



The role of diffusion weighted imaging in magnetic resonance to evaluate breast masses

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ABSTRACT

Aim: To investigate the role of diffusion weighted magnetic resonance imaging (MRI) in differentiation of benign and malignant breast lesions using apparent diffusion coefficient (ADC) values preoperatively.

Methods: A total of 30 women between the ages of 14-75 years (mean, 47, 6 years) with 30 histopathologically verified breast lesions were investigated in this study. The patients were examined by a 1, 5 T MRI device using bilateral phased array breast coil. Spin echo planar diffusion imaging was used to scan patients. Images were obtained by b values 0 and 500 seconds/mm². Mean ADC values of the benign and malignant lesions were measured and calculated. The comparison between the histopathological diagnoses and the mean ADCs were performed by Mann Whitney U test.

Results: The diagnosis of 30 patients with 30 breast lesions were as follows; malign lesions (n=13), benign lesions (n=17). The ADC values were as follows (in units of 10⁻³mm² /sec): benign breast lesions (range: 1, 09-1, 98, mean: 1, 45) and malignant breast lesions (range: 0, 59-1, 08, mean: 0, 76). The mean ADC obtained from malignant breast lesions was statistically different from that observed in benign solid lesions ($p < 0, 01$).

Conclusion: Diffusion imaging can be used in differentiation of malign and benign breast lesions.

Keywords: Magnetic resonance imaging, diffusion, breast masses.

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Introduction

Breast cancer is the most common type of cancer in women. Despite significant

improvements in treatment, it is still one of the major causes of cancer-related mortality worldwide with an estimated 500,000 deaths per year [1]. Accurate diagnosis is of critical importance because early diagnosis and treatment increases quality of life and survey [2].

Mammography is still the main imaging method for screening and detecting breast

lesions with a sensitivity of 69–90% [3-5]. In the presence of dens parenchyma or breast implant, where mammography is insufficient, ultrasonography (USG) is complementary to mammography in patients evaluated postoperatively or after radiotherapy, and it has a very significant place in breast imaging. However, USG alone is inadequate to detect microcalcifications and ductal carcinoma in situ cases [6].

MRI is increasingly used as a problem-solving method in the diagnosis of breast cancer [2]. Conventional dynamic breast MRI has a sensitivity of 94-99% in the diagnosis of invasive breast cancer, while its specificity varies between 37-86% [7-8]. In addition, it may not be possible to differentiate benign lesions from malignant lesions by conventional MRI sequences because sometimes morphological features and contrast enhancement patterns of benign and malignant lesions may be similar [9]. Therefore, more specific imaging techniques are needed to characterize breast lesions. DWI is an MRI technique based on different diffusion rates of water molecules in normal and pathological tissues. Compared with conventional MRI, this technique has been shown to have a higher specificity in differentiating benign and malignant lesions from 84% to 37% [10].

In addition, ADC maps are generated automatically by high-capacity computers over DWI, and measurements can be made on these maps. In many studies in the literature, it was found out that the average ADC values correlated with the cell density of breast tumors [10-11]. Studies have suggested that DWI and ADC measurements have high accuracy rate in differentiating malignant-benign breast lesions [11-14].

In this study, it was aimed to determine the contribution of signal abnormalities detected in

DWI to diagnosis in breast MRI and, additionally, DWI planned in selected cases for different reasons, and to compare the ADC values measured with histopathological results for the lesions.

Materials and Methods

Thirty female patients whose lesion differentiation between malignant and benign could not be assessed by mammography or USG, and who had BI-RADS 4 and 5 lesions with a mass size of 1 cm or over were included into our study. MRI examinations of premenopausal patients were performed at the 2nd and 3rd weeks of the cycle to avoid possible effects of menstrual cycle on ADC values. After getting approval of the ethics committee (MoH Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Evaluation Commission, 26.08.2010, Decision No: 03), all participants were informed and their written consent was obtained.

Breast MRI examinations of all patients were performed by 1,5 Tesla MRI (Signa HDxt, GE, USA). 34 cm imaging area was obtained by using a standard breast coil in the prone position, TSE T1 and T2 weighted fat saturated axial, gradient echo T1 weighted axial, and contrast gradient echo T1 weighted dynamic and late phase axial sequences as conventional sequences. For pre-contrast FSE T1-weighted images TR: 650msec, TE: 9.6 msec, matrix: 512X512, sections with a cross-sectional thickness of 3 mm and a cross-section of 0.5 mm; For FSE T2-weighted images, TR: 10550 msec, TE: 83.8 msec, matrix: 256x256, cross-sectional thickness 3 mm and 0.5 mm cross-sectional range were obtained. 8 images for each section in the axial plane for dynamic operation TR: 6.6 msec, TE: 3.2 msec, angle of roll: 20 °, matrix: 512X512, cross-sectional thickness: 3 mm and cross-sectional range: 0.5

mm with 30 sec intervals in the T1-weighted FSE sequence were obtained. Gadolinium-containing contrast agent 0.1 to 0.2 mmol / kg dose was given intravenously within 20 seconds. Subtracted series were obtained by using the subtraction program as standard in the MRI console, and time signal intensity curves of the lesions were plotted.

Diffusion-weighted MRI images were obtained in the axial plane prior to contrast agent injection, through breath-hold command and single-shot echoplanar spin echo sequence by using the following parameters: TR / TE: 2500 / 74.4 msec ; matrix: 256X256; imaging area: 34 cm; section thickness: 3mm; gap between sections: 0.5mm. Two different b-values were used for each section, with $b = 0$ and $b = 500$ sec / mm². Both breasts were examined in 22 sections. In the console of the MRI device, ADC values were automatically measured and ADC map images were prepared. ADC measurements were made using a standard measuring area (ROI) of 25.0 mm². During ADC measurement, necrotic and cystic components of the tumors were excluded from the measurement area. ADC measurements were taken three times in each case in the lesion, and normal breast parenchyma, and a numerical value was determined by taking arithmetic mean for each localization. ADC value was measured by standard deviation in ROI.

Statically analysis

Statistical package for social sciences (SPSS) computer program was used for statistical evaluations. Descriptive statistics (mean, standard deviation, minimum maximum interval), were used in statistical evaluation on computer, and Mann Whitney U test and Chi-square test were used to compare continuous variables with each other. It was accepted that

“p” value should be less than 0.05 ($p < 0.05$) as the statistical significance limit.

Results

The age of the patients ranged from 14 to 75 years, and the mean age was determined as 47.6 years. Lesions were detected in the right breast of 13 patients (43.3%), in the left breast of 17 patients (56.6%), in the upper outer quadrant of 17 patients (56.6%), in the upper internal quadrant of 7 patients (23,3 %), in the lower outer quadrant of one patient(3.3%) and in the lower inner quadrant of 5 patients (16.6%) by conventional breast imaging methods. None of the patients had BI-RADS (Breast Imaging-Reporting and Data System) 4-5 lesions in the contralateral breast. The size of the lesions detected were between 1.5 and 4 cm (mean: 2.3 cm). 30 lesions in total were detected on routine MRI. All patients had only one lesion. The smallest lesion detected on MRI was 1 cm and the largest lesion was 4 cm (mean: 2.06 cm). It was seen that the lesions covered a single quadrant correlated with conventional breast imaging methods. Of the 30 lesions sampled histopathologically 13 were malignant and 17 were benign. All patients underwent diffusion weighted breast MRI. The smallest lesion detected in DWI was 1 cm and the largest lesion was 4 cm in size, and signal abnormalities were detected in all of the lesions. There was, visually, diffusion limitation in 14 lesions (46.6%) and diffusion increase in 16 lesions (53.3%) in DWI. On ADC maps, the mean ADC value of 13 lesions with malignant histopathologic diagnosis was calculated as 0.76×10^{-3} mm² / sec \pm 0.14 (highest value 1.08×10^{-3} mm² / sec, lowest value 0.59×10^{-3} mm² / sec) (Figure 1).

The mean ADC value for measurements from seventeen benign lesions was 1.45×10^{-3} mm² / sec. \pm 0.26 (highest value $1,98 \times 10^{-3}$ mm² / sec,

lowest value $1,09 \times 10^{-3} \text{ mm}^2 / \text{sec}$). However, each lesion group was evaluated within itself, and ADC values of lesion subgroups were calculated (Table 1).

sensitivity rate in detecting breast cancer compared to mammography and USG [16]. Conventional breast MRI and dynamic phase contrast MRI, which is a part of this

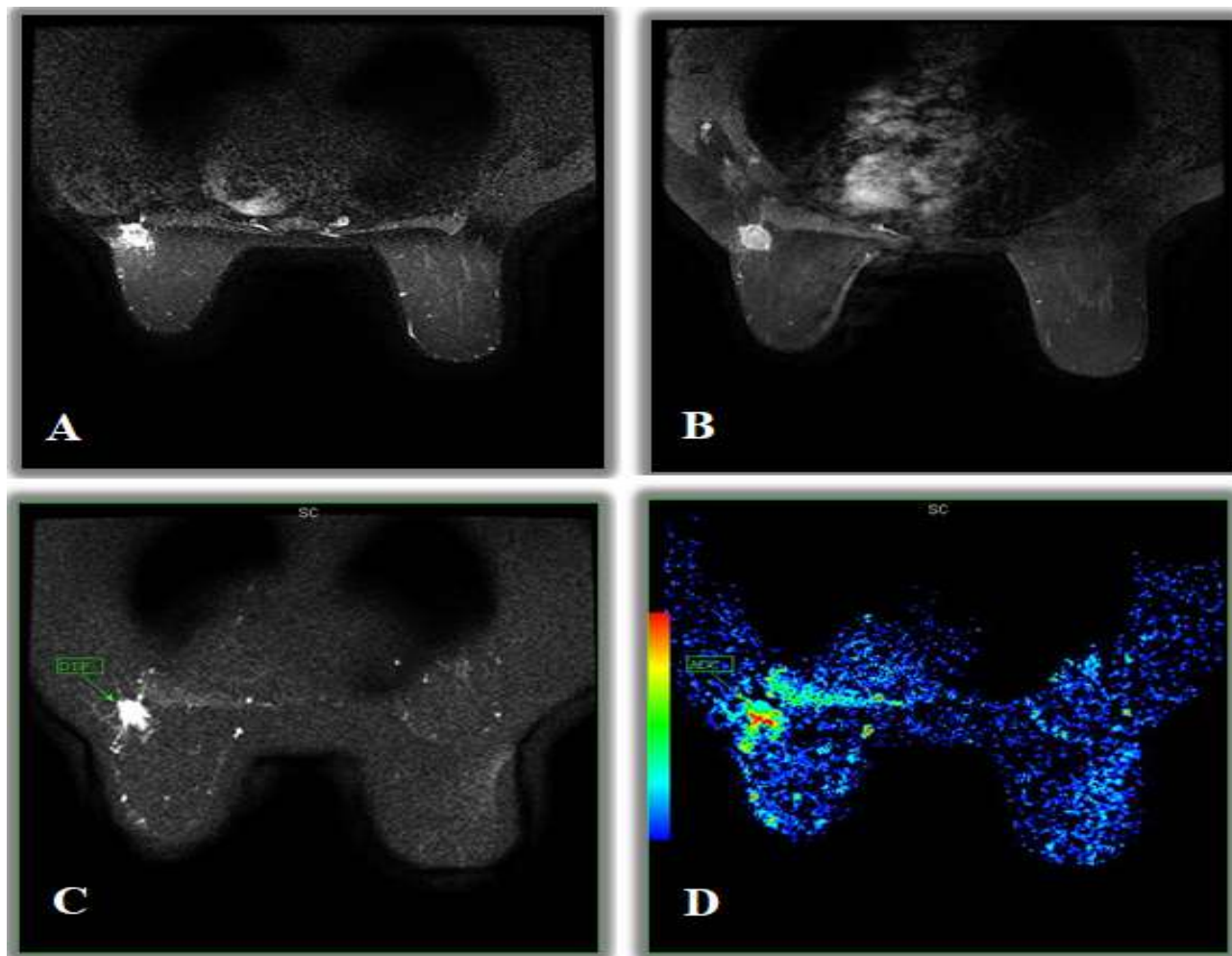


Figure 1 A-D. Conventional dynamic and diffusion weighted MR images from a patient with histologically proved invasive ductal carcinoma in the left breast. **A.** Fat saturated T2-weighted image shows a mass with high signal intensity compared with normal fibroglandular tissue **B.** Contrast-enhanced T1-weighted image demonstrates peripherally enhancement of the mass **C.** Diffusion-weighted image shows restricted diffusion compared to normal breast tissue in the left side and **D.** On ADC maps calculated mean ADC values of the mass was low ($0,755 \times 10^{-3} \text{ mm}^2 / \text{sec}$)

Discussion

Breast cancer, affecting 2.1 million women each year, is becoming an increasing health problem in both developed and developing countries. It is the primary cause of cancer-related deaths in women [15]. MRI has a higher

examination, are now widely used in breast evaluation in many centers. However, it may cause unnecessary biopsies with a high false-positive rate [17]. Dynamic examination reflects tissue vascularity, vascular

Table 1. Distribution of ADC values in lesion subgroups (ADC value x 10⁻³ mm²/sec).

Pathological Diagnosis of Lesions	Number of Lesions	ADC Values (10 ⁻³ mm ² /sec)			
		The Lowest ADC	The Highest ADC	Mean ADC	Standard Deviation
Invasive ductal carcinoma	6	0,60	0,97	0,75	0,13
Infiltrative ductal carcinoma	5	0,59	0,85	0,73	0,11
Invasive lobular+ductal carcinoma	1	–	–	0,65	–
Invasive lobular carcinoma	1	–	–	0,88	–
Fibroadenoma	6	1,15	1,57	1,35	0,17
Fibrocystic changes of breast	4	1,32	1,58	1,47	0,1
Atypical hyperplasia	3	1,45	1,92	1,75	0,14
Tubular adenoma	1	–	–	1,05	–
Fat necrosis	1	–	–	1,43	–
Intraductal papilloma	1	–	–	1,15	–
Stromal fibrosis of the breast	1	–	–	1,98	–

permeability, changes in interstitial pressure, and changes in extracellular space content. This technique is directly related to the vascularity of the lesions, but there is no direct correlation between tumor cellularity and contrast enhancement pattern [18]. The only imaging method that reflects cellular cellularity in recent conditions is DWI [12]. The term diffusion is

used for the randomized microscopic movement of molecules known as Brownian motion and measured by ADC values [19]. DWI and ADC maps obtained from them reduce the false positivity rates caused by conventional MRI in breast imaging by examining the biophysical properties of tissues [17]. Magnetic susceptibility and chemical shift

artifact are evident in the images obtained by echo planar imaging (EPI) technique, which is the most widely used diffusion sequence in clinical practice [13,20]. Especially in breast imaging, the sensitivity of the EPI sequence to the indicated artifacts increases because the breast tissue is surrounded by very dense adipose tissue and the air-tissue interface is high due to the anatomical localization of the breast. The resulting artifacts both create image distortion and cause the edges of the lesion to fade in isotropic diffusion images. In today's technological conditions, especially in breast imaging, it is recommended that the spatial resolution of DWI should be low, and the lesion to be examined should be larger than 2x2 pixels. The resulting image distortion does not significantly change the functional sensitivity of the diffusion up to a certain limit. Because the ADC map where measurements are made is created by making measurements per pixel [11]. Studies have shown that these artifacts and the disadvantages of the EPI sequence are eliminated by the DWI technique obtained by the HASTE (Half Fourier Single Shot Turbo Spin Echo) sequence [21,22]. In our study, in 3 of the DWI obtained by the EPI sequence, the artifacts which we think were caused by the above mentioned features and the dense fat tissue found in the breast tissue in the BI-RADS type 1 breast pattern were observed. The basis of the use of DWI in malignant lesions of the breast is constituted by its histological properties due to the microstructure of tumors. There is a direct correlation between tumor cellularity and ADC values. In a study on brain tumors carried out for the first time, ADC values of low-grade gliomas were shown to be higher than high-grade gliomas [23]. In many studies on breast lesions, it was shown that ADC values in malignant breast lesions with high cellularity were significantly lower

compared to benign lesions, and it increased sensitivity in the differentiation of benign and malignant lesions. In the study performed by Kinoshita et al. [21], it has been reported that the average ADC value in 10 masses diagnosed with invasive ductal carcinoma in DWI obtained by HASTE sequence: $1.216 \pm 189.10^{-3} \text{ mm}^2 / \text{sec}$, and the average ADC value in 6 lesions diagnosed with fibroadenoma: $1.495 \pm 0.181.10^{-3} \text{ mm}^2 / \text{sec}$. In this study, "b" value is taken as 0 and 700 sec / mm^2 . In our study, the mean ADC value in 11 masses with pathologic diagnosis of invasive ductal carcinoma was obtained as : $0,74 \pm 0.12 .10^{-3} \text{ mm}^2 / \text{sec}$ while the mean ADC value of the lesion from 6 pathological diagnosis of fibroadenoma was found out to be : $1,35 \pm 0.17 .10^{-3} \text{ mm}^2 / \text{sec}$.

The ADC values determined in some studies obtained with the EPI sequence were as follows; the average ADC value of 17 malignant lesions: $1,60 \pm 0,36 .10^{-3} \text{ mm}^2 / \text{sec}$, the mean ADC value of 6 benign lesions : $2,01 \pm 0,46.10^{-3} \text{ mm}^2 / \text{sec}$ in the study in which b value was taken as 400 sec/ mm^2 by Sinha et al [11], the average ADC value of 31 malignant lesions: : $0,97 \pm 0,20 .10^{-3} \text{ mm}^2 / \text{sec}$, the mean ADC value of 24 benign lesions: $1,57 \pm 0,23 .10^{-3} \text{ mm}^2 / \text{sec}$ in the study in which b value was taken as 1000 sec/ mm^2 by Guo et al [22], again in another study in which b value was taken as 1000 sec/ mm^2 by Marini et al [24] it was found out that the average ADC value of 42 malignant lesions: $0,95 \pm 0,18 .10^{-3} \text{ mm}^2 / \text{sec}$ and the mean ADC value of 21 benign lesions: $1,48 \pm 0,37 .10^{-3} \text{ mm}^2 / \text{sec}$. In another study in which Partridge et al [25] took b value as 600 sec / mm^2 , the values were calculated as follows : the mean ADC value of 27 malignant lesions : $1,32 \pm 0,23 .10^{-3} \text{ mm}^2 / \text{sec}$ and the mean ADC value of 91 benign lesions: $1,71 \pm 0,43 .10^{-3} \text{ mm}^2 / \text{sec}$.

Table 2. Comparison of previous studies with current study about diffusion imaging of breast lesions and ADC values (ADC value x 10⁻³ mm²/sec).

Previous Studies	Methods of Study		ADC Value (10 ⁻³ mm ² /sec)	
	DWI Sequence	“b” Value (mm ² /sec)	Malignant Lesions	Benign Lesions
Kinoshita et al.	HASTE	0-700	1,21 ± 0,18	1,49 ± 0,18
Sinha et al.	EPI	0-400	1,60 ± 0,36	2,01 ± 0,46
Guo et al.	EPI	0-1000	0,97 ± 0,20	1,57 ± 0,23
Marini et al.	EPI	0-1000	0,95 ± 0,18	1,48 ± 0,37
Partridge et al.	EPI	0-600	1,32 ± 0,23	1,71 ± 0,43
Current study	EPI	0-500	0,76 ± 0,14	1,45 ± 0,26

The ADC values obtained in our study and in the literature show numerical differences for lesion groups (Table 2). This difference is thought to be caused by the differences in the value of “b”. The gradient intensity applied in diffusion measurement is expressed with the value of “b”. The unit is a parameter, s/mm², which shows the power and time of the gradient. As the gradient intensity increases, the phase distribution in the moving protons increases, and thus the signal loss increases. Therefore, in the selected studies with high “b” values diffusion weights are high while their ADC values are low. The value of “b” is of great importance while obtaining DWI. When the value “b” is chosen as 400 sec / mm² and lower than this value, the image is not only affected by the molecular diffusion of water, but also by the microcirculation of the blood in the capillary bed of tissues and thus by the perfusion [12]. As predicted in malignant tumors, an increase in the number and size of these capillary vessels is observed

[26,27]. Therefore, when the low “b” value is selected, the perfusion effects that will occur in the ADC value will be higher for malignant tumors rather than benign tumors.

In our study, diffusion-weighted images were used to determine and compare the mean ADC values of malignant and benign lesions. In the images, “b” value is selected as 0-500 sec / mm². The common result obtained from all studies in this field in the literature is that the ADC values of malignant and high-grade tumors are significantly lower compared to benign tumors. In the results of our study, a statistically significant difference was observed between the malignant lesions and benign breast lesions (p <0.01) in the mean ADC values in accordance with the literature data. This difference is due to the fact that malignant tumors have low ADC values due to the reasons mentioned above. The ADC results of benign and malignant lesion groups obtained by Padridge et al. [25] (0-600 sec/mm²) and Sinha et al. [11] (0-400 sec/mm²), who took “b”

values close to the one in our study, and our findings showed numerical differences. In addition to this, it was found out that malignant and benign lesions could be differentiated with 100% sensitivity and 100% specificity with a cut-off value of $1.08 \cdot 10^{-3} \text{ mm}^2 / \text{sec}$ in our patient group. However, we think that these high sensitivity and specificity rates and the numerical differences observed in the closest “b” values stems from our limited patient group of thirty. It is estimated that sensitivity and specificity rates and ADC values may change if the patient group is expanded and diversified because the ADC values of the lesions are associated with tumor cellularity, the sensitivity and specificity values of the threshold values specified in the literature are lower [22]. In fact, in some studies done using DWI, it has been shown that ADC values in invasive breast carcinomas are lower than noninvasive breast carcinomas and that ADC values may be useful for histopathological differentiation [28,29].

ADC measurement values vary depending on the structure of the tissues. Changes in ADC values of normal breast fibroglandular tissue during the menstrual cycle have been demonstrated by studies [20]. During the first and second weeks of the cycle, ADC values showed a steady decrease, but increased in the third and fourth weeks. These changes were not statistically significant. It was established that histopathologically indicated ADC changes were due to the varying water and epithelial tissue content of the breast parenchyma at different stages of the menstrual cycle, and in this study it was shown that fibroglandular tissue density of the breast also affected ADC values [30]. ADC values of adipose tissue located close to breast tissue are very low. While there is no fat tissue between the voxels measured in the breast tissue in the dense sclerosed pattern, the liposclerosis and

lipomatous breast pattern inevitably have fat tissue in the voxels within the scope of measurement, which leads to a decrease in the measured ADC values. It is reported that, in order to remove the signal of adipose tissue, signal spectral-spatial RF pulses were inserted in single-shot turbo spin echo diffusion weighted sequences thanks to new technical advances [29]. Furthermore, free diffusion of water is limited in very dense fibrosis and it increases in liquids compared to solid lesions. In line with this information, it should be kept in mind that in a benign lesion such as fibrous fibroadenoma, ADC values may decrease depending on significant fibrous content and increase in malignant tumors showing intense central necrosis. In our study, DWIs were performed in premenopausal patients in the second and third weeks of menstrual phase as recommended in the literature.

Conclusion

DWI is a special MRI sequence, and when used together with conventional MRI sequences, it increases the diagnostic usefulness for differentiating malignant and benign lesions. One of the important advantages of DWI is the ability to obtain numerical data by measuring ADC. Thus, with the help of ADC measurements from breast lesions of sufficient size, a more accurate prediction can be made about the malignancy potential of the lesions before histopathological sampling. When DWI is being evaluated, ADC maps should be evaluated together with it. In this way, the T2 shine-through effect imitating limited diffusion can be eliminated.

There are some limitations to our study. The first is that we have conducted studies with limited number of patients, and if the patient group is expanded and diversified, the sensitivity and specificity rates will change. The second is the formation of artifacts due to

the use of EPI sequence with low spatial resolution. Finally, ADC measurements were performed by a single observer and there was no intra-observer correlation.

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