Can Breast MRI Findings Predict Molecular Subtypes of Breast Cancer?

Meme MRG Bulguları Meme Kanserinin Moleküler Alt Tiplerini Öngörebilir mi?

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ABSTRACT

Objective: To investigate the association between the morphologic and kinetic results obtained with the dynamic contrast-enhanced magnetic resonance imaging (MRI), and the apparent diffusion coefficient (ADC) values obtained using diffusion-weighted imaging (DWI) in breast cancer with the histopathologic subtypes of tumors.

Material and Methods: The MRI results of 271 breast lesions of 258 patients were retrospectively evaluated. Lesion morphology and contrast-enhancement characteristics were evaluated using conventional MRI, and ADC measurements were performed with DWI.

Results: An association was detected between regular margins in the masses, the presence of intratumoral necrosis, and annular contrast enhancement with triple-negative type (TN), spiculated margin luminal A type. Higher histological grade was mostly detected in TN (45.7%), and human epidermal growth factor receptor 2 positive (HER2+) tumors (47.1%) ($p<0.001$). The mean ADC value was measured as $1001x10^{-6}$ mm^2/second. No significant difference was detected in molecular subtypes considering the ADC values ($p=0.396$). No correlation was detected between the Ki-67 proliferation index and the mean ADC values ($p=0.207$).

Conclusion: Although the morphological results of dynamic contrast-enhanced breast MRI indicated particular molecular subtypes, it may be suggested that the ADC values obtained using DWI were not decisive in identifying molecular subtypes.

Key Words: Diffusion-weighted MRI, Breast cancer, ADC, Molecular subtype

ÖZ

Amaç: Meme kanserinde dinamik kontrastlı manyetik rezonans görüntüleme (MRG) ile saptanan morfolojik ve kinetik bulgularla, difüzyon ağırlıklı görüntüleme ile elde edilen apparent diffusion coefficient (ADC) değerlerinin tümör histopatolojik alt tipleri ile ilişkisini araştırmak.

Gereç ve Yöntemler: 258 kadın hastaya ait 271 meme lezyonunun MRG bulguları geriye dönük olarak değerlendirildi. Konvansiyonel MRG'de lezyon morfolojisi ve kontrastlanma özellikleri değerlendirilirken, difüzyon ağırlıklı MRG'de ADC ölçümleri yapıldı. Morfolojik, kinetik özellikler ve ortalama ADC değerleri ile tümör boyutu, histolojik grade, aksiller lenf nodu tutulumu, ki-67 indeksi ve histolojik subtipler arasındaki ilişki analiz edildi.

Bulgular: Kitlelerde düzgün kenar, tümör içi nekroz varlığı ve halkasal kontrastlanma bulgularıyla triple negatif tip; spiküle kenar luminal A tip, aksilla lenf nodu tutulumu ile human epidermal growth factor reseptör 2 pozitif (HER2+) tip arasında ilişki saptandı. Yüksek histolojik grade en fazla TN (%45,7) ve HER2 (+) (%47,1) tümörlerde saptandı ($p=0.000$). Ortalama ADC değeri $1001x10^{-6}$ mm2/sn olarak ölçüldü. Triple negatif (TN) tümörlerde ortalama ADC değeri diğer subtiplerden daha yüksekti. Ancak, ADC değeri moleküler subtipler arasında önemli farklılık göstermedi ($p=0,396$). Östrojen ve progesteron reseptörü pozitif (ER/PR+) subgrubun ADC değerleri HER2+ ve TN grupla karşılaştırıldığında iki grup aralarında anlamlı farklılık saptanmadı ($p=0,556$). Ki-67 proliferasyon indeksi ve ortalama ADC değerleri arasında korelasyon saptanmadı ($p=0,207$).

Sonuç: Dinamik kontrastlı meme MRG morfoloji bulguları özellikle bazı moleküler alt tipleri işaret ederken, DAG ile saptanan ADC değerlerinin moleküler alt tip belirlemede iddialı olmadığı söylenebilir.

Anahtar Sözcükler: Difüzyon ağırlıklı MRG, Meme kanseri, ADC, Moleküler subtip

INTRODUCTION

Breast cancer is not a uniform disease, it is a heterogeneous group of diseases. The estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER 2), and the Ki-67 proliferation index identify the molecular subtype of the tumor. In recent years, the classification of breast cancers is performed according to the gene expression profile. Accordingly, luminal A breast cancer is ER/PR positive, HER2 negative and displays low levels of the protein Ki-67 index. This molecular subtype is low-grade with a good prognosis. Luminal B breast cancer is ER/PR positive and either HER2 positive or negative with high levels of Ki-67 proliferation index. The prognosis is slightly worse than the prognosis of luminal A. Triple negative breast cancer is ER/PR negative and HER2 negative while HER2 positive breast cancer is ER/PR negative and HER2 positive. This molecular subtype grows faster than luminal subtypes with a worse prognosis.

The clinical characteristics, response to treatment, and prognosis vary in accordance with molecular subtypes in breast cancer. In addition to various indications, breast magnetic resonance imaging (MRI) has high specificity and sensitivity, which provides beneficial information in preoperative staging in patients with breast cancer. Researchers have shown that there was an association between molecular subtypes and characteristics such as tumor shape, margin characteristics, enhancement type with contrast agent, and the contrast kinetics detected in dynamic contrast-enhanced breast MRI (1-4).

Diffusion MRI is a relatively new imaging technique that provides images according to the Brownian motion of water molecules in the tissue. Quantitative evaluation is performed on the images showing the diffusion amount of water molecules in the apparent diffusion coefficient (ADC) map obtained from the diffusion weighted images by special software. A low ADC value is expected in malignant lesions due to the restriction of the movement of water molecules. Diffusion MRI provides qualitative and quantitative information about the tumor biology. ADC provides biological information such as tumor cellularity and water content. ADC may be affected by factors such as the tumor matrix and cellularity. In the evaluation of breast tumors, diffusion MRI may be beneficial in the differentiation of benign and malignant, and in the evaluation of the neoadjuvant chemotherapy (NAC) response. Some studies have demonstrated that diffusion MRI might predict the histopathological subtypes of tumors (5-8). It is important to classify breast cancer according to molecular subtypes so that suitable and specific treatment can be used. Predicting molecular subtypes from ADC values measured in ADC maps is non-invasive and needs shorter time to reach the diagnosis compared to a biopsy procedure. Therefore, the treatment can be started as soon as possible.

The aim of the present study was to investigate the association of the morphological and kinetic results detected using dynamic contrast-enhanced MRI in breast cancer, and the ADC values obtained in diffusion-weighted imaging with the various tumor histopathological subtypes.

MATERIALS and METHODS

We retrospectively evaluated the clinical, radiologic, and histopathologic results of 258 women with a diagnosis of breast cancer who underwent preoperative MRI, and were treated at our hospital between January 2013 and January 2017. Inclusion criteria for this study were: the diagnosis of invasive breast cancer at biopsy; the performance of breast MRI before or at least 3 weeks after biopsy, the absence of post-procedural artifacts; the performance of surgery within 3 weeks after MRI; and the availability of complete immunohistochemistry pattern with biomarkers (hormonal receptors status, HER-2, Ki-67 proliferation index). There was no ethnic differences between study subjects. All the patients were caucasian. The patients who were planned to undergo neoadjuvant chemotherapy and those who underwent surgery after NAC were excluded from the study. Lesion morphology and contrast enhancement characteristics were evaluated using conventional MRI, and ADC measurements were performed using diffusion-weighted MRI.

All patients underwent mammography, digital breast tomosynthesis, and ultrasonography before biopsy. After obtaining the MRI results from the digital radiology archive, 4 different radiologists with 3 years, 5 years, and 14 years of experience in breast imaging retrospectively evaluated the MRI results of the patients with breast cancer, whose MRIs were performed with the aim of preoperative staging. The radiologists were informed about the cancer diagnosis; however, they did not know the details of the histopathological evaluation. The radiologists performed the evaluation in pairs, and the decision was taken with consensus in undecided cases. Additionally, histopathological evaluation was performed by a pathologist with 10 years of experience in the radiology of the breast.

MRI was performed with the patient in the prone position using a dedicated 7-channel breast coil with 1.5 Tesla MRI (Achieva, Philips MS, Best, the Netherlands). Precontrast T1- and T2-weighted images, and diffusion-weighted images were obtained from all patients (along the x, y, z axes,TR/TE 7329/71 ms, FOV: 34, st: 3 mm). Then, high-resolution postcontrast fat-suppressed axial T1A images were taken. The dynamic fat-suppressed axial images were obtained 2, 4, 6, and 8 minutes after injecting the contrast agent (0.1-0.2 mmol/kg Dotarem®; Guerbet, Aulnay-sous-Bois, France).

All images were evaluated using a PACS (Picture Archiving and Communication System) work station. ADC maps were automatically generated in a special software package (Myrian, Imoios, Montpellier, France) in 0-600 sec/mm^2 b values. The mean ADC values were measured using a circular region of interest (ROI) that was placed on the solid part of the lesion, and on the central part of lesions demonstrating non-mass enhancement (Figure 1A-D).

In the histopathological investigation, tumor size, histologic type, histologic grade, axillary lymph node involvement, and immunohistochemical parameters were evaluated. Histological grade was evaluated between 1 and 3 according to tubule formation (score 1: Tubule formation accounts for more than 75% of the tumor, score 2: Tubule formation accounts for 10-75% of the tumor, score 3: Tubule formation accounts for less than 10% of the tumor); nucleus characteristics (score 1, 2, 3: Nucleus shape and size differs slightly, moderately, and markedly, respectively) , and mitotic activity (the number of mitoses is scored as 1, 2 and 3). The histological grade was determined according to the total score obtained (Histologic grade 1: Total score 3-5; grade 2: Total score 6-7, grade 3: Total score 8-9) (modified Bloom-Richardson system) (9).

In the immunohistochemical investigation, ER, PR, HER2 amplification, and the labeled Ki-67 index were evaluated.

Currently malignant breast tumors are divided into 4 groups as luminal A, luminal B, triple-negative (TN), and HER2-positive in accordance with the molecular characteristics. Luminal A subtype breast cancer is the most common subtype and accounts for the 50-60% of these cancers. It is ER and/or PR- positive, HER2-negative, and has a low Ki-67 index. ER- positive tumors have gene expression and cytokeratin profiles similar to the luminal cells of mammary glands with a good prognosis. A nuclear enhancement of more than 10% of the cancer cells was described as ER or PR positive. The demonstration of nuclear Ki-67 expression of less than 20% of the tumor cells was evaluated as luminal A, and the opposite was evaluated as luminal B. Luminal B subtype breast cancer accounts for 10% to 20% of all breast cancers. This subtype is ER and/or PR-positive, HER2-negative, and has a high Ki-67 index. When compared to luminal A, the luminal B subtype is more aggressive with a higher histological grade and proliferative index and a poor prognosis. Some of the ER-negative tumors are positive for human growth factor 2 receptor (CerbB2) or can be shown to amplify the human epidermal growth factor receptor-2 (Her-2) gene in tumor cells. This group is known as HER-2 positive tumors. 15% of breast cancers are in the HER-2 positive subtype. It is characterized by a poor prognosis. The most important feature of TN (similar to basal) subtype tumors is the absence of three receptors.

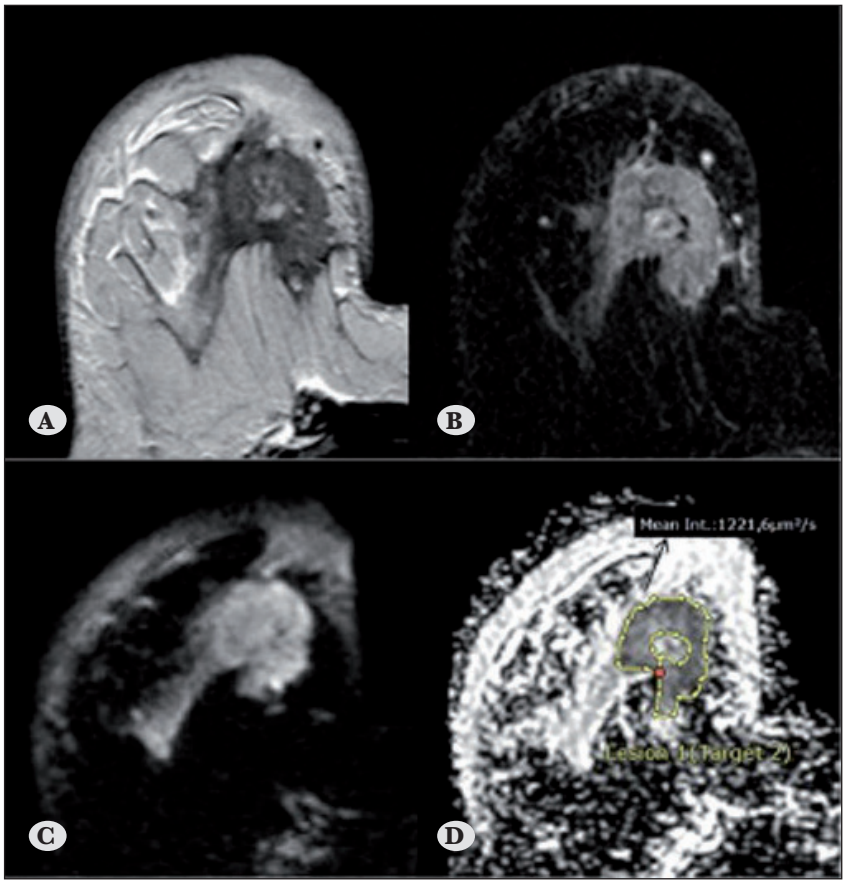

Figure 1: Axial T2W (**A**), T1a C+ (**B**), DWI (**C**) and ADCmap (**D**): ROI was measured particularly in the very vascular and solid areas of the tumor. In large lesions, the ROI was placed carefully. Areas of necrotic tissue and hemorrhagic component as identified from the morphologic and contrast-enhanced images were avoided.

They have a worse prognosis than luminal subtypes. The TN subtype has large tumor size, high histological grade, and frequent lymph node involvement. We first assessed HER2 expression immunohistochemically. Accordingly, scores of 0 and 1 were accepted as negative, and scores of 2 and 3 were accepted as positive. The HER2 gene amplification was then evaluated using the fluorescence in situ hybridization (FISH) technique and a score of 2+ (5-9).

The data were evaluated using the Statistical Package for the Social Sciences (SPSS) Ver. 17.0 program (SPSS Inc., Chicago, IL). Continuous data in descriptive statistics are given as mean±standard deviation (minimum-maximum values), and categorical data are given as frequency (percentage) values. Student's t-test was used in inter-group comparisons for parametric continuous data, and the Chi-square test was used for categorical data. The type-1 error levels were regarded as 0.05.

RESULTS

The MRI results of 271 breast lesions detected in 258 patients with breast cancer were retrospectively evaluated. The mean age of the patients was 52.5±10 years (range, 26-84 years). One hundred eighteen (46%) of the patients were in the premenopausal period, and 140 (54%) were in the postmenopausal period. Bilateral cancer was detected in 26 (9.5%) patients. The lesions were single in 187 (69%), multifocal in 39 (14%) and multicentric in 45 (17%). The mean dimension of the lesions was 26.93±16.9 mm (range, 4-100 mm).

The MRI results of lesions were as follows: there were 183 masses (67.5%), 37 of which were non-mass enhancing (NME) (13.7%), and 51 (18.8%) were masses and other findings (NME or focal focus). Ninety-six (41%) masses had irregular margins, 89 (38%) lesions were spiculated, 29 (12.4%) lesions had regular margins, and 20 (8.5%) lesions had infiltrative characteristics ($p<0.001$). Ten (15.4%) of the NME lesions demonstrated segmental distribution, 15 (23.1%) were regional, 14 (21.5%) were linear, 11 were focal (16.9%), 10 (15.4%) were multiple, and 5 (7.7%) lesions showed diffuse distribution. Heterogenous enhancement was present in 177 (75.6%) masses, 42 (17.9%) had annular enhancement, and 15 (6.4%) showed homogeneous enhancement. The MRI contrast kinetics of 40 (15.7%) lesions were type 1, 126 (49.4%) were type 2, and 89 (34.9%) were type 3 (Table I).

Sixty-two (22.9%) lesions were detected as stage Ia, 23 (8.5%) as stage Ib, 57 (21%) as stage IIa, 64 (23.6%) as stage IIb, 9 (3.3%) as stage IIIa, 22 (8.1%) as stage IIIb, and 34 (12.5%) as stage IV.

In the histopathological evaluation, 238 (87.5%) of the 271 lesions were diagnosed as invasive ductal carcinoma, 11 (4.0%) as invasive lobular carcinoma, and 21 (7.7%) were other histologic types.

The subtype distribution of 271 lesions observed on MRI showed that 100 lesions were luminal A (37%), 107 (39.6%) were luminal B, 39 (14.4%) were TN, and 24 (8.9%) were HER2+. The pathologic classification of one lesion could not be established. Of all the subtypes, the majority was

Table I: MRI morphological features of mass and non-mass lesions according to molecular subtype.

		Luminal A	Luminal B	HER2(+)	TN	P value
Mass Margin						
1	Smooth	5	7	4	13	0.000
2	Irregular	35	40	11	9	
3	Spiculated	40	37	3	9	
4	Infiltrative	3	12	3	2	
Mass- internal enhancement						
1	Homogeneous	5	6	2	1	0.000
2	Heterogeneous	68	83	12	14	
3	Rim	11	5	7	19	
Non-mass distribution						
1	Focal	5	4	1	1	0.267
2	Linear	6	4	2	2	
3	Segmental	3	5	0	2	
4	Regional	6	3	2	4	
5	Multiple	4	2	3	1	
6	Diffuse	0	5	0	0	

found in the BIRADS 5 category, one (0.9%) luminal B lesion was evaluated as BIRADS 2, one TN (2.6%) subtype lesion was evaluated as BIRADS 3; 5 luminal A (5%), 4 luminal B (3.7%) and 5 TN (12.8%) cases were evaluated as BIRADS 4; 95 luminal A (95%), 101 luminal B, 33 TN (84.6%) and 24 HER2+ (100%) were evaluated as BIRADS 5; one luminal B (0.9%) was evaluated as BIRADS 6. However, it was not statistically significant (p=0.215).

In the evaluation of subtypes in accordance with tumor staging, the highest number of lesions in luminal A was found in stage Ia (32 lesions, 32%). In luminal B, it was in stage IIa (21 lesions, 19.6%). The highest number of lesions in the TN subtype was in stage Ia (10 lesions, 25.6%). With HER2+, it was in stage IIa (7 lesions, 29.2%) (Table II) (p=0.181).

Lower tumor stages were mostly detected in luminal A and TN tumors, and higher tumor stages were detected in luminal B and HER2+ tumors.

The mean lesion dimensions in luminal A, luminal B, TN, and HER2+ subtypes were found as 23.34±13.2 mm, 28.5±17.4 mm, 26.6±19.5 mm, and 34.8±21.4 mm, respectively (p=0.013). When two groups were separated as luminal A and luminal B (good prognosis) and HER2 + and TN (poor prognosis), the mean lesion size was statistically significantly higher in the worst case group compared to the good course group (p=0.008). The mean dimension of the lesions was 24.2±15.2 mm, 29.6±18.2 mm, respectively.

Masses with regular margins were mostly detected in the TN subtype (39.4%) (p<0.001). Perilesional T2A brightness (edema), inflammatory cancer symptoms (46.2%, 18.2%) (p>0.05), and tumor necrosis were mostly detected in the TN subtype (52.8%) (p=0.009). No statistically significant association was detected between the lesion type found on MRI (mass and NME), and molecular subtype (p>0.05). No significant association was detected between the distribution of lesions demonstrating NME in MRI and the subtypes (p>0.05).

Annular contrast enhancement of the masses on dynamic contrast-enhanced MRI was mostly detected in TN tumors (55.9%), and heterogeneous contrast enhancement was detected in luminal A and B tumors (81% and 88.3%, respectively) (p<0.001).

The most commonly detected contrast kinetics type for all molecular subtypes was type 2 (p=0.038).

The rate of axillary lymph node metastasis in the group with poor prognosis was higher compared with the group with good prognosis (p=0.044). No statistically significant association was detected between distant metastasis and subtypes (p=0.346).

Multicentricity and multifocality in MRI was mostly detected in the HER2+ subgroup; multicentricity was detected in 9 (37.5%) lesions, and multifocality in 6 (25%) lesions, respectively (p=0.541). Contralateral breast involvement was mostly detected in the HER2+ subtype (12.5%) (p=0.901).

Higher histologic grade was mostly detected in TN (45.7%) and HER2+ (47.1%) tumors (p<0.001).

The apparent diffusion coefficient could be measured in 261 out of 271 lesions identified in MRI. ADC could not be measured in 10 lesions because the ROI could not be placed due to artefact, or due to the small dimensions of the lesions. The mean ADC value was 1001 x 10^{-3} mm^2/sec. The mean ADC values for luminal A, luminal B, TN, and HER2+ subtypes were 991 x 10^{-6} mm^2/sec, 988 x 10^{-6} mm^2/sec, 1055 x 10^{-6} mm^2/sec, 1017 x 10^{-6} mm^2/sec, respectively (p=0.396) (Table III) (Figure 2A-D).

The mean ADC values were 1000 x10^{-6} and 990 x10^{-6} in the classification of subtypes with good prognosis (luminal A and B) and poor prognosis (TN and HER2+), and the difference was not statistically significant (p=0.556).

The Ki-67 proliferation index in the group with poor prognosis was higher compared with the group with good prognosis (p<0.001). The mean ADC values with a low Ki-67 proliferation index were lower compared to the high Ki-67 proliferation index group (p=0.207) (Table IV).

No significant association was detected between the ADC value, histologic grade, and lymph node metastasis (p=0.473 and p=0.412, respectively).

Table II: Tumor stage distribution according to molecular subtypes.

Tumor Staging	Molecular Subtype				
	Luminal A	Luminal B	HER2(+)	TN	Totally
Stage I	40 (40%%)	24 (23.4%)	5 (20.8%)	16 (41%)	85 (31.5%)
Stage II	41 (41%)	54 (53.4%)	13 (54.2%)	13 (35.3%)	121 (44.8%)
Stage III	10 (10%)	16 (14.9%)	4 (10.2%)	4 (10.2%)	31 (11.4%)
Stage IV	9 (9%)	13 (12.1%)	6 (15.4%)	6 (15.4%)	33 (12.2%)

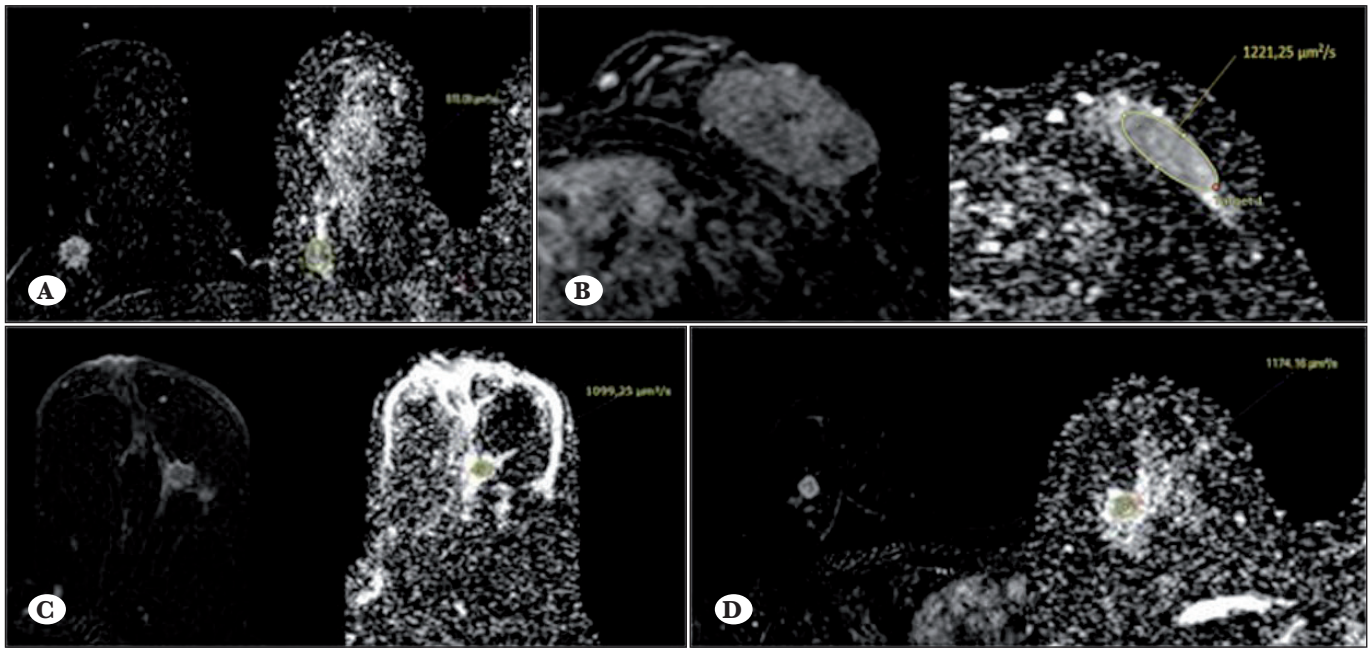

Figure 2A-D: These are some examples of our cases: in this patient diagnosed with Invasive Ductal Cancer-Luminal A (**A**), 1.12 sec/mm² in this patient with Luminal B (**B**); ADC was calculated as 1.09 sec/mm² in the patient with subtype of HER2 positive (**C**). the mean ADC value was 0.97 sec/mm²; 1.17 sec/mm² in this patient who was Triple Negative (**D**).

Table III: Mean ADC values according to molecular subtypes.

	Molecular Subtype					
	Luminal A (n=95)	**Luminal B (n=106)**	**HER2 (+) (n=23)**	**Triple (-) (n=37)**	**F**	**p**
ADC*(Mean)	0.99±0.21	0.98±0.23	1.02±0.16	1.05±0.23	0.995	0.396
	Good prognosis (Luminal A, Luminal B)		Poor prognosis (HER2 (+), Triple (-))		t	p
	1.0±0.21		0.99±0.21		0.589	0.556

***:** Apparent Diffusion Coefficient (x 10 -3 mm²/s), **F:** The Anova test value, **t:** Student t-test value, **p=** Statistical significance

Table IV: Mean ADC values according to the Ki-67 proliferation index.

	Low Ki67	**High Ki67**	**t**	**p**
ADC(Mean)	Mean ±SS	Mean ±SS	1.265	0.207
	0.98±0.21	1.02±0.21		

DISCUSSION

In the present study, we investigated the association of tumor morphology and kinetic evaluation results detected on dynamic contrast-enhanced breast MRI, and mean ADC values found using the diffusion-weighted imaging in patients with breast cancer, with tumor histopathologic subtypes.

Researchers in previous studies have reported that smooth border characteristics, larger dimension of lesion, intratumoral necrosis, annular contrast enhancement, and high grade were associated with TN subtype (5,9). In compliance with the literature, in the present study we found that regular margin characteristics, annular contrast enhancement, and presence of intratumoral necrosis were statistically significantly associated with the TN subtype.

The association of spiculated border characteristics with low grade, low Ki-67 index (<20%), and association of annular contrast enhancement with high histologic grade and ER/PR negative subtype were reported in the literature (10,11). Similarly, we demonstrated that spiculated border characteristics were associated with ER/PR positive cancers, particularly with luminal A subtype. Spiculated border characteristics seem to be a good indicator for differentiating the two groups.

Tumor size is a significant factor for indicating prognosis, and is associated with the chance of longer survival in breast cancer. Researchers in recent publications reported the association of larger tumor size and ER-negative cancers (8,10). A higher mean lesion size was detected in the HER2+ subtype in the present study, and was found statistically significantly higher in the ER- negative group, compatible with the literature.

Researchers reported that HER2+ tumors were more malignant than HER2- tumors (12). Although statistically insignificant in that study, irregular margin characteristics, multicentricity, multifocality, and contralateral breast involvement were observed more frequently in the HER2+ subtype. It may be suggested that HER2+ tumors are more aggressive.

The presence of lymph node metastasis is one of the significant prognostic factors of breast cancers. The presence of metastasis increased the mortality rate 4 to 8 times (13). Although some studies have reported that the ratio of lymph node positivity was associated with TN tumors, others reported no significant difference between the subtypes (5,14,15). Lymph node metastasis was mostly observed in the HER2+ subtype, and no statistically significant difference was detected between the subtypes (p=0.044). No significant association was detected between ADC values and lymph node metastasis.

Some studies in the literature have evaluated the association of breast MRI findings and breast cancer molecular subtypes (1-4). Some recent studies reported that ADC measurements were beneficial in the identification of breast tumor subgroups; however, other researchers detected no association between hormone receptors and mean ADC values (16-20-22). In addition, the mean ADC value of the TN subtype was reported to be higher compared with the other subtypes (5). Although we detected the highest mean ADC value in the TN subtype in the present study, no significant association was detected between ER-positive and ER-negative tumors regarding the ADC value.

Apparent diffusion coefficient values are affected by both diffusion and perfusion. However, the effect of perfusion decreased in higher b values, and the effect of diffusion became more dominant (21). Various imaging parameters such as magnetic sensitivity, spatial resolution, and signal-noise ratio, and also the methods used in measurement of ADC affect the ADC value. The detection of different results for ADC values in the literature may be due to these reasons.

A direct association between tumor cellularity and histologic grade has not yet been proven. Although some researchers reported an association between tumor cellularity and ADC, other authors have detected no association between the histologic grade of breast cancer and ADC (6,16,23,24). We also detected no association between the histologic grade and ADC.

The Ki-67 proliferation index is a well-identified indicator in cancer cells. Some researchers in a small number of studies investigating the association of Ki-67 proliferation index and mean ADC values emphasized the negative correlation between these two parameters but other researchers reported no correlation (21,25-28). We detected no correlation between the Ki-67 index and mean ADC values. Higher Ki-67 proliferation shows higher cell proliferation, and lower ADC values show higher cellular density. Accordingly, a negative correlation between this pair seems to be an expected outcome; however, this might not always be the case. Cellular density may be affected by various factors such as necrosis and structural heterogeneity. In addition, ADC values may be affected by the perfusion parameters of the tumor.

The most important limitations of this study are that it was a single-center retrospective study, and the evaluators were informed about the diagnosis of cancer. Biopsies were performed before MRI in some patients, and changes due to biopsy might have affected the ADC values. A significant advantage of this study was that the number of patients was adequate, and therefore, the distribution and number of molecular subtypes was adequate.

The joint evaluation of DWI findings with morphologic characteristics may provide more information about the role of magnetic resonance imaging.

Conclusion

In conclusion, although dynamic contrast-enhanced breast MRI morphology findings show some molecular subtypes in particular, the ADC values detected in DWI may not be suggested to be decisive in the identification of molecular subtypes.

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Statement of Ethics:

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Concept, Design, Writing the manuscript, Research, Literature search-Y.D.P.; Materials, Data collection and/or Processing-V. S.Ö, Materials, Data collection and/or Processing -R.Ö, Analysis and/or interpretation-İ.E., F.A; Critical review, supervision-F.T.

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