Transarterial Chemoembolization Of Hepatocellular Carcinoma: Can Early Diffusion Weighted Imaging Predict Response?

Gulzar asma[1] , Shera tahleel[2] , Shah omair[3] , Choh naseer[4] , Gojwari Tariq[5] , Bhat mudaisr[6] , Maqsood shadab[7] .

1

1. MD Department of Radiology, SKIMS SOURA , J&K,INDIA
2. MD (Assistant professor),Department of Radiology, SKIMS SOURA , J&K,INDIA
3. MD (Senior Resident),Department of Radiology, SKIMS SOURA , J&K,INDIA
4. MD (Additional professor), Department of Radiology, SKIMS SOURA , J&K,INDIA
5. MD (Professor), Department of Radiology, SKIMS SOURA , J&K,INDIA
6. MD (Assistant Professor), Department of Radiology, SKIMS SOURA , J&K,INDIA
7. MD (Assistant Professor), Department of Radiology, SKIMS SOURA , J&K,INDIA

Corresponding author
Omair Ashraf Shah, shahomair133@gmail.com. 167 nursingh garh karanagar Srinagar J&K India 190010

ABSTRACT

Purpose: We evaluated the role of early diffusion weighted imaging (DWI) in predicting response to TACE in patients with HCC and compare the results with contrast enhanced magnetic resonance imaging.

Methods: 24 patients with documented HCC were taken up for TACE after a pre-procedural contrast CT and MRI. Post procedural DWI was taken on day 5-7 and the mean ADC values were documented and compared to pre procedural values. The change in ADC values was grouped into 4 categories: group 1- <25%, group 2 26-50%, group 3- 51-75% and group 4- >75%. The increase in ADC values signifying response was correlated with 5 week CEMRI scan (which has been the traditional gold standard for response evaluation) and a threshold ADC increase signifying response in majority of the cases was calculated.

Results: The mean ADC of the lesions changed from $1.21 \times 10\text{-}3$ (pre TACE) to $2.02 \times 10\text{-}3$ mm2/sec (post TACE) [p<0.001]. Taking CE MRI as gold standard, DWI imaging had a sensitivity of 80%, specificity of 94.7% with a positive predictive value of 80%, negative predictive value of 94.7% and overall accuracy of 91.7%. Complete response was seen in19 (79%) and incomplete in 5 (21%) patients in our study. The change in ADC was significantly higher in responders (884.15 ± 161.60) as compared to non responders (564.80 ± 221.05) [p =0.001].

Conclusion: Early DWI after TACE can predict response of a HCC lesion to chemoembolization. The change in ADC values can earmark responders from non-responders. Early DWI results are concordant with CEMRI results in most of the cases. DWI can act as a substitute to CEMRI when contrast administration is not advised.

Keywords: Transarterial Chemoembolization, Magnetic Resonance Imaging, Hepatocellular Carcinoma, Diffusion Weighted Imaging, Apparent Diffusion Coefficient.

INTRODUCTION:

Hepatocellular carcinoma (HCC) is an epithelial tumor originating in the liver and is the fifth most common tumor in the world [1]. Cirrhosis is the most important clinical risk factor for HCC with approximately 80% of cases of HCC developing in cirrhotic livers [2]. The prognosis of HCC depends largely on the stage at which the tumor is detected with symptomatic patients having a dismal prognosis while patients in whom HCC is detected at an early stage may benefit from curative and palliative treatments [3]. Imaging plays a very important role in the diagnosis of HCC with multiphasic CT and MR imaging with contrast agents as first-line modalities for this purpose [4, 5]. Pathological and biochemical evaluation also help in diagnosing this entity. The role of angiography is now limited to the administration of therapies such as chemo-embolization [6].

The management of HCC is dependent on its staging. (. The proposed treatment according to the Barcelona Clinic Liver Cancer (BCLC) stage (figure 1) includes [7]: Treatment options for HCC include curative treatments like surgery including resection or liver transplant and loco-regional therapies including thermal ablation (radiofrequency ablation [RFA] and microwave ablation) or chemotherapy-based conventional trans-arterial chemoembolization (TACE). Palliative treatments are trans-catheter therapies including TACE, drug eluting bead TACE (DEB-TACE), bland trans arterial embolization (TAE), trans arterial radio-embolization (TARE) or systemic therapy (sorafenib) [5].

TACE is widely used in the treatment of malignant liver tumors .The best candidates for TACE are patients with preserved liver function (Child Pugh class A) and multi-nodular or isolated large tumor (> 3 cm), without vascular invasion, extra hepatic spread or tumor related symptoms and those not eligible for surgical or percutaneous curative approaches. Patients with liver functional decompensation (either Child B or C class) are excluded [8, 9]. The response to TACE has remained an enigma over the years with various modalities being used to assess therapeutic response. The accumulation pattern of iodized oil observed on CT has been used previously but it is more informative about the techni-
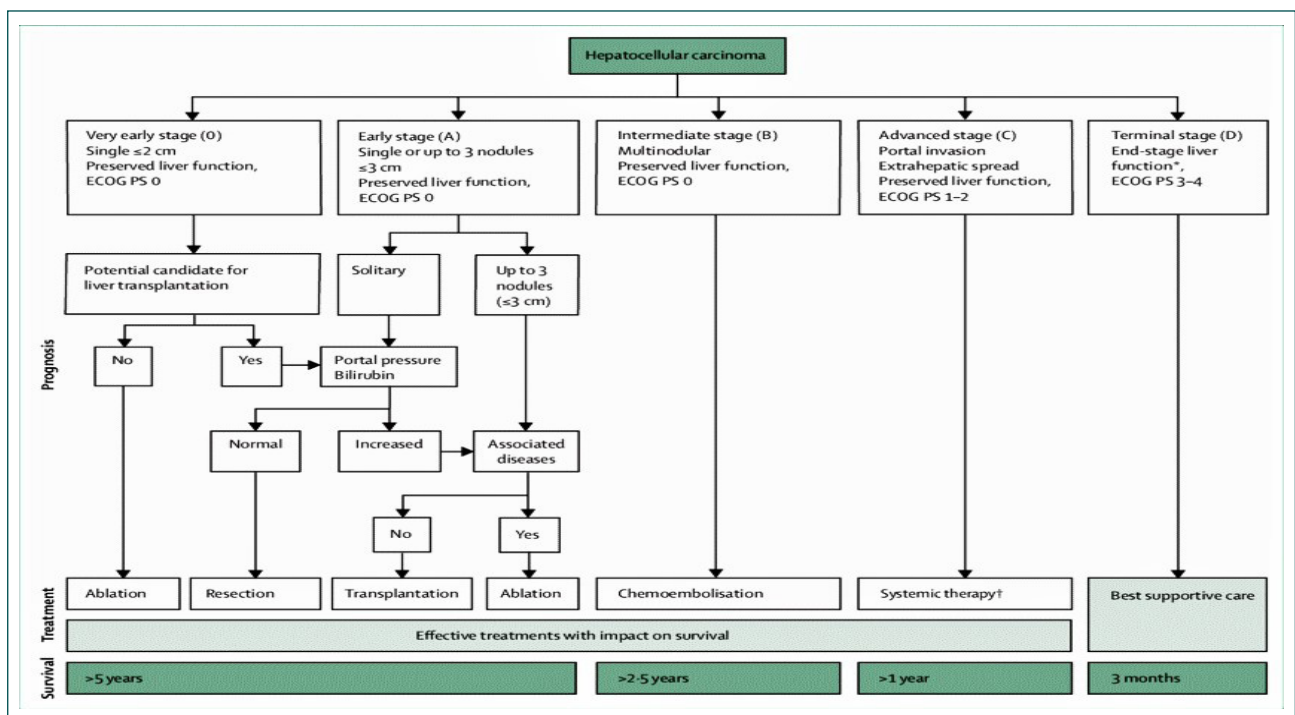

Figure.1. Flowchart showing the management protocol of HCC patients based on BCLC staging system[7].

cal success rather than actual tumor necrosis response. Contrast enhancement on CT post TACE is a difficult proposition owing to beam- hardening artifacts produced by iodized oil. The signal characteristics of HCC post TACE on conventional MRI sequences (T1/T2) are quite variable, therefore contrast enhanced multiphase MRI has been the investigation of choice for TACE assessment and detection of residual viable tumor. However there are some limitations to CEMRI including its difficulty in assessing the enhancing capsule in the early and late phases of dynamic enhancement. This enhancing capsule can represent either viable tumor or post treatment changes [10-12].

Diffusion-weighted imaging (DWI) has emerged in the last decade as a useful modality in assessing post TACE tumor necrosis. An increase in the ADC values of the tumor can be assessed as early as the first week predicting the response to treatment and the need for retreatment, if any. It can be used in patients with contraindication to gadolinium based contrast agents. DWI facilitates distinction between viable and necrotic tumor areas and helps in diagnosis of residual or recurrent tumor. The improved results with DWI imaging are based on its ability to assess response earlier than anatomical imaging, quantifiable ADC values used for assessment, short time of acquisition and no requisition of post processing. However difficulties might emerge when evaluating lesions close to diaphragm owing to motion artifacts and an overall tendency of this sequence to have poor signal to noise ratio [13-15].

Our study aims to solve the puzzle of post TACE tumor assessment especially with regard to the use of DWI imaging as a predictor of response to treatment and its role in guiding further management based on the presence or absence of residual tumor. We also aimed at comparing the results of DWI imaging with Dynamic post contrast CEMRI imaging which has remained the main stay of post TACE assessment over the years.

Material and methods

Our prospective observational study was conducted in the Department of Radio diagnosis and Imaging, Sheri-Kashmir Institute of Medical Sciences (SKIMS) over a period of 3 years (2017-2020) including patients who were diagnosed with HCC based on imaging, biopsy or biochemical (AFP levels >400) [presence of any two of three modalities] and were candidates for TACE based on BCLC staging. We excluded patients with severe renal failure, coagulopathy, portal vein thrombosis, untreated esophageal varices. After assessing the demographic profile and biochemical values (AFP), the patients were admitted to our institute.

STUDY DESIGN

Patients to be taken up for TACE were evaluated with Diffusion Weighted MRI 1 day prior to the procedure and on the 5th – 7th day post procedure assessing the percentage change in ADC values. Patients underwent contrast enhanced MRI 4-6 weeks post procedure to evaluate the response to chemoembolization and compare the results to early DWI. We also assessed the role of pre-procedure DWI in predicting response to TACE.

Imaging:

Magnetic Resonance Imaging:

Pre procedure evaluation was done using 1.5-T MRI scanner (Magnetom Avanto, Siemens Medical Systems, Germany) equipped with phased array torso surface coil to cover the whole liver using following sequences:

- T1 weighted (T1W) (FLASH 2d)(FS axial):Time to Repeat (TR)- 7.15ms, Time to Echo (TE)- 2.3 ms, flip angle- 70 degree and band width -230 Hz.
- T2 weighted (T2W) images (single shot fast spin echo sequence) (HASTE):TR - 900 ms, TE - 92 ms, flip angle - 15 degrees and band width - 411 Hz.
- DIFFUSION Weighted Imaging (DWI): Respiratory-triggered fat-suppressed single-shot echo planar DW imaging with b values 0, 500, and 800 sec /square millimeter. TR1852 ms, TE =70 ms, number of excitations (NEX) = 3, matrix 150 x 236 with a field of view as small as possible, slice thickness= 4 mm, slice gap =0.5 mm and a scan time of approximately 5 minutes.
- DYNAMIC CONTRAST ENHANCED MRI (CEMRI):Dynamic imaging using VIBE technique was performed using TR = 4.3ms, TE=1.97, Flip angle- 10 degrees and bandwidth = 400 Hz after injection of gadolinium based contrast agent (Gadodiamide, OMNIS-

CAN) 0.05-0.1 mmol/Kg at a rate of 2mL/s. Following a non contrast image, scans were obtained in early arterial phase, late arterial phase, portal phase and a delayed phase (3-5 min).

Trans-arterial Chemoembolization (TACE):

TACE was performed in a Digital subtraction angiography (DSA)suite (SEIMENS ARTIS ZEE DSA) by an interventional radiologist with more than 5 years of experience. After selective cannulation of the feeding arteries embolization was done using chemotherapeutic emulsion of 20 mL of iodized oil (Lipiodol Ultrafluid) and 7 mL(60 mg) of epirubicin hydrochloride (Farmarubicin, Pfizer) and 7 mL of contrast, total volume depending on the size of the target lesion followed by gelatin particle infusion in that particular vessel. An intraprocedure DYNA CT was done in all patients to assess the drug deposition and technical success of chemoembolization.

Post-chemoembolization MRI

After treatment, follow-up imaging was done on 5-7th day to assess early response using conventional (T1 and T2) and DWI sequences. The final response of the lesion to chemoembolization was assessed after 4- 6 weeks using T1 WI, T2 WI (HASTE), DWI and post contrast T1 WI (VIBE) sequences. Alpha fetoprotein levels were assessed 3 months post-TACE and compared with pre TACE levels.

IMAGING EVALUATION

The MRI data obtained was transferred to a dedicated work station and the lesions were assessed with regard to their size, T2 signal characteristics taking background liver and paraspinal muscles as references, diffusion weighted imaging signal and quantitative ADC values and contrast enhancement within the lesion using subtraction methods. ADC measurements were done by placing the region of interest (ROI) over any sustained hyper-intense area on diffusion images, and if no high signal was identified, the whole lesion was measured. Measurement of the viable tumor was performed on MRI obtained in the arterial phase, when the contrast between viable vascularized tumor tissue and non-enhancing necrotic tissue was the highest.

Assessment of response:

The response of the lesion to TACE was classified based on CEMRI done at 4-6 weeks as under:

● Complete response- lesion had no enhancement or thin rim of enhancement that is expected after treatment.

● Partial Response- at least a 30% decrease in sum of diameters of viable (enhancement in arterial phase) target lesions. Stable Disease- Criteria of neither partial response nor progressive disease fulfilled.

● Progressive Disease- an increase of at least 20% in the sum of diameters of viable(enhancing) target lesionsand/or the appearance of a new lesion (>1cm lesion with typical features of HCC).

STATISTICAL ANALYSIS

The data obtained was compiled and statistical analysis done using SPSS 17.0. Categorical variables were analyzed using Chi Square test. Quantitative variables were analyzed using paired t-test. P value less than 0.05 was considered to be statistically significant.

RESULTS:

Patient Profile:

We included 24 patients in our study with a male to female ratio of 21(87.5%): 3(12.5%) having a mean age of 59.4 ± 9.4 years (range 42 -73 years).

Clinical Profile:

We had 13 (54%) patients who were known cirrhotic while 11 (46%) others were non cirrhotic. The cause of cirrhosis among our patients included chronic viral hepatitis (hepatitis B and C) (n= 5), non-alcoholic steatohepatitis (n=4), chronic alcohol abuse (n=2) and cryptogenic (n=2).

Among non-cirrhotics, 6 patients were hepatitis B surface antigen positive (HBsAg) and two patients were positive for hepatitis C serology, however the disease had not progressed to cirrhotic stage. The three remaining patients had no obvious risk factors for cirrhosis or HCC.

The overall clinical assessment of the patients was done based on Child Pugh scoring. 13 (54%) patients were in class A whereas 11(46%) patients were classified into

class B of Child Pugh score. Class C patients were excluded from study.

Diagnosis:

. 18 (75%) patients were diagnosed by imaging and raised AFP levels (>400) whereas 6 (25%) patients had to undergo biopsy for diagnosis of HCC in view of the atypical imaging appearance or low AFP levels.

Imaging evaluation:

Intraprocedural DYNA CT:

Type 1b and 2 accumulation of drug within the lesion was the most common pattern seen in 14 (58%) of our patients. 8 (33%) patients had type 3 deposition while 2 (9%) had type 4 deposition after initial injections. All

patients with type 3 or type 4 deposition underwent further injection of drug in the same setting achieving type 2 deposition in all but two patients.

T2 Weighted Imaging:

The Pre (1 day prior) and Post (Day 5-7) TACE T2 weighted images were evaluated to calculate T2 signal characteristics of the lesion, background liver and paraspinal muscles [Table 1]. Taking paraspinal muscles as reference standard, ratios of T2 signal intensity of lesion and background liver to paraspinal muscles was also calculated to remove individual differences in the liver and muscle signal characteristics [Table 2].

T2 signal intensity	Mean	Std. Deviation	Std. Error Mean	p-value
Lesion Pre-TACE	312.96	49.988	10.204	
Lesion Post-TACE	452.67	96.174	19.631	≤0.0001
Liver Pre-TACE	239.46	58.158	11.871	
Liver Post -TACE	256.71	72.544	14.808	0.003
Muscle Pre-TACE	99.63	17.873	3.648	
Muscle Post-TACE	100.29	10.618	2.167	0.79

Table 1. Comparison of pre and post TACE signal intensities of lwesion, liver parenchyma and para spinal muscles on T2 HASTE.

T2 signal intensity	Mean	n	Std. Deviation	Std. Error Mean	p-value
Liver to Muscle Ratio Pre-TACE	2.4667	24	0.686	0.140	0.33
POST TACE T2 SI RATIO LIVER TO MUSCLE	2.5518	24	0.632	0.129	
PRE TACE T2 SI RATIO LESION TO MUSCLE	3.2197	24	0.707	0.144	≤0.0001
POST TACE T2 SI RATIO LESION TO MUSCLE	4.5137	24	0.845	0.172	

*T2 SI= T2 Signal Intensity, n= number of patients.

Table 2. Comparison of pre and post TACE signal intensity ratios of liver parenchyma to paraspinal muscle and that of the lesion to para spinal muscle.

Diffusion Weighted Imaging:

The quantitative assessment of ADC values of the lesion, liver and paraspinal muscles as well as the ratios were calculated showing a significant increase in the ADC values of the lesion as well as the lesion to paraspinal muscle ratio (p<0.001). [Table 3, 4] [Figure 2].

Correlation of ADC values with lesion response based on CEMRI:

We divided the patients into four groups based on degree of increase in ADC values: Group 1-<25%, Group2- 25-50%, Group 3- 50-75% and Group 4- >75%. The ability of early diffusion weighted imaging to predict TACE response was assessed by comparison with CEMRI done 4-6weeks post procedure [Table 5]. Taking DCE MRI as gold standard, DWI imaging provided
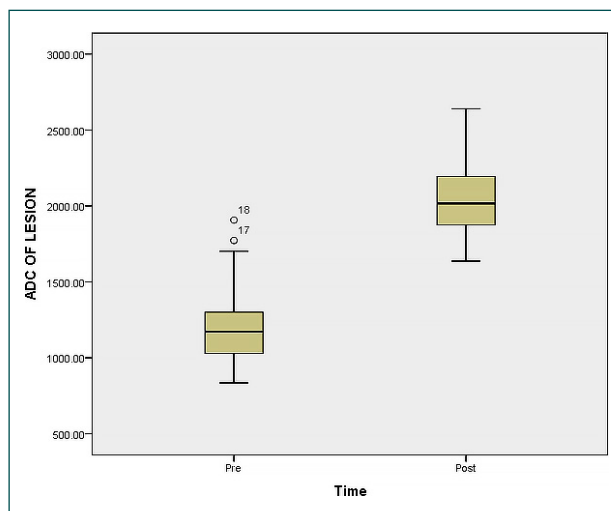

Figure.2. Box plots distribution of pre- and post-TACE ADC values in tumor lesions. 2 out of 24 lesions showed values out of the distribution plot.

Apparent Diffusion Coefficient (ADC Values)	Mean	Std. Deviation	Std. Error Mean	p-value
Pre TACE ADC Of Lesion	1212.13	272.457	55.615	
Post TACE ADC Of Lesion	2029.33	250.221	51.076	≤0.0001
Pre TACE ADC Of Liver	1230.67	173.944	35.506	
Post TACE ADC Of Liver	1380.33	183.666	37.491	≤0.0001
PRE TACE ADC OF MUSCLE	1427.13	134.660	27.487	
POST TACE ADC OF MUSCLE	1434.33	96.225	19.642	0.69

Table 3. Comparison of pre and post TACE ADC values of lesion, liver and para-spinal muscle.

ADC RATIOS	Mean	Std. Deviation	Std. Error Mean	p-value
ADC RATIO LESION TO MUSCLE (PRE TACE)	0.8417	0.15578	0.03180	≤0.0001
ADC RATIO LESION TO MUSCLE (POST TACE)	1.4221	0.18552	0.03787	
ADC RATIO LIVER TO MUSCLE (PRE TACE)	0.8546	0.12382	0.02527	≤0.0001
ADC RATIO LIVER TO MUSCLES (POST TACE)	0.9583	0.13691	0.02795	

Table 4. Comparison of pre and post TACE ADC ratios of the lesion and background liver.

CEMRI response-5wk				
		Incomplete responders.	Complete responders	Total
%AGE CHANGE IN ADC OF LESION	0-25%	1	0	1
		20.0%	0.0%	4.2%
	26-50	3	1	4
		60.0%	5.2%	16.7%
	51-75	1	8	9
		20.0%	42%.2%	37.5%
	>75%	0	10	10
		0.0%	52.6%	41.7%
Total		5	19	24
		100.0%	100.0%	100.0%

Table 5. Comparison of percentage ADC changes in the lesion with CEMRI response assessed at 5 weeks.

a sensitivity of 80%, specificity of 94.7% with a positive predictive value of 80%, negative predictive value of 94.7% and overall accuracy of 91.7%.The overall response in our study was complete in 19 (79%) and incomplete in 5 (21%) patients based on CEMRI findings.

Change in ADC values (ΔADC) among responders and incomplete responders:

The mean ΔADC of incompletely responding lesions was 564.80± 221.05 while that of completely responding lesions was 884.15 ± 161.60. This difference was statistically significant with a P value of 0.001.

Alpha Feto-Protein (AFP) levels:

The pre TACE mean AFP level was 14444.25 ± 372.64 and post TACE mean AFP level was 149.96 ± 140.25. The difference was statistically significant (p value < 0.0001).

DISCUSSION

Response assessment after local therapy in HCC patients is an important aspect related to management as it guides further interventions. Local treatment including TACE is believed to act predominantly by tumor necrosis rather than tumor shrinkage and hence tumor size or volume is not always a good indicator of tumor response.. A total of 24 post TACE patients with male predominance (M:F=7:1) having a mean age of 59 years

were recruited in our study. We had a mix of both cirrhotic and non cirrhotic patients with hepatitis B and C being the most common underlying etiological agent. The clinical status of our patients was assessed by Child Pugh score with patients equally distributed in class A and B. The number of patients in our study is comparable to studies done by Ibrahim YA et al[14] , Afifi et al[15] and Tantawy HI et al[16]. The numbers are significant in a resource constrained region like ours where procedures like TACE are in its inception. The male predominance is in keeping with known male preference of the disease.

In our study comparing pre and post TACE mean signal intensity of the lesion on T2 HASTE, we observed increase in the mean signal intensity of the lesion on T2 weighted images (figure 2)[Table 1] . Afifi et al.[15] and Ebeed et al.[17] in their studies showed that treated lesions exhibit hyperintensity on conventional T1 weighted images and hypo-intensity T2 weighted images with T2 hyperintensity indicating tumor viability. However, signal changes on conventional T1 and T2 weighted images are non-specific and do not correlate with tumor necrosis. Hyper- intense signal on T2 weighted imaging not only represent residual tumor but could be seen in case of lesional hemorrhage inflammation, or cystic necrosis
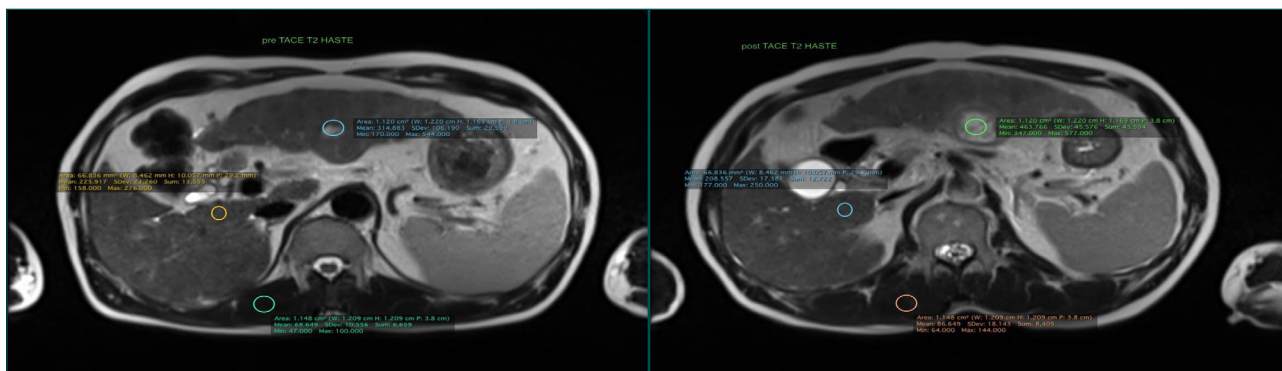
Figure.2. Pre and post TACE T2 weighted images of a patient with aleft lobe lesion showing a significant increase in the T2 signal of the lesion in comparison to the background liver. The T2 signal of the paraspinal muscles was used to obtained reference ratios.
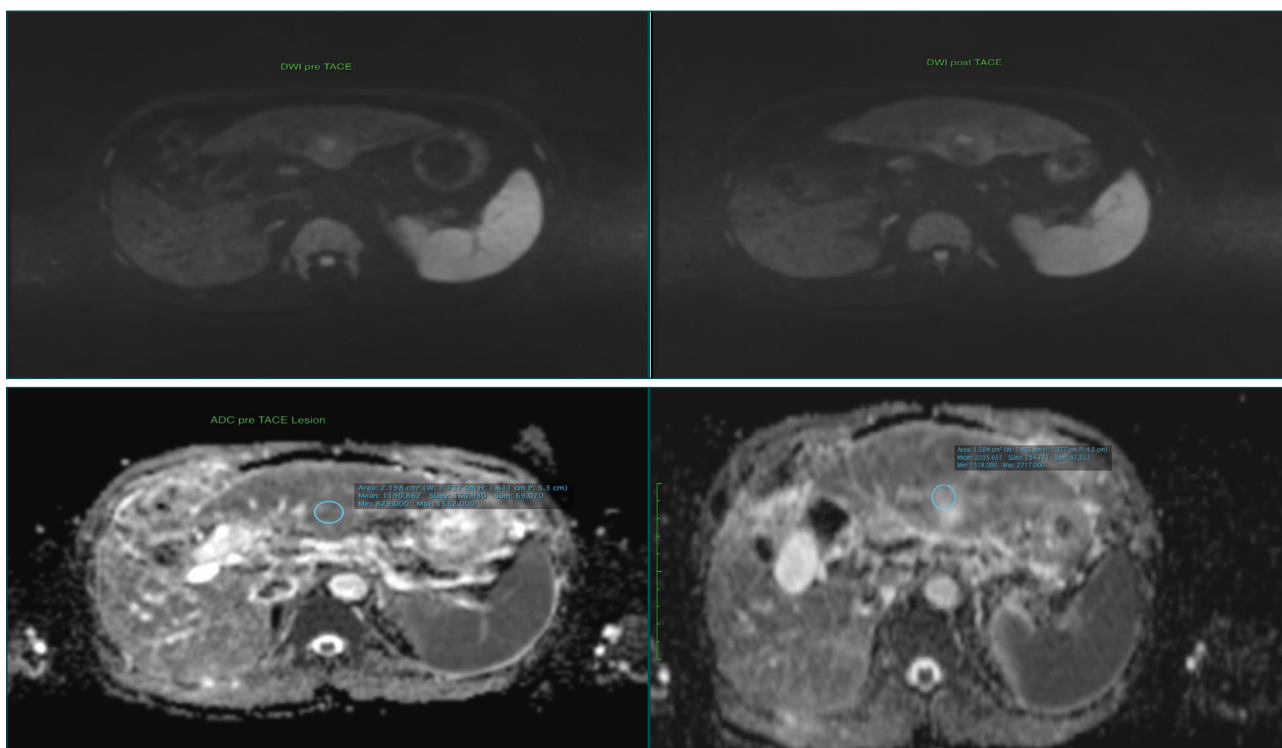

Figure.3. Pre (a, c) and post TACE (b, d) axial images of the same patient in figure 1 showing a marked increase in the ADC value of the lesion from 1.109 to 2.035 mm/s2 indicating a good response.

as well. So, it is difficult to assess the viable HCC tumors after TACE by conventional spin echo imaging[18]. The conflict between our study and Ebeed et al.[17] is likely because of the post-TACE cystic necrosis or intra-lesional hemorrhage in our study. Also we found an increase in T2 signal of the background liver post TACE procedure probably as a part of a generalized increase in T2 signal of body tissues post chemotherapy.

This was confirmed by keeping the paraspinal muscles as standard and obtaining ratios of T2 signal of normal liver and the lesion to the signal of paraspinal muscles. While lesion to paraspinal muscle signal ratio showed a significant change post TACE, the normal background liver to para spinal muscle signal ratio changed insignificantly [Table 2]. We therefore believe that although conventional MRI may help in understanding the un-

derlying mechanisms of local chemotherapy action, however their role vis-à-vis residual tumor viability is limited.

DWI has emerged as a robust means of assessing tumor viability and can detect early signal changes post TACE procedure.. In our study, DWI with b values of 0, 500, and 800 s/mm2 was applied using parallel imaging with respiratory triggering. Mean pre TACE ADC value of the liver parenchyma was 1.23 ± 0.17 x 10-3mm2/s while that of HCC lesions was 1.21 ±0.27x 10-3 mm2/s with no significant statistical difference (p value >0.1). This observation was also recorded by Kubota et al[19] and Lu et al[20] in their studies. However we found a significant increase (p value <0.001) in the post TACE ADC values of the lesions when compared to pre TACE values (2.0x 10-3 mm2/s versus 1.21x 10-3 mm2/s) indicating significant response and a mean increase of ADC signal of approximately 60%[Table 3 and 4, Figure 3 and 5]. The increase in ADC values has been documented in many previous studies including those of Kamel et al[13], Ibrahim YA et al[14] , Afifi et al[15] and Tantawy HI et al[16]. However in most of these studies the percentage increases in ADC value is not as high as our study probably owing to lack of other loco-regional therapies like radiofrequency ablation

used in our center. RF ablation prior to TACE can lead to necrosis and therefore a less increase in ADC values post TACE because of pre-existing necrosis.. We also found a significant increase in the ADC values of the background liver from 1.23x10-3 to 1.38x 10-3 (p value <0.0001) which was not in line with the previous studies. The possible reasons for this could be intracellular edema, tissue cellular death, and microcirculation disturbances due to systemic absorption of the drug post chemoembolization. This aspect needs further investigation however the fact that the mean ADC values of the normal liver reduced almost to pre TACE levels (1.26x10-3) on the 5 week scan is an indication of the transient nature of this change with no clinical or functional significance.

In our study out of 24 patients, 19 patients (79%) showed complete CEMRI response as assessed by m-RECIST (figure 4 and 5) while 5 patients (21%) showed partial response with viable tumor tissue in the form of mass like enhancement in 2 patients and peripheral nodular enhancement in 3 patients on DCE-MRI (figure 6). According to the percentage change in ADC values we divided our patients into four groups [Table 5]. We had 5 patients with less than 50% ADC value increase post TACE out of which 4 (80%) patients
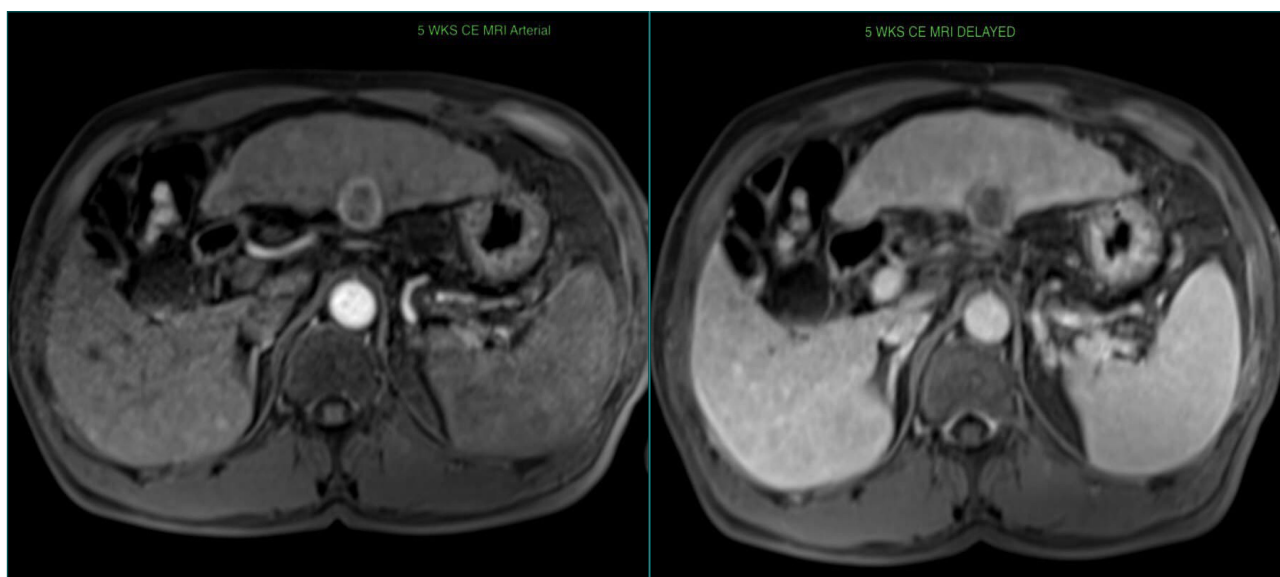

Figure.4. Pre-TACE (a) and post-TACE (b) contrast enhanced T1 vibe images in the same patient as figure 1 and 2 showing no evidence of any significant nodular or irregular peripheral enhancement suggesting a good response post-TACE.
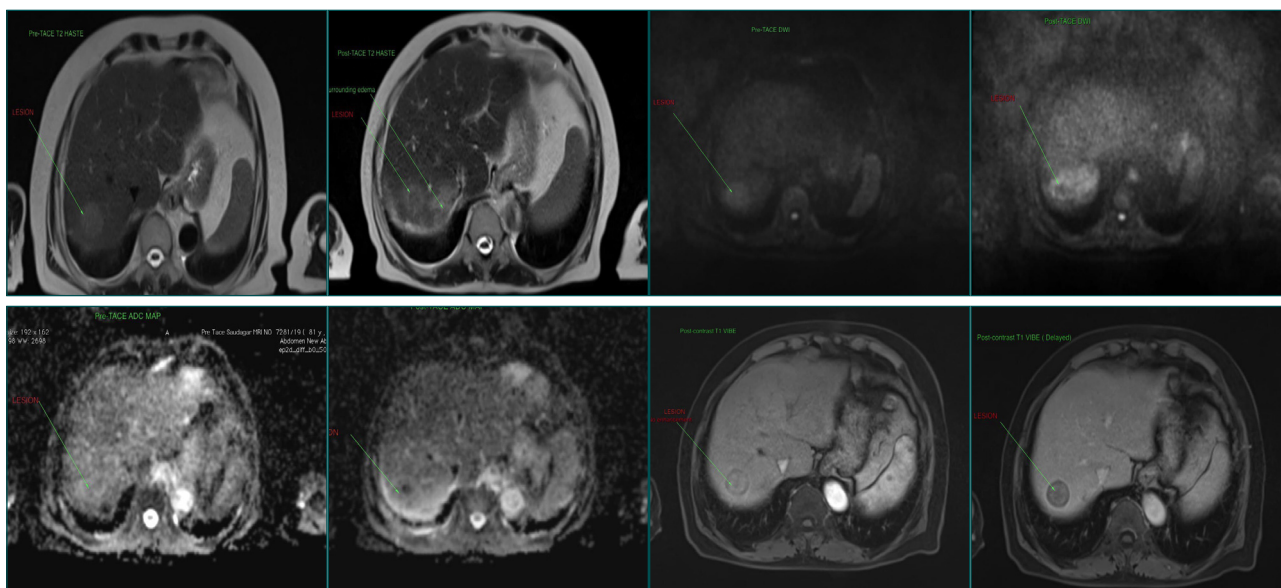
Figure.5. Pre- (a) and post-TACE (b) T2 HASTE images showing an increase in signal intensity in post TACE images suggesting edema. Pre (c ,e) and post TACE (d, f) axial images of the same patient in showing an increase in the ADC value of the lesion. The hypointensity in (f) is likely secondary to necrosis. 5 weeks post TACE CEMRI of the patient showing no residual lesion on arterial (g) and delayed (h) phase images.

showed partial response on 5 week CEMRI scan and one (20%) patient had complete CEMRI response. One false positive case in our study is possibly because of increase in signal intensity on DW MRI due to intra-lesional hemorrhage which showed diffusion restriction. Studies of Holtås et al.[21] and Tung et al.[22] stated that sterile liquefactive necrosis and intracavitary micro- hemorrhage may be the cause of high signal intensity in DWI of malignant necrotic lesions. 19 patients had facilitated diffusion with more than 50% post treatment ADC change. Among these 19 patients one (5%) patient showed partial response while 18 (95%) others showed complete response on 5 week CEMRI scan. Causes of false negative results of DWI may be due to increased ADC of tumor in well differentiated HCC or incorrect ROI placement including part of normal liver ,areas of nearby necrotic tissue or peritoneal fat. In our study, mean ΔADC in responders was higher than that of non-responders with a P value of 0.001 similar to the observations of Kubota et al.[19]. Although a specific threshold couldn't be obtained owing to the wide range of distribution of the ADC values, we believe that an ADC change of 50% in a HCC lesion (not previously treated) on day 5-7 DWI is a good indicator of future

complete response. However further inquest into this aspect is required. Similar problems in determining an ADC threshold was also encountered by Goshima et al[23]. The patients with partial response were taken up for a second session of TACE and are being followed for further recurrences.

DWI in our study as an indicator of early therapeutic response to TACE had a sensitivity, specificity, PPV and NPV of 80%, 94.7%, 80%, and 94.7%,respectively. Overall diagnostic accuracy of DWI was 91.7%. These numbers are quite similar to previous studies done by Ebeed Ebrahim et al[17] and Mohamed et al[24]. Our study had several limitations. First, technical difficulties of DWI such as poor signal-to-noise ratio and partial loss in spatial resolution were caused by increased sensitivity to pulsatile artifacts which could have introduced calculation errors. We tried to overcome these difficulties by placing the smallest possible ROI and having multiple measurements. Another limitation in our study was relatively small sized sample diminishing the statistical analysis power. Small sized sample could be attributed to the strict inclusion and exclusion criteria carried out for this research and the early days of TACE procedure.
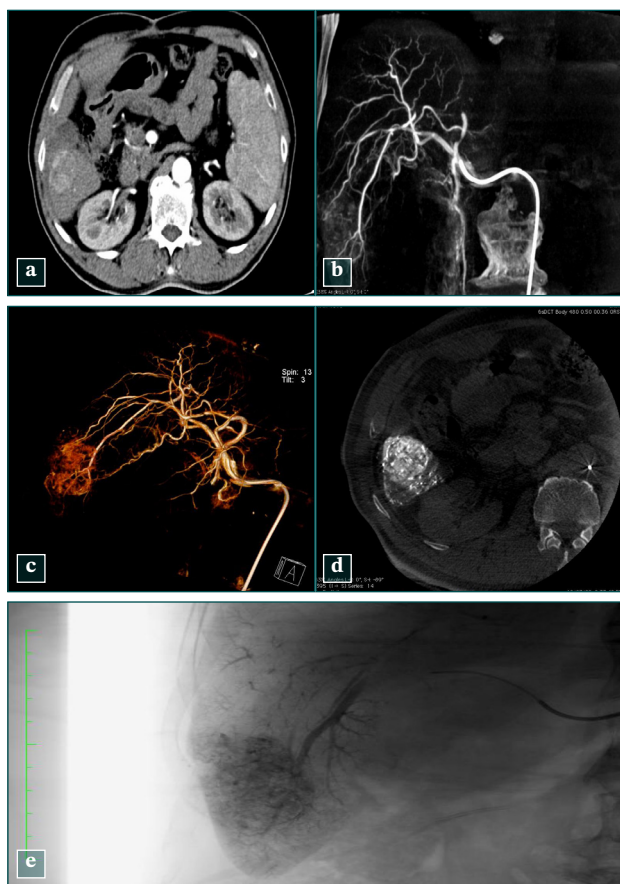
Figure.7. Shows a 57-year-old male with HCC in right lobe of liver. Pre-procedural CECT (a) showing arterial phase enhancing HCC lesion in segment 6 (blue arrow). MIP imaging (b) of rotational Dyna CT showing segmental arterial branches supplying the lesion. VRT images (c) showing the vascular anatomy of the lesion. Lipiodol deposition (d) in the lesion on DSA. Post TACE completion Dyna CT (e) showing homogenous type 1 deposition of contrast in the lesion.

Figure.6. Pre-TACE (a, b) and post-TACE axial DWI and ADC images (c, d) of the lesion respectively showing some increase in the ADC values of the lesion but significant areas of diffusion restriction in post TACE images. Corresponding post-TACE 5 week CEMRI image (e) arterial phase shows nodular enhancement in the lesion suggestive of residual lesion (partial response). This patient required a second session of TACE.

CONCLUSION

Post TACE HCC lesion assessment remains a tricky situation for the radiologist, however the early use of DWI can act as a path breaker. A significant increase (>50%) in mean ADC values of the lesion is a good indicator of complete response in most of the cases. Post-TACE mean ADC value of normal hepatic parenchyma can show a significant increase, however this change is clinically and functionally insignificant and partially reversible. DWI is a robust modality for early post TACE assessment with promising diagnostic accuracy and should be used in all cases.
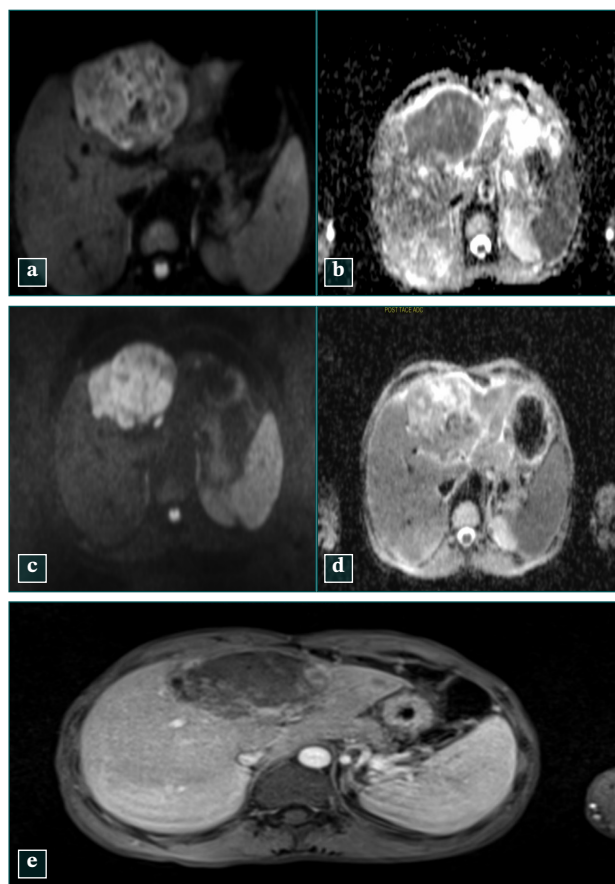
REFERENCES

1. El-Serag HB, Davila JA, Petersen NJ, et al. The continuing increase in the incidence of hepatocellular carcinoma in the United States: an update. Ann Intern Med 2003;139(10):817–823.
2. McGlynn KA, London WT. Epidemiology and natural history of hepatocellular carcinoma. Best Pract Res Clin Gastroenterol 2005;19(1):3–23.
3. Trevisani F, Cantarini MC, Wands JR, et al. Recent advances in the natural history of hepatocellular carcinoma. Carcinogenesis 2008;29(7):1299–1305.
4. Bruix J, Sherman M; American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma: an update. Hepatology 2011;53(3):1020–1022.
5. European Association For The Study Of The Liver; European Organisation For Research And Treatment Of Cancer. EASL- EO-

RTC clinical practice guidelines: management of hepatocellular carcinoma. J Hepatol 2012; 56(4):908–943.

6. Krinsky GA, Nguyen MT, Lee VS, et al. Dysplastic nodules and hepatocellular carcinoma: sensitivity of digital subtraction hepatic arteriography with whole liver explant correlation. J Comput Assist Tomogr 2000;24;628-634.

7. Hepatocellular carcinoma - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Barcelona-Clinic-Liver-Cancer-BCLC-staging-and-treatment-strategy-The-BCLC-system_fig2_322267682.

8. Bruix J, Sherman M; Practice Guidelines Committee, American Association For The Study Of Liver Diseases. Management of hepatocellular carcinoma. Hepatology 2005; 42: 1208-1236.

9. Baffy G, Brunt EM, Caldwell SH. Hepatocellular carcinoma in non- alcoholic fatty liver disease: an emerging menace. J Hepatol 2012;56(6):1384–1391.

10. Ito K, Honjo K, Fujita T, et al. therapeutic efficacy of transcatheter arterial chemoembolization for hepatocellular carcinoma: MRI and pathology. J Comput Assist Tomogr 1995; 19:198-203.

11. Semelka RC, Worawattanakul S, Mauro MA, et al. Malignant hepatic tumours: changes on MRI after hepatic arterial chemoembolization – preliminary findings. J Magn Reson Imaging 1998; 8:48-56.

12. Kubota K, Hisa N, Nishikawa T, et al. Evaluation of hepatocellular carcinoma after treatment with transcatheter arterial chemoembolization: comparison of lipoidol-CT, power Doppler sonography, and dynamic MRI. Abdom Imaging 2001; 26; 184-190.

13. Kamel IR, Liapi E, Reyes DK. Unresectable hepatocellular carcinoma: serial early vascular and cellular changes after transarterial chemoembolization as detected with MR imaging. Radiology 2009;250:466-473.

14. Ibrahim YA, ElGharib M, Sheha DM. Chemoembolization follow- up of hepatocellular carcinoma with diffusion-weighted MR imaging. The Egyptian Journal of Radiology and Nuclear Medicine (2015) 46, 871-878.

15. Afifi AH, Naguib AM, Seragaldin F. Diffusion weighted magnetic resonance imaging in assessment of hepatocellular carcinoma after chemoembolization. The Egyptian Journal of Radiology and Nuclear Medicine (2010) 47, 61-71.

16. Tantawy HI, Mohamed FF (2016) Diagnostic value of apparent diffusion coefficient (ADC) in evaluating hepatocellular carcinomas post trans-catheter arterial chemoembolization and radiofrequency ablation. Egypt J Radiol Nucl Med 47(3):699–706.

17. Ebraheem Ebeed A, Abd El-hamied Romeih M, Mohamed Refat M et al (2017) Role of dynamic contrast-enhanced and diffusion weighted MRI in evaluation of hepatocellular carcinoma after chemoembolization. Egypt J Radiol Nucl Med 48:807–815

18. Ozkavukcu E, Halilog lu N, Erden A. Post-treatment MRI findings of hepatocellular carcinoma. Cardiovasc Intervent Radiol 2010; 33(3):532-40.

19. Kubota K, Yamanishi T, Itoh S, et al. Role of diffusion weighted imaging in evaluating therapeutic efficacy after transcatheter arterial chemoembolization for hepatocellular carcinoma. Oncology Reports 24: 727-732, 2010.

20. Lu T-L, Becce F, Bize P, et al. Assessment of liver tumor response by high-field (3 T) MRI after radiofrequency ablation: short- and mid-term evolution of diffusion parameters within the ablation zone. Eur. J. Radiol.2012;81:944–50.

21. Holtås S, Geijer B, Strömblad LG, et al. A ring enhancing metastasis with central high signal on diffusion-weighted imaging and low apparent diffusion coefficients. Neuroradiology 2000; 42(11):824–7.

22. Tung GA, Evangelista P, Rogg JM, et al. Diffusion-weighted MR imaging of rim-enhancing brain masses: is markedly decreased water diffusion specific for brain abscess? AJR Am J Roentgenol 2001;177(3):709–12. doi:https://doi. org/10.2214/ajr.177.3.17 70709.

23. Goshima S, Kanematsu M, Kondo H, et al. Evaluating local hepatocellular carcinoma recurrence post-transcatheter arterial chemoembolization: is diffusion-weighted MRI reliable as an indicator? J Magn Reson Imaging 2008;27:834-839

24. Mohamed IY, Medhat MR, Mohamed HF. Role of diffusion-weighted magnetic resonance imaging in the evaluation of hepatocellular carcinoma response to transcatheter arterial chemoembolization using drug eluting beads; correlation with dynamic MRI. Egypt J Radiol Nucl Med 2017; 48: 817-24.