ORIGINAL ARTICLE

Diffusion weighted magnetic resonance imaging in assessment of hepatocellular carcinoma after chemoembolization

A.H. Afifi *, A.M. Naguib, F. Seragaldin

Department of Radiology, Alexandria University, Egypt

Received 29 June 2015; accepted 4 October 2015
Available online 2 November 2015

KEYWORDS
Diffusion; MRI; H.C.C.; Liver; Post-TACE

Abstract
Objective: To evaluate role of DWI in assessment of H.C.C. after TACE.

Patients and methods: Twenty patients with H.C.C., mainly in sixth and seventh decades underwent TACE therapy. The baseline hepatic MRI before chemoembolization used 1.5-T closed magnet and then follow-up 3 weeks post-TACE included axial T1, T2 WI, DWI and dynamic contrast study. DWI used b values 0, 300, and 600 s/mm² then measured ADC value on dedicated workstation.

Results: ADC measurement within H.C.C. tumor was significantly lower than normal liver parenchyma before TACE with increased ADC in the necrotic tissue after TACE. Fifteen patients showed a partial response with increased tumor necrosis. Complete response occurred in five patients as absent residual viable tumor tissue on DWI. Statistical analysis showed that DWI has sensitivity of 86.67%, specificity of 80%, positive predictive value of 92.86% and negative predictive value of 66.67%.

Conclusions: MRI DWI offers quick and non-invasive technique to distinguish between viable and necrotic tumor areas and helps the diagnosis of residual tumor. Potential effect of treatment can be detected as increase in the diffusion coefficient. We recommend that optimal follow-up after image guided trans-catheter tumor therapy should include DWI and contrast-enhanced MRI.

1. Introduction

Hepatocellular carcinoma (HCC) is the commonest hepatic malignancy. In Egypt, between 1993 and 2009, there was an almost two and half fold increase in HCC among chronic liver patients. With the highest prevalence of hepatitis C worldwide, increasing urbanization, smoking rates, environmental exposures, and aging, HCC will continue to rise in next few decades forming major health problem (1,2).

HCC is an aggressive tumor with a median survival following diagnosis of approximately 6–20 months. Surgical resection is considered to be the only curative treatment for HCC, but only a small number of patients were able to undergo such treatment (3).
Selective arterial treatment of liver tumors with chemotherapeutic and embolic agents has been used for almost 20 years. Trans-arterial chemoembolization causes acute ischemic damage to HCC and results in coagulative necrosis because HCC is nourished only by the hepatic artery. Prior studies have shown survival benefits of trans-arterial chemoembolization (TACE), with cumulative survival probability superior to that achieved with the best systemic chemotherapy (4).

Viable neoplastic tissue may remain in some cases after TACE, so assessment of post-TACE tumor response is important in determining treatment success and in guiding future therapy. Early identification of treatment failure is also critical in patient management, since a repeat treatment cycle can be performed if liver function is maintained. The decision to repeat TACE or look for alternative treatment should be based on the assessment of residual tumor (5).

Follow-up using sonography, computed tomography and magnetic resonance imaging has been used to assess therapeutic efficacy. However, conventional imaging necessitates injection of contrast material and shows some limitations in the evaluation of therapeutic efficacy (6).

Diffusion-weighted imaging (DWI), a functional MRI technique that detects signal changes in tissues due to water proton motion varies based upon degree of cell membrane integrity (7,8).

The intact membranes of viable tumor cells restrict water diffusion, whereas necrotic tumor cells with disrupted cell membranes exhibit increased water diffusion. Previous preclinical and clinical studies have shown that tumor necrosis is associated with an increase in ADC value, thereby allowing differentiation between viable and necrotic portions of tumor (7).

With advances in hardware and coil systems, DWI can now be applied to liver imaging with improved image quality. DW MR imaging enables qualitative and quantitative assessment of tissue diffusivity (by apparent diffusion coefficient) without the use of gadolinium chelates, which makes it a highly attractive technique, particularly in patients with severe renal dysfunction (9).

2. Aim of the work

The aim of the current work was directed to study the role of diffusion weighted magnetic resonance imaging in the assessment of hepatocellular carcinoma after chemoembolization.

3. Patients and methods

Current prospective study included 20 patients diagnosed as H.C.C. who further underwent trans-arterial chemoembolization. All the studied patients subjected to radiological assessment through initial US followed by triphasic MDCT (16 slices) and baseline then follow-up hepatic MRI including DWI. The medical ethics were considered and patients’ agreement was obtained including informed consent that was enrolled prior to the study.

Inclusion criteria comprised unresectable tumor, patent portal vein based on Doppler, no ascites, satisfactory liver function and no major contraindications to angiography (Normal coagulation and renal function), whereas exclusion criteria included clinically apparent jaundice, hepatic encephalopathy, occluded PV, extra-hepatic tumors and non-correctable coagulopathy.

Unenhanced CT is obtained following conventional TACE to reveal lipiodol distribution and assess adequate tumor targeting. It is sometimes difficult to detect viable tissue, because beam hardening artifacts produced by iodized oil can impair evaluation of arterial enhancement.

MRI for the liver was performed using 1.5-T MRI scanner (Philips Intera) equipped with phased-array torso surface coil. The baseline study was obtained before chemoembolization procedure and included axial T2 weighted and DWI. The follow-up MRI study was obtained 21 days after chemoembolization and included pre-contrast axial T1 in-phase/out-phase imaging, T2 weighted, and dynamic contrast study.

T2 weighted images were obtained by T2 fast spin-echo sequence (repetition time msec/echo time msec; 508/100, matrix; 272 x 237, field of view; 380 mm, section thickness; 10 mm, and flip angle 90°). DWI was obtained by applying three different b values (0, 300, and 600 s/mm²). The parameters of diffusion sequence are as follows: repetition time/echo time; 1.2 s/61 ms, matrix; 124 x 124, field of view; 369 mm, section thickness; 10 mm, flip angle; 90° and Number of averages; 4.

DCEMRI study was performed after bolus injection of 0.1 mmol/kg body weight of Gd-DTPA. Contrast and saline injection was performed manually. DCE using T1 THRIVE (High Resolution Isotropic Volume Examination) technique was performed in triphasic way; A dynamic series consisted of one pre-contrast series followed by four successive postcontrast series including early arterial, late arterial, and portal phases imaging with 18–21 s intervals followed by 5-min delayed phase imaging. Imaging done at end of expiration to limit the risk of image distortion.

3.1. Image analysis

(a) Conventional image analysis: lesions assessed regarding size and T2 signal characteristics.
(b) Dynamic image analysis: Arterial hyper-vascularty was regarded as suggestive findings of viable HCC. Meanwhile benign conditions were considered in progressive persistent enhancement. In some lesions with spontaneous T1 hyper intensity, inclusion of subtraction images was done using a commercially windows workstation (PHILIPS).
(c) DWI analysis: Signal intensity on DWI with ADC values was evaluated side to side using windows workstation. Pattern of diffusion restriction was classified into heterogeneous or nodular and rim. Benign conditions were considered when lost signal on diffusion images (no restriction) or mild sustained hyperintensity with bright ADC map (shine through effect).
(d) ADC measurement: Pixel-based ADC maps were generated on the workstation using the three b values (0, 300, and 600 s/mm²). Normal liver parenchyma was evaluated with randomly drawn region of interest from different slices. Artifacts caused by physical limitations and image distortions were considered. ADC measurement in heterogeneous lesions with different signals on DWI was evaluated by placing ROI on corresponding ADC map at the most restricted solid region where ADC value is considered to be the lowest in the entire tumor.
3.2. Statistical analysis

Statistical analysis was performed with web based calculator. Mean, minimum, and maximum ADC values of the lesions were evaluated by Wilcoxon signed-rank test. Mean ADC values of the liver parenchyma were also compared by Wilcoxon signed-rank test. Differences were considered significant when \(P\) values were less than 0.05.

4. Results

The examined group included eighteen males and two females with 9:1 ratio. Their ages ranged between forty-two years and sixty-nine years and mean age was fifty-six years. The peak age was targeting the sixth and seventh decades.

According to tumor burden, patients were classified according to Child classification as follows: 12 patients (60%) with Child A classification and 8 patients with Child B classification (40% of cases). Five patients underwent first time TACE while others received previous loco regional by either TACE or RFA or combination. Conventional TACE procedure was done in seventeen patients and beads thereby were used in three patients in view of multiplicity of lesions. The procedures were performed successfully in all patients without 24 h major complication.

Table 1 represents the distribution of lesions according to baseline lesion characteristics including T2 WI baseline signals, size of the lesions, growth pattern and internal structure.

<table>
<thead>
<tr>
<th>Character</th>
<th>Parameter</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>3–5 cm</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>5–8 cm</td>
<td>12</td>
<td>60</td>
</tr>
<tr>
<td>T2 Signal</td>
<td>Hyper-intense</td>
<td>19</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>iso-intense</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Pattern</td>
<td>Nodular</td>
<td>19</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>Infiltrative</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Internal structure</td>
<td>hemorrhage/fatty metamorphosis/necrosis</td>
<td>17</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>Homogenous</td>
<td>3</td>
<td>15</td>
</tr>
</tbody>
</table>

Diffusion and ADC map analysis before TACE showed significantly lower ADC value of the cellular parts in the lesion than normal appearing liver parenchyma. Mean ADC value in lowest signal intensity areas before TACE was 1.25 mm²/s (range 0.75–1.3 mm²/s) while the mean ADC value of the liver was 1.69 mm²/s (range 1.11–1.8 mm²/sec). Fig. 1 represents the graph that demonstrates liver and tumor ADC values before TACE.

After TACE the change in tumor size on the T2-weighted images was not statistically significant \(P\) value 0.4. The normal appearing liver parenchyma also showed no significant changes before and after TACE.

Fifteen out of twenty patients “75% of the study group” showed partial response and residual viable tumor tissue was defined by arterial enhancement (Cases 1 and 2). The diffusion imaging showed diffusion restriction "sustained hyper-intensity with high b value and low ADC value on ADC map" in thirteen patients (65% of cases). The pattern of diffusion restriction was focal nodular and heterogeneous. Two patients with lesions in the liver dome showed residual tumor and were not detected by diffusion imaging.

The necrosis induced after TACE was noted on dynamic study as non-enhancing portions showed bright signal on the diffusion images with high ADC value “mean 1.85 mm²/sec” (Case 3).

Table 2 represents correlation between tumor and Liver ADCs and size before and after TACE. Fig. 2 shows changes of ADC values of the hepatic lesions after TACE. Fig. 3 shows comparison between the changes in ADC values of the lesions measured before and after TACE.

False positive results with diffusion restriction were noted in two cases (10%) while it shows no enhancement after dynamic contrast study excluding no residual active tumor tissue (Case 4).

Five patients “25% of the study group ” showed complete response defined by disappearance of arterial enhancement in the target lesions and DWI showed no nodular or heterogeneous diffusion restriction in four lesions. One lesion showed heterogeneous diffusion restriction with no enhancement in the dynamic study. The complete response lesions showed delayed persistent peripheral enhancement in all five lesions with corresponding thin rim of sustained peripheral hyper-intensity and restriction (Case 5).

![Fig. 1](graph.png)  
*Fig. 1* Graph showing liver and tumor ADC values before TACE.
Results of ROC analysis for non-responding versus responding lesions and pretreatment ADC values were not significant (P. 84). Statistical analysis shows that diffusion imaging had sensitivity of 86.67%, specificity of 80%, positive predictive value of 92.86% and negative predictive value of 66.67% to arterial phase enhancement in the dynamic MRI.

5. DISCUSSION

Change in tumor size on cross-sectional imaging is the gold standard for noninvasive assessment according to Response Evaluation Criteria in Solid Tumors (RECIST) (6).

However, results from a number of previous clinical studies in HCC have demonstrated that RECIST criteria could not apply adequately for interventional therapies (10).

Discrepancy between the reduction in tumor size seen on imaging and the degree of necrosis at histopathology may be explained by the delayed resorption of the necrotic material due to the occlusion of the feeding artery and hepatic sinusoids. As acknowledged in the original RECIST publication, assessments based solely on changes in tumor size could be misleading (1).

In recent study by Kamel et al. performed at 2009, a series of MRI performed before TACE, 24 h and 1, 2, 3, and 4 weeks after therapy had been demonstrated that mean tumor size was unchanged up to 4 weeks after TACE (11).

In the present work, we did once follow-up examination obtained three weeks after TACE and showed no significant changes regarding the size of the lesion which is consistent with Kamel et al. study.

European association for the study of liver (EASL) and American association for the study of liver diseases (AASLD) adopted a modification of the RECIST criteria in recent guidelines, in which evaluation of the treatment response should take into account the induction of intra-tumoral necrotic areas.

Fig. 2 Graph demonstrating the linear changes of ADC values between pre and post TACE procedure in examined patients.

Fig. 3 Graph demonstrating, for every individual patient, the differences between the average ADC values before TACE procedure (blotted as blue line) and those values after TACE procedure (blotted as red line). Notice elevated ADC value in the follow up after TACE in all patients with variable degrees.
in estimating the decrease in tumor load, and not just a reduction in tumor size. Thus the diameter of the target lesions with viable tumor should guide all measurements (1).

The study done by Kamel et al. (11) demonstrated poor correlation between lipiodol deposition and tumor enhancement. So, main value of CT is to document the technical success of the procedure. Kloeckner et al. (12), stated that MRI was found to be superior to CT for detection of viable tumor residuals after lipiodol based TACE, since Iodized oil does not affect MRI signals.

Signal changes on conventional (T1 and T2) MR imaging are non-specific and do not correlate with tumor necrosis. It was reported that T2 hyper-intensity not only represents residual tumor but could also represent hemorrhage, liquefactive necrosis, or inflammatory infiltrate. So, it was difficult to assess the viable HCC tumors after TACE by conventional spin echo imaging (13).

Current study results matched with the mentioned ones as T2 signal characteristic showed no significant changes in seventeen patients. Three patients however showed difference in the T2 appearance manifested by variable degrees of increased signal, so we found that assessment of HCC necrosis after TACE based on pre-contrast sequences considered a deficient issue.

Use of DWI to probe tumor response is promising, as it characterizes highly cellular tumor regions versus necrotic regions as viable tumor cells with intact membranes causing restricted diffusion whereas necrotic tumors with disrupted cell membrane have increased water diffusion (14).

DWI offers the advantage of earlier signals of treatment response, even prior to obvious anatomic changes. In addition, ADC values add a quantifiable measure of tumor cell death by directly reporting the state of water diffusion within the tumor, which is especially valuable because of the wide spectrum of histopathologic findings after TACE, ranging from total viability to complete necrosis. Successful tumor treatment after TACE results in diminished blood supply with subsequent diminished tissue fluid (13).

Several Preclinical animal studies were conducted on animal models (Geschwind et al. and Yuan et al.) that showed that following minimally invasive therapies, an increase in the ADC value may be observed in those responding to treatment (15, 16).

Case 1  Male patient 50 years old underwent second time TACE. (a) T2-weighted images after TACE with well-defined right hepatic lobe lesion showing mild internal heterogeneity. (b and c) DWI and ADC map at b value 600 mm²/sec. Note peripheral nodular restriction interpreted as neoplastic residual tissue (star). (d and e) DCE MRI showing nodular arterial enhancement and early washout denoting residual tumor tissue.
Estimating necrosis after TACE through diffusion MR was studied initially by Kamel et al in 2003 (11). They studied patients with HCC who underwent chemoembolization as a bridge for transplantation and found direct correlation between increasing ADC and increasing necrosis within the explanted surgical specimen.

They also found that diffusion imaging can quantify necrosis after TACE to a greater degree than can gadolinium-enhanced MRI. However their study had limitations as it included only a small number of patients, and did not assess image subtraction and the details of acquisition and processing of the histopathologic specimens were not reported (11,17).

Another study by Mannelli et al., with larger number of patients demonstrated that DCE MRI with subtraction technique had more significant correlation than diffusion imaging with the histopathologic correlation in the evaluation of necrosis of HCC after TACE whereas there was no difference between the two methods in diagnosis of complete tumor necrosis (18).

In the study in hand, although histopathologic analysis of the tumor remains the only reliable method to determine necrosis, we could not obtain histologic correlation due to obvious ethical reasons as the patients were not suitable for lesion resection or liver transplantation.

Both studies by Kamel et al. and Mannelli et al. showed that DWI can be used to assess necrosis which is concomitant with our results.

Early response of HCC to TACE by DW and MR Spectroscopy was assessed by Chen et al. (20) and Bonekamp et al. (21). Both demonstrated an increase in ADC values and decreased choline levels significantly which was useful for assessing the early therapeutic responses.

In the current study, we confirmed that increased intraleSIONal ADC post-TACE was concomitant with therapy-induced necrosis; however, technical, time and cost factors precluded MR spectroscopy and future studies are recommended to establish choline level changes post-TACE.

Sahin et al. (22) using 3.0-T MR showed that there was increased ADC value from $1.10$ to $1.27 \times 10^{-3} \text{mm}^2/\text{s}$ for the lesion while those for normal liver and spleen remained unchanged.

The abovementioned studies obtained ADC values of liver and tumor with considerable variation. Our explanation this may be a consequence of differences in parameters of DWI.

**Case 2** Male patient 56 years old underwent first time TACE. (A and B) T1 in-phase and out-phase showing no signal drop in out-phase image. (C and D) DWI and ADC map showing central necrosis and peripheral restriction. (E and F) DCE MRI arterial phase and subtraction image showing central non-enhancing necrosis.
and ADC used among different studies. In our opinion, adequate exploitation of ADC changes in monitoring response after TACE necessitates agreement on the appropriate time interval, DWI parameters including b value and uniform ADC measurement methodology in order to establish a functioning cutoff values.

Case 3  Female patient 61 years with large hepatic mass. (a) Axial T2-weighted image before TACE shows sizable hyperintense HCC. (b) Diffusion weighted image “b value 600 mm²/sec” reflecting high signal intensity with diffusion restriction. (c and d) T2-weighted and T1-weighted images after TACE shows areas of increased signal intensity (arrow). (e) Corresponding diffusion weighted image “b value 600 mm²/sec”. (f) Corresponding ADC map and area of high ADC value denoting necrosis (arrow). (g) Arterial phase dynamic MRI with same region points to non-enhancing area of necrosis (arrow).

According to current study, the impact of ADC value is limited as nine lesions exceeded 8 cm making overall tumor ADC measurement impossible, however the ADC maps can be used as complementary for DWI to eliminate T2 shine through and visualize the necrosis. Although the reproducibility in ADC was reported in some studies as a limiting factor,
we demonstrated no significant changes in the ADC of normal appearing liver parenchyma before and after TACE while the targeted lesions showed significant changes.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Tumor and Liver ADC and size before and after TACE.</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Tumor ADC pre-TACE mm²/sec</td>
<td>1.357</td>
</tr>
<tr>
<td>Tumor ADC post-TACE mm²/sec</td>
<td>1.606</td>
</tr>
<tr>
<td>Liver ADC pre-TACE mm²/sec</td>
<td>1.696</td>
</tr>
<tr>
<td>Liver ADC post-TACE mm²/sec</td>
<td>1.698</td>
</tr>
</tbody>
</table>

P value: Less than .001

Tumor size pre-TACE (cm) | 5.4 | 1.15 | 3–8
Tumor size post-TACE (cm) | 5.2 | 1.18 | 3–8
P value | 0.418

A study carried out by Yuan et al. (19) investigated the value of pretreatment ADC and proposed that high pretreatment ADC was predictive of poor response. Their results produced controversy with the current study. Although the reason for this is unclear, we performed dynamic scan in all patients as the response depends on the presence of early enhancement, which was not clearly described by Yuan study.

In a study by Mannelli et al. (14), they used subtraction images of dynamic post-TACE MRI to assess the necrosis and correlated with the pretreatment ADC values. They concluded that pre-TACE ADC can potentially be used as predictor of subsequent response to TACE.

The present study suggests a more clinically significant value of pretreatment diffusion imaging as it could be useful in patients with multiple focal lesions where ADC can be road map for conventional TACE on repeated sessions where visualization of enhancement is difficult so it can direct thereby to the most active non-necrotic lesion without invasive techniques or contrast administration. It is interesting to mention that, to the best of our knowledge, no previous study reports such issue, however naturally to say further studies are needed to reach firmer conclusion.

Case 4  Male patient 65 years old underwent third time TACE. (a and b) T2 and T1 weighted images after TACE showed segment IV heterogeneous HCC with arrow points to anterior cystic portion. (c and d) Diffusion image and ADC map. Anterior portion is showing to T2 shine through. The posterior portion shows diffusion restriction “False positive”. (e and f) Early and delayed arterial phases show no enhancement.
Treated HCC may show a thin perilesional enhancement depicted on DCE-MRI that may be mistaken for residual tumor yet it may be attributed to various benign conditions as reactive edema or reactive granulation tissue due to adjacent inflammation or other non-tumorous arterioportal shunts (13,23).

Yu et al. (23) measured the ADC value to differentiate between the marginal recurrences of HCC from perilesional benign conditions and they found that the ADC values varied widely for the non-tumorous lesions and grossly overlapped with the viable tumor portion making it impossible to determine any cutoff points.

Case 5  Male patient 66 years old undergoing second time TACE. (a) DCE-MRI arterial phase CT before TACE showing partly enhancing solid portion and partly necrotic posterior component. (b) T2-weighted image confirmed heterogeneous necrotic high signals component. (c) DWI at different b value 600 with area of sustained high signal. (d) ADC map showing necrosis confirmed residual viable tissues. (e) DCE MRI arterial phase CT after Conventional TACE showing no residual enhancement. (f and g) DWI and ADC map reflecting T2 shine through effect and thin peripheral restriction. (h) Arterial dynamic MR with no residual enhancing lesions apart from persistent capsular rim enhancement.
DWI increased sensitivity for detection of post-TACE residual HCC but increased false positives, that decreased specificity, will compromise the increased sensitivity gained by DWI and so decreased overall diagnostic accuracy. They referred the increase in false positive findings to perilesional parenchymal insults that showed hyperintensity with increased b factors and explained that hyper-cellularity within fibrotic content in inflammatory granulation tissue could cause restricted diffusion (23).

Our results are concordance with Yu et al. as there was no significant difference between the ADC values of perilesional benign looking restriction and residual tumor. The discrimination, based on DWI, between thin rim hyperintensity and focal nodular hyperintensity may have decreased the false positive results and increased the specificity and sensitivity of diffusion imaging in our study.

In a study performed by Goslima et al., where DWI was compared with dynamic MR study, they found that DWI was not a reliable predictor of local HCC recurrence after TACE as compared with gadolinium enhanced MR imaging (24).

In our study, we did not aim to make a comparative study; we used dynamic MR as a reference. Among our study group we found one lesion with false positive result, that showed diffusion restriction and no arterial enhancement noted.

In the studies of Holtas et al. (25), sterile liquefactive necrosis and intra-cavitary micro-hemorrhage are accepted causes of hyperintensity in DW MR images of malignant lesions.

False positive finding in our study is likely originating from intralesional hemorrhage that caused diffusion restriction.

We found that DW MRI had some advantages to DCE MRI. First, contrast administration, with its known hazards, was not required, so examination is obtained in a relatively short time. Second, the technique is easy to be repeated, allowing close follow-up during and after tumor treatment. Third, image post-processing is less time-consuming compared to DCE MR imaging. At last, Diffusion-weighted MR imaging allows easy evaluation of the entire tumor.

This study had several limitations. First, technical difficulties of DWI such as relatively poor signal-to-noise ratio and partial loss in spatial resolution were caused by increased sensitivity to pulsatile and magnetic susceptibility artifacts.

Lesions close to the diaphragm posed a challenge to DW-MRI evaluation, as they are more sensitive to motion, susceptibility artifacts, as well as artifacts arising from the heart. We had two sub-diaphragmatic HCC cases that were excluded because of low image quality.

Although we placed the smallest ROI possible in the viable parts of the lesions on the ADC map and made multiple measurements, partial volume effects and uncontrollable image noise caused unavoidable errors. Second, the sample group was small with possible selection bias. Third regarding follow-up data on patient outcomes were not available because of lack of adequate registration systems and poor patient compliance. Last, we did not assess DWI as a standalone sequence; instead, DCE MRI was used as guidance to define necrosis and residual tumor, and this decision may have introduced bias. It would be interesting to perform future studies comparing DWI with contrast-enhanced imaging in a more independent manner.

Studies exploring the potential for using DW-MRI for the early detection of therapeutic-induced changes in tumors are ongoing. Future studies with high magnetic gradient systems with new technical developments are needed to improve the image quality and sensitivity of DWI.

6. Conclusion

DWI is a promising technique that proved useful in evaluating HCC depending on its capability of microscopic tissue characterization. It facilitates distinction between viable and necrotic tumor areas and helps the diagnosis of residual tumor. Potential effect of treatment can be detected as an increase in the diffusion coefficient.

In the follow-up after TACE, changes in lesion size alone could not be used as markers of response and recent guidelines take into consideration the residual viable tumor. So we recommend that optimal follow-up after TACE therapy should include DWI and contrast-enhanced MRI.

DW images are rather difficult to interpret since it is very sensitive to artifacts especially in the lesions near the dome of the diaphragm, and also standardizing liver diffusion protocols must be pursued in order to provide reproducible parametric quantification.

Conflict of interest

We have no conflict of interest to declare.

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