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Evaluation of the diagnostic value of DWI with multiple synthetic b-values of breast lesions compared to dynamic contrast-enhanced breast MRI

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Abstract---Background: Several studies have demonstrated that the sensitivity of unenhanced MRI with DWI was equal or superior to mammography; however, there is still room for improvement. Diffusion sensitivity, better known as “b- value,” has important implications for tumor conspicuity and can be controlled by modifying the magnitude and duration of the diffusion gradients. **Aim:** The aim of our study was to assess lesion visibility and the diagnostic

performance of DWI for breast cancer detection by the addition of different synthetic b-values. **Patients and Methods:** this prospective study is IRB approved. Patients presented for both screening and diagnostic purpose were included. All patients underwent breast MRI with DWI with addition of different synthetic b-values. Three readers evaluated DWI with acquired synthetic b-800, b-1000, b-1200, b-1500, and b-1800 s/mm² images. The readers determined the preferred b-value based on lesion visibility and conspicuity. **Results:** One hundred and fourteen patients met our study criteria. One hundred twenty-five breast lesions in 114 women were detected. The mean age of our population is (39.6 ± 5.9 years old) ranged from 30 to 50 years old.. Lesion size ranged from 5 to 100 mm with mean size of (25.9 ± 16.9 mm). The percentage of enhancing lesions identified on DWI was 75.2% for reader 1 (r1), 76.8% for reader 2 (r2), and 70.4% for reader 3 (r3). DWI visualized 86–90% of the malignant enhancing lesions. there was a consensus agreement between all readers that, synthetic b-values 1500–1800 s/mm² was preferred for lesion conspicuity, especially in moderate and marked background enhancement. b- 800 and synthetic b-1000/b-1200 s/mm² values allowed the visualization of 57–70% of benign lesions, while b-1500/b-1800 s/mm² allowed the visualization of 82–85% of benign lesions. DWI was more specific (84.8 % vs 67.4%, $p < 0.001$) but less sensitive (62% vs 89.9%, $p < 0.001$) and accurate (73.4% vs 78.7%, $p = 0.010$) than DCE-MRI for breast cancer detection, where mpMRI was the most accurate modality accounting for less false positive cases. **Conclusion:** Addition of synthetic high b-values (e.g., 1200 s/mm²) improves tumor conspicuity without increasing the time of scan, which is particularly helpful in moderate and marked background enhancement. Nevertheless, the role of DWI for the visualization of NME and small lesions and its performance in breast cancer detection are still not definite.

Keywords---*DWI, Synthetic b-values, Breast Cancer.*

Introduction

Breast MRI techniques are progressively including diffusion-weighted imaging (DWI). DWI with apparent diffusion coefficient (ADC) mapping has been shown to identify breast lesions with up to 96% sensitivity and 100% specificity (1).

The diagnosis of breast lesions on MRI depends on the presence of suspicious enhancement after gadolinium contrast injection, which identifies regions of aberrant vascularity, a typical feature of breast cancers. Several of the most recent high-risk screening studies showed that breast MRI specificity and positive predictive value may surpass those of traditional breast imaging modalities, such as mammography and ultrasound, despite the fact that MRI was previously linked to relatively high false-positive rates (2).

Breast cancer is a diverse set of illnesses with a biological composition that influences therapy and clinical outcome; its death rate is 2.5% annually. As a result, it is now evident that a disease exhibiting notable intratumoral and inter-tumoral variations cannot be adequately classified using the conventional reliance on appearance alone (3).

To avoid needless breast biopsies, the main goal of DWI is to distinguish between benign and malignant tumors. (4,5).

A few studies have shown that the sensitivity of unenhanced MRI with DWI was better than mammography. By altering the strength and length of the diffusion gradients, one may regulate diffusion sensitivity, sometimes referred to as "b-value," which has significant effects on tumor conspicuousness. Higher b-values seem to reduce the T2 shine-through effect and inhibit normal breast tissue, improving lesion conspicuity (6). However, because of their poor signal-to-noise ratio, they need lengthy investigation durations and may result in reduced picture quality (7).

These restrictions could be circumvented using synthetic b-values. synthetic b-values are produced voxel wise from at least two distinct lower b-values using a mathematical computation technique without lengthening the scan time or lowering image quality (in fact, synthetic b-values present a higher image quality than the acquired b-values) (7,8) The purpose of this research was to evaluate DWI's diagnostic ability for characterizing breast lesions by adding multiple b-values.

Patients and Methods

This prospective study is Institutional Review Board "IRB" approved. all patients presented for screening or diagnostic purposes with BI-RADS categories 2, 3, 4 or 5 (according to Breast Imaging Reporting and Data System) (9) were included in this study. patients on chemotherapy, and patients with biopsy- proven malignancy (BI-RADS 6), were excluded from the study.

MR imaging:

MRI of the breasts were performed on high field 1.5 Tesla MR Scanner (Philips Medical Systems, Achieva), using dedicated breast coils. IV contrast was utilized (0.1 mmol of gadolinium-DTPA/kg) and there were no complications. The following pulse sequences were acquired:

- Axial T1, STIR WIs, DWIs & ADC map.
- Pre-contrast axial 3D T1 WI
- Post Gd-DTPA Dynamic axial 3D T1 WI
- Post Gd-DTPA one sagittal 3D T1 WI
- Post processing subtraction and MIP were reconstructed.
- Kinetic time-intensity curves when needed.
- The study was reviewed on high resolution monitors.

Reader study:

Three dedicated breast radiologists with 2- 10 years of experience in interpretation of breast MRI evaluated the images independently. Each reader reviewed the DWI with multiple synthetic b-values (b- 800, b-1000, b-1200, b-

1500, and b-1800 s/mm²) and ADC maps blinded to the DCEMRI. These items were evaluated

☐ Visibility of the lesion using each b-value (yes/no).

1. location, and laterality.

☐ If more than one lesion were visible, all lesions were assessed.

☐ A visual grading image quality score using Likert score (1 = bad quality, 2 = average, 3 = good quality) was assigned by each reader for all the b-values based on artifacts and fat suppression.

☐ In addition, a preferred b-value was selected by each reader based on lesion conspicuity defined as the visual difference in lesion contrast with the surrounding parenchyma.

☐ One 2D region of interest (ROI) per lesion and reader were drawn manually on ADC maps derived from acquired b-values using the ROI that was placed in a slice containing the tumor maximum diameter and within the area with the lowest ADC values.

☐ Each lesion was assigned a final BI-RADS category according to the ACR BI-RADS lexicon 2013, using acquired and preferred synthetic b-values for each visible lesion. BIRADS 4 and 5 were considered suspicious for malignancy, whereas scores 1, 2, and 3 were considered non-suspicious.

☐ The criteria for this score included qualitative parameters based upon the previous literature as well as quantitative ADC values extracted from ADC maps as shown in Table1.

Table 1: Criteria for DWI malignancy score (10)

Descriptor	DWI + ADC map	
	Suspicious	Not suspicious
Internal signal	Heterogeneous	Homogeneous
Shape	Irregular/angulated	Round/oval
ADC	$\leq 1.3 \times 10^{-3} \text{ mm}^2/\text{s}$	$> 1.3 \times 10^{-3} \text{ mm}^2/\text{s}$

After a wash-out period of at least 14 days, DCE-MRI alone was evaluated by each reader. Readers classified lesions according to ACR BI-RADS lexicon, 2013. Lesions categorized as BI-RADS 2 or 3 were considered non- suspicious, whereas categories BIRADS 4 or 5 was considered suspicious for malignancy. Consequently, the results for both readings will be reviewed for missed lesions on DWI or a lesion characterization mismatch between DCE-MRI and DWI. A consensus was considered obtained when two of the three readers agreed on a same division. Readers were aware of the presence of lesions in all the examinations but were blinded to the biopsy results and prior imaging.

Histopathology

The final diagnosis was established by histopathology using image- guided true cut needle biopsy. In the event of discordant findings between histopathology and imaging, the final diagnosis was established surgically.

Statistical analysis

We used SPSS Statistics for Windows, Version 25.0, a statistical tool for the social sciences, to edit, code, tabulate, and import the data we gathered onto a personal computer. For each parameter, data was displayed and analyzed appropriately

based on the kind of data gathered. To determine if there is a statistically significant difference between the means of two groups, the Student T Test was used. One way to look at the connection between two qualitative variables is via the chi-square test. When comparing AB-MRI with FD-MRI ratings of categorical data, one statistical tool to use is Cohen's Kappa Score, also called the Kappa Coefficient. The following is Cohen's proposed interpretation of the Kappa result: Values: ≤ 0 denotes absence of agreement and ≤ 0.01 -0.20 denotes negligible to mild. The following ranges are considered fair: 0.21–0.40, moderate: 0.41–0.60, substantial: 0.61–0.80, and almost perfect agreement: 0.81–1.00. To determine the Fast MRI's validity in detecting breast lesions, the diagnostic performance was evaluated by generating 2×2 contingency tables with breast lesions analysis serving as the reference or gold standard. A number of statistical measures were determined, including sensitivity, specificity, accuracy, PPVs, NPVs, and 95% confidence intervals for each. Be aware that a p-value less than 0.05 with a 95% confidence interval is considered significant.

Results

one hundred twenty-five breast lesions in 114 women met our study criteria. The mean age of our population is (39.6 ± 5.9 years old) ranged from 30 to 50 years old. We found 125 lesions in 114 women. Most of lesions 83.2% of lesions were unilateral and 16.8% were bilateral. Lesion size ranged from 5 to 100 mm with mean size of (25.9 ± 16.9 mm) as in table 2. Table 3 showed that IDC made up the majority of the malignancy (32.8%), followed by DCIS (17.6%) and lastly ILC (12.8%). the most common benign pathology is fibroadenoma composing 20% of all benign pathology. In table 4, the percentage of enhancing lesions identified on DWI was 75.2% for reader 1 (r1), 76.8% for reader 2 (r2), and 70.4% for reader 3 (r3). DWI visualized 89.6% of the malignant enhancing lesions.

Table 5 showed that b-800 and synthetic b-1000/b-1200 s/mm² values allowed the visualization of 57– 70% of benign lesions, while b-1500/b-1800 s/mm² allowed the visualization of 82–85% of benign lesions. This study readers found that, synthetic b-values 1500–1800 s/mm² were preferred for lesion conspicuity, especially in dense breast. Table 6 describe mean ADC value of benign and malignant lesions for each reader for benign and malignant lesions. The readers have looked at the DWI alone and some lesions went undetected. This table describe false negative cases diagnosed by DWI for each reader. Reader 2 had the highest number of false negative cases (26) with histopathological subtypes and mean size as in Table 7.

Table 8 showed that DWI was more specific (84.8 % vs 67.4%, $p < 0.001$) but less sensitive (62% vs 89.9%, $p < 0.001$) and accurate (73.4% vs 78.7%, $p = 0.010$) than DCE-MRI for breast cancer detection, where mpMRI was the most accurate modality accounting for less false positive cases. DWI inter-reader agreement was low to high for benign lesion visibility ($\kappa = 0.31$ –0.91), for malignancy score was high ($\kappa = 0.71$ –0.91), and DCE- MRI assigned BI-RADS ($\kappa = 0.57$ –0.63). The highest level of inter-reader agreement for benign lesion was b-800 s/mm² (average $\kappa = 0.87$), whereas the lowest κ value was for b-1200 s/mm² (average $\kappa = 0.31$). The highest level of inter-reader agreement for malignant lesion was b-1800 s/mm² (average $\kappa = 0.81$).

Discussion

By reducing the T2-shine-through effect and suppressing the normal breast tissue, higher b-values seem to increase lesion visibility. But, they need lengthy examination durations, and the picture quality can be diminished as a result of a poor signal-to-noise ratio. These restrictions could be circumvented by using synthetic b-values. The sensitivity of breast cancer detection could be enhanced using synthetic b-values, which are created using a mathematical computation technique from at least two distinct lower b-values in a voxel wise fashion. This process does not increase the scan time or degrade image quality—in fact, synthetic b-values display a higher image quality than the acquired b-values (11,12).

For the purpose of MRI screening for malignant lesions, DWI has been introduced as a non-enhanced alternative. Without increasing the collection time and without sacrificing visibility, synthetic b-values enhance lesion visibility. In this project we tried to evaluate the diagnostic ability of DWI's diagnostic in characterization of breast lesions utilizing different synthetic b-values. we evaluated DWI for tumor visibility and breast cancer identification using a mix of collected b-values (800 s/mm²), its ADC maps, and the addition of various synthetic b-values (1000, 1200, 1500, and 1800 s/mm²). At the same time, 84% of the malignant enhancing tumors could be seen and the accuracy reached 73.4% using the synthetic b-1000/1200 s/mm² values and the acquired b-800 values (6).

Daimiel et al. found that 78% - 82% of the lesions seen using DCE-MRI, including both benign and cancerous breast lesions, could be seen with DWI alone. According to previous research on DWI with ADC mapping, most of the lesions that were missed were either tiny (≤ 10 mm) or non-melanomaous (13), which is consistent with the findings of our study.

While DWI is useful for characterizing lesions seen in other imaging modalities, it may pose problems when used only for breast cancer screening. It would be ideal if DWI sequence resolution could be improved in order to make cancer detection more effective.

The number of tumors that could be identified using the obtained b-value of 800 s/mm² and the synthetic b-values of 1000/1200 s/mm² were same. Alternatively, simulated b-values of 1500 and the decrease in picture quality likely explains why 1800 s/mm² missed more lesions.

When it came to detecting breast cancer, DWI was more specific (84.8 % vs 67.4%, $p < 0.001$), less sensitive (62% vs 89.9%, $p < 0.001$), and less accurate (73.4% vs 78.7%, $p = 0.010$) than DCE-MRI. The most accurate modality, accounting for fewer false positive instances, was mpMRI (13,14).

By combining the strengths of DCE-MRI and DWI, mpMRI was able to achieve a far higher level of accuracy than each modality could on its own. Whereas mpMRI achieved an accuracy rate of 80-90% while producing fewer false positive instances.

Between 57% and 71% of benign lesions could be seen with B-800 and synthetic b-1000/b-1200 s/mm² values, 82% to 85% of benign lesions could be seen with b-1500/b-1800 s/mm², and 15% to 50% of malignant lesions could be seen with synthetic b-1500/b-1800 s/mm² values.

The majority of the lesions that were overlooked were either tiny (≤ 10 mm) or non-melanomalous liver erosions (NMLE), and our analysis shown that between 78% and 82% of lesions may be seen with DCE-MRI and had been seen with DWI alone.

According to Pinker et al., who explored this topic, previous research on dynamic contrast imaging (DWI) plus angiography (ADC mapping) confirmed that DWI missed very tiny or non-massive lesions (NMLE) (15).

Compared to the surrounding parenchyma, malignant tumors were brighter at high b-values (1500 and 1800 s/mm²), but benign lesions were more noticeable at lower b-values (800 and 1000 s/mm²). Similar to what Chen et al. found, several investigations using a broader range of b-values have shown that breast cancer is more noticeable at high b-values (16).

Tamura et al. determined cDWIs with b-values of 1400, 2100, 2800, and 3500 s/mm². They concluded that aDWIs may seem less prominent if cDWIs with high b-values were created from pictures with low signal-to-noise ratios. In dense breasts, such as ACR C and D, where there is a lot of fibroglandular tissue and lesions, especially little ones, might be mammographically disguised and hidden, an increase in the visibility of malignant tumors at high b values could be very useful (17).

Based on our findings, b-1200 s/mm² may be the ideal dose for dense breast lesion imaging, which in turn may improve lesion characterisation via improved correlation on ADC maps and more precise ADC values. I should clarify that ADC (maps and values) can only be obtained from DW photos that have been captured without extending the acquisition period. Assuming a Gaussian model, signals recorded at lower b-values (e.g., 0 and 800 s/mm²) are extrapolated to produce synthetic high b-value pictures. We observed that benign lesions had a higher mean ADC value than malignant lesions in the present research.

The strategy of using synthetic high b-values to improve contrast in lower b-value images without adding more sequences to the examination could be helpful for detecting and depicting lesions, but it doesn't have the power of non-Gaussian diffusion to characterize tissues. For example, a study by Rosenkrantz A et al. demonstrated that DW images obtained with a b-value of 2000 s/mm had significantly higher sensitivity than 1000 s/mm ($P < 0.001$), but there was no difference in sensitivity between ADC maps calculated using the two b-values ($P \geq 0.309$) (18).

The results of our investigation showed that the simplified model could also account for the heterogeneity of malignant lesions, since the diagnostic effectiveness of ADC_{avg}-ADC_{fast} was identical to that of ADC_{avg}-ADC_{fast- α} (AUC = 0.807). In addition, ADC_{avg}-ADC_{fast} provided the best possible differential

diagnosis in clinical practice, with the highest Youden indices of 68.42% and 87.8%, respectively, making it a more feasible non-invasive technique than other standard quantitative tests.

For example, for high b-values, unenhanced MRI is more likely to miss cancers like DCIS or NMLE because their signal intensity is lower in DWI. Given that screening tumors are often smaller in size and NMLE lesions are clinically undetected, it is necessary to overcome these constraints in order to use unenhanced MRI in this context. Also, these lesions are the reason why some DWI tests come out negative. Although our research's sensitivity for DWI was significantly lower than previous studies (approximately 65%), it was very specific in detecting such lesions (84.8%), similar to a study conducted by Amornsiripanitch et al. because a large proportion of IDC patients had concomitant DCIS (19).

Our findings suggest that DWI should not be used in isolation for the evaluation of ambiguous lesions (such as BI-RADS IVa and IVb lesions) at this time, particularly for smaller lesions (less than 10mm) because its accuracy was reduced due to a loss of sensitivity. Since differentiating morphological characteristics is challenging, DCE-sensitivity MRI's was similarly lowered in this subgroup, reaching 78.7 percent. Despite the lack of statistically significant differences between mp-MRI and DCE-MRI, mp-MRI maintained its position as the most accurate method, achieving 85.5% in these instances.

However, combining DWI with DCE-MRI had an extra benefit: it reduced the amount of false positives. Most of the benign lesions in our research sample belonged to the category of tiny lesions < 10 mm, where this was very important. In order to keep expenses down and alleviate patient worry, it is crucial to avoid doing needless follow-up exams or biopsies on ambiguous or benign tumors. These findings are consistent with those of other research that looked at using DWI and DCE-MRI together to identify breast cancer (20,21).

Our research has a number of limitations that we are aware of. To start, in order to keep clinical acquisition durations constant, no comparison was made with obtained high b-values. To add to that, the findings and their applicability could be impacted by the fact that malignant lesions tend to be bigger than benign ones, and that there aren't as many pure cases of DCIS, ILC, and NMLE as there are invasive carcinomas that showcase a mass.

However, according to the radiology department's stated inclusion criteria, this sample represented the clinical practice in our screening and tertiary care facility. Finally, there is a possibility that visual and image quality outcomes can vary when synthetic b values are produced from various DWI sequences. Our work only used a singleshot EPI DWI with a short TI inversion- recovery (STIR) fat suppression sequence, hence the findings may not be applicable to other sequences.

Conclusion

In conclusion, the addition of synthetic high b-values (e.g., 1200s/mm²) improves tumor conspicuity without increasing the time of scan, which is particularly helpful in dense breasts. Nevertheless, the role of DWI for the visualization of NMLE and small lesions and its performance in breast cancer detection are still not definite.

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Table 2: Basic demographic data of the studied patients

(n = 114)	
Age (years)	
Range	30.0 – 50.0
Mean ± SD	39.6 ± 5.9
Lesion side (no, %)	
Unilateral	104(83.2%)
Bilateral	21(16.8%)
Lesion size (mm)	
Range	5.0 – 100.0
Mean ± SD.	25.9 ± 16.9

Abbreviations: SD: **Standard deviation.**

Table 3: Distribution of histopathology results of all lesions (n=125).

Group I (n = 40)	
Benign lesions	46(36.8%)
Fibro adenoma	25(20%)
Fibrocystic changes	8(6.4%)
Benign parenchyma	4(3.2%)
Stromal fibrosis	4(3.2%)
Lymph node	3(2.4%)
Periductal mastitis	2(1.6%)
Malignant lesions	79(63.2%)
IDC	41(32.8%)
DCIS	22(17.6%)
ILC	16(12.8%)

Abbreviations: IDC: **Invasive Ductal Carcinoma**, DCIS: **Ductal Carcinoma In Situ**, ILC: **Invasive Lobular Carcinoma.**

Table 4: Percentage of detected and missed lesions by DWI compared to Dynamic MRI among different readers (n=125).

	Reader 1	Reader 2	Reader 3	Read by all
Malignant	15(12%)	14(11.2%)	17(13.6%)	13(10.4%)
Benign	16(12.8%)	15(12%)	20(16%)	13(10.4%)
Total	31(24.8%)	29(23.2%)	37(29.6%)	26(20.8%)

Table 5: Preferred synthetic b value for lesions diagnosis for all readers among the study patients (n=125)

	Reader 1		Reader 2		Reader 3	
	Benign	malignant	Benign	malignant	Benign	malignant
800	22(17.6%)	0(0%)	13(10.4%)	0(0%)	11(8.8%)	0(0%)
1000	8(6.4%)	0(0%)	9(7.2%)	0(0%)	4(3.2%)	0(0%)
1200	0(0%)	0(0%)	9(7.2%)	0(0%)	11(8.8%)	0(0%)
1500	0(0%)	46(36.8%)	0(0%)	37(29.6%)	0(0%)	35(28%)
1800	0(0%)	18(14.4%)	0(0%)	28(22.4%)	0(0%)	26(20.8%)

Table 6: Average of ADC mean values for each reader in benign and malignant lesions (n=125)

	Reader 1	Reader 2	Reader 3	P value
Benign lesions	1.47±0.23	1.50±0.20	1.52±0.30	0.003
Malignant lesions	1.10±0.18	1.11±0.15	0.96±0.22	

*Units: $\times 10^{-3} \text{ mm}^2/\text{s}$ for all the values Abbreviations: ADC, apparent diffusion coefficient.

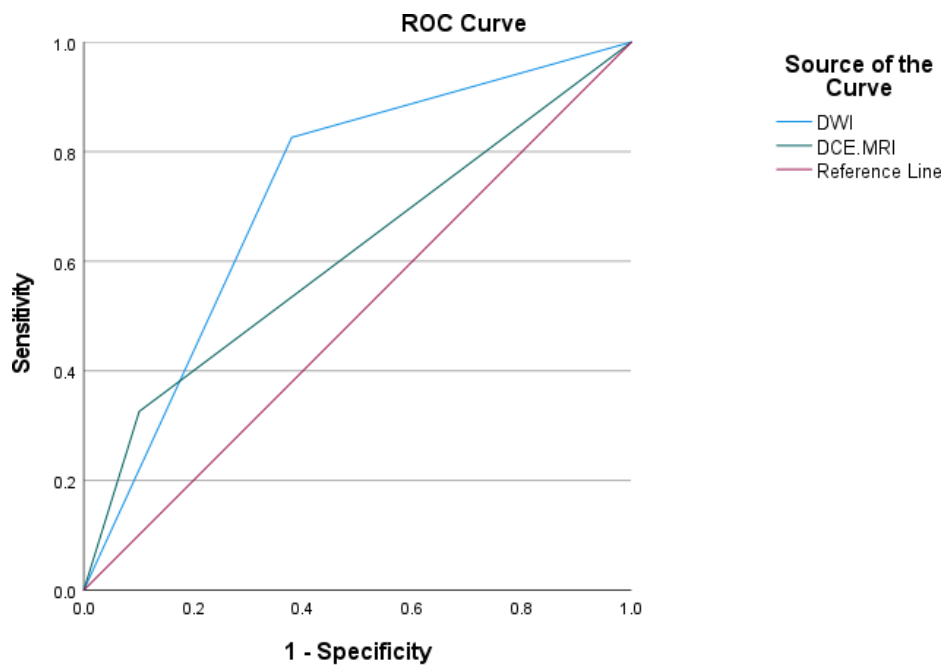
Table 7: False negative cases with DWI (n=125)

Reader	Histology	Mean size mm (range)	Total of false negatives
1	13 IDC	15 (6-50)	25
	6 DCIS	10.5 (7-12)	
	6 ILC(3 of them NME)	11 (8-14)	
2	16 IDC	14.3 (6-45)	26
	4 DCIS	11.5 (7-29)	
	6 ILC(3 of them NME)	12 (8-16)	
3	12 IDC	10 (6-24)	23
	5 DCIS	11.5 (7-20)	
	6 ILC(3 of them NME)	10 (8-14)	

Table 8: Average values of the diagnostic parameters for DWI, DCE, and multiparametric MRI

		DWI	DCE-MRI	mpMRI	p values		
					DWI vs DCE-mpMRI	DWI vs mpMRI	DCE-MRI vs mpMRI
Overall	Sensitivity	62%	89.9%	94.9%	<0.001	<0.001	<0.001
	Specificity	84.8%	67.4%	76.1%	<0.001	0.011	0.058
	Accuracy	73.4%	78.7%	85.5%	0.010	0.017	0.108
≤ 10 mm	Sensitivity	20.3%	75.5%	91.1%	<0.001	<0.001	<0.001
	Specificity	97.8%	72.6%	91.3%	0.092	0.056	0.022
	Accuracy	59.05%	74.05%	91.2%	0.074	0.029	<0.001
> 10 mm	Sensitivity	74.7%	97.4%	98.7%	0.010	0.014	0.625
	Specificity	96.9%	43.5%	84.7%	0.005	<0.001	<0.001
	Accuracy	85.8%	70.5%	91.7%	0.009	0.018	0.082

Abbreviations: DWI, diffusion-weighted image; ADC, apparent diffusion coefficient; DCE-MRI, contrast-enhanced magnetic resonance image; mpMRI, multiparametric magnetic resonance image.



Diagonal segments are produced by ties.

Figure 1: Results of pairwise comparisons between the receiver operating curves (ROCs) and the area under the curve (AUC) for DWI vs DEC-MRI diagnostic modality

1800			0.77		0.91		0.76	0.81
1200								
ADC mean		0.89	0.74	0.75	0.86	0.81	0.69	0.76
DCE-MRI	BI-	0.63		0.57		0.61		0.60
RADS								

Abbreviations: K: **kappa coefficient**.

Table 9: Inter-reader agreement (weighted κ values) for diffusion-weighted images (DWI) and dynamic contrast-enhanced MR images (DCE-MRI) parameters ($n=125$)

	r1 vs r2		r2 vs r3		r1 vs r3		K
DWI	Benign	Malignant	Benign	Malignant	Benign	Malignant	
800	0.87		0.90		0.84		0.87
1000	0.88		0.80		0.86		0.85
1200	0.31		0.87		0.20		0.46
1500		0.75		0.89		0.71	0.78