ORIGINAL ARTICLE

Value of diffusion weighted imaging (DWI) and apparent diffusion coefficient factor (ADC) calculation in differentiation of solid breast lesions

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Received 10 July 2015; accepted 21 October 2015
Available online 17 November 2015

Abstract  Objective: To study the utility of DWI and ADC in increasing the specificity of MRI in differentiating benign from malignant solid breast lesions.

Patients and methods: 56 female patients were included in our study. All patients referred to MRI unit-Radiology Department – Ain Shams University Hospitals to do bilateral breast MRI using conventional sequences, DWI, ADC calculation and post-contrast dynamic study with time/intensity curve using Philips superconductive magnet at 1.5 T with breast surface coil. All the patients were subjected to clinical examination, sonomammography as well as written consent. Also, the histopathological results were recorded.

Results: 56 lesions were detected, 30 were benign lesions while the rest 26 were malignant lesions. The sensitivity of the DWI was 100% while the specificity was 80%. The ADC values for the benign lesions were $1.1-2.2 \times 10^{-3} \text{ mm}^2/\text{sec}$, while the malignant lesions showed ADC values of $0.46-0.99 \times 10^{-3} \text{ mm}^2/\text{sec}$. The ADC value of $1.1 \times 10^{-3} \text{ mm}^2/\text{sec}$ can be used as the cutoff value in differentiating the benign from the malignant lesions.

Conclusion: DWI and ADC calculation are short unenhanced sequence that can be inserted easily into MRI protocols to accurately differentiate between the benign and malignant breast lesions.

1. Introduction

Breast lesions were classified as benign or malignant lesions with the majority of the breast lesions are benign. So, it is important to differentiate the benign lesions from the malignant one (1). Breast cancer is the most common female malignancy representing 31% of the tumors affecting the female patients and considered the second leading cause of death among the female population (2). The increasing rate of breast cancer incidence markedly raises the concern of both clinicians and researchers. Also, the increase in the awareness of breast cancers among the population leads to more frequent physical examination and using more frequent diagnostic imaging procedures needed for early diagnosis and improved the prognosis (3).

http://dx.doi.org/10.1016/j.ejrnm.2015.10.013
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Mammography is the first tool in diagnosis and detection of different breast lesions and usually used for screening. However, it is known to have high false positive results in detection of breast malignancy (about 60–80%), resulting in unnecessary biopsies (4). Breast ultrasound examination has been used as a complementary exam for the mammography especially to differentiate whether the mammography seen lesions represent cystic or solid masses (5).

Breast MRI has become an important tool for breast lesions characterization with the dynamic contrast enhanced MRI technique is highly sensitive in detection of breast cancers especially those that are occult on physical examination, mammography and ultrasonography (6). The typical MRI protocol involves contrast enhanced sequences to highlight the lesion and increase the sensitivity for detecting the malignant lesions. However, many false positive results were obtained (7). Various benign lesions of the breast can be difficult to distinguish from the malignant lesions on MRI, such as sclerosis adenosis, atypical hyperplasia, lobular carcinoma in situ (LCIS) and breast papillomas. All these lesions can produce enhancement pattern that is similar to the malignant lesions. This overlap can lead to decrease the specificity of the MRI (8). Also, MRI may miss some lesions causing false negative results such as ductal carcinoma in situ (DCIS) and invasive lobular carcinoma (9).

Also, some malignant lesions have benign morphology with absent malignant architecture features as in medullary and colloid cancers with the dynamic study gives continuous enhancement with subsequent false negative result (10).

DWI provides important biological information about the composition of the tissue, their physical properties, their microstructure and their architecture. DWI provides images based on the molecular motion of the water inside the tissue which is altered with the change in the tissue criteria (11,12). The motion of water molecules is more restricted in tissues with high cellularity i.e. tumoral tissue with the malignant one being more cellular than the benign lesions (13).

The value of diffusion of the water inside the tissue can be calculated numerically and is called apparent diffusion coefficient (ADC). The ADC is calculated for each pixel of the image and is displayed as a parametric map. The areas of restricted diffusion represent high cellular areas with low ADC value (11,14). Many studies are focusing on the role of DWI and ADC in differentiating benign from malignant lesions with the malignant lesions showing restricted diffusion with subsequent lower ADC values (15).

Also, the DWI has a great role in differentiating the local recurrence and the operative bed surgical scar (16). Finally, DWI by the help of ADC has important role in monitoring and predicting the early tumoral response to the chemotherapy and evaluation of the peri-tumoral tissue (17,18).

### 2. The aim of the work

The aim of this work was to evaluate the role of DWI and ADC value calculation in increasing the specificity and sensitivity of the MRI in diagnosis and differentiation of the benign from the malignant breast lesions.

### 3. Patients & methods

#### 3.1. Patients

The study conducted over 56 female patients referred for bilateral breasts MRI at MRI unit-Radiology department-Ain Shams University over the period from January 2013 to August 2014. Written consents were taken from all the patients before examination and any radiological investigation. All patients were subjected to clinical examination and sonomammography before the MRI study. We excluded patients with bad general conditions, patients with contraindications for MRI (e.g. patients with implanted magnetic device), patients with claustrophobia, patients whom contrast medium safety not yet approved (e.g. lactating females or patients with severe renal failure being more susceptible for nephrogenic sclerosis)

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Illustrate the different parameters used during different MRI pulse sequences.</th>
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<tbody>
<tr>
<td></td>
<td>Axial T1WI</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>540</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>10</td>
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<tr>
<td>NEX</td>
<td>1</td>
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<tr>
<td>ST (mm)</td>
<td>3</td>
</tr>
<tr>
<td>Gap (mm)</td>
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</tr>
<tr>
<td>FOV (cm)</td>
<td>$34 \times 34$</td>
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<td>Matrix</td>
<td>$256 \times 160$ or $256 \times 192$</td>
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**Fig. 1** The ADC value calculated in both the benign and malignant lesions showing that $1.1 \times 10^{-3}$ mm$^2$/sec ADC value was the cutoff value to differentiate between the benign and malignant breast lesions.
and patients with only cystic lesions or multiple lesions on sonomammography.

3.2. Patient preparation

There was no specific preparation apart from fasting and better evaluation during the second or the third week of the cycle. The patients were informed about the importance of complete prevention of the movement. Also, venous line (18–20 G) cannula was inserted for post-contrast study. Serum creatinine was checked for all patients.

3.3. Patient position

We used Philips superconductive magnet system at 1.5 T with breast surface coil. The patients were placed on prone position with the breast positioned dependant inside the coil and the arms placed along the body.

3.4. MRI techniques

We started with conventional sequences namely axial T1WI, axial T2WI, axial T2 fat suppression and STIR ± Sagittal STIR. This was followed by DWI which was performed prior to the contrast study to exclude any possibility about the effect of the contrast agent on the diffusion criteria of the examined lesions. We used EPI-DW (echo-planar imaging) in transverse axial plane using $b$-values of 0, 400, 800 s/mm$^2$. The other parameters were illustrated in Table 1.

For quantitative analysis, the DWI and ADC values were calculated and measured for each lesion and if the lesion was less than 3 cm in average size, the ADC value was calculated twice to ensure that the same areas were measured. Finally, dynamic study was performed for all the patients using Gadolinium as a contrast agent at a dose of 0.1 mmol/kg using a pump followed by saline flush to ensure that the contrast

![Fig. 2 The relation between the different types of the dynamic curve and different pathological types of breast lesions.](image)

![Fig. 3 28 years old female with right breast lump. MRI study revealed: (A) T1WI shows right breast well defined lesion involving the upper outer part exhibiting low SI. (B) T2WI: Intermediated to high SI. (C) STIR showing high SI. (D) DWI showing hyperintense lesion. (E) The ADC value was $1.3–1.5 \times 10^{-3}$ mm$^2$/sec. (F) The dynamic time/intensity curve was type I. The previous MRI features more with benign lesion. The case was proved histopathologically to be a fibroadenoma.](image)
enhanced images could be obtained immediately after contrast injection. This is followed by performance of a time/intensity curve.

3.5. Images interpretation

Each lesion detected by MRI was evaluated as regards the morphology, location, extent, Signal intensity in different pulse sequences, signal intensity on DWI, the ADC value, the enhancement pattern after contrast injection and the type of dynamic time/intensity curve. From all the previous parameters, the lesions were classified into benign versus malignant lesions and compared with the histopathological results that were obtained from the patients after surgery or biopsy.

4. Results

The analysis data were done using IBM SPSS (Statistical Program for Social Science version 22.0, IBM Corp., USA, 2013). Diagnostic validity tests were used including diagnostic sensitivity, specificity and efficacy.

Our study included 56 patients with 56 different lesions (one lesion for every patient), and their ages ranged between 14 years old and 73 years old with a mean age 45.14 ± 13 SD. 35.7% of the studied cases were presented by breast lump which was the main clinical presentation. This was followed by previous history of surgery or skin thickening which represented 17.8% and 14.2% respectively. 30 cases out of 56 cases had benign lesions (i.e. fibroadenoma, fibrosis, glandular condensation or postoperative scar) representing 53.6% of the cases with the fibroadenoma was the commonest benign lesion representing 70% of all benign lesions. The rest 26 cases had malignant lesions (i.e. invasive ductal and lobular carcinoma, undifferentiated, malignant phylloides and recurrent malignancy) representing 46.4% of the cases with the invasive ductal carcinoma (IDC) was the commonest malignancy representing 65.4% of the malignant lesions.

All the malignant lesions showed restricted diffusion. Also, 6 benign lesions showed restricted diffusion. So, the DWI alone showed sensitivity about 100%, specificity about 80% and efficacy about 89.3%. The ADC value of these lesions was calculated and was $0.46-0.99 \times 10^{-3} \text{mm}^2/\text{sec}$ (mean = $0.8 \text{mm}^2/\text{sec} \pm 0.17 \text{SD}$) for malignant lesions, while the ADC value of the benign lesions was ranging from $1.1-2.2 \times 10^{-3} \text{mm}^2/\text{sec}$ (mean = $1.67 \text{mm}^2/\text{sec} \pm 0.37 \text{SD}$). The ADC value of $1.1 \times 10^{-3} \text{mm}^2/\text{sec}$ was the cutoff value to differentiate between the benign and malignant breast lesions (Fig. 1).

Regarding the dynamic time/intensity curve, 25 cases show type I curve (benign form) and were diagnosed histopathologically as benign lesions. 11 cases showed type II curve (equivocal form) with 6 of them showed low ADC value and proved histopathologically to be malignant while the rest 5 showed high ADC value and proved histopathologically to be benign lesions. 20 cases showed type III curve (malignant form) with low ADC value and restricted diffusion and proved histopathologically to be malignant (Fig. 2). The sensitivity and specificity of the dynamic time/intensity curve alone was

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Fig. 4 A female patient 60 years old with history of left lumpectomy for breast cancer. On followup, operative bed suspicious mass lesion noted. MRI study revealed: (A) T2WI shows low SI irregular mass. (B) T1WI + C show low SI mass with no definite enhancement. (C) DWI: No diffusion restriction. (D) STIR: Heterogeneous SI. (E) ADC map with ADC value = $1.5 \times 10^{-3} \text{mm}^2/\text{sec}$. (F) Dynamic time/intensity curve reveals type II curve. The case was proved histopathologically to be operative bed scar.
Fig. 5 A female patient 70 years old with bilateral MRM for bilateral cancer breasts. On follow-up, irregular mass lesion noted at the left breast implicating the left pectoralis major. (A) T1WI shows hypointense mass lesion. (B) DWI shows restricted diffusion. (C) STIR images show heterogeneous SI. (D and E) Axial and sagittal T1WI + Contrast show positive enhancement of the mass lesion. (F) Dynamic time/intensity curve shows type III curve. The ADC value of this case was $0.75 \times 10^{-3}$ mm$^2$/sec. Collectively, the MRI criteria were with local recurrence. The case was proved histopathologically to be local recurrence for invasive ductal carcinoma.

Fig. 6 A 57 years old female presented with suspicious lymphadenopathy detected during the routine follow-up after right radical mastectomy. (A) The lymph nodes express low SI on T1WI with absent central fatty hilum. (B) T2WI shows intermediated SI. (C) STIR shows low SI. (D) DWI shows hyperintense signal. (E) The ADC value was $0.82 \times 10^{-3}$ mm$^2$/sec. (F) The dynamic time/intensity curve was type III curve characteristic for malignancy. The case was histopathologically proved to be metastasis from invasive ductal carcinoma.
77% and 83.3% respectively. Type II curve showed low sensitivity and specificity of 19% and 83% respectively while type III curve showed 80% sensitivity and 100% specificity.

Also, with the use of ADC calculation the sensitivity reached 93.3% with specificity about 100%.

5. Discussion

Breast cancer is the most common malignancy in women with the usual assessment methods such as physical examination and radiographic imaging using ultrasound and mammography have well known limitations, such as inaccurate differentiation between the benign and malignant lesions. Also, these conventional methods are inaccurate for detection of local recurrence and differentiation between the operative bed recurrence and operative bed scarring (19).

MRI is an established supplementary technique in evaluation of suspicious breast lesions. Conventional MRI is based on combined analysis of the morphology and enhancement kinetics of the lesions. So, information about tumor physics, vascularity and vascular permeability was obtained (20). Recently, different parameters have been evaluated to increase the specificity and accuracy of breast MRI (21).

DWI provides important biological information about the composition of tissues, their physical properties, their microstructures and their architectural organization. The DWI is based on molecular motion of water, which is altered by disease (12).

By using DWI sequence, one can calculate the ADC value, a quantitative measure that is directly proportional to the water diffusion. High cell proliferation in malignant tumor increases the cellular density, reducing the ADC and resulting in signal loss (18).

In this study, we attempted to investigate the validity of DWI and ADC calculation in evaluation of suspicious solid breast lesions with finding correlation with the histopathological data aiming to increase the specificity of MRI study in differentiation of breast solid lesions.

We conducted the study over 56 patients having 56 solid breast lesions (one lesion for each case) with 30 of them were proved histopathologically to have benign lesions representing 53.6% of the cases while the rest 26 patients proved to have malignant lesions representing 46.4% of the cases.

The mean age of the patients was 45.1 ± 13 years old. The main complain was breast lump sensation representing 35.7% of the cases and this was followed by cases with history of cancer breast removal representing 17.8% of cases. The most benign lesion was fibroadenoma accounting 70% of the benign cases while the most malignancy was invasive ductal carcinoma representing 65.4% of the malignant cases. This is comparable with Li et al., 2005 who showed in their breast cancer survey that the invasive ductal carcinoma accounts for 76% of all cases (22).

22 cases showed typical benign appearance in conventional MRI being well defined and regular with smooth outer margin exhibiting low signal on T1WI and intermediate to high signal intensity on T2WI. All appeared isointense or not identified on...
The dynamic time/intensity curve was typically type I curve (continuous rising curve) characteristic for benign lesions. The ADC value was ranging from 1.1 to $2.2 \times 10^{-3}$ mm$^2$/sec. This is consistent with Partridge et al. and Tozaki and Fukuma (23,24).

All proved histopathologically to be benign lesions either fibroadenoma or fibrosis versus glandular condensations. All these benign lesions are characterized by low cellularity explaining the low signal on DWI due to high water motion. Therefore, high ADC value is obtained.

Another 6 cases showed well defined and regular lesions with low signal on T1WI and intermediate to high signal on T2WI yet with hyperintense signal on DWI. 3 of them showed type II dynamic time/intensity curve (equivocal form) with the rest showed type I curve. All showed high ADC of $1.3-2 \times 10^{-3}$ mm$^2$/sec. The histopathology proved their benign natures namely fibroadenomas. This is consistent with Belli et al. (21). He found that, the fibroadenomas may have high signal on DWI which may be due to stromal myxoid changes and consequently increased mobility of water (Fig. 3).

Among the studied group, 10 patients representing 17.8% had history of surgical removal of cancer breast and showed irregular speculated suspicious mass lesion on regular follow-up by sonomammography. All these patients underwent MRI to differentiate between local recurrence versus operative bed scarring. 2 of them showed type II curve (equivocal form) which was not conclusive and maintained the dilemma of the diagnosis. The DWI showed isointense signal with ADC value 1.5 and $2.2 \times 10^{-3}$ mm$^2$/sec, results more with benign features and this was proved histopathologically to be operative bed scarring. These results were almost similar to Rinaldi et al. (16), who reported that the combination of DWI with the contrast MRI showed high diagnostic value evaluation of scar in patients operated for breast cancer and ADC value can be a specific parameter in differential diagnosis between recurrence, and found that in benign scar lesions ADC values were more than $1.4 \text{cm}^2$/sec associated with low signals on DWI while recurrence showed ADC values less than $1.4 \text{cm}^2$/sec associated with hyperintense signal on DWI (Fig. 4).

The rest 8 postoperative cases showed local recurrence with typical malignant criteria in MRI in the form of irregular speculated lesion showing type III curve as well as high signal intensity on DWI with low ADC value characteristic for malignancy. This was almost similar to Seely et al. (25). This is consistent with the basis that the malignancy shows high cellularity leading to decrease the mobility of water and restricted diffusion as well as low ADC value (Fig. 5).

2 other cases among the study population presented with suspicious looking axillary lymphadenopathy. They underwent MRI with the lymph nodes showing high signal intensity on DWI with typical type III curve characteristic for malignancy with low ADC value of 0.50 and $0.82 \times 10^{-3}$ mm$^2$/sec. This was proved histopathologically to be malignant axillary lymphadenopathy. This is consistent with Kohn and Collins, 2007 as well as Pereira et al. (14,18). They reported that the DWI as well as the ADC calculation can be used to detect lymph nodes affected by malignant cells. The malignant lymph nodes show increased cellularity leads to diffusion restriction and low ADC values (Fig. 6).

**Fig. 8** 14 years old female presented with left breast lump. The left breast shows a large well defined soft tissue mass lesion exhibiting heterogeneous SI on both T1WI and T2WI (A and B). Also, it shows restricted diffusion (C) with ADC value = $0.90 \times 10^{-3}$ mm$^2$/sec (D). The dynamic time/intensity curve was type II (equivocal) (E). The case was proved histopathologically to be malignant phylloides.
The rest 16 patients diagnosed to have primary malignancy with the invasive ductal carcinoma (IDC) were the commonest representing 65.4% of the malignant cases consistent with Rosal et al. (26) which considered IDC the most common tumor involving the breast. All lesions showed high signal intensity on DWI with 10 of them showed typical type III curve while 6 showed equivocal type II curve yet all showed low ADC value with mean value of 0.8 × 10^{-3} mm²/sec. This is explained by high cellularity of the malignant lesions with subsequent decreased water motion and increased signal on DWI and low ADC value (Figs 7 and 8).

In our study, we notice that there is still some overlap between the benign and malignant lesions regarding the type of the dynamic curves. We obtained type II curve in 11 patients with 5 of them were diagnosed to have benign lesions. This is consistent with Ikeda, 2001 (27). The sensitivity and specificity of the dynamic curve alone was 77% and 83.3% respectively. Also, we found that the combination between the DWI and the dynamic curve parameters increased the sensitivity and specificity of the MRI study.

We found that all malignant lesions showed diffusion restriction with most of the benign lesions showed isointense signal on DWI or couldn’t be identified. Some benign lesions showed diffusion restrictions with the sensitivity of the DWI alone was 100% while the specificity was 80%.

Also, the ADC value calculation is an important parameter to differentiate between the benign and malignant lesions with our study revealing that, the cutoff value between the benign and malignant lesions was 1.1 × 10^{-3} mm²/sec. This is almost similar to the previous studies by Tsushima et al., Rubesova et al., Yabuuchi et al. and Portridge et al. (28–30,23). The minimal difference in ADC threshold can be explained by the difference in many technical variables that affect the ADC value, such as pulse sequences and b-value.

6. Conclusion

DWI is a short unenhanced scan that can be inserted easily into standard breast MRI protocols as a potential adjunct that can be added routinely to conventional breast MRI. Also, the ADC values derived from it can be accurately used to differentiate benign from malignant breast lesions with high sensitivity and specificity.

Conflict of interest

We have no conflict of interest.

References

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