

The Comparison of Diffusion Weighted Imaging (DWI) with Other Breast MRI Parameters in the diagnosis of Breast Masses

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ABSTRACT

The breast MRI parameters such as morphologic features, enhancement kinetics and diffusion restriction can be used for the differential diagnosis. We aimed to compare the Apperant Diffusion Coefficient (ADC) values of masses with other MRI parameters in diagnosis of breast masses.

Between March 2014 and September 2017, 49 female patients in whom a breast mass was diagnosed, determined using ultrasound and mammography and who were further examined with MRI, were enrolled to this study. Total 51 lesions were detected. Routine breast MRI protocol was performed and images were evaluated. The ADC cut-off value was taken as $1,1 \times 10^{-3} \text{mm}^2 / \text{s}$ according to the literature.

Fifty-one lesions were diagnosed with biopsy. Of these lesions, 23 (45.1%) were malignant (20 invasive ductal carcinoma and others) and 28 (54.9%) were benign (20 fibroadenomas and others). The accuracy rate of DCE assessment of MRI was 90,9% for benign lesions in with a type 1 curved lesions, and 81,8% for malign lesions in with a type 3 curved lesions. The accuracy rate of ADC values was 93,1% for benign lesions and 95,5% for malign lesions.

We believe that the ADC value can provide a higher diagnostic accuracy with the combination of morphological characteristics and contrast kinetics of the lesion and that ADC can be used alone because of its high diagnostic accuracy in some cases.

Key Words: ADC, Breast MRI, Breast masses

Introduction

The magnetic resonance imaging (MRI) is a supplementary diagnostic method of the breast lesion. The breast MRI parameters such as morphologic features, enhancement kinetics and diffusion restriction can be used for the differential diagnosis. The diagnostic superiority of Dynamic Contrast Enhancement (DCE) and Diffusion Weighted Imaging (DWI) are assessed separately in the studies (1,2,3,4). Among these parameters, DCE is the most sensitive MRI technique for the detection of breast cancer in general (5,6). In the characterization of breast masses, the contour characters of the lesion and the qualitative values of contrast enhancement (within 2 minutes after contrast administration) are important criteria (3,4). The increased cell density in tumors leads to diffusion restriction of intercellular water motion and is pointed as malignancy (1,2). The apparent diffusion coefficient (ADC) on DWI is quantitative value of diffusion restriction within the lesion. Our goal was to compare the ADC values of

breast masses with other MRI parameters in the diagnosis of breast masses.

Materials and Methods

Patients: Our institutional ethics committee confirmed this retrospective study and waived the informed consent requirement. Between March 2014 and September 2017, 49 female patients (aged 18-81, mean 43.4) in whom a breast mass was diagnosed, determined using ultrasound and mammography and who were further examined with MRI, were enrolled to this study. The inclusion criteria were as follows: had ≥ 1 cm solid lesion which was clearly defined on the ADC map. The exclusion criteria were as follows: had cystic lesion and < 1 cm diameter of the lesion or indistinguishable on ADC map. Total of 51 breast masses were pathologically sampled and reported. The solid lesions were examined with three diagnostic MRI criteria. The morphological properties, enhancement kinetics and ADC values of the solid lesions were compared with pathological results of them retrospectively.

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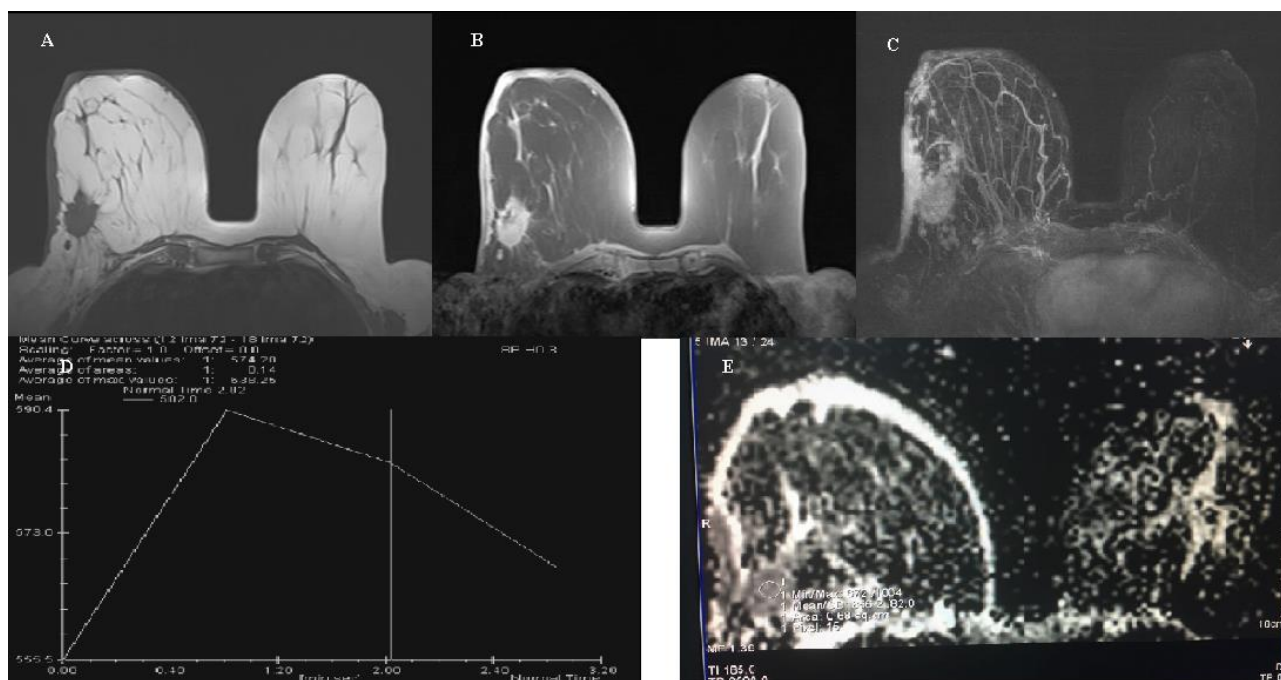


Fig. 1. An outer quadrant located lesion in T1 Weighted images (A), T2 Weighted images (B), a subtracted image with dynamic contrast (C). Time curve of contrast enhancement (D). A diffusion restriction image at ADC (E) due to hypointensity correlation with histopathology with at quantitative evaluation ADC with $0,86 \times 10^{-3} \text{mm}^2/\text{s}$. Histopathology: Invasive ductal carcinoma

MRI Examinations and Image Analysis: The MRI examinations were performed with 1.5 Tesla MR apparatus (Magnetom Avanto Siemens, Erlangen, Germany) and breast coil. Routine breast MRI protocol was performed during breast MRI examination protocol and 0.1 mmol / kg gadolinium was used as contrast agent. In DWI, b values were taken as 0, 200, 400, 600, 800 and 1000 s / mm². MR images were separately evaluated at the workstation by two radiologists. We used Breast Imaging Reporting and Data System (BI-RADS) for lesions at morphological assesment. The American College of Radiology (ACR) developed the BI-RADS system for common language at classify the lesions in imaging systems. It is widely accepted as a risk assessment and quality assurance tool in breast lesions. This classification consists of seven classes (7).

BI-RADS 0: Incomplete. It is used for inadequate or incomplete evaluation. Requires additional examination.

BI-RADS I: Normal. Totally normal and symmetric. There is no mass, structural abnormality or calcification.

BI-RADS II: Benign findings. Lesions that are certain to be benign. They have characteristic appearances.

BI-RADS III: These all probaply benign lesions. Recommended to follow-up at frequent intervals.

BI-RADS IV: It raises suspicion in terms of malignancy. Biopsy should be considered. It have three subgroups.

BI-RADS IVa: Low doubt for malignancy

BI-RADS IVb: Intermediate doubt for malignancy

BI-RADS IVc: Moderate doubt for malignancy

BI-RADS V: There is a view suggesting highly malignancy. An additional procedure should be considered.

BI-RADS VI: They are pathologically diagnosed as malignancy.

In the evaluation of the lesion, the algorithm is as follows: Firstly, lesion or lesion were detected on the dynamic 3D T1 - weighted subtracted images. Secondly, the morphological features of lesion were examined in T1 and T2 weighted sequences together with contrasted series. Third, the enhancement kinetic was examined in the dynamic series. Lastly, in the ADC map, the quantitative evaluation of the diffusion limitation was adjusted with a round region of interest (ROI) according to the size of the mass. In order to calculate the value in ROI more easily and accurately in the ADC map, those larger than 1 cm were included in the study. Necrotic areas were not measured. ROI was measured at 5 different points and the average of the 3 closest RIO's were taken (3). For comparison, ADC measurements in normal fibroglandular tissues in the contralateral breasts of all patients were performed at the same level as the localization of the lesion. The ADC cut-off value was taken as $1.1 \times 10^{-3} \text{mm}^2/\text{s}$ according to the literature (8). An example MRI apperance of the invasive ductal carcinoma (Figure 1).

Table 1. Morphological features of breast lesions evaluated according to BIRADS

| MR BIRADS | Total lesions | Pathological result | Ratio (%) | |
|-----------|---------------|---------------------|-----------|------|
| BI-RADS 3 | 25 | Benign | 22 | 88 |
| | | Malign | 3 | 12 |
| BI-RADS 4 | 8 | Benign | 3 | 37,5 |
| | | Malign | 5 | 62,5 |
| BI-RADS 5 | 18 | Benign | 3 | 16,7 |
| | | Malign | 15 | 83,3 |

Table 2. Contrast-enhanced MRI was performed in 51 lesions and the dynamics of these 51 lesions are given in table 2

| Contrast Curve | Total lesions | Pathological result | Ratio (%) | |
|----------------|---------------|---------------------|-----------|------|
| Type 1 | 22 | Benign | 20 | 90,9 |
| | | Malign | 2 | 9,1 |
| Type 2 | 7 | Benign | 4 | 57,1 |
| | | Malign | 3 | 42,9 |
| Type 3 | 22 | Benign | 4 | 18,2 |
| | | Malign | 18 | 81,8 |

Results

The fifty one lesions detected on MRI were all pathologically diagnosed. Twenty three (45,1%) of these lesions were malignant (20 invasive ductal carcinomas, 2 invasive lobular carcinomas, 1 apocrine carcinoma) and 28 (54,9%) were benign (20 fibroadenoma, 3 inflammatory changes, 3 fibrocystic changes and 2 adenoses).

On MRI, morphologically features of breast lesions evaluated according to BIRADS. The results are given in table 1. On morphological MRI evaluation; despite being evaluated as BI-RADS 5, 3 out of 18 patients had benign pathology results. Additionally, despite being evaluated as BI-RADS 3, 3 out of 25 patients had malign pathology results. The accuracy rate of morphological assessment of MRI was 88% for benign masses in BI-RADS 3 lesions and 83,3% for malign masses in BI-RADS 5 lesions. BI-RADS 4 lesions are masses that are difficult to diagnose as a benign-malignant lesion, as determined statistically.

Contrast-enhanced MRI was performed in 51 lesions and the dynamics of these 51 lesions are given in table 2. MRI evaluation according to curve types; despite being evaluated as type 3, benign pathology was the result in 4 of 22 patients. There were also malignant pathology results in 2 of 22 patients, although they were evaluated as type 1. The accuracy rate of DCE assessment of MRI was 90,9% for benign lesions in with a type 1 curved lesions., and 81,8% for malign lesions in with a type 3 curved lesions. Type 2 curved

lesions are lesions that are difficult to diagnose as a benign-malignant lesion, as determined statistically.

ADC values of these 51 lesions are given in table 3. The cutt off value of ADC was taken as $1,1 \times 10^{-3} \text{mm}^2/\text{s}$. The ADC values of 51 lesions demonstrated a good correlation with the histopathology. 2 out of 29 lesions above the ADC value of $1,1 \times 10^{-3} \text{mm}^2/\text{s}$ which evaluated as benign were pathologically malignant. In addition, 1 of the 22 lesions below the ADC value of $1,1 \times 10^{-3} \text{mm}^2/\text{s}$ which evaluated as malign were pathologically benign. ADC values of 51 patients in Diffusion MRI: The average ADC value of 23 malignant lesions were $0,85 \pm 0,07$ (mean \pm 2SE) $\times 10^{-3} \text{mm}^2/\text{s}$ (the minimum ADC value was $0,26 \times 10^{-3} \text{mm}^2/\text{s}$ and the maximum ADC value was $1,2 \times 10^{-3} \text{mm}^2/\text{s}$). The average ADC value of the 28 benign lesions were $1,22 \pm 0,16$ (mean \pm 2SE) $\times 10^{-3} \text{mm}^2/\text{s}$ (the minimum ADC value was $0,87 \times 10^{-3} \text{mm}^2/\text{s}$ and the maximum ADC value was $1,8 \times 10^{-3} \text{mm}^2/\text{s}$). In the differentiation of malignant and benign masses, the cutt-off value of ADC was found to be $1,1 \times 10^{-3} \text{mm}^2/\text{s}$. The accuracy rate of ADC values was 93,1% for benign lesions and 95,5% for malign lesions.

In our study, ADC values of the lesions showed almost good correlation with pathology. In one patient, the lesion contour showed irregularity supporting the malignancy. However, ADC value was calculated as $1,2 \times 10^{-3} \text{mm}^2/\text{s}$ and was in benign group. Its pathology result was IDC.

Table 3. ADC values of these 51 lesions are given in table 3

| ADC Value | Total lesions | Pathological result | | Ratio (%) |
|--|---------------|---------------------|----|-----------|
| Above $1,1 \times 10^{-3} \text{ mm}^2 / \text{ s}$ | 29 | Benign | 27 | 93,1 |
| | | Malign | 2 | 6,9 |
| Below and equal to $1,1 \times 10^{-3} \text{ mm}^2 / \text{ s}$ | 22 | Benign | 1 | 4,5 |
| | | Malign | 21 | 95,5 |

Discussion

Although the sensitivity of breast MRI is high, its specificity is low. The parameters of MRI for evaluating lesion are the contrast enhancement, the morphological property of the lesion and the ADC value. However, there are some limitations for each of three parameters.

In literature for morphological evaluation, the macrolobular shape was accepted as benign by *Guo et al.*(9). However, *M. Tozaki et al.* (10) reported that macrolobular shape was insufficient to discriminate benign from malignant lesions and the enhancement kinetics should be evaluated in such cases. The lesion should be considered in favor of malignant if type 3 time – intensity curve was present. In our study, we accepted macrolubular shape as benign, among malignant lesions two patient had round shape and smooth contour (invasive ductal carcinoma) but its ADC value ($0,87 \times 10^{-3} \text{ mm}^2 / \text{ s}$ and $0,80 \times 10^{-3} \text{ mm}^2 / \text{ s}$) was correlated with the histopathology. In contrast, the contours of two benign lesions were irregular and looked like malignant. However, ADC values were in the benign group ($1,0 \times 10^{-3} \text{ mm}^2 / \text{ s}$ and $1,8 \times 10^{-3} \text{ mm}^2 / \text{ s}$), correlated with the histopathologic results and enhancement kinetics were type 1 and type 3, respectively.

It was reported that the enhancement kinetics in some malignant breast lesions had slow initial enhancement and persistent time-intensity curve, especially in small cell breast cancer with predominantly fibrosis, papiller carcinoma, medullar carcinoma and some intraductal papilloma, metastasis and lymphoma (10). In contrast, some benign breast lesions with hyperplastic parenchymal cells and proliferative activity could mimic the enhancement kinetics of malignant lesions (11). Rapid and intense contrast enhancement at the early period of time – intensity curve could be seen in fat necrosis (especially during the early phase), proliferative dysplasia, scar tissue after an operation (at first 6 months), some myxoid fibroadenoma and after radiotherapy (at first 18 months) (12). In our study, 3 malignant and four benign lesions had type 2 contrast enhancement which could be seen in both malignant and benign lesion. In type 3 time-intensity curve, histopathology

of four lesions was benign lesions (3 granulomatous mastitis, 1 fibroadenoma) and other 18 lesions were reported as malignant. Tree of these lesions had irregular margin and only one had regular margin. ADC value was correlated with the histopathology ($1,1 \times 10^{-3} \text{ mm}^2 / \text{ s}$ – $1,2 \times 10^{-3} \text{ mm}^2 / \text{ s}$). Two lesions of 22 lesions with type 1 time – intensity curve were malignant lesions. Lesion contours could not be distinguished as malignant or benign in case of poor temporal and spatial resolution of breast MRI. Contrast kinetics and morphological features can be evaluated together to improve the specificity of breast MRI for differentiating malignant and benign lesions (10).

The technique based on contrasted examinations was directly related to the vascularity of the lesions. There was no direct relationship between tumor cellularity and contrast retention dynamics (13). The ADC was the only method providing the tumor cellularity and numerical data. It provides important information about the structural composition, physical properties of tissues and their interaction (13). In Figure 1, there is a pathologically diagnosed case of invasive ductal carcinoma. In most studies, ADC values of malignant tumors were significantly lower than benign tumors (1, 3, 15). However, Reiko W. et al. (11) reported that ADC was still insufficient in the qualitative evaluation of the lesion; ADC values are indicated as unreliable, especially in fibrocystic diseases, ductal ectasia, intraductal papilloma and some types of fibroadenoma (11). It also reports that it is possible to obtain high ADC values in mucinous carcinoma, DCIS and malignant phyllodes tumors (11). They also suggested that as a cause of this abnormality, there could be unclear small necrotic foci or conditions that cause susceptibility studies such as bleeding. In our study, we observed that there was not a correlation between ADC value and histopathological findings only in one patient, and we considered that it might be caused by an undetectable necrotic focus.□

The value of ADC in mucinous carcinoma is generally accepted to be high like benign lesion, however, Woodhams et al. (16) reported that mucinous carcinoma could be clearly differentiated from other breast tumors by ADC. In our study we had no mucinous carcinoma case, therefore we cannot comment on the subject.

The limitations of this study are the lack of case numbers and retrospective work.

In conclusion; We believe that the combination of ADC value, the morphological and contrast kinetics features of the lesion can provide a higher diagnostic accuracy for breast MRI and ADC value can be used in the MRI BIRADS criteria. In some patients whose chronic renal failure, pregnancy or have contrast allergy, ADC and morphological evaluation of MRI can provide high accuracy in the diagnosis of lesions.

References

1. Palle L, Reddy B. Role of diffusion MRI in characterizing benign and malignant breast lesions. *Indian J Radiol Imaging* 2009; 19(4): 287-290.
2. Pereira FP, Martins G, Carvalhaes de Oliveira Rde V. Diffusion magnetic resonance imaging of the breast. *Magn Reson Imaging Clin N Am* 2011; 19(1): 95-111.
3. Sonmez G, Cuce F, Mutlu H, Incedayi M, Ozturk E, Sildiroglu O, Velioglu M, Bashekim CC, Kizilkaya E. Value of diffusion-weighted MRI in the differentiation of benign and malign breast lesions. *Wien Klin Wochenschr* 2011; 123: 655-661.
4. Baltzer P.A, Bickel H, Spick, C, et al. Potential of Noncontrast Magnetic Resonance Imaging With Diffusion-Weighted Imaging in Characterization of Breast Lesions: Intraindividual Comparison With Dynamic Contrast-Enhanced Magnetic Resonance Imaging. *Investigative radiology* 2018; 53: 229-235
5. Warner E, Messersmith H, Causer P, et al. Systematic review: using magnetic resonance imaging to screen women at high risk for breast cancer. *Ann Intern Med* 2008; 148: 671-679.
6. Mann R.M, Mus RD, van Zelst J, Geppert C, Karssemeijer N, Platel B.A. novel approach to contrast-enhanced breast magnetic resonance imaging for screening: high-resolution ultrafast dynamic imaging. *Investigative radiology* 2014; 49: 579-585.
7. ACR BI-RADS Atlas. American College of Radiology. 2013; 125-143, ISBN:155903016X
8. Bansal, R, Shah, V. & Aggarwal, B. Qualitative and quantitative diffusion-weighted imaging of the breast at 3T-A useful adjunct to contrast-enhanced MRI in characterization of breast lesions. *The Indian journal of radiology & imaging* 2015; 25: 397-403.
9. Guo Y, Cai YQ, Cai Z. et al. H. Differentiation of clinically benign and malignant breast lesions using diffusion-weighted imaging. *Journal of magnetic resonance imaging* 2002; 16: 172-178.
10. Mitsuhiro T. Interpretation of breast MRI: Correlation of kinetic and morphological parameters with pathological findings. *Magnetic Resonance in Medical Sciences* 2004; 3: 189-1979.
11. Reiko W, Keiji M, Keiichi I, et al. ADC mapping of benign and malignant breast tumors. *H. J Comput Assist Tomogr* 2005; 29: 644-649.
12. Heywang SH, Wolf A, Pruss E, Hilbertz T, Eiermann W, Permanetter W. MR imaging of the breast with Gd-DTPA: use and limitations. *Radiology* 1989; 171: 95-103.
13. Matsubayashi R.N, Fujii T, Yasumori K, Muranaka T, Momosaki S. Apparent diffusion coefficient in invasive ductal breast carcinoma: correlation with detailed histologic features and the enhancement ratio on dynamic contrast-enhanced MR images. *Journal of oncology* 2010.
14. Basser PJ. Diffusion and diffusion tensor imaging. In: Atlas SW, editor. *Magnetic resonance imaging of brain and spine*. 3rd ed. Philadelphia: Lippincot Williams and Wilkins; 2002; 197-212.
15. Yabuuchi H, Matsuo Y, Okafuji T, et al. Enhanced mass on contrast-enhanced breast MR imaging: Lesion characterization using combination of dynamic contrast-enhanced and diffusion-weighted MR images. *J Magn Reson Imaging* 2008; 28: 1157-1165.
16. Woodhams R, Kakita S, Hata H, Iwabuchi K, Umeoka S, Mountford CE, Hatabu H. Diffusion-weighted imaging of mucinous carcinoma of the breast: evaluation of apparent diffusion coefficient and signal intensity in correlation with histologic findings. *AJR Am J Roentgenol* 2009; 193: 260-266.