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Full Length Research Paper

Assessment of Breast Lesions: A Magnetic Resonance Imaging Study

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The purpose of our study was to evaluate the combination of the Diffusion-Weighted Imaging (DWI), Dynamic Contrast Enhancement Magnetic Resonance Imaging (DCE-MRI) and BI-RADS in the improvement of the diagnosis of breast MRI benign and malignant Lesions. This retrospective study included 50 breasts with lesions, their ages were between 26 and 80 years (mean age: 41.78±12.48years). All patients were examined on MRI: T1, T2 weighted images, and underwent consequent biopsy. (DWI) was obtained and (DCE-MRI), BI-RAD were applied and the findings were evaluated .The study took place during the period from June 2012 up to June 2014, at Dr. Suleiman Alhabib Medical Center-Olaya. Findings were 34 benign lesions out of 50 including: breast hematoma, breast cyst, degeneration, fibro-adenoma, fat necrosis, fibrocystic change, myxoid fibroid, papilloma and pseudoangiomatous hyperplasia. Malignant lesions totaled 16 out of 50, including: infiltrating ductal carcinoma, ductal papillary carcinoma and breast calcification. The average of diameter of the benign lesions was 1.7x1.5cm and that of breast malignant lesions was 2.1x2.0cm. The diagnostic assessment of breast lesions in combination with the assessment of signal intensity and lesion morphologic features, as well as the (DWI), (DCE-MRI), BI-RADS, and dynamic curve assessment with detailed histopathology for each lesion showed significant relationship at P- Value <0.05. Histological results and MRI Findings showed sensitivity of 82%, specificity of 71%, accuracy of 75% and positive predictive value (PPV) of 64%. The additive diffusion-weighted imaging, contrast enhancement MRI, dynamic curves and BIRADS values to T1, T2-weighted MR imaging, for the assessment of breast lesions, would be useful in the analysis of breast MR images. It is likely that all the MR breast imaging combined procedures would be revealed to have an acknowledged task in breast MR imaging without the need of the invasive unnecessary biopsies.

Keywords: BIRAD, Breast, Diffusion-Weighted Imaging, MRI

INTRODUCTION

Magnetic resonance imaging (MRI) is a widely-used tool for the diagnosis of breast lesions. However, the conventional breast MRI is a morphological diagnostic technique which provides anatomical information including signal intensity, size and shape (Zhang et al., 2009).

New MRI technology is the diffusion-weighted imaging (DWI) which is an unenhanced MRI sequence that measures the different and potentially complementary information to DCE-MRI. DWI is sensitive to biophysical

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characteristics of tissues (Le Bihan et al., 1992). DWI is based on the thermal motion of water molecules in extracellular fluid and enables the acquisition of images that reflect histological structure and therefore it can detect the changes of tissue structure (Manenti et al., 2006). It also enables the quantitative evaluation of apparent diffusion coefficient (ADC), which may be useful for distinguishing malignant from benign tissues (Koyama and Togashi, 2007; Woodhams et al., 2005). This imaging possession is unique and provides a different contrast mechanism than that observed on conventional T_1- and T_2- weighted MR images (Reiko et al., 2011).

Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) of the breast has a high sensitivity for breast cancer detection (Kriege et al., 2004). The high sensitivity of this technique results from the differential enhancement between normal and malignant tissue on T_1-weighted imaging. It uses morphologic and kinetic enhancement criteria that can present additional challenges by detecting many benign lesions (Savannah et al., 2011). A recent study reported high accuracy for characterizing enhancing breast lesions through a combination of DWI and Dynamic contrast-enhanced - MRI texture (Le Bihan et al., 1992).

The BI-RADS MRI method was established to standardize breast MRI technique and lesion classification (Ikeda et al., 2001). In BI-RADS, attention is given to biologic differences in lesion growth patterns through differentiation of breast lesions (Ikeda et al., 2001). Recent study gives specificities of 81–97% (Leach et al., 2005). To the best of our knowledge, no research has been conducted to systematically examine the characteristics of breast MRI findings in conventional breast MRI assessment, DWI, DCE-MRI, BI-RADS MRI compared with the classification analysis of biopsy-proven lesions on breast MR images

MATERIALS AND METHODS

Study Sample

Fifty cases with 50 breast lesions were examined by MRI during the period from June 2012 up to June 2014, at Dr. Suleiman Alhabib Medical Center-Olaya. All patients were females and aged between 26 and 80 years (mean age: 41.78±12.48years).

Histological Findings

The results of histopathologic examination were chosen as the reference standard for lesion evaluation. Findings could either be benign or malignant, and the tumor type was recorded. Findings were 34 benign lesions out of 50 including: breast hematoma, breast cyst, degeneration, fibro-adenoma, fat necrosis, fibrocystic change, myxoid fibroid, papilloma and pseudoangiomatous hyperplasia. Malignant lesions totaled 16 out of 50, including: infiltrating ductal carcinoma (IDC), ductal papillary carcinoma and breast calcification.

Breast Lesion Size and Shape

The average of diameter of the benign lesions was 1.7x1.5cm and that of breast malignant lesions was 2.1x2.0cm. Also lesions were classified according to their shapes as regular and irregular.

MRI protocols and imaging

MRI was performed with a 1.5 T MR system (GE Signa HDX 1.5T, GE Optema 450w 1.5T and a dedicated 8-channel phased-array bilateral breast coil, with the patient lying in prone position and the breast in a holder. The imaging protocols included a sagittal T1-weighted (matrix = 5000, slice thickness (ST)= 5 mm, slice space(SP)=1mm, band width=31.25 Flip angle(FA) = 90.0,TR=6000-7000ms,TE=10ms, ETL=3; a T2-weighted turbo spin-echo (TSE) pulse sequence (matrix = 5000, slice thickness (ST)= 5 mm, slice space(SP)=1mm ,band width=31.25 Flip angle (FA)= 90.0; TR=2000-5000ms,TE=85-97ms, ETL=16. And DWI pulse sequence, slice thickness (ST)= 5 mm, Flip angle (FA)= 90.0, TR=6000-7000ms, TE=74-75ms, diffusion mode (DM) = SE, NSA = 1. The contrast media used was Gadolinium DTPA (20ml). Two basic weighted images, dynamic curves and BIRAD classes were obtained. The analysis of magnetic resonance images of the diagnosis of 50 lesions was shown as frequencies and percentages see table 1, as well as the classification of the lesions according to age groups was noted in table 2. Dynamic contrast enhancement was assessed by placement of a region of interest in the most suspect part of the lesion and consecutive signal intensity analysis of unenhanced and Contrast-enhanced images. The increase in signal intensity in the first minute after IV contrast injection (SI_{1min}) was calculated in percentage relative to the unenhanced signal intensity (SI_{native}) as follows: (SI_{1min} – SI_{native})/SI_{native}. According to the BI-RADS lexicon, initial enhancement was ordinally classified as slow (< 50%), intermediate (50–100%), or fast (> 100%). Type of delayed enhancement curve type was classified according to the BI-RADS classification (American College of Radiology, 2003).

Statistical analysis

The Independent-Sample *T*-test and One-Way ANOVA were used to determine statistical significance. *P* value < 0.05 was regarded as statistically significant. All statistical analyses were performed using the SPSS version 16 software package (SPSS Inc, Chicago, IL, USA). Sensitivity, specificity, and accuracy, positive predictive values (PPV) were evaluated according to the equations:-

$$Sensitivity = \frac{TP}{(TP + FN)} \quad \textit{Eq (1)}$$

$$Specificity = \frac{TN}{(TN + FP)} \quad \textit{Eq (2)}$$

$$Accuracy = \frac{(TN + TP)}{(TN + TP + FP + FN)} \quad \textit{Eq (3)}$$

$$PPV = \frac{TP}{(TP + FP)} \quad \textit{Eq (4)}$$

Abbreviations:- True positive (TP),True negative (TN), False positive (FP),False negative (FN).

RESULTS

Table 1. MRI Diagnoses and Classification of 50 Breast Lesions

	MRI Classification of Breast Lesion		
MRI Diagnoses/Findings	***Benign***	***Malignant***	***Total***
Suspicious Breast Masses	0	5	5
Hematoma	1	0	1
Cyst	1	0	1
Degeneration	1	0	1
Fibro Adenoma	13	0	13
Fat Necrosis	4	0	4
Fibrocystic Change	8	0	8
Infiltrating Ductal Carcinoma	0	9	9
Intraductal Papillary Cancer	0	1	1
Myxoid Fibroid	2	0	2
Papilloma	3	0	3
Pseudoangiomatous Hyperplasia	1	0	1
Popcorn Calcification	0	1	1
Total	34	16	50

Table 2. MRI Diagnoses And Classification of 50 Breast Lesions According to Age Classes

		Age Classes/Years				**Total**
		26-40	41-55	56-75	>76	
MRI Diagnosis	**Benign Lesions**	21	6	1	0	28
	Malignant Lesions	7	9	5	1	22
Total		28	15	6	1	50
P- Value =0.002 <0.05						

Table 3. Analysis of Magnetic Resonance Images of the 50 Breast lesions signals intensity in T_1, T_2, DWI Techniques.

Classification	NO	Signal Intensity at T_1Weighted Imaging	Signal Intensity at T_2Weighted Imaging	Signal Intensity at Diffusion Weighted Imaging DWI
Suspicious Breast Masses	5	1=hyperintense 4=hypointense	3=hyperintense 2=hypointense	5=isointense
Hematoma	1	1=hyperintense	1=hyperintense	1=hyperintense
Cyst	1	1=hypointense	1=isointense	1=hyperintense
Degeneration	1	1=hypointense	1=hypointense	1=isointense
Fibro Adenoma	13	13=hypointense	8=hyperintense 3=hypointense 2=isointense	13=hyperintense
Fat Necrosis	4	4=hyperintense	4=hyperintense	4=hypointense
Fibrocystic Change	8	2=hyperintense 6=hypointense	8=hyperintense	7=hyperintense 1=hypointense
Infiltrating Ductal Carcinoma	9	8=hypointense 1=isointense	3=hyperintense 5=hypointense 1=isointense	4=hyperintense 4=hypointense
Intraductal Papillary Cancer	1	1=hypointense	1=isointense	1=hyperintense
Myxoid Fibroid	2	2=hypointense	2=hyperintense	2=hyperintense
Papilloma	3	2=hyperintense 1=hypointense	2=hyperintense 1=hypointense	2=hyperintense 1=hypointense
Pseudoangiomatous Hyperplasia.	1	1=hypointense	1=isointense	1=isointense
Popcorn Calcification	1	1=hypointense	1=hypointense	1=isointense
Statistical Correlations	50	(Pearson Chi-Square =48.5) P-Value =0.118 >0.05	(Pearson Chi-Square =58.8) P- Value =0.017 <0.05	(Pearson Chi-Square =84.9) P- Value =0.000 <0.05

Table 4. Analysis of Magnetic Resonance Images of the 50 Breast lesions in Dynamic Curve and BI-RAD Techniques.

Classification	*No*	*Dynamic Curve*			*BI-RAD*			
		1.0	**2.0**	**3.0**	**2.0**	**3.0**	**4.0**	**5.0**
Suspicious Breast Masses	5	-	-	5	-	1	2	2
Hematoma	1	1	-	-	-	1	-	-
Cyst	1	1	-	-	-	1	-	-
Degeneration	1	1	-		-	1	-	-
Fibro Adenoma	13	11		2	-	13	-	-
Fat Necrosis	4	2	2	-	1	2	1	-
Fibrocystic Change	8	7	1	-	-	7	1	-
Infiltrating Ductal Carcinoma	9	-	-	9	-	5	1	3
Intra Ductal Papillary Cancer	1	-	-	1	-	-	1	-
Myxoid Fibroid	2	2	-		-	2	-	-
Papilloma	3	2	-	1	-	3	-	-
Pseudoangiomatous Hyperplasia.	1	1	-	-	-	-	1	-
Popcorn Calcification	1	1	-	-	-	1	-	-
Total Lesions	50	29	3	18	1	37	7	5
		(Pearson Chi-Square= 55.6) P- Value =0.032 <0.05			Pearson Chi-Square =73.53) P- Value =0.069 >0.05			

Table 5. Morphologic Characteristics of 50 breast Lesions in DWI

	Morphologic Characteristics in DWI		Total
	Irregular	Regular	
Suspicious Breast Masses	5	0	5
Hematoma	0	1	1
Cyst	0	1	1
Degeneration	0	1	1
Fibro Adenoma	0	13	13
Fat Necrosis	2	2	4
Fibrocystic Change	2	6	8
Infiltrating Ductal Carcinoma	7	2	9
Intra Ductal Papillary Cancer	1	0	1
Myxoid Fibroid	1	1	2
Papilloma	2	0	2
Pseudoangiomatous Hyperplasia	1	0	1
Popcorn Calcification	0	1	1
Total	22	28	50
	44.0%	56.0%	100.0%
	(Pearson Chi-Square =35.11)		
	P- Value =0.014 <0.05		

Table 6. MRI contrast enhancement of the breast lesions cross tabulated with MRI diagnosis results

		MRI FINDINGS		Total
		Benign Lesions	Malignant Lesions	
MRI Contrast Enhancement of Lesions	**Intermediate**	16	1	17
	Slow	10	5	15
	Strong	2	16	18
Total		28	22	50
P –value = 0.000				

Table 7. Cross Tabulation between the Histological Results and MRI Findings

		HISTOPATHOLOGY FINDINGS		*Total*
		Benign Lesions	**Malignant Lesions**	
MRI Findings	Benign Lesions	12	5	17
	Malignant Lesions	2	9	11
Total		14	14	28
(Pearson Chi-Square =443.9) P- Value =0.002 <0.05				

Sensitivity=82%, Specifity=71%, Accuracy=75% and Positive Predictive Value (PPV) =64%

Table 8. MRI Contrast Enhancement of the Breast Lesions Cross Tabulated With Histopathology Results

		HISTOPATHOLOGY FINDINGS			Total
		NA	Benign Lesions	Malignant Lesions	
MRI Contrast Enhancement of Lesions	Intermediate	10	4	3	17
	Slow	5	9	1	15
	Strong	7	2	9	18
Total		22	15	13	50
NA stands for: not applicable		*P* –value = 0.005			

Table 9. Cross Tabulation between the Histological Results with BI-RAD MRI values.

		BI-RAD MRI				Total
		2.00	3.00	4.00	5.00	
HISTOPATHOLOGY FINDINGS	Benign	1	29	2	0	32
	Malignant	0	7	5	6	18
Total		1	36	7	6	50
P –value = 0.001						

Table 10. Cross Tabulation between the Histological Results with MRI dynamic curve values.

		MRI Dynamic Curve			Total
		1.00	2.00	3.00	
HISTOPATHOLOGY FINDINGS	**Benign**	27	2	3	32
	Malignant	2	1	15	18
Total		29	3	18	50
P –value = 0.000					

Table11. Published Breast MRI Screening Study Results (12)

	Nether Lands	Canada	United Kingdom	Germany	United States	Italy	Our Study
No of Women	1.909	236	649	529	390	105	50
Age Range	25-70	25-65	35-49	≥30	≥25	≥25	26-80
No of Cancers	50	22	35	43	4	8	50
Sensitivity	80	77	77	91	100	100	82
Specificity	90	95	81	97	95	99	71
Accuracy	-	-	-	-	-	-	75
(PPV)	-	-	-	-	47%	-	64%

DISCUSSION

In conventional breast MRI investigation, precontrast imaging was started either with T_1 or T_2 weighted images. Table 3 showed the characterization of lesions according to signal intensity. In the T_2-weighted images water-containing lesions or edematous lesions have an intense signal, and in this sequence cysts and myxoid fibro adenomas were very well identified. In most cases cancer as infiltrating ductal carcinoma, intraductal papillary cancer, and popcorn calcification does not give up a high signal on T_2 weighted images; therefore, these sequences can be useful in the differentiation between benign and malignant lesions, also most of these lesions can also be identified on T_1 weighted images. Therefore previous studies suggested using either T_1 or T_2 as they have the same value in that cases (Kelez, 2006; Kuhl et al., 1999). Signal intensity at diffusion-weighted imaging is inversely proportional to the degree of water molecule diffusion, that was influenced by the histological structure. The motion of water molecules is more limited in tissues with a high cellular density as tumor tissue or with lipophilic cell membranes and less restricted in areas of low cellularity or where cell membranes have been damaged (Yoshikawa et al., 2007). The correlation between the MRI findings and the signal intensity is found to be significant at P value<0.05 in both T_2 and DWI as 0.017 and 0.000 respectively.

The presence of isointense signal in DWI in the suspicious mass, degeneration, pseudoangiomatous hyperplasia and popcorn calcifications suggested that DWI may have lower sensitivity than DCE-MRI for detecting breast cancer. This was similar to what has been described previously by Yoshikawa et al. (2007). Therefore, and for more information, the study used the dynamic contrast enhanced MRI which uses curve type as it was recommended by the study done by Schnall et al. (2006).

Hematomas containing intracellular components (oxyhemoglobin, deoxyhemoglobin, or methemoglobin) showed significantly reduced diffusion as compared with hematomas containing lysed red blood cells (extracellular methemoglobin) (Fischbein et al., 2000). However some hematomas have high signal intensity on precontrast T_1-weighted images as shown in the study results. Therefore, T_1-weighted images should be evaluated

together with diffusion-weighted images to avoid misdiagnosis.

Several studies suggest the diagnostic assessment of breast diffusion-weighted images in combination with the assessment of signal intensity and lesion morphologic features on T_2-weighted images (Baltzer et al., 2010). The combination of high signal intensity at diffusion-weighted imaging, an irregular margin, and iso- to hypointensity at T_2-weighted imaging is a potential indication for malignancy. This combination method may improve the specificity of breast cancer assessment (Tozaki and Fukuma, 2009). Table 3 showed the signal intensities at diffusion-weighted imaging, T_1 and T_2-weighted imaging for various pathologic conditions of the breast.

Dynamic Contrast Enhancement DCE-MRI scans were interpreted for each lesion and were assessed using the American College of Radiology (ACR) BI-RADS breast MRI lexicon (American College of Radiology, 2003) integrating morphologic and kinetic features, see table 4. The correlation was found to be significant between the MRI findings, Dynamic curves and BIRADS results as 0.032and 0.069 respectively at P value<0.05

Similar findings were discussed by Berg et al. (2004) who found that the BI-RADS MRI morphologic descriptors were not significantly predictive of the malignancy of lesions with non mass like enhancement. Also Jansen et al. (2008), in an evaluation of the effectiveness of kinetic analysis of both masses and lesions with non mass like enhancement, found that DCE-MRI kinetic information effectively differentiated benign from malignant mass lesions.

The lesions were additionally described on the basis of their size, shape, margin and enhancement pattern. The kinetic curve evaluation includes a description of the contrast enhancement (American College of Radiology, 2003). Lesion characteristics, including, shape regularity and irregularity were presented, see table 5, 22(44.0%) of the lesions were found to be irregular and 28(56.0%) were found to be regular in their borders. The correlation between the diagnosis and the shape was found to be significant at *P*-value <0.05=0.014 .And our results showed that the malignant lesions were greater in dimensions than the benign one.

DCE-MRI scans were interpreted, they showed 17 lesions had intermediate curve (16 were benign and 1was malignant), 15 lesions had slow curve (10 were benign and 5 were malignant), 18 lesions had strong curve (2 were benign and 16 were malignant). The correlation between the MRI conventional diagnosis and contrast enhancement curves was found to be significant at *P*-value=0.000, see table 6. The Diffusion-weighted MRI (DWI) findings, DCE-MRI, BI-RADS, and dynamic curve assessment were recorded .This information was registered with detailed histopathology for each lesion. The consignment between histopathology results and MRI diagnosis, was found to be significant at P-Value <0.05 as 0.002. DCE-MRI results were significantly correlated with histopathology results at *P*-Value <0.05 as 0.005, One study revealed the specificity of DCE-MRI according to morphologic and kinetic criteria and reported to be between 37% and 97% (Orel and Schnall, 2001). The variable specificity of DCE-MRI is a limitation that can result in unnecessary biopsy (Elmore et al., 1998).

According to the definitions of American College of Radiology; masses categorized as BI-RADS 4 were considered to be suspicious for malignancy. Masses categorized as BI-RADS 5 were highly suggestive of malignancy. Masses were assigned BI-RADS category 3, is probably benign (Hiroko et al., 2011). Correlation between the histopathology and BIRADs results were found to be significant at p value <0.05 as 0.001 and 0.000 with the dynamic curve results see tables 7-10. The cross tabulation between the histological results and MRI findings showed sensitivity of 82%, specificity of 71%, accuracy of 75% and positive predictive value (PPV) of 64%. Table 11 presented our study results and the comparison with other similar studies (Debbie et al., 2007).

A review of studies about the MRI breast cancer, found a wide variation in the positive predictive value (PPV). Calculated as the percentage of lesions considered suspicious on MRI and found to be malignant on biopsy, PPV ranged from 24% to 89% (Elmore et al., 2005). Another study reported a PPV for MRI of 25% (Lehman et al., 2007), with 91 false-positive findings among 121 biopsies performed as a result of suspicious findings on MRI. Techniques used in this study could improve the specificity of breast MRI and could reduce unnecessary biopsies and thus improve the overall accuracy of this highly sensitive tool for detecting breast cancer.

When assess the study findings, it showed that the diffusion-weighted breast imaging as a diagnostic imaging method can differentiate between the benign and malignant breast lesions without the use of contrast material. Ei Khouli et al (2010) showed an increase in diagnostic accuracy by adding diffusion-weighted imaging to conventional breast MR imaging. Similarly our results showed the highly significant correlations between the diagnosis of breast lesions and signal intensity changes in T_2 weighted and DWI at P- Value =0.017 and 0.000 respectively. Therefore diffusion-weighted imaging findings cannot be assessed in isolation from findings obtained with other MR imaging sequences (T_1 and T_2-weighted imaging). Diffusion-weighted imaging has a low specificity for breast cancer and a low sensitivity (Woodhams et al., 2009) for the detection of infiltrating ductal carcinoma, and because the benign and malignant lesion signal intensity may be overlapped in different imaging sequences, therefore this combination method may improve the specificity of breast cancer assessment. However, the assessment of all these findings in combination indicates that diffusion-weighted imaging

should be added to conventional and contrast-enhanced breast MR imaging as well as the diagnostic assessment by the curve types taking into accounts the increasing importance of detailed morphological and dynamic information. BIRADS gives acknowledged results when compared with the histopathology findings and illustrates many of the morphological findings seen on contrast-enhanced breast MRI. It also includes a lexicon that should be used for uniform reporting of the features seen on MRI (American College of Radiology, 2003).

CONCLUSION

Appreciation of the significance of the additive diffusion-weighted imaging, T1, T2-weighted MR imaging, Contrast enhancement MRI, Dynamic curves and BIRADS values for the assessment of breast lesions, could be useful in the analysis of breast MR images. It is likely that diffusion-weighted breast imaging could be revealed to have an acknowledged task in breast MR imaging without the need of the invasive unnecessary biopsies.

REFERENCE

American College of Radiology (2003). BI-RADS: MRI,1st ed. In: *Breast imaging reporting and data system:BI-RADS atlas.* Reston, VA: American College of Radiology.

American College of Radiology (2003). *Breast imaging reporting and data system (BI-RADS)*, 4th ed. Reston, VA: American College of Radiology.

Baltzer PA, Benndorf M, Dietzel M, Gajda M, Camara O, Kaiser WA (2010). Sensitivity and specificity of unenhanced MR mammography (DWI combined with T2-weighted TSE imaging, ueMRM) for the differentiation of mass lesions. Eur. Radiol. 20(5): 1101–1110.

Berg WA, Gutierrez L, NessAiver MS, et al (2004). Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. *Radiol.* 233:830–849

Debbie Saslow, Carla Boetes, Wylie Burke, Steven Harms, Martin O Leach, Constance D Lehman, Elizabeth Morris, Etta Pisano, Mitchell Schnall, Stephen Sener, Robert A Smith, Ellen Warner, Martin Yaffe, Kimberly S Andrews, Christy A Russell (2007). American Cancer Society Guidelines for Breast Screening with MRI as an Adjunct to Mammography, CA Cancer J. Clin. 57:75–89

Ei Khouli RH, Jacobs MA, Mezban SD, et al (2010). Diffusion-weighted imaging improves the diagnostic accuracy of conventional 3.0-T breast MR imaging. Radiol. 256(1):64–73.

Elmore JG, Armstrong K, Lehman CD, Fletcher SW (2005). Screening for breast cancer. *JAMA*. 293:1245–1256

Elmore JG, Barton MB, Moceri VM, Polk S, Arena PJ, Fletcher SW (1998). Ten-year risk of false positive screening mammograms and clinical breast examinations. *N. Engl. J. Med*. 338:1089–1096

Fischbein NJ, Roberts TP, Dillon WP (2000). Bleed or stroke? diffusion measurements in intracranial hematomas. AJNR. Am. J. Neuroradiol. 21(7): 1179–1180.

Hiroko Satake, Akiko Nishio, Mitsuru Ikeda, Satoko Ishigaki, Kazuhiro Shimamoto, Maki Hirano, Shinji Naganawa, tak H, Nishio A (2011). Ikeda Predictive Value for Malignancy of uspicious Breast Masses of BI-RADS Categories 4 and 5 Using Ultrasound Elastography and MR Diffusion-Weighted Imaging *AJR*. 196:202–209

Ikeda DM, Hylton NM, Kinkel K, et al (2001). Development, standardization, and testing of a lexicon for reporting contrast-enhanced breast magnetic resonance imaging studies. *J. Magn. Reson. Imaging*. 13:889–895

Jansen SA, Fan X, Karczman GS, et al (2008). DCEMRI of breast lesions: is kinetic analysis equally effective for both mass and nonmass-like enhancement? *Med. Phys*. 35:3102–3109

Kelez F (2006). Quantitative Assessment of T2 Imaging information in differential diagnosis of enhancing breast lesions. Eur. Radiol. 16(Suppl 5):E51–E53

Koyama T, Togashi K (2007). Functional MR imaging of the female pelvis. *J. magnetic resonance imaging*. 25(6):1101-1112.

Kriege M, Brekelmans CT, Boetes C, et al (2004). Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *N. Engl. J. Med*. 351:427–437

Kuhl CK, Klaschik S, Mielcarek P, Gieseke J, Wardelmann E, Schild HH (1999). Do T2-weighted pulse sequences help with the differential diagnosis of enhancing lesions in dynamic breast MRI? J. Magn. Reson Imaging. 9:187–196

Le Bihan D, Turner R, Douek P, Patronas N (1992). Diffusion MR imaging: clinical applications. *AJR*. 159:591–599

Leach MO, Boggis CR, Dixon AK, et al (2005). Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). *Lancet*. 365:1769–1778

Lehman CD, Gatsonis C, Kuhl CK, et al (2007). MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. *N. Engl. J. Med.* 356:1295–1303

Manenti G, Squillaci E, Di Roma M, Carlani M, Mancino S, Simonetti G (2006). In vivo measurement of the apparent diffusion coefficient in normal and malignant prostatic tissue using thin-slice echo-planar imaging. *Radiol. Med.(Torino)*. 111(8):1124-1133.

Orel SG, Schnall MD (2001). MR imaging of the breast for the detection, diagnosis, and staging of breast cancer. *Radiol.* 220:13–30

Reiko Woodhams, Saadallah Ramadan, Peter Stanwell,Satoko Sakamoto, Hirofumi Hata, Masanori Ozaki, Shinichi Kan, Yusuke Inoue (2011). Diffusion-weighted Imaging of the Breast: Principles and Clinical Applications Radio Graphics. 31:1059–1084

Savannah C Partridge, Wendy B DeMartini, Brenda F Kurland, Peter R Eby, Steven W White, Constance D Lehman (2011). Quantitative Diffusion-Weighted Imaging as an Adjunct to Conventional Breast MRI for Improved Positive Predictive Value *AJR*. 196:202–209

Schnall MD, Blume J, Bluemke DA, DeAngelis GA, DeBruhl N, Harms S, Heywang-Kobrunner SH, Hylton N,Kuhl CK, Pisano ED, Causer P, Schnitt SJ, Thickman D, Stelling CB, Weatherall PT, Lehman C, Gatsonis CA(2006). Diagnostic architectural and dynamic features at breast MR imaging: multicenter study. Radiol. 238:42–53

Tozaki M, Fukuma E (2009). 1H MR spectroscopy and diffusion-weighted imaging of the breast: are they useful tools for characterizing breast lesions before biopsy? AJR. Am. J. Roentgenol. 193(3):840–849

Woodhams R, Kakita S, Hata H, et al (2009). 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. 193(1): 260–266.

Woodhams R, Matsunaga K, Kan S, Hata H, Ozaki M, Iwabuchi K,Kuranami M, Watanabe M, Hayakawa K (2005). ADC mapping of benign and malignant breast tumors. *Magnetic resonance in medical sciences*, 4(1):35-42

Yoshikawa MI, Ohsumi S, Sugata S, et al (2007). Comparison of breast cancer detection by diffusionweighted magnetic resonance imaging and mammography. *Radiat. Med.* 25:218–223

Zhang Yili, Huang Xiaoyan, Du Hongwen, Zhang Yun, Chen Xin, Wang Peng, Guo Youmin (2009). The value of diffusion-weighted imaging in assessing the ADC changes of tissues adjacent to breast carcinoma *BMC Cancer*. 9:18