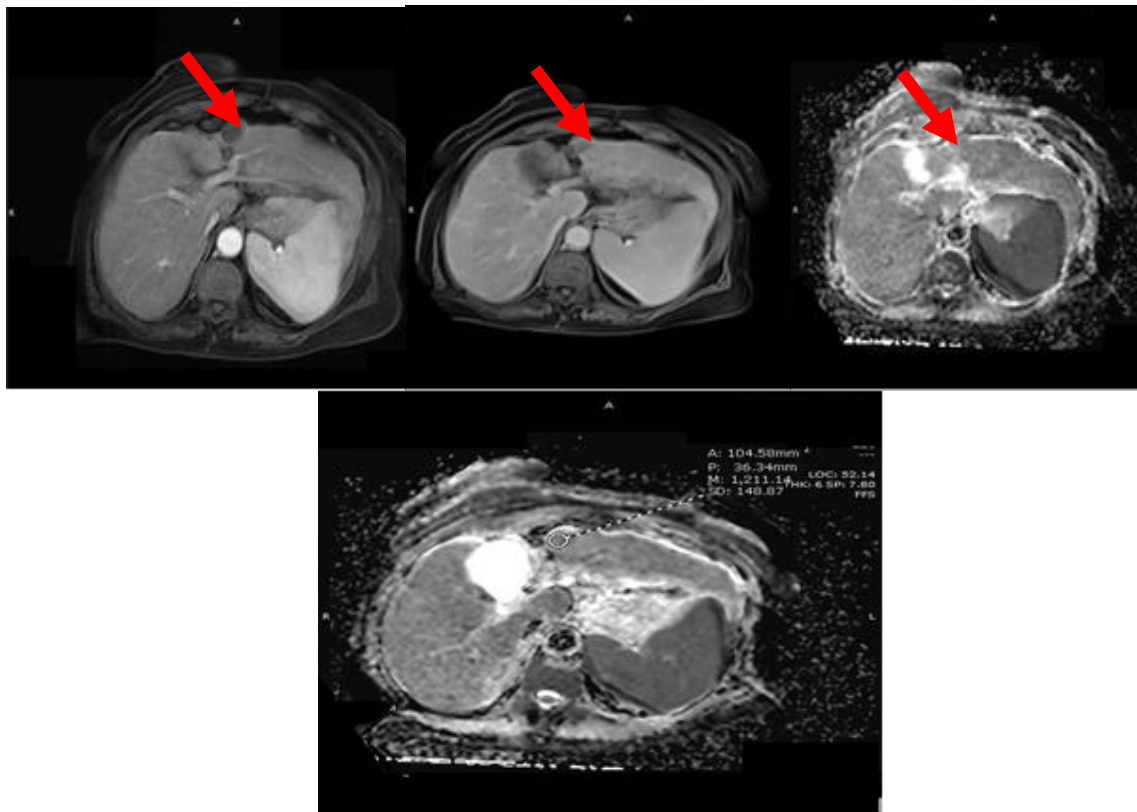
Table (3): Validity of DCE MRI & and DWI/ADC in detecting active lesions.

DWI/ADC		dynamic MRI		Total	Agreement Kappa
		Positive	Negative		
DWI/ADC	Positive	7	1	8 (26.7%)	0.684
	Negative	3	19	22 (73.3%)	
	Total	12 (33.3%)	20 (66.7%)	30 (100%)	

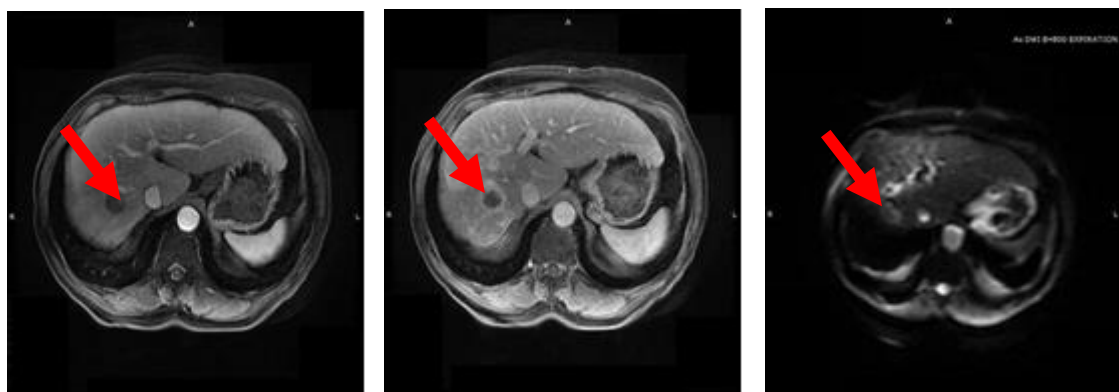
**Table 4:** An agreement between dynamic-MRI and DWI/ADC in detecting active lesions.



**Fig. 1:** ROC curve of DCE MRI and dynamic MRI in detecting treatment response /residual tumor.



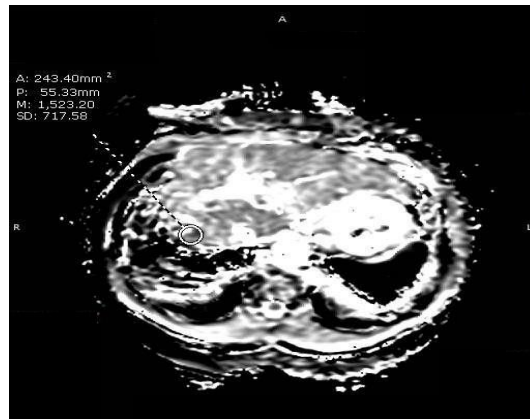
**Fig. 2 :** 68 years old female patient with liver cirrhosis and HCV + VE underwent TACE of left hepatic lobe lesion segments II focal lesion. Dynamic MRI with diffusion weighted study and ADC mapping was done 3 months after embolization. (A) Axial arterial phase image showing no enhancement (B) Axial delayed phase image showing delayed washout , (C) the lesion showing no restricted diffusion on (DWI),(D) ADC mapping and ADC value decreased  $1.2 \times 10^{-3}$  denoting well ablated.



**A**

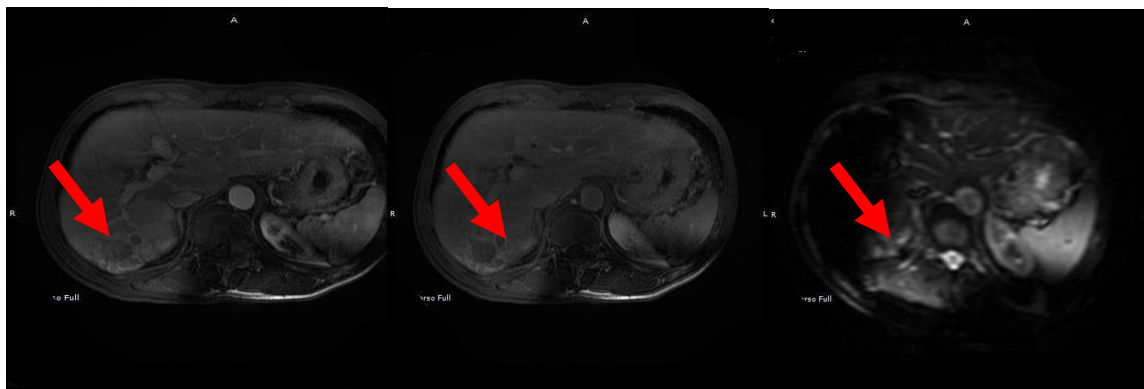
**B**

**C**



**D**

**Fig. 2:** 51 years old male patient with liver cirrhosis and HCV + VE underwent TACE of right hepatic lobe lesion segments VI focal lesion. Dynamic MRI with diffusion weighted study and ADC mapping was done 3 months after embolization. (A) Axial arterial phase image showing early peripheral enhancement and (B) Axial delayed phase image showing delayed washout, (C) the lesion showing partially restricted diffusion on (DWI). (D) ADC mapping and ADC value  $1.0 \times 10^{-3}$  denoting residual activity.



**A**

**B**

**C**



**D**

**Fig. 4:** 59 years old male patient with liver cirrhosis and HCV + VE underwent TACE of right hepatic lobe lesion segments VII focal lesion. Dynamic MRI with diffusion weighted study and ADC mapping was done 3 months after embolization. (A) Axial arterial phase image showing early enhancement and (B) Axial delayed phase image showing washout, (C) the lesion showing partially restricted diffusion on (DWI). (D) ADC mapping and ADC value  $1.3 \times 10^{-3}$  denoting recurrent activity.



## DISCUSSION

Diffusion-weighted imaging (DWI) may be vulnerable to modifications in the tumour microenvironment after therapy, that could be quantified for the computation of the ADC. DWI may indicate the extent of tumour necrosis in huge HCC after TACE, and the data can guide patient therapy. The ADC value can predict the survival of HCC cases after TACE.<sup>8</sup>

The present study showed that as regard MRI, DWI/ADC characteristics in the studied HCC patients. Regarding dynamic MRI, there was 10 (33.3%) cases showed positive changes while 20 (66.7%) cases showed negative changes. As regards to DWI/ADC, there was 8 (26.7%) cases showed positive changes while 22 (73.3%) cases showed negative changes. The mean ( $\pm$  SD) ADC value was  $2.15 \pm 0.124 \times 10^{-3}$  mm<sup>2</sup>/s. 2 (6.7%) cases had mean ADC value  $< 1.2 \times 10^{-3}$  mm<sup>2</sup>/s while 28 (93.3%) cases had mean ADC value  $> 1.2 \times 10^{-3}$  mm<sup>2</sup>/s. While, in the study of ZENAT et al.<sup>9</sup> the mean ( $\pm$  SD) ADC value was  $1.47 \pm 0.37$  ( $\times 10^3$  mm<sup>2</sup>/sec).

In the study of Tantawy & Mohamed,<sup>10</sup> that involved 40 HCCs evaluated by DWI and ADC value, thirty-two HCCs responded to treatment. With b value 500, the mean ADC value was comparable between responding and non-responding lesions. While with b value 1000, there was a significance with higher mean ADC values in responding lesions than in non-responding (P=0.03).

Our results showed that DCE-MRI and DWI/ADC assessments regarding active lesions showed; comparable sensitivity, specificity, PPV, NPV and accuracy in HCC patients; without significance. There was a good agreement between dynamic-MRI and DWI/ADC evaluation of reactivity between HCC cases (kappa =0.684). By using ROC-curve analysis, Dynamic-MRI can detect cases with residual active pathology, with excellent (96.7%) accuracy, sensitivity= 100% and specificity= 95% (p <0.001). DWI/ADC value at a cutoff point ( $\leq 2.17$ ) can detect cases with residual active pathology, with good (83.3%) accuracy, sensitivity= 87.5% and specificity= 81.8% (p < 0.001).

Our findings similar to study of ZENAT et al.<sup>9</sup> as they discovered a moderate agreement between DCE-MRI and DWI/ADC reactivity evaluations in HCC cases. DCE-MRI identified patients with residual active pathology with excellent (92%) accuracy, sensitivity (92%) and specificity (91%) by ROC curve (p0.01). DWI/ADC value at a cut-off point (1.33) identified cases with remnant active pathology with good (84%) accuracy, sensitivity= 84%, and specificity= 83% (p=0.0001).

Similarly, Goshima et al.<sup>11</sup> who discovered that DWI had a 100% sensitivity, a 65.5% specificity, a 67.7% PPV, a 100% NPV, and a total agreement of 80%.

In the study of Abdelrahman et al.<sup>12</sup> The qualitative DWI had a sensitivity and specificity of 77.8% and 75% for detecting remnant viable HCC after TACE, respectively. The quantitative ADC value had a higher sensitivity than the DWI for detecting remnant HCC, with a sensitivity and specificity of 81.5% and 75%, respectively, at an ADC cut off value of  $1.32 \times 10^3$  mm<sup>2</sup>/s. regarding to logistic regression analysis, the optimal ADC value  $1.35 \times 10^3$  mm<sup>2</sup>/s was the best imaging tool for detection of active HCC with 88.6% accuracy.

Ebeed et al.<sup>7</sup> recorded a higher cut-off value of  $1.38 \times 10^{-3}$  mm<sup>2</sup>/s with a sensitivity of 76.5% and a specificity of 65.2% at a cut-off value of  $1.38 \times 10^{-3}$  mm<sup>2</sup>/s. DWI had an 82.3% sensitivity and 73.9% specificity for detecting remnant active HCC after TACE.

Saleh et al.<sup>13</sup> noticed a similar finding, revealing an accuracy of 82.5% at a cut-off value of  $1.35 \times 10^{-3}$  mm<sup>2</sup>/s. They found variant diagnostic values, with a reduced sensitivity of 52.6% and a raised specificity of 90.5%; however, their study included 1R-TR non-evaluable HCC, which was not included in our study.

In meta-analysis conducted by Liu et al.<sup>14</sup> DWI had a pooled sensitivity, specificity, and AUC value of 85%, 83%, and 0.90, respectively in identifying remnant or relapsed HCCs following TACE and lower than that of necrotic tumours (P= 0.01).

## CONCLUSION

Authors conclude that dynamic MRI is useful and the standard in identifying relapsed pathology but, this value is enhanced by DWI/ADC protocol which will significantly be of great value in increasing the confidence in our diagnosis.

Conflict of interest : none

## REFERENCES

1. Machida K. NANOG-dependent metabolic reprogramming and symmetric division in tumor-initiating stem-like cells. In *Alcohol and Cancer* 2018 (pp. 105-113). Springer, Cham.
2. Llovet JM, Pavel M, Rimola J, Diaz MA, Colmenero J, Saavedra-Perez D, et al. Pilot study of living donor liver transplantation for patients with hepatocellular carcinoma exceeding Milan Criteria (Barcelona Clinic Liver Cancer extended criteria). *Liver Transplantation*. 2018;24(3):369-79.
3. Sugawara Y, Yamamoto H, Hibi T. Living donor liver transplantation for patients with hepatocellular carcinoma in Japan. *Hepatology Research*. 2018;4:2-7.
4. Liu S, Guo L, Li H, Zhang B, Sun J, Zhou C, & et al. Postoperative adjuvant trans-arterial chemoembolization for patients with hepatocellular carcinoma and portal vein tumor thrombus. *Annals of surgical oncology*. 2018;25(7):2098-104.
5. Kierans AS, Elazzazi M, Braga L, Leonardou P, Gerber DA, Burke C, & et al. Thermoablative treatments for malignant liver lesions: 10-year experience of MRI appearances of treatment

- response. *American Journal of Roentgenology*. 2010;194(2):523-9.
6. ElSaid NA, Kaddah RO, Fattah MS, Salama NM. Subtraction MRI versus diffusion weighted imaging: Which is more accurate in assessment of hepatocellular carcinoma after Trans Arterial Chemoembolization (TACE)?. *The Egyptian Journal of Radiology and Nuclear Medicine*. 2016;47(4):1251-64.
  7. Ebeed AE, Romeih MA, Refat MM, Yossef MH. Role of dynamic contrast-enhanced and diffusion weighted MRI in evaluation of hepatocellular carcinoma after chemoembolization. *The Egyptian Journal of Radiology and Nuclear Medicine*. 2017;48(4):807-15.
  8. Dong S, Ye XD, Yuan Z, Xu LC, Xiao XS. Relationship of apparent diffusion coefficient to survival for patients with unresectable primary hepatocellular carcinoma after chemoembolization. *European journal of radiology*. 2012;81(3):472-7.
  9. ZENAT A, MONA AA, ABDEL AZIZ MD, MOHAMED M. Role of Apparent Diffusion Coefficient (ADC) Mapping in Assessment of Therapeutic Response of Hepatocellular Carcinoma Post Trans-Catheter Arterial Chemoembolization. *The Medical Journal of Cairo University*. 2021;89(9):1533-41.
  10. Tantawy HI, Mohamed FF. Diagnostic value of apparent diffusion coefficient (ADC) in evaluating hepatocellular carcinomas post trans-catheter arterial chemoembolization and radiofrequency ablation. *The Egyptian Journal of Radiology and Nuclear Medicine*. 2016;47(3):699-706.
  11. Goshima S, Kanematsu M, Kondo H, Yokoyama R, Tsuge Y, Shiratori Y, & et al. Evaluating local hepatocellular carcinoma recurrence post-transcatheter arterial chemoembolization: Is diffusion-weighted MRI reliable as an indicator?. *Journal of Magnetic Resonance Imaging: An Official Journal of the International Society for Magnetic Resonance in Medicine*. 2008;27(4):834-9.
  12. Abdelrahman AS, Abdel-Rahman AS, Taha NM. The role of functional imaging; DWI, ADC and 18F-FDG PET/CT in the evaluation of HCC treatment response after transarterial chemoembolization. *Egyptian Journal of Radiology and Nuclear Medicine*. 2021;52(1):1-7.
  13. Saleh TY, Bahig S, Shebrya N, Ahmed AY. Value of dynamic and DWI MRI in evaluation of HCC viability after TACE via LI-RADS v2018 diagnostic algorithm. *Egyptian Journal of Radiology and Nuclear Medicine*. 2019;50(1):1-1.
  14. Liu Z, Fan JM, He C, Li ZF, Xu YS, Li Z, & et al. Utility of diffusion weighted imaging with the quantitative apparent diffusion coefficient in diagnosing residual or recurrent hepatocellular carcinoma after transarterial chemoembolization: a meta-analysis. *Cancer Imaging*. 2020;20(1):1-10.