Diagnostic value of apparent diffusion coefficient (ADC) in evaluating hepatocellular carcinomas post trans-catheter arterial chemoembolization and radiofrequency ablation

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Received 30 March 2016; accepted 8 May 2016
Available online 2 June 2016

KEYWORDS
ADC; Hepatoma; Chemoembolization; Radiofrequency

Abstract  Background: Trans-arterial chemoembolization (TACE) and radiofrequency ablation (RFA) are widely used interventional procedures in treatment of HCCs. ADC value can be used in evaluating their efficacy in order to rule out or in residual tumor tissue.

Aim: To assess the role of DWI and ADC value in evaluating HCCs post TACE and REA.

Patients and methods: 36 patients with 40 HCCs were included, and 28 lesions were treated with TACE and 12 with RFA. All lesions were evaluated by DWI and ADC value measurement before and after interventional management.

Results: 32/40 lesions responded to treatment and 8 lesions had not. ADC values were significantly higher in lesions that responded to TACE or RFA than in non-responding lesions. The mean ADC of the lesions before treatment was 1.27 ± 0.25 \( \times 10^{-3} \) mm\(^2\)/s, and increased after treatment in responding lesions to reach 1.57 ± 0.22 \( \times 10^{-3} \) mm\(^2\)/s with a statistically significant difference (\( P = 0.002 \)). Responding lesions showed significantly higher % ADC than non-responding lesions 23.6% vs. –21%, respectively (\( P = 0.001 \)).

Conclusion: ADC is a reliable quantitative assay in assessing the efficacy of TACE and RFA in treating HCC and can replace contrast studies.

1. Introduction

Hepatocellular carcinoma (HCC) is the most common primary malignant hepatic tumor which is in need for surgical resection and transplantation as the only potentially curative options; however, they are contraindicated in the majority of patients (1). Only 10–20% of patients with hepatocellular carcinoma (HCC) or metastatic disease are eligible for hepatic transplantation (2).

Imaging guided interventional procedures for treatment of HCC are radiofrequency ablation (RFA), ethanol injection, trans-arterial chemoembolization (TACE) and radioembolization...
which are not curative, but they increase survival and to down
stage patients in order to be suitable for liver transplantation
(3).

Viable neoplastic tissue remains in some cases after TACE
and RFA. Therapeutic efficacy after treatment is assessed by
different imaging modalities such as computed tomography
(CT), magnetic resonance imaging (MRI) and functional
MRI including diffusion weighted image and apparent diffusion
coefficient (DWI and ADC). Contrast enhanced CT and MRI
are necessary with some limitations in evaluating the therapeu-
tic efficacy (4).

The mean ADC before and after TACE or RFA is signifi-
cantly increased among patients with HCC (4). ADC values
map the thermally induced changes on water molecular motion
in tissues are able to provide insight into tumor microstructure
(5).

The aim of this study was to assess the role of DWI and
ADC value in evaluating HCCs post TACE and REA.

2. Patients and methods

This research is a prospective study conducted with institu-
tional review board (IRB) approval and informed consents
were taken from all patients.

Thirty-six patients in number with (40) HCCs were
included in the study, which was conducted in Radiodiagnosis
Department, Zagazig University Hospitals, during the period
from February 2015 to October 2015. The patients were 28
males and 8 females, and their ages ranged from 40 to 75 year.

The HCCs were diagnosed according to characteristic
imaging findings (early enhancement on dynamic contrast
enhanced CT or MRI at the arterial phase with rapid washout
at the portal venous phase) and positive Laboratory results for
viral hepatitis and elevated level of alpha fetoprotein (AFP).

The 40 HCCs (mean diameter, 2.6 cm; range, 1.5–7.7 cm)
were treated by interventional management, (28 HCCs) with
TACE and (12 HCCs) with RFA.

We excluded Patients with contraindication to MRI study
(pacemaker or vascular clips).

Patients were subjected to the following:

1. Clinical and laboratory assessment including the following:
   liver function tests, serum albumin, bilirubin and AFP
   level.

2. Radiological assessment:

   All patients underwent baseline and follow-up MR imaging
   performed with a 1.5-T MR imaging unit (Philips Achieva,
superconducting MR imager). Abdominal coil was used with respi-
atory triggering. The imaging protocol included the following:

A. Non-contrast MR imaging preliminary to the diffusion
   weighted examination.
   - T1-weighted images were performed with the
     following parameters: (TR = 400 ms, TE = 20 ms,
     385 × 385 mm field of view (FOV), 256 × 256 matrix,
     section thickness 5–7 mm).
   - T2-weighted images with the following param-
     eters (TR = 3000 ms, TE = 90, 385 × 385 mm FOV,
     256 × 256 matrix and section thickness: 5–7 mm).

B. Diffusion weighted MR imaging (DWI) and ADC value
   calculation:

   DWI was obtained using a transverse a single-shot echopla-
nar imaging with two b-values (500, 1000 mm2/s) applied in
   the z direction. These b-values were chosen to acquire
   images with a sufficient contrast-to-noise ratio.

   - DWI with b value 0 & DWI with b value 500 (TR/TE,
     1300/65, FA 90°, matrix:128 × 128, section thickness
     5–7 mm, intersection gap 1 mm and FOV 385 × 385 mm)
     and DWI with b value 1000 (TR/TE, 1500/80, FA 90°,
     matrix:128 × 128, section thickness 5–7 mm, intersection
     gap 1 mm and FOV 385 × 385 mm).

   - Quantitative ADC maps were calculated using commer-
cially available software and an imaging workstation.

ADC maps were generated from the DWI, and values were
recorded by placing ROIs over the center and peripheral area
of the treated mass (Mean ADC of the ROIs was calculated),
as observed on the axial image.

Evaluation with DWI was performed before TACE or
RFA. The first follow-up was performed between four and
six weeks post-interventional management by DWI and tripha-
sic CT study. Further follow-up was done after 2 months using
triphasic CT and/or DWI and ADC Value for the responding
lesions, and we considered unchanged ADC value or the
absence of tumor enhancement as a gold standard to confirm
the absence of tumor activity or recurrence.

For evaluation of treatment response, in the follow-up
study, responsive lesions were defined as complete and partial
response tumors (> 50% decrease in the product of the longest
diameter and length of the perpendicular diameter of the
lesion, or > 50% increased necrosis), while non-responsive
lesions were defined as stable and progressive disease.

The presence of any residual tumor and the extent of tumor
necrosis were assessed. The apparent diffusion coefficient
(ADC) values of the entire area of the treated mass and the
viable and necrotic tumor tissues were recorded.

Changes in the ADC values, obtained 4–6 weeks after
TACE or RFA, were determined by calculating the percent
change in ADC from baseline study (before TACE or RFA),
with each patient serving as his/her own control. The percent
change in ADC (% ADC) from before to after TACE or
RFA was calculated based on the following formula:

\[
\% \text{ ADC} = \left( \frac{\text{ADC}_{\text{after}} - \text{ADC}_{\text{before}}}{\text{ADC}_{\text{before}}} \right) \times 100
\]

where ADC-b is ADC of HCC before TACE or RFA and
ADC-a is ADC of HCC after TACE or RFA.

3. Statistical analysis

Data were checked, entered and analyzed using, Response
Evaluation Criteria in Solid Tumors (RECIST) (6). Data were
expressed as mean ± SD for quantitative variables, numbers
and percentage for qualitative ones. Unpaired t-test, paired
t-test, Chi-squared ($X^2$) or fishers exact were used when appropriate. $P < 0.05$ was considered statistically significant.

4. Results

This study included 36 patients with 40 HCCs. They were 28 males (77.8%) and 8 females (22.2%), and their ranged between 40 and 75 years with a mean age 57.1 ± 10.9 years. The most common age group was 50–60 years (20 patients). The most common clinical symptoms were right hypochondrial pain, nausea, vomiting and fatigue. Laboratory findings included elevated alpha fetoprotein in 34 patients, elevated serum bilirubin in 8 patients, elevated liver enzymes in 30 patients and decreased total proteins in 11 patients, and 70% were treated by TACE as shown in Table 1.

Diffusion-weighted imaging (DWI) was performed for all patients before TACE or RFA. The follow-up study was performed between four and six weeks post-interventional management (Figs. 1 and 2).

The mean (± standard deviation) ADC in 40 HCCs before TACE or RFA was $1.27 ± 0.25 \times 10^{-3} \text{mm}^2/\text{s}$ using $b$ value 500 and $1.26 ± 0.28 \times 10^{-3} \text{mm}^2/\text{s}$ using $b$ value 1000, with no significant difference from that in normal liver parenchyma ($1.23 ± 0.26 \times 10^{-3} \text{mm}^2/\text{s}; P = 0.1$).

On the follow-up study (4–6 weeks post-interventional management) of the 40 HCCs evaluated by DWI and ADC value calculation, 32 HCCs responded to treatment and 8 HCCs had not.

With $b$ value 500, the mean ADC value before treatment did not differ significantly between responding ($1.27 ± 0.26 \times 10^{-3} \text{mm}^2/\text{s}$) and non-responding lesions ($1.27 ± 0.20 \times 10^{-3} \text{mm}^2/\text{s}; P = 0.97$). While with $b$ value 1000, there was a significant difference with higher mean ADC values before interventional management in responding lesions than in non-responding ($1.32 ± 0.28 \times 10^{-3} \text{mm}^2/\text{s}$ in responding lesions and $1.04 ± 0.00 \times 10^{-3} \text{mm}^2/\text{s}$ in non-responding, respectively; $P = 0.03$).

Responding lesions showed significantly larger percent change in ADC (% ADC) than in non-responding lesions, and it was 18.9% vs. 5.7%, respectively ($P = 0.01$) using $b$ value 500 and 23.6% vs. (−21%), respectively ($P = 0.001$) using $b$ value 1000.

Most of the lesions (90%) were of low signal intensity on T1WI before treatment. After treatment, 60% of them retained low signal intensity, while the remaining became of high or intermediate signal on T1WI. The high signal intensity represents subacute hemorrhage.

There was significant difference of T1WI signal intensity before and after treatment ($P < 0.05$) as shown in Table 2.

Most of the lesions (80%) were of high signal intensity on T2WI before treatment. After treatment, 60% of them retained high signal intensity, while the remaining became of low or intermediate signal which is not conclusive and may represent Liquefactive necrosis or residual tumor. There was significant difference of T2WI signal intensity before and after treatment ($P < 0.05$) as shown in Table 3.

All lesions (100%) were of high signal intensity on DWI before treatment, 90% of them were still high after treatment, while the remaining became of low signal intensity. This is not conclusive and should be enforced by quantitative diffusion using ADC value measurement (Table 4).

<table>
<thead>
<tr>
<th>Type of treatment</th>
<th>No. of HCC lesions</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TACE</td>
<td>28</td>
<td>70</td>
</tr>
<tr>
<td>RFA</td>
<td>12</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>100</td>
</tr>
</tbody>
</table>

Mean ADC value before treatment was $1.27 ± 0.25 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD), while after treatment it was $1.46 ± 0.3 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD). The % ADC change was 19.8% (±7.05) which is significant by statistical analysis (Table 5).

Mean ADC value before treatment was $1.26 ± 0.28 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD), while after treatment it was $1.46 ± 0.24 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD). The % ADC change was 19.7% (±6.01) which is significant by statistical analysis (Table 6).

The mean ADC value of the lesions treated with TACE was $1.2 ± 0.22 \times 10^{-3} \text{mm}^2/\text{s}$ before treatment and $1.47 ± 0.33 \times 10^{-3} \text{mm}^2/\text{s}$ after treatment with significant difference ($P = 0.02$), while in lesions treated with RFA it was $1.375 ± 0.26 \times 10^{-3} \text{mm}^2/\text{s}$ before treatment and $1.44 ± 0.01 \times 10^{-3} \text{mm}^2/\text{s}$ after treatment with significant difference ($P = 0.04$) as shown in Table 7.

The mean ADC value of the lesions treated with TACE was $1.225 ± 0.24 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) before treatment and $1.435 ± 0.26 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) after treatment with significant difference ($P = 0.004$).

While in lesions treated with RFA it was $1.33 ± 0.24 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) before treatment and $1.52 ± 0.1 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) after treatment with significant difference ($P = 0.03$) as shown in Table 8.

The mean ADC value (at $b$ value 500) of the responding HCCs with no residual tumor was $1.32 ± 0.28 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) before treatment and $1.54 ± 0.12 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) after treatment with statistically significant difference ($P = 0.02$).

While in non-responding HCCs with residual tumor it was $1.04 ± 0.0 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) before treatment and $1.1 ± 0.07 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) after treatment with non-significant difference ($P = 0.06$) as shown in Table 9.

The mean ADC (at $b$ value 1000) of the responding HCCs ($N = 32$) with no residual tumor was $1.27 ± 0.26 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) before treatment and $1.57 ± 0.22 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) after treatment with statistically significant difference ($P = 0.002$).

While in non-responding HCCs ($n = 8$) with residual tumor, it was $1.27 ± 0.2 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) before treatment and $1.002 ± 0.005 \times 10^{-3} \text{mm}^2/\text{s}$ (mean ± SD) after treatment with non-significant difference ($P = 0.18$) as shown in Table 10.

5. Discussion

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors all over the world (7).

Most of patients with hepatocellular carcinoma are unfit for surgery or liver transplant, and the alternative treatment is locoregional therapy (2). Post loco-regional therapy or
systemic therapy evaluation is mandatory to evaluate its success and whether further treatment is needed (2). RF ablation (RFA) is the most widely used ablation therapy, and consists of placing a needle electrode directly into the tumor, guided by US or CT, and heating tissue to temperatures exceeding 60°C to induce coagulative necrosis of the tumor. Ablation zone should be 5–10 mm larger in comparison with the pre-existing tumor (8).

Trans-arterial chemoembolization (TACE) consists of trans-arterial administration of a mixture of chemotherapy (Doxorubicin or Cisplatin in most cases) and iodized oil (Lipiodol, Guerbet, France), followed by embolizing agents.

Fig. 1  Female patient 45-year-old diagnosed with HCC at segment III and VI. (A) Axial T2WI reveals two ill-defined heterogeneous hyperintense and hypointense lesions at segments III and VI respectively. (B) Diffusion weighted image (DWI) with (b = 500) displays the lesion of high signal intensity that is consistent with diffusion restriction. (C) DWI with (b = 1000) shows hyperintense signal of both lesions that are consistent with diffusion restriction. (D) ADC map reveals hypointense lesion with ADC value of 1.037 × 10⁻³ mm²/s at segment III and 1.21 × 10⁻³ mm²/s at segment VI. (E) Axial T2WI after RFA displays low signal intensity of the lesion with peripheral high intensity rim. (F) Diffusion weighted image (DWI) with (b = 500) after RFA displays low signal intensity denoting free diffusion. (G) DWI with (b = 1000) after RFA shows hypointense signal of segment III focal which is consistent with free diffusion while the lesion in segment VI displays low SI centrally with high restricted margins. (H) ADC map of the lesion after RFA reveals isointense lesion with ADC value of 1.06 × 10⁻³ mm²/s with % ADC change = 0.09% in keeping with residual tumor after RFA at segment III. ADC value of lesion at segment VI was 1.03 × 10⁻³ mm²/s with % ADC change = 6.6% in keeping with residual tumor after RFA at segment VI. (I) Arterial phase of triphasic CT study 1 month later reveals moderate heterogeneous contrast enhancement revealing residual tumoral activity of both lesions.
Fig. 2  Male patient 57-year-old diagnosed with HCC occupying most of right lobe. (A) Axial T2WI reveals ill-defined large heterogeneous hyperintense lesion. (B) DWI with \((b = 500)\) shows the lesion of high signal intensity denoting restricted diffusion. (C) DWI with \((b = 1000)\) shows hyperintense signal of the lesion. (D) ADC map reveals hypointense lesion with ADC value of \(0.95 \times 10^{-3} \text{mm}^2/\text{s}\) in the peripheral and \(1.19 \times 10^{-3} \text{mm}^2/\text{s}\) in the central area of the lesion. (E) Axial T2WI after TACE shows the lesion of high signal intensity with central areas of low signal intensity. (F) DWI with \((b = 500)\) after TACE displays hyperintense signal of the periphery of the lesion with central hypointensity. (G) DWI with \((b = 1000)\) after TACE displays hyperintense signal of the periphery of the lesion with central hypointensity. (H) ADC map of the lesion after TACE reveals isointense lesion with ADC value of \(1.62–1.69 \times 10^{-3} \text{mm}^2/\text{s}\) with % ADC change = 72.9% denoting successful TACE. (I) Arterial phase of triphasic CT study one month after TACE revealed no contrast enhancement denoting no residual tumoral activity. (J) Follow-up DWI with \((b = 1000)\) 2 months after TACE displays hyperintense signal of the periphery of the lesion with central hypointensity. (K) Follow-up ADC map of the lesion 2 months after TACE using multiple ROIs reveals isointense lesion with ADC value of \(1.66–1.68 \times 10^{-3} \text{mm}^2/\text{s}\) denoting successful TACE. (L) Triphasic CT study after 2 months revealed no contrast enhancement denoting no residual tumoral activity.
MRI is one of the most valuable techniques in the evaluation of post therapeutic response (5). DWMRI is the most accurate non-invasive method to evaluate tumoral cellularity, particularly in patients with renal impairment and cannot receive CT contrast material (10).

The current study included 36 patients (28 males and 8 females) with 40 HCC lesions, and 28 lesions were treated with TACE and 12 lesions with RFA. Their ages ranged from 40 to 75 years and the mean age was 57.1 years, which means that hepatic tumors are more predominant after the age of 50 which was in line with Miller et al. (11) who performed a study including 382 patients with age ranging from 15 to 88 years and mean age was 59.2 years. In addition, Vergara et al. (12) carried out a study including 26 patients with age ranging from 30 to 73 years and the mean age was 51.5 years. Koike et al. (13) also carried out a study including 70 patients with age ranging from 39 to 86 years and mean age 65.3 years.

DWI and ADC value measurements were used 4–6 weeks after TACE or RFA. Kamel et al. (14) found that ADC significantly increased within the first day after TACE and reaches its maximum after 2 weeks, and this was followed by gradual decreases to reach the pre-therapeutic level. Lu et al. (15) stated that there were significant differences from the pre-treatment ADC values and 1 and 6 months after RF ablation of the HCC.

Post TACE or RFA for HCC treatment there were different patterns of T1 and T2 signal intensity. Hypointense T2 weighted images suggest coagulative necrosis while hyperintense T2 weighted images represent residual tumor tissue and

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Variation in T1WI signal intensity before and after treatment.</th>
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</thead>
<tbody>
<tr>
<td>T1WI</td>
<td>Before</td>
</tr>
<tr>
<td>Low</td>
<td>36</td>
</tr>
<tr>
<td>Intermediate</td>
<td>4</td>
</tr>
<tr>
<td>High</td>
<td>0</td>
</tr>
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</table>

* Significant.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Variation in T2WI signal intensity before and after treatment.</th>
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</thead>
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<td>T2WI</td>
<td>Before</td>
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<td>0</td>
</tr>
<tr>
<td>Intermediate</td>
<td>8</td>
</tr>
<tr>
<td>High</td>
<td>32</td>
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* Significant.

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<tr>
<th>Table 4</th>
<th>Variation in DWI before and after treatment.</th>
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<td>Before</td>
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<tr>
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<td>Intermediate</td>
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<tr>
<td>High</td>
<td>40</td>
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</tbody>
</table>

* Significant.

<table>
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<tr>
<th>Table 5</th>
<th>ADC measurements with b value 500 before and after treatment.</th>
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<tbody>
<tr>
<td>ADC 500</td>
<td>Mean ± SD (range)</td>
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<tr>
<td>Before treatment</td>
<td>1.27 ± 0.25 (0.968–1.67)</td>
</tr>
<tr>
<td>After treatment</td>
<td>1.46 ± 0.3 (1–1.86)</td>
</tr>
</tbody>
</table>

N.S = non-significant. * Significant.

<table>
<thead>
<tr>
<th>Table 6</th>
<th>ADC measurements with b value 1000 before and after treatment.</th>
</tr>
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<tbody>
<tr>
<td>ADC 1000</td>
<td>Mean ± SD (range)</td>
</tr>
<tr>
<td>Before treatment</td>
<td>1.26 ± 0.28 (1–1.7)</td>
</tr>
<tr>
<td>After treatment</td>
<td>1.46 ± 0.24 (1.04–1.86)</td>
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</tbody>
</table>

N.S = non-significant. ** Highly significant.

<table>
<thead>
<tr>
<th>Table 7</th>
<th>Variation in ADC measurements using b value 500 in each type of the management.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>No</td>
</tr>
<tr>
<td>T1.639</td>
<td>28</td>
</tr>
<tr>
<td>R1.75</td>
<td>12</td>
</tr>
</tbody>
</table>

T = 1.639 | P = 0.11 N.S

<table>
<thead>
<tr>
<th>Table 8</th>
<th>Variation in ADC measurements using b value 1000 in each type of the management.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>No</td>
</tr>
<tr>
<td>T1.639</td>
<td>28</td>
</tr>
</tbody>
</table>
| R1.75 | 12 | 1.33 ± 0.24 (1–1.7) | 1.52 ± 0.1 (1.3–1.82) | 1.93 | 0.03 | ** Highly significant.

N.S = non-significant. * Significant.

Post TACE or RFA for HCC treatment there were different patterns of T1 and T2 signal intensity. Hypointense T2 weighted images suggest coagulative necrosis while hyperintense T2 weighted images represent residual tumor tissue and including 70 patients with age ranging from 39 to 86 years and mean age 65.3 years.

DWI and ADC value measurements were used 4–6 weeks after TACE or RFA. Kamel et al. (14) found that ADC significantly increased within the first day after TACE and reaches its maximum after 2 weeks, and this was followed by gradual decreases to reach the pre-therapeutic level. Lu et al. (15) stated that there were significant differences from the pre-treatment ADC values and 1 and 6 months after RF ablation of the HCC.
may also represent hemorrhage, tumor liquefactive necrosis or inflammatory process Vossen et al. (5).

In our study, the signal intensity on T1 and T2 weighted images was significantly variable. Thirty-six HCCs lesions (90%) showed low signal intensity on T1WI before treatment and 24 HCCs (67%) of them retained low signal intensity after treatment while 8HCCs (20%) depicted high signal intensity which represents subacute hemorrhage, and the reminder 4 lesions (10%) depicted intermediate signal intensity. On T2WI, 32 HCCs (80%) lesion showed high signal intensity before treatment which represents active tumoral tissue and varied after treatment with 24 out of 32 HCCs (75%) retained high signal intensity which is not conclusive and may correspond to residual tumor. However, this hyperintensity can also represent hemorrhage, Liquefactive necrosis or inflammatory infiltration. While 12 HCCs (30%) showed low signal after treatment, with statistically significant difference (p < 0.05), 8 HCCs (20%) were intermediate before treatment, 50% of them retained intermediate signal, and so we cannot depend on the signal intensity only in monitoring the effect of treatment.

In this study we use high b values (500 and 1000 s/mm²) to overcome the effect of capillary perfusion and water diffusion in extracellular extravesicular space, as high b value will result in reduction in signal from moving protons in the bile ducts, cysts, vessels, and fluid in the bowel. This will result in an increased contrast between the lesion and liver. This was similar to the b value used in studies carried out by Koike et al. (13), Demir et al. (16), and Hosni (17).

In our study we found that the mean ADC value of the liver parenchyma was (mean ± SD) 1.23 ± 0.26 × 10⁻³ mm²/s which was in line with the study done by Lu et al. (15) who reported that the mean ADC value of normal liver was (mean ± SD) 1.286 ± 0.234 × 10⁻³ mm²/s.

The mean (± standard deviation) ADC in 22 HCCs before TACE or RFA was 1.27 ± 0.25 × 10⁻³ mm²/s using b value 500 and was 1.26 ± 0.28 × 10⁻³ mm²/s using b value 1000, with no significant difference from that in normal liver parenchyma (1.23 ± 0.26 × 10⁻³ mm²/s; P = 0.1). This was similar to Kubota et al’s (4) study, who found that the mean (± standard deviation) ADC in 36 HCCs from 25 patients before TACE was 1.27 ± 0.395 × 10⁻³ mm²/s, with no significant difference from that in normal liver parenchyma (1.286 ± 0.234 × 10⁻³ mm²/s; P = 0.901).

The mean ADC value before management did not differ significantly with b value 500 between responding (1.27 ± 0.26 × 10⁻³ mm²/s) and non-responding lesions (1.27 ± 0.20 × 10⁻³ mm²/s, P = 0.97). While with b value 1000, there was a significant difference with higher mean ADC values before interventional management in responding lesions than in non-responding (1.32 ± 0.28 × 10⁻³ mm²/s) in responding lesions and 1.04 ± 0.00 × 10⁻³ mm²/s in non-responding, respectively; P = 0.03). This was in agreement with the results of Kubota et al. (4), who found that the ADC showed no significant difference between responding (1.22 ± 0.355 × 10⁻³ mm²/s) and non-responding lesions (1.357 ± 0.46 × 10⁻³ mm²/s; p = 0.33) using b value 500.

On the short term follow-up study of the 40 HCC lesions, 32 HCCs responded to treatment and 8 HCCs had not according to DWI and ADC value calculation.

In our study, responding lesions showed significantly higher percent change in ADC (% ADC) than in non-responding lesions. It was 18.9% vs. 5.7%; P = 0.01 using b value 500 and 23.6% vs. (−21%), respectively using b value 1000; P = 0.001. Kubota et al. (4) found that the mean (± standard deviation) ADC in 36 HCCs from 25 patients before TACE was 1.27 ± 0.395 × 10⁻³ mm²/s, while after TACE responding lesions showed significantly higher % ADC than in non-

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### Table 9 Variation in ADC values at b 500 in responding and non-responding HCCs (residual tumor).

<table>
<thead>
<tr>
<th>Residual tumor</th>
<th>No</th>
<th>Before X ± SD (range)</th>
<th>After X ± SD (range)</th>
<th>Paired T</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responding (−ve)</td>
<td>32</td>
<td>1.32 ± 0.28 (1–1.7)</td>
<td>1.54 ± 0.12 (1.3–1.86)</td>
<td>2.66</td>
<td>0.02*</td>
</tr>
<tr>
<td>Non-responding (+ ve)</td>
<td>8</td>
<td>1.04 ± 0.0 (1–1.01)</td>
<td>1.1 ± 0.07 (1.04–1.16)</td>
<td>1.1</td>
<td>0.06 N.S</td>
</tr>
</tbody>
</table>

N.S = non-significant. * Significant. ** Highly significant.

### Table 10 Variation in ADC values at b 1000 in responding and non-responding HCCs (residual tumor).

<table>
<thead>
<tr>
<th>Residual tumor</th>
<th>No</th>
<th>Before X ± SD (range)</th>
<th>After X ± SD (range)</th>
<th>Paired T</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responding (−ve)</td>
<td>32</td>
<td>1.27 ± 0.26 (0.96–1.67)</td>
<td>1.57 ± 0.22 (1.047–1.86)</td>
<td>3.56</td>
<td>0.002**</td>
</tr>
<tr>
<td>Non-responding (+ ve)</td>
<td>8</td>
<td>1.27 ± 0.2 (1.09–1.45)</td>
<td>1.002 ± 0.005 (1–1.01)</td>
<td>1.73</td>
<td>0.18 N.S</td>
</tr>
</tbody>
</table>

N.S = non-significant. ** Highly significant.
responding lesions (85.2 ± 12.4% vs. 8.0 ± 56.7%, respectively).

Kamel et al. (18) demonstrated that mean tumor ADC increased after TACE by 20% (P = 0.026), while Yuan et al. (10) found the mean ADC value of the entire area of the treated mass on the axial image was 1.92 ± 0.29 × 10⁻³ mm²/s (range, 1.01–2.57 × 10⁻³ mm²/s; median, 1.93 × 10⁻³ mm²/s).

This was similar to the study done by Lu et al. (15) who found that the ADC value at one month after RFA was significantly higher than the pre-treatment value.

6. Conclusion

DWI and ADC value correlation should be added in the protocol of hepatocellular carcinoma imaging in pre- and post-interventional procedures as initial ADC is a predictor for therapeutic response and the % changes in ADC value is valuable in monitoring the cases.

Conflict of interest

We have no conflict of interest to declare.

Acknowledgment

The authors acknowledge Professor Tarek Mohammed Sobhy and Dr. Rola Mahoud, for their assistance.

References