

Follow-up after Radiofrequency Ablation of Hepatocellular Carcinoma; Diffusion Weighted & Dynamic Contrast Enhanced MRI Characteristics

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Abstract

Background: Monitoring tumor response to loco-regional therapy is an increasingly important task in oncologic imaging.

Aim of Study: The aim of the study is to highlight the growing role of diffusion and dynamic MRI in the follow-up of patients with hepatocellular carcinoma after radiofrequency ablation, and hence playing a crucial role in evaluating treatment effectiveness and therefore in taking important decisions in the management of these patients.

Patients and Methods: This study included 80 patients, 61 males and 19 females, patients ages ranged from 32 to 85 years with the mean age of 60 years underwent Radiofrequency ablation of 100 hepatic focal lesions over a period of 19 months (July 2018-February 2020). The study was conducted in the Radiology Department at a private radiology centre.

Results: 69 lesions (69%) were resolved lesions while 31 lesions (31%) had residual/recurrent tumor viability. The measured cut off value between the completely ablated lesions and residual/recurrent lesions was $1.18 \pm 0.24 \times 10^{-3} \text{mm}^2/\text{s}$ after the 1st month and $1.22 \pm 0.30 \times 10^{-3} \text{mm}^2/\text{s}$ after 3-4 months. The ablated zones can be differentiated from liver parenchyma visually in the DWIs and by means of ADC in all patients. There is no statistical difference in the mean ADC values between the ablated zones of the resolved and unresolved lesions. All the 31 malignant lesions show arterial phase enhancement with 16 lesions out of 31 show persistent enhancement on the portal phase and show washout of the contrast on the delayed phase with 15 malignant lesion show washout of the contrast on the portovenous and delayed phases of the study. The enhancement is considered only if proved by the subtracted images.

Conclusion: MRI is a powerful tool in detection of tumour viability and response after RFA of hepatocellular carcinoma. Imaging protocols should include dynamic study, diffusion imaging with post processing of the images to obtain subtracted images and ADC measurements for precise tissue characterization and should be performed at regular time intervals.

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Key Words: Dynamic MRI – Hepatocellular carcinoma – Radiofrequency ablation.

Introduction

HEPATOCELLULAR Carcinoma (HCC) is one of the most common causes of cancer death worldwide [1]. Liver transplantation is the best curative option with good survival rates, although its use is restricted by the shortage of donor organs [2]. The tumors in most patients are unresectable because of a variety of factors including: Poor hepatic reserve, multifocal disease or inability to obtain an optimal tumor free margin [3].

The image guided locoregional treatment for patients with unresectable HCC includes chemical or thermal ablative techniques and catheter based approaches. Among the ablative techniques, Radiofrequency Ablation (RFA) has been used as the most popular method for treating early stage HCC [4].

Post-treatment follow-up is usually accomplished with both Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) but the MRI is found to be superior in detecting residual or recurrent tumors after treatment. MRI is also used for diagnosing post-treatment complications. For radiologists, familiarity with post-treatment MRI findings is critical for the correct interpretation of these examinations and for guiding further therapies [5]. The aim of the present study is to highlight the growing role of MRI in the follow-up of patients with hepatocellular carcinoma after radiofrequency ablation and evaluating treatment effectiveness and hence in taking clinical decisions in the management of these patients.

Patients and Methods

This study was performed on 80 cases of HCC who underwent radiofrequency ablation of 100 hepatic focal lesions over a period of 19 months (July 2018-February 2020), written informed consent was obtained from all patients before each procedure. The institutional review board of our institute approved the study. The patients were treated by radiofrequency ablation in Theodor Bilharz Research Institute and the follow-up imaging was conducted in the Radiology Department at a private radiology center. The patients' ages ranged between 32 to 85 years (mean age 60); 61 patients were males and 19 patients were females. Most of the patients had liver cirrhosis related to chronic viral hepatitis. Inclusion criteria are patients who were candidates for radiofrequency ablation & already underwent the procedure: Both sexes

are included and no age group predilection. Exclusion criteria are contraindications to MRI, contraindications to contrast media and liver tumour other than hepatocellular carcinoma. All cases had been subjected to the following: Full clinical assessment, revision of the patient's laboratory investigations including mandatory renal function tests (urea and creatinine) and liver functional test (if available), revision of the previous radiological investigations done for the patients. In our study the 80 patients were examined 1 month after the ablation and 3- 4 months after the ablation.

MRI protocol:

44 cases were performed using Philips 3 Tesla MRI scanner (Ingenia) and the other 36 cases were performed using Philips open 1 Tesla MRI scanner (Panorama HFO) with the following parameters.

- Pre-contrast imaging (Table 1):

Table (1): Pre-contrast imaging.

Sequence	TR (msec)		TE (msec)		FOV (mm)		Flip angle		Slicethickness	
	1 tesla	3 tesla	1 tesla	3 tesla	1 tesla	3 tesla	1 tesla	3 tesla	1 tesla	3 tesla
Axial T1 TFE	14	10	6.9	2.3	300-350		15	15	7mm	
Axial T2 TSE	1082	639	80	100	300-350		15	15	7mm	
Axial T2 WI SPAIR 991		842	80	70	300-350		15	15	7mm	

- Diffusion study:

Diffusion MR imaging was performed before the dynamic study using respiratory triggered fat-suppressed single-shot spin echo echoplanar sequence that combined the two diffusion (motion-probing) gradients before and after the 180° pulse. The acquisition parameters for 1 Tesla machines were TR 2270 msec, TE 78msec, matrix 100 X 83 with a field of view as small as possible, slice thickness 10mm, slice gap 1-2mm, scan time 4-5 min. We used b values of 0, 400 and 800s/mm². The acquisition parameters for 3 Tesla machines were: TR 7953msec, TE 64msec, matrix 104 X 89 with a field of view as small as possible, slice thickness 9mm, slice gap 1-2mm, scan time 3-4 min. We used b-values of 0, 500 and 1000s/mm².

- Dynamic study:

Dynamic study was performed after manual bolus injection of 0.1mmol/kg body weight of Gd-DTPA. Dynamic imaging using 3D fat-suppressed T1-weighted gradient echo sequence (THRIVE i.e. T1 high resolution isotropic volume examination). A dynamic series consisted of one pre contrast series followed by four successive post contrast series including early arterial, late arterial, and portal phases with 19-21 seconds intervals (17 seconds for image acquisition with breath-holding and 2-4 seconds for re-breathing) this is followed

by 5-min delayed phase imaging. All patients were imaged in end expiration to limit the risk of image misregistration. Acquisition parameters for open 1 Tesla machine were TR 3.3msec, TE 1.6msec, flip angle 10°, matrix size, 136 X 108, field of view 300-350mm and slice thickness 2-3mm. Acquisition parameters for 3 Tesla machines were TR 2.9msec., TE 1.3msec., flip angle 10°, matrix size, 160 X 160, field of view 300-350mm and slice thickness 2-3mm.

Analysis of the MR images:

Images were sent to the workstation (Phillips Extended MR Workspace) for further image processing. The morphological features of each lesion were recorded including size, border and signal intensity at T1, T2 and SPAIR images. Assessment for the presence of complications, residual or recurrent tumor viability.

ADC map measurement:

ADC maps were generated on the workstation. Calculation of the ADC value is an automated process available on the workstation. The ROI included the entire ablation zone. Another area of 2cm diameter in the surrounding cirrhotic liver parenchyma was also measured in each case. In case of focal hyperintensity within or at the margins of the ablation zone; its ADC value was calculated.

The ADC was measured three times and the three measurements were averaged.

Dynamic study analysis:

We perform arterial and portal phasesubtraction which is automated process available on the workstation. Pattern of enhancement in the dynamic imaging and subtracted images was then studied.

Interpretation of the MR image:

Signal of the ablation zone at T1, T2, SPAIR and diffusion WIs was classified as: High, low or heterogeneous. ADC measurement (mean and ADC ratios) of the cirrhotic parenchyma, ablation zone, surrounding parenchymal changes and any focal hyperintensity.

Dynamic study interpretation:

Arterial phase enhancement: That should be confirmed by the subtraction images (to prove that the high signal in the arterial phase is due to enhancement and not due to the original pre-contrast high T1 signal). Contrast washout: Decrease in the enhancement on delayed phase imaging compared with early phase imaging. Presence of ill-defined perilesional parenchymal enhancement: Post interventional reactive changes: This is defined as early phase enhancement beyond the ablated cavity on the surrounding liver parenchyma that persists in the delayed phase. Perfusion abnormalities (transient hepatic intensity difference): Ill-defined parenchymal enhancement during the arterial phase. This occurs in cases of injury of the portal vein or traumatic arteriportal shunting. Well defined enhancement at the margin of the ablation zone which may be either: Granulation tissue rim: Persistent or delayed phase enhancement. Nodular or hallow enhancement: That suggest tumour recurrence.

Types of tumour progression:

We follow the classification reported by Chopra et al., 2001 [6] as follow: Halo type: Irregular, thick rim of enhancement around the ablation zone. Nodular type: Nodular foci of enhancement at the margins of the ablation zone. Gross enlargement type: Overall increase in the size of the ablation zone.

We categorize the patients into two groups:

Resolved group: No MRI signs of residual or recurrent viability (regardless the presence of newly developed lesions). Unresolved group: If there is evidence of residual or recurrent tumor.

Standard of reference:

It was difficult to obtain pathologic confirmation in patients who underwent radiofrequency ablation

because most of them did not undergo surgery. In addition, biopsy could have resulted in sampling error as recurrent lesions are mostly small nodules. So, the standard of reference was: - Benign findings (resolved lesions) are considered if the finding becomes stationary, regressed or disappeared in the follow-up studies. Residual/recurrent HCC (unresolved lesions) is considered if: Increased in the size of the ablation zone when comparing the images obtained 3-4 months after treatment with those 1 month after treatment. Focal area at the margin of the ablation zone that shows: Diffusion hyperintensity (restriction) and low ADC value, early or late arterial phase enhancement that must be proved by the subtraction images, contrast washout: The lesion becomes hypointense relative to the liver parenchyma in the delayed phase.

Statistical analysis:

Results are expressed as mean \pm standard deviation or number (%). Comparison between mean values of ADC in the studied groups was performed using unpaired *t*-test. *p*-value less or equal to 0.05 was considered significant and less than 0.01 was considered highly significant.

Results

The study group consisted of 80 patients underwent RFA for 100 hepatic focal lesions, 61 were males (76.25%) and 19 were females (23.75%). Age of these patients ranged from 32 to 85 years (mean age: 60). We classified the ablated lesions into two groups; resolved (benign) group: No MRI signs of residual or recurrent viability at the ablated lesion (regardless the presence of other lesions). Unresolved (malignant) group: If there's evidence of residual or recurrent viability.

69 lesions (69%) were resolved lesions while 31 lesions (31 %) had residual/recurrent tumor viability. The formentioned 31 lesions showing residual/recurrent tumoral activity, they showed the following types of tumoral activity based on their pattern of enhancement: Nodular type: The most common type and detected in 13 lesions (41.9%), Halo type: Detected in 8 lesions (25.8%), gross enlargement type: Detected in 6 lesions (19.4%), more than one type: Detected in 4 lesions (12.9%) where there were nodular and halo recurrence.

In our study the signal intensity of the of the 31 unresolved lesions showing the following signal intensity in the following T1, T2 WI and DCE-MRI was, 20 (61.5%) was intermediate, 8 (25.8%) was low and 3 (9.7%) was high on T 1 WI while 10

(32.3%) was intermediate and 21 (67.7%) was high on T2WI and 31 (100%) showing arterial enhancement, 16 (19.4%) showing persistent portovenous enhancement, 15 (48.4%) showing wash out on the portovenous phase and 31 (100%) showing washout in the delayed phase on the DCE-MRI. The enhancement is considered only if proved by the subtracted images. We correlates the DCE-MRI findings of the lesions 1 month after the ablation to the final diagnoses and showing 27 (27%) was true positive lesions, 3 (3%), 66 (66%) was true negative lesions and 4 (4%) was false negative lesions. The signal intensity of unresolved lesion of DW-MRI as compared to the ablative zone was 26 (81.5%) was high signal and 5 (16.1%) was intermediate in the 1st month after ablation and 23 (74.2%) was high and 8 (25.8%) was intermediate in 3-4 months follow-up after ablation.

Table (2): Statistical significance of the ADC values of the entire liver parenchyma, entire ablation zones, malignant lesions and reactive tissue changes.

Category	No. of the lesions		Mean ADC		± SD	
	1st month	3-4 month	1st month	3-4 month	1st month	3-4 month
Cirrhotic parenchyma	100	100	0.966	0.988	0.20	0.22
Entire ablation zone in RFA lesions	100	100	1.18	1.22	0.24	0.30
Malignant lesions	27	31	0.87	0.92	0.24	0.33
Reactive tissue change	100	100	1.02	1.29	0.23	0.12

Significance of the ADC value measured at the entire ablation zone, cirrhotic liver parenchyma, residual/recurrent tumoral tissue, post ablation changes (Table 3).

Table (3): Statistical significance of different ADC values.

	Mean ADC value	p-value	ce
• Entire ablation zone versus cirrhotic liver parenchyma.	1.220	0.0001 **	Significantly higher
• Residual/recurrent tumoral tissue versus entire ablation zone.	0.92	0.0008 **	Significantly lower
• Residual/recurrent tumoral tissue versus cirrhotic liver parenchyma.	0.92	0.003	Significantly lower
• Post ablation changes versus residual/recurrent tumoral tissue.	1.29	0.0001 **	Significantly higher

We correlates the DW-MRI findings of the lesions 1 month after the ablation to the final diagnoses and showing 22 (22%) was true positive lesions, 4 (4%) was false positive lesions, 66 (66%) was true negative lesions and 8 (8%) was false negative lesions while after 3-4 months 23 (23%)

We studied presence of perilesional parenchymal enhancement and was found to be benign finding (based on the follow-up study) that represents reactive inflammatory and vascular changes of the liver parenchyma adjacent to the ablation zone. These areas exhibited mild hyperintensity on the diffusion imaging. This was present in 74 out of the 100 lesions imaged within the 1st month after ablation (74%) which persists in 72 lesions out of 100 imaged at 3-4 months after ablation (72%).

We used the following ADC values of the entire ablation zones, recurrent lesions, surrounding parenchymal changes and cirrhotic liver parenchyma at b-value of 0, 400, 800 or 0, 500, 1000s/mm² were calculated for the different study groups to avoid intravoxel perfusion effect which result from low b-values (<50s/mm²) as well as image degradation from high b-value (>1000s/mm²) (Table 2).

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 Table (4): Sensitivity, specificity, accuracy, PPV, NPV of the dynamic and diffusion WI.

	MRI 1 month follow-up	D W I 1 month follow-up	D W I 3-4 follow-up
• Sensitivity	87.09%	73%	74%
• Specificity	95.5%	94%	96%
• Accuracy	93%	88%	89%
• Positive predictive value(PPV)	90%	85%	88%
• Negative predictive value(NPV)	94.3	89%	89%

Regarding complication detected after intervention, was found in 33 lesions in the form of biliary complication secondary to injury in 5 lesions (5%), portal vein thrombosis without secondary perfusion changes in 5 lesions (5%), portal vein thrombosis with secondary perfusion changes in 11 lesion

(11%) and perihepatic collection in 12 lesions (12%) with no detectable other major complications

such as hemorrhage, infection or seedling of malignant cells along the ablation tract Figs. (1,2).

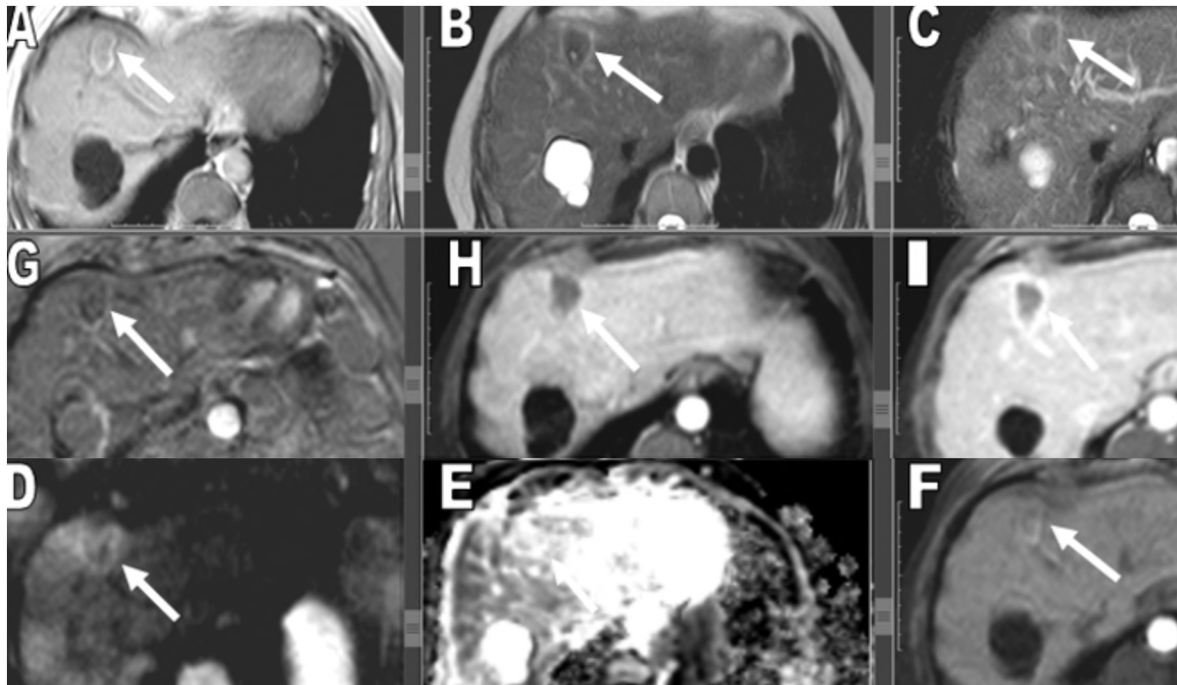


Fig. (1): 57-year-old male patient with liver cirrhosis underwent radiofrequency ablation of left hepatic lobe segment IV focal lesion. The patient underwent dynamic MRI with diffusion study of 1 & 4 months after the ablation. (A, B & C) axial T1, T2 & SPAIR WI 1 months after the ablation showing the ablated segment IV lesion displaying coagulative necrosis of high T1, low T2 and SPAIR signal (arrows). (D) Diffusion WIs and (E) ADC map at the same level show no diffusion restriction, the ADC value of the entire ablation zone is $1.42 \times 10^3 \text{mm}^2$ and of the ADC value of the cirrhotic liver parenchyma is $0.96 \times 10^3 \text{mm}^2$ (arrows). (F, G, H & I) Dynamic post contrast axial arterial, arterial subtraction, portal and delayed phase images showed no significant early arterial post contrast enhancement (best appreciated on the dynamic subtraction images) denoting successful ablation with marginally enhancing rim detected on the delayed phase denoting granulation tissue (arrows). Non-enhancing right hepatic lobe cyst is also noted.

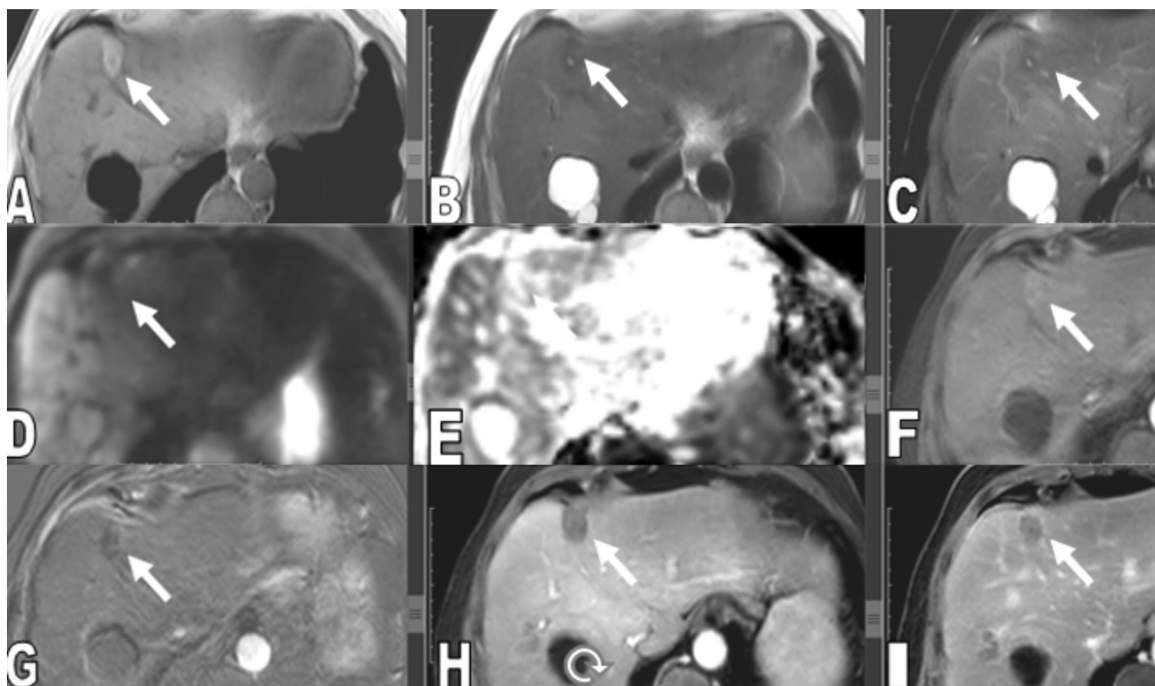


Fig. (2): (A, B & C) Axial T1, T2 & SPAIR WI 4 months after the ablation showing mild size regression of the ablated segment IV lesion still displaying high T1, low T2 and SPAIR signal (arrows). (D) Diffusion WIs and (E) ADC map at the same level still show no diffusion restriction, the ADC value of the entire ablation zone is $1.2 \times 10^3 \text{mm}^2$ and of the ADC value of the cirrhotic liver is $0.9 \times 10^3 \text{mm}^2$ (arrows). (F, G, H & I) Dynamic post contrast axial arterial, arterial subtraction, portal and delayed phase images showed no significant post contrast enhancement on the arterial and portovenous phases (best appreciated on the dynamic subtraction images) denoting successful ablation (arrows). Still noted surrounding fine enhancing rim on the delayed phase denoting granulation tissue. Final diagnosis: Well ablated lesion with marginal granulation tissue rim.

Discussion

Monitoring tumor response to loco-regional therapy is an increasingly important task in oncologic imaging. Early favorable response generally indicates effectiveness of therapy, and may result in significant survival benefit. Early identification of treatment failure is also critical in patient management, since a repeat treatment cycle can be performed if liver function is maintained, before disease progression occurs. DWI has been shown to be sensitive to micro environmental changes in tumors at molecular level that result from treatment and hence may be able to predict early response to locoregional therapy [7]. Dynamic contrast enhanced MR imaging can assesses the change in tumor vascularity and perfusion after TACE or local ablation therapy [8].

The signal intensity of the entire ablation zone on non enhanced T1 & T2 weighted images were studied and we found that on the 1st month after ablation, homogenous high T1 & T2 in 80% and 25%, heterogenous T1 & T2 in 13% and 18% while was homogenous low in 7% and 57% respectively while after 3-4 months follow-up, the ablation zone was homogenous high in both T1 & T2 in 81% and 23% respectively and heterogenous in 7% and 12% and homogenous low in 12% and 65% respectively. The heterogeneity of the ablation zone in the early post ablation imaging could be explained by the different tissue changes after ablation including oedema, haemorrhage and inflammatory reaction. Such changes mostly resolved within 3-4 months after ablation leaving the coagulation necrosis with the characteristic homogenous high T1 and low T2 signal.

Our findings agreed with Kierans et al., 2010 [9] who performed a study over 203 ablated lesions for which MRI was acquired <4, 4-9, and >9 months after radiofrequency ablation, cryoablation, and microwave ablation. They found that 87.8% of the ablation zones imaged within the first 4 months after ablation show high T1 signal with persistence of the high signal in about 84.1% in patients imaged >9 months after ablation. This is also agreed with Dromain et al., 2002 [10] examined 50 hepatic tumours treated with RFA underwent MR imaging at 2, 4, and 6 months. They found at the 2 months follow-up that 28% of the RF-treated areas were hypointense and homogeneous and 72% was heterogeneous with a peripheral hyperintense ring at T1-weighted images. On T2-weighted MR images, 54% of the RF treated areas were hypointense and homogeneous, 14% were isointense and

homogeneous, 32% were heterogeneous with foci of high signal intensity.

We didn't find significant difference in the signal intensity of the entire ablation zone between the resolved and unresolved groups at the early imaging follow-up. This agreed with Kierans et al., 2010 who detected no significant signal changes at the follow-up within the first 4 months after ablation. This could be explained by the fact that the recurrence is mostly at the margin of the ablation zone. This is also may be contributed to the post-treatment reactive changes that occur within the ablation zone which may mask any recurrent lesions within the center of the ablation zone [9].

We also studied the signal intensity of the recurrent lesions on unenhanced T1 and T2 WI and we classified the signal intensity of the lesion into intermediate, high or low signal (relative to the ablation zone). We found 67.7% of the recurrent lesions eliciting high T2 signal relative to the ablation zone and only 23.3% of the lesions elicits intermediate signal on T2. On T1 WI 64.5% of the lesions elicit intermediate signal, 25.8% elicit low T1 signal and 9.7% elicit high T1 WI signal. This shows that T2 weighted images is superior to non enhanced T1 WI weighted images in detection of tumour recurrence. This agreed with Dromain et al., 2002 [10] who found 8 recurrent lesions (out of the 9 local recurrence detected within 2 months after the ablation), six of the eight local regrowths (75%) exhibited moderate high signal intensity on T2-weighted images and contrast material uptake on T1-weighted images. The two remaining local regrowths (25%) were detected only on T2-weighted images as hyperintense nodules abutting the hypointense necrotic area, without suspicious areas being detectable on T1-weighted images before or after contrast medium injection. So an assessment of HCC post RFA ablation based on precontrastsequencies signal intensity is a conflict issue. The ADC values of the entire ablation zones, recurrent lesions and surrounding parenchymal changes and cirrhotic liver were calculated for the different study groups and we found that the mean ADC value of the entire ablation zone in the RF ablated lesions (whether resolved or non resolved) was $1.18 \pm 0.24 \times 10^{-3} \text{mm}^2/\text{s}$ after the 1st month and $1.22 \pm 0.30 \times 10^{-3} \text{mm}^2/\text{s}$ after 3-4 months. We found the mean ADC value of the recurrent or residual lesions in the malignant group was $0.87 \pm 0.24 \times 10^{-3} \text{mm}^2/\text{s}$ after the 1st month and $0.92 \pm 0.33 \times 10^{-3} \text{mm}^2/\text{s}$ after 3-4 months while the mean ADC value of the surrounding parenchymal changes was $1.02 \pm 0.23 \times 10^{-3} \text{mm}^2/\text{s}$ after the 1st month and $1.29 \pm 0.12 \times 10^{-3} \text{mm}^2/\text{s}$ after 3-4 months.

Then comparison between different study groups was done and we found that: The mean ADC value of the entire ablation zones in all the 100 ablated focal lesions (whether resolved or unresolved) in the study was significantly higher than mean ADC of the cirrhotic liver parenchyma ($p=0.0001$ * *). The mean ADC value of the recurrent or residual malignant lesions in the 31 focal lesions in the unresolved group was significantly lower than the mean ADC of the entire ablation zones in all the 31 lesions in the study ($p=0.0008$ **).

The mean ADC value of the recurrent or residual malignant lesions in the 31 focal lesions in the unresolved group was significantly lower than the mean ADC of the cirrhotic liver parenchyma ($p=0.003$ **). The mean ADC value of the post treatment reactive tissue changes was significantly higher than the mean ADC of the recurrent or residual malignant lesions ($p=0.0001$ * *). There was no statistical difference in the mean ADC values between the entire ablation zones of the resolved and unresolved groups ($p=0.70$ **).

Our results agreed with Schraml et al., 2009 [11] who studied 148 consecutive follow-up MR examinations of 54 patients after RFA of malignant focal lesions. Apparent Diffusion Coefficient (ADC) values of ablation zones and liver parenchyma were assessed. ADC values of ablation zones and adjacent signal alterations identified in DWI were analysed with regard to local tumour recurrence. They found that mean ADC values of the entire ablation zones was $1.19 \pm 0.30 \times 10^{-3} \text{ mm}^2/\text{s}$ while for the liver parenchyma was $1.06 \pm 0.21 \times 10^{-3} \text{ mm}^2/\text{s}$ ($p=0.0003$). No evident changes in ablations' ADC values over time could be identified. They also found that ADC values obtained from the entire ablation zones did not significantly differ between the resolved group ($1.22 \pm 0.30 \times 10^{-3} \text{ mm}^2/\text{s}$) and the unresolved groups ($1.19 \pm 0.30 \times 10^{-3} \text{ mm}^2/\text{s}$). They also found that the mean ADC value of the recurrent lesions differs significantly from the mean ADC value of the surrounding parenchymal tissue changes ($p=0.0124$). Lu, T-L., et al., 2012 [12] performed a study over 43 malignant liver lesions underwent liver MRI (3.0 T) before and after RFA (at 1, 3 and 6 months) using T2-, gadolinium-enhanced T1- and DWI-weighted MR sequences. They measured the ADC value of the entire ablation zones in cases without tumour recurrence. The pre-treatment value was $1.20 \pm 0.26 \times 10^{-3} \text{ mm}^2/\text{s}$. At 1 month, it was 1.46 ± 0.33 while at 6 months they found it to be 1.52 ± 0.33 . The values at 1 month and at 6 months were significantly higher than the pre-treatment value ($p=0.007$ and $p=0.026$, respectively).

In our study, all the 31 malignant lesions show arterial phase enhancement with 16 lesions out of 31 show persistent enhancement on the portal phase. All the 31 malignant lesion show washout of the contrast on the delayed phase with 15 malignant lesion show washout of the contrast on the portovenous and delayed phases of the study. The enhancement is considered only if proved by the subtracted images. We followed the study of Yu et al. (2009), Goshima et al. (2008) and Boll D & Merkle E.M. (2009) [13-15], who considered that the follow-up MRI is the standard of reference. We considered the dynamic MRI on 3-4 months to be the standard of reference and we calculated the sensitivity, specificity, accuracy, PPV & NPV of the dynamic MRI 1 month after the RFA, the diffusion MRI after 1 month and 3-4 months following the RFA as compared to the dynamic MRI findings after 3-4 months of the RFA. We correlated the dynamic findings on the 1st month following the ablation to the final diagnoses (findings on the dynamic study performed 3-4 months following the ablation), 27 lesions (27%) were true positive, 3 lesions (3%) were false positive, 66 lesions (66%) were true negative and 4 lesions (4%) were false negative. We correlated the diffusion findings on the 1st month follow-up compared to the final diagnoses (findings on the dynamic study performed 3-4 months following the ablation), 22 lesions (22%) were true positive, 4 lesions (4%) were false positive, 66 lesions (66%), were true negative and lesions (8%) were false negative. We correlated the diffusion findings on the 3-4 month follow-up compared to the final diagnoses (findings on the dynamic study performed 3-4 months following the ablation), 23 lesions (23%) were true positive, 3 lesions (3%) were false positive, 66 lesions (66%), were true negative and 8 lesions (8%) were false negative.

Our study revealed that the dynamic MRI of the 1st month follow-up as compared to the dynamic MRI done 3-4 months follow-up had a sensitivity of 87.09%, a specificity of 95.5%, accuracy of 93%, PPV of 90% and NPV of 94.3%. The diffusion weighted MRI on the 1st month follow-up has a sensitivity of 73%, specificity of 94%, accuracy of 88%, PPV of 85% & NPV of 89% as compared to the dynamic MRI done 3-4 months follow-up, while the diffusion weighted MRI on the 3-4 months follow-up has a sensitivity of 74%, specificity of 96%, accuracy of 89%, PPV of 88% & NPV of 89% as compared to the dynamic MRI done 3-4 months follow-up. Our results are matching with those of Yu et al. (2009) and Goshima et al., (2008) showing dynamic contrast enhanced MRI to be superior to diffusion weighted MRI in

evaluating HCC response to treatment as dynamic MRI had a sensitivity of 90.5%, a specificity of 96.6% as compared to 100% and 65.5% respectively of diffusion weighted imaging [13,15].

Limitation of our study. First, the lack of histologic proof in our cases, but this is related to clinical practice where histology is not always indicated. Second, the MR examinations were performed on systems at two different field strengths with a small variance of sequences but we believe that these factors did not affect our results. Third, limitation of the DWI is that the measurement of the ADC of the entire ablation zone is not accurate in detection of the recurrent lesion within the center of the ablation zone as it could be masked by the post ablation changes, however the fact that most of the recurrence occur at the periphery of the ablation zone rather than within its center should be considered. Fourth, limitation in diffusion analysis includes absence of pre interventional MRI in most cases so we didn't have the ADC before the treatment. In conclusion, we are certain that diffusion weighted and dynamic MRI play a crucial role, complete each other in the assessment of response of HCC to RFA measurements for better tissue characterization, and should be performed at regular time intervals.

References

- 1- RAWLA P., SUNKARA T., MURALIDHARAN P. and RAJ J.P.: Update in global trends and aetiology of hepatocellular carcinoma. *Contemp. Oncol. (Pozn)*, 22 (3): 141-50, 2018.
- 2- AZZAM A.Z.: Liver transplantation as a management of hepatocellular carcinoma. *World J. Hepatol.*, 7 (10): 1347-54, 2015.
- 3- ARIF-TIWARI H., KALB B., CHUNDRU S., SHARMA P., COSTELLO J., GUESSNER R.W., et al.: MRI of hepatocellular carcinoma: An update of current practices. *Diagn. Interv. Radiol.*, 20 (3): 209-21, 2014.
- 4- N'KONTCHOU G., MAHAMOUDI A., AOUT M., GANNE-CARRIE N., GRANDO V., CODERC E., et al.: Radiofrequency ablation of hepatocellular carcinoma: long-term results and prognostic factors in 235 Western patients with cirrhosis. *Hepatology*, 50 (5): 1475-83, 2009.
- 5- OZKAVIUKCIE HALILOGLU N. and ERDEN A.: Post-treatment MRI findings of hepatocellular carcinoma. *Diagn. Interv. Radiol.*, 15 (2): 111-20, 2009.
- 6- CHOPRA S., DODD G.D., 3rd, CHINTAPALLI K.N., LEYENDECKER J.R., KARAHAN O.I. and RHIM H.: Tumor recurrence after radiofrequency thermal ablation of hepatic tumors: Spectrum of findings on dual-phase contrast-enhanced CT. *AJR Am. J. Roentgenol.*, 177 (2): 381-7, 2001.
- 7- MOSTAFA M.M.S.: Diffusion weighted and dynamic contrast enhanced magnetic resonance imaging in assessment of malignant liver tumors after percutaneous radiofrequency ablation. *The Egyptian Journal of Radiology and Nuclear Medicine*, 7 (10): 1347-54, 2016.
- 8- KIM K.W., LEE J.M. and CHOI B.I.: Assessment of the treatment response of HCC. *Abdom. Imaging*, 36 (3): 300-14, 2011.
- 9- KIERANS A.S., ELAZZAZI M., BRAGA L., LEONARDOU P., GERBER D.A., BURKE C., et al.: Thermoablative treatments for malignant liver lesions: 10-year experience of MRI appearances of treatment response. *AJR Am. J. Roentgenol.*, 194 (2): 523-9, 2010.
- 10- DROMAIN C., De BAERE T., ELIAS D., KUOCH V., DUCREUX M., BOIGE V., et al.: Hepatic tumors treated with percutaneous radio-frequency ablation: CT and MR imaging follow-up. *Radiology*, 223 (1): 255-62, 2002.
- 11- SCHRAML C., SCHWENZER N.F., CLASEN S., REMPPH. J., MARTIROSIAN P., CLAUSSEN C.D., et al.: Navigator respiratory-triggered diffusion-weighted imaging in the follow-up after hepatic radiofrequency ablation-initial results. *J. Magn. Reson. Imaging*, 29 (6): 1308-16, 2009.
- 12- LU T.L., BECCE F., BIZE P., DENYS A., MEULI R. and SCHMIDT S.: Assessment of liver tumor response by high-field (3T) MRI after radiofrequency ablation: Short- and mid-term evolution of diffusion parameters within the ablation zone. *Eur. J. Radiol.*, 81 (9): e944-50, 2012.
- 13- YU J.S., KIM J.H., CHUNG J.J. and KIM K.W.: Added value of diffusion-weighted imaging in the MRI assessment of perilesional tumor recurrence after chemoembolization of hepatocellular carcinomas. *J. Magn. Reson. Imaging*, 30 (1): 153-60, 2009.
- 14- BOLL D.T. and MERKLE E.M.: Diffuse liver disease: Strategies for hepatic CT and MR imaging. *Radiographics*, 29 (6): 1591-614, 2009.
- 15- GOSHIMA S., KANEMATSU M., KONDO H., YOKOYAMA R., KAJITA K., TSUGE Y., et al.: Diffusion-weighted imaging of the liver: Optimizing *b*-value for the detection and characterization of benign and malignant hepatic lesions. *J. Magn. Reson. Imaging*, 28 (2): 201-7, 2008.

دور التصوير بواسطة الرنين المغناطيسي الديناميكي بعد حقن الصبغة والرنين المغناطيسي باستخدام خاصية الانتشار في متابعة مرض سرطان الكبد بعد التردد الحرارى

تعتبر أورام الكبد الأولية الخبيثة من أكثر الأورام السرطانية إنتشاراً على مستوى العالم ونتائجها المستقبلية سيئة إذا لم تعالج بطريقة صحيحة. ويعتبر التردد الحرارى من الطرق الواعدة فى علاج أورام الكبد فى المرضى الذين لا تسمح حالتهم الصحية بإجراء الجراحة. ولذلك أصبح من الضرورى متابعة إستجابة الورم للعلاج الحرارى حيث أن الإستجابة الجيدة تدل على مدى فاعلية العلاج. وقد أضافت التقنيات الحديثة للرنين المغناطيسى القدرة على متابعة التغيرات الميكروسكوبية لخلايا الورم مما يسمح بالمتابعة الدقيقة لإستجابة الورم للعلاج والتفرقة بين عودة نشاط الورم والتغيرات الحميدة التى تحدث فى خلايا الكبد المحيطة بالورم نتيجة العلاج الحرارى. ومن هذه التقنيات الحديثة، فحص الصبغة الديناميكي والتصوير بالرنين المغناطيسى باستخدام خاصية الإنتشار وأجريت هذه الدراسة على مئة بؤره كبدية تم تشخيصها على أنها سرطان الكبد الأولي وأجرى لهم التردد الحرارى حيث تم إجراء فحص الرنين المغناطيسى وقد تم فحص البؤر الكبدية من حيث الشكل، الحجم، إشارة الرنين المغناطيسى الإعتيادى وإشارتها بعد التصوير بخاصية الإنتشار وأيضاً بعد حقن الصبغة. وقد وجدنا أهمية الفحص الديناميكي بالصبغة فى تشخيص عودة النشاط السرطاني بأنواعه المختلفة بينما أضاف الرنين الإنتشارى القدرة على التفرقة بين عودة نشاط الورم والتغيرات الحميدة التى تحدث فى خلايا الكبد المحيطة بالورم نتيجة العلاج الحرارى. أظهرت نتائج هذه الدراسة إرتفاع أداء التشخيص بفحص الرنين المغناطيسى الديناميكي مقارنة مع الرنين بطريقة الإنتشار. وقد وجدنا أن التصوير بالرنين المغناطيسى بخاصية الإنتشار يزيد من حساسية الرنين المغناطيسى فى تشخيص وجود نشاط للمرض. كما وجدنا أن الفحص الديناميكي بالصبغة هو حجر الزاوية فى تشخيص وجود النشاط السرطاني.