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Research Article

The Importance of Diffusion MRI Imaging in Differentiating Malignant and Benign Breast Lesions

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Abstract

Aim: The aim of this study is to research the seperation benign and malign breast masses with diffusion-weighted magnetic resonance imaging (MRI).

Material and Method: 66 patients (26 benign, 40 malign) who have taken MRG for any purpose have been incorporated to the research. Rutin contrast enhancement dinamic MRI and diffusion weighted imaging (DWI) applied on 66 lesions. Contrast enhancement MRI and DWI charecteristics of lesions have been evaluated as retrospective for each lesion. Kinetic curves of contrast enhancement pattern of lesions have been evaluated in accordance with BI-RADS classifications. Apparent diffusion coefficient (ADC) measurements have been obtained numerical from DWI's at work stations. Also, ADC values of normal fibrogranduler tissue (NFT) at opposite breast of each patient have been measured. ADC values of NFT, benign and malign lesions have been compared.

Results: Avarage ADC values of benign and malign lesions, NFT in benign and malign patients, were respectively: $1.535x10^{-3}$ mm^2/s, $1.169x10^{-3}$ mm^2/s, $1.879x10^{-3}$ mm^2/s, $1.852x10^{-3}$ mm^2/s. Avarage ADC values of NFT were statistically significant higher than values of bening and malign lesions. Avarage ADC values of malign lesions were statistically significant lower than ADC rates of bening lesions ($p<0.001$).

Conclusion: Distinguish between bening and malign breast lesions with ADC values is an auxiliary paremeter which can be used together with dinamic contrast enhancement curves of lesions and morphological criterias. In our study, we found that the use of DWI in addition to contrast-enhanced MRI can easily distinguish between NFT, benign and malignant masses. We suggest routinely usage of DWI during breast MRI.

Keywords: Magnetic resonance imaging, diffusion, breast cancer, malign, benign

INTRODUCTION

Breast cancer is one of the most common cancers in women in our country. Mortality rates due to cancer are gradually increasing (1,2). Currently, mammography (MG) is the first radiological diagnostic method used in the evaluation of breast lesions (3). The sensitivity of MG increases with age (4). However, 10% of palpable breast cancers cannot be detected by MG (5). In the evaluation of breast lesions, Magnetic Resonance Imaging (MRI) is used in addition to Ultrasonography (USG) and MG, especially in evaluating multicentricity, breast-sparing surgical planning, distinguishing residual lesions and granulation tissue, and follow-up after treatment (3,6,7). The most important limitation of MRI is its inability to detect microcalcifications, an important indicator of breast cancer (8). The American Cancer Society (ACR) has developed the MRI BI-RADS classification system and the MRI dictionary to ensure standardization in MRI reports, as in MG (9).

DWI is one of the new techniques and is a method with a short imaging requires no time and no contrast material. Recently, diffusion weighted imaging (DWI), which reflects the histological structure and cellularity of the tissue, and MRI, which reflects the morphological features and contrast enhancement patterns of the lesion, have been increasingly used in the evaluation of breast lesions (10). Hypercellularity and underdeveloped neovascularity in

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tumoral tissue cause diffusion restriction. Therefore, this difference makes cancer detectable in DWIs (11). DWI was first used by Englander et al. in 1997 (12,13). Sinha et al. used it in 2002 to detect breast masses (14). Diffusion-weighted MRI imaging is known to be effective in showing benign-malignant differentiation as well as tumor aggressiveness in breast lesions (15,16).

The numerical equivalent of diffusion in living tissue is apparent diffusion coefficient (ADC) value. Benign tumors of the breast often have high ADC values. ADC value is affected by tissues characteristics, in fibrotic and necrotic tissues with reduced cellularity. Therefore, the ADC value decreases in masses with dense fibrosis such as fibroadenomas or invasive ductal carcinoma (11,17). It is observed that ADC values of cysts increase according to fluid ratios. Serous substances cause less restriction in diffusion, whereas mucinous substances cause slightly higher diffusion restriction (18-20). In different studies conducted in the literature, it is stated that the specificity will be increased when DWIs are evaluated together in the characterization of breast masses (21).

In our study, we planned to evaluate how the use of DWI findings, one of the functional imaging techniques, in the differentiation of malignant and benign solid breast masses would contribute to the literature.

MATERIAL AND METHOD

Characteristics of Patients

The images of the women undergoing breast MRI due to abnormal MG, USG, and clinical findings in the Radiodiagnostic Department of Dicle University Faculty of Medicine between January 2012 and May 2015 were retrospectively analyzed. Patients receiving chemotherapy and radiotherapy were not included in the study. 66 patients in total were included in the study. Average age of patients was 41.07 (25-76 years). The lesions in the patients were evaluated by the same radiologist. 40 of the lesions were malignant and 26 were benign. The mean age of the patients with malignant lesions was 42.8 years, while it was 38.4 years in those with benign lesions. Ethical approved for the study was obtained from Dicle University Faculty of Medicine, Non-Interventional Clinical Research Ethics Committee (Ethics Committee approval no: 12.06.2015/346).

MRI Protocol

3 Tesla MRI device (Philips Achieva 3.0T MRI Scanner 2013 was used for MRI examination (using a 4-channel double superficial breast wrap, covering the whole breast). The patient was laid on the table in the face down posture and both breast scanning was carried out at the same time. The files of the premenopausal patients who would undergo MRI were scanned and confirmed to be between the 7th and 14th days of the menstrual cycle. In all cases, T1 and T2, fat-suppressed T2 axial view was evaluated. After obtaining fat-suppressed 3D T1-weighted FLASH sequence images, 0.1 mmol/kg gadolinium was injected intravenously with an autoinjector at a speed of 2 ml/s followed by 20 ml saline.

DWI was achieved prior to dynamically contrast-enhanced views. It was determined that a 2D spine echo- plane imaging (EPI) series was used in axial plane images. A diffusion gradient with a b value of 0 and 600 s\mm^2 was applied. ADC mapping is automatically generated at the workstations.

Evaluation of MRI

All MR scans were analysed at the central station. The pathology result was unknown while the evaluation was performed. Fat-suppressed non-contrast sections were removed from the contrast-enhanced sections and evaluated. Suspicious lesions were evaluated with the help of T2 images with removal and fat suppression. The lesion type was classified as mass or non-mass according to BI-RADS (11) (Table 1). The mean tumor diameter was measured using T2 images with axial contrast or fat suppression. ADC values of the lesions were calculated by placing them in the peripheral enhancing part of the lesion using the region of interest (ROI). In particular, the ROI was placed in the solid and contrasted part of the lesion. At least three analyses were performed and the values averaged. Care was taken not to place the ROI in areas with necrosis in the middle and not contrasted. The ROI size was kept between 20-25 mm^2. ADC measurements were also made from the normal breast of each patient, especially from the retroareolar area, and from normal fibroglandular tissues (NFT) (Table 2).

Table 1. MRI BI-RADS classification of malignant and benign lesions

	Malign (40)	Benign (26)	Total (66)
BI-RADS 1	0	0	0
BI-RADS 2	0	0	0
BI-RADS 3	0	22	22 (33.3%)
BI-RADS 4	1	4	5 (7.5%)
BI-RADS 5	39	0	39 (59.1%)

Table 2. NFT minimum, maximum, average ADC values

	Benign	Malign
NFT minimum ADC	1.550x10^{-3} mm^2/sn	1.560x10^{-3} mm^2/s
NFT maximum ADC	2.328x10^{-3} mm^2/sn	2.650x10^{-3} mm^2/s
NFT mean ADC	1.879x10^{-3} mm^2/sn	1.852x10^{-3} mm^2/s

Statistical Analysis

The data were evaluated using the SPSS programme. Results are reported as mean±standard variance and as a percentage. It was checked whether the data fit the normal distribution, and an independent sample t-test was used in pairwise comparisons for those that fit the normal distribution and the Mann-Whitney U test was used for those that did not display a normal distribution. Receiver operating characteristic (ROC) analysis was used to calculate the ADC threshold value in the differentiation of benign and malignant lesions.

RESULTS

The study included 66 patients aged 25-76 years. The findings of 66 lesions in 66 operated patients DWI were evaluated. Of the 66 lesions, 26 (39.4%) were benign and 40 (60.6%) were malignant. The age range of patients with benign lesions was 25-67 years (mean age 38.42 years). The definitive diagnosis was made with histopathological diagnosis in 13 (19.6%) benign and 40 malignant (60.8%) lesions, while it was made with radiological follow-up in 13 benign (19.6%) lesions. Lesions were evaluated histopathologically in 53 cases, and radiological follow-up was performed in 13 cases.

Characteristics of Benign Lesions

A totally of 26 tumours were benign. 13 of the 26 benign tumours were evaluated as benign in the histopathological examination. The other 13 lesions were evaluated to be benign after 2 years of follow-up and no histopathological evaluation was required. Of the lesions diagnosed histopathologically, 2 were reported as adenosis, 1 as apocrine metaplasia, 2 as fibroadenomatoid change, 1 as phylloides tumor, and 7 as fibroadenoma.

Characteristics of Malignant lesions

The age range of patients with malignant tumours was 29-76 years (average age 42.80 years). Lesion sizes were between 17-90 (mean size 39.33) mm. For this reason, dimension measurement could not be made. Only 1 of the malignant lesions had a smooth contour.

40 cases with malignant lesions were evaluated histopathologically, and of these, 1 was Ductal Carcinoma Incitu (DCIS), 1 was malignant mesenchymal tumor (MMT), 5 were malignant epithelial tumor (MET), 4 were Invasive Lobular Carcinoma (ILC), and 29 were Invasive Ductal Carcinoma (IDC).

When the patient ages were compared, the mean patient ages in the benign (first group) and malignant (second groups) were 38.42 and 42.80 years, respectively. When the lesion sizes were compared, the mean volume of malignant tumors was measured as 39.33 mm and the mean size of benign tumours was found to be 17.65 mm, and a statistically considerable variance between them was observed ($p<0.05$).

The mean ADC value of NFT was 1.879 (1.550-2.328x10^{-3}) mm^2/s in the primer group and 1.852 (1.560-2.650x10^{-3}) mm^2/s in the seconder group. There was no significance between the average ADC measurements of the NFTs of the two groups ($p=0.653$) (Table 2). There was a statistically considerable variance between the mean ADC results of NFT and lesions ($p<0.05$).

The mean ADC values of benign and malignant lesions were 1.535x10^{-3} (1.206-1.858x10^{-3}) mm^2/s, and 1.169x10^{-3} (0.997-1.597x10^{-3}) mm^2/s, respectively. And there was a statistically considerable variance between these measurements ($p<0.001$) (Table 3).

Table 3. Minimum, maximum and mean ADC values in malignant and benign lesions

	Benign	Malign
Minimum ADC	1.206x10^{-3} mm^2/s	0.997x10^{-3} mm^2/s
Maximum ADC	1.858x10^{-3} mm^2/s	1.597x10^{-3} mm^2/s
Mean ADC	1.535x10^{-3} mm^2/s	1.169x10^{-3} mm^2/s

In the ROC analysis of benign-malignant differentiation of the lesions, the sensitivity 92.3% and the specificity 82.5% when 1.238x10^{-3} mm^2/s was taken as the threshold value. Area under the curve: 94.8 (95% confidence interval: 0.901-0.995) (Figure 1).

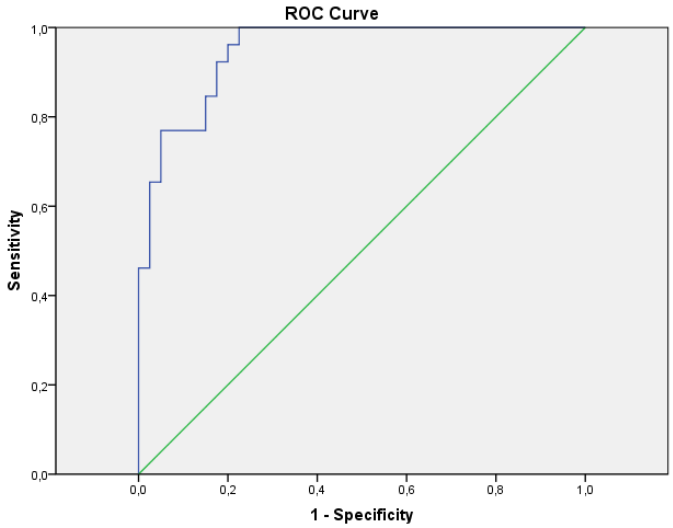

Figure 1. ROC analysis curve of ADC values, area under the curve: 94.8 (95% confidence interval: 0.901-0.995)

DISCUSSION

In this study, we compared the NFT-ADC and ADC ratings malignant and benign lesions to investigate the importance of DWI in benign-malignant differentiation of breast masses. However, in the last years, DWI has been used in breast lesions to make this distinction better. DWI is the most important imaging method that reflects cellularity (22). Many researchers report that the evaluation of DWI features along with the contrast enhancement pattern of breast lesions facilitates the diagnosis (23).

There are significant differences between the mean ADC values of normal breast tissue and benign and malignant breast mases. This difference depends on the physiological characteristics of the lesion, the technical parameters used in imaging, and the different software programs used to statistically evaluate the ADC values found (24). Unfortunately, there is no consensus among the authors about a standard maximum b value that can be used in terms of ADC values in the examination of breast masses. At low b values (<400 mm^2/s for breast tissue), the perfusion effect is evident, and ADC values higher than expected are obtained. Especially in invasive ductal carcinoma, the perfusion effect is evident at low b values due to capillary proliferation, and ADC values higher than expected are obtained (24,25).

In studies conducted using different b values in the literature, it was seen that the perfusion effect decreased and ADC values decreased proportionally as the b value increased in the same lesion (24,26). While Partridge et al. used a b value of 600 s/mm^2, b values such as 750 and 1000 were used in other studies (24,27-29). In our study, a b value of 600 was used.

Palle and Reddy showed that ADC measurements at low b values were higher than ADC measurements at high b values due to perfusion effect. The sensitivity and specificity values for benign and malignant lesions were found to be higher than other studies with a threshold value of 1.3-1.5x10^{-3} mm^2/s and 0.85-1.1x10^{-3} mm^2/s, respectively (30).

There is no established threshold value for ADC value in differentiating benign and malignant masses. Different threshold values have been found in many studies (14,24,26-29,31-33) (Table 4). Sinha et al. found the average ADC values in the first DWI for breast masses as 1.01x10^{-3} mm^2/s in malign, 1.35x10^{-3} mm^2/s in benign lesions, and 1.90x10^{-3} mm^2/s in NFT (14). Using ADC values, they were able to make the benign-malignant distinction between lesions with NFT.

Table 4. Sensitivity and specificity ratios for DWI at different b values and cut-off values in the literature and in our study

Study	Number of lesions	b value (mm^2/s)	Limit value	Sensitivity (%)	Specificity (%)
Pereira (133)	138	250	1.47	81.5	87.7
		500	1.34	91.4	91.2
		750	1.24	91.4	93.0
		1000	1.12	91.0	91.2
Kul (151)	84	1000	0.92	91.5	86.5
Partridge (148)	118	600	1.60	96.0	55.0
Tozaki (147)	124	1000	1.13	97.0	56.0
Stadlbauer (146)	36	1000	1.21	69.0	100
Our work	66	600	1.23	92.3	82.5

Imamura et al. found the mean ADC values to be 0.968x10^{-3} mm^2/s in non-mass malignant lesions and 1.238x10^{-3} mm^2/s in benign ones. At the threshold value of 1.1x10^{-3} mm^2/s, the sensitivity was 68.8% and the specificity was 72.7% (26). Imamura et al. accepted the threshold value as 1.1x10^{-3} mm^2/s in the differentiation of non-mass forming formations of malignant-benign character, while Yabuuchi et al. determined this threshold value as 1.30x10^{-3} mm^2/s (34).

Partridge found the mean ADC value at 600 mm^2/s to be 1.30x10^{-3} mm^2/s and 1.71x10^{-3} mm^2/s in malignant and benign lesions, respectively. At the threshold value of 1.60x10^{-3} mm^2/s, sensitivity was determined to be 96% and specificity was found to be 55% (27,35). In our study, the b value was used as 600, but our threshold value was accepted as 1.238x10^{-3} mm^2/s. Different threshold values can be found in studies using the same b values.

In the studies conducted different threshold values were found at different and the same b values. In their study, Pereira et al. found that as the b value increased, the average ADC ratios of benign and malign breast masses decreased compared to each other, and sensitivity and specificity ratios changed. When the b value was selected as 750 mm^2/s, they found better sensitivity (91.4%) and better specificity (93%) ratios compared to other b value combinations (0, 250, 500, 750 and 1000 mm^2/s) (143) (Table 4). When the threshold value was taken as 1.24x10^{-3} mm^2/s at b value 750, sensitivity 91.4%, specificity 93% (24), and when the threshold value was taken as 1.21x10^{-3} mm^2/s at b value 1000, sensitivity 69%, specificity 100% (28), while in another study, when the threshold value was accepted as 1.23x10^{-3} mm^2/s at b value 1000, sensitivity 97.4%, specificity 85.7% (29), and in our study, when the ADC threshold value was taken as 1.238x10^{-3} mm^2/s, sensitivity 92.3%, and specificity 82.5%. These rates we found are compatible with the literature.

Luo et al. determined ADC values as 1.98x10^{-3} mm^2/s in NFT, 1.59x10^{-3} mm^2/s in benign lesions, 0.87x10^{-3} mm^2/s malignant lesions, and they found a statistically considerable variance in ADC values in the differentiation of NFT-malign-benign lesions ($p<0.05$). At the threshold value of 1.22x10^{-3} mm^2/s, the sensitivity was 88.9% and the specificity was 87.9% (33,36).

In our study, the average ADC values of NFT were found to be statistically significantly higher than the ADC values of malignant and benign lesions (Table 2). A statistically considerable variance was found between the ADC values of malign tumours and benign tumours ($p<0.001$) (Table 3). When the ADC threshold value was set as 1.238x10^{-3} mm^2/s for the identification of benign and malign masses, sensitivity and specificity were 92.3% and 82.5%, respectively.

CONCLUSION

MRI is a common radiologic diagnostic modality for evaluation and identification of breast masses. Contrast-enhanced MRI is very successful in detecting lesions. However, the use of contrast-enhanced MRI alone leads to difficulties in differentiating benign and malignant masses. DWI provides information about morphologic and physiologic changes in tissues caused by some

changes at the cellular level. However, it is difficult to use it alone in in the differentiation of breast masses due to its low resolution. For this reason, contrast-enhanced MRI and DWI can be evaluated together in the characteristic features of breast masses. In conclusion, we believe that the use of DWI in addition to contrast-enhanced MRI can easily to separate from each other between NFT, benign and malignant masses. We recommend that DWI should be used routinely to differentiate breast lesions.

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