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5 **ABSTRACT** 6

Aims: The aim of this study was to emphasize magnetic resonance imaging (MRI) protocols to characterize breast tumors, using different pulse sequences, and compare it with histopathological findings.

Accuracy of Magnetic Resonance Imaging (MRI) in

Original Research Article

Detecting Breast Tumors

Study Design: This prospective study included 254 patients (4 males and 250 females; ages range between 15-78 years) underwent breast MRI examination.

Place and Duration of Study: This study was conducted in different MRI departments in Khartoum, Sudan between June 2014 and July 2016.

Methodology: Patients were examined using two sequences of MRI; routine and dynamic contrast enhanced MRI (DCE-MRI). Signal intensities were evaluated from different MRI sequences in different tumors; the histopathology result was used as a reference for each case.

Results: The sensitivity and specificity of MRI were 82.6 and 73.2 respectively. In addition, the breast cancer was more enhanced with fat suppression images. Contrast enhanced MRI (CE-MRI) has been shown to be more sensitive than routine sequences in detecting ductal carcinoma in situ (DCIS). Image subtraction technique showed that breast cancer has heterogeneous features (89.9%), and ring enhancement was clearly seen on (8.7%). DCE-MRI has been used to evaluate focal breast lesions. Adding information derived from the kinetic curve type of architectural features of a lesion, improves the specificity of breast MRI. On the other hand, it revealed that most cases of cancer represented on type 111 curves or rapid wash out. However, quantitative measurements of kinetic curve type resulted in significantly higher diagnostic performance and increasing specificity of MRI.

Conclusion: The accuracy of MRI in this study was more than other imaging modalities in characterizing breast abnormalities and tumors. Therefore, it offers a new method to detect breast cancer in its early stage, and help improve the survival rate.

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Keywords: Accuracy, breast tumors, histopathology, imaging, MRI, protocols.

9 10 **1. INTRODUCTION**

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Breast cancers are the most common type of cancer among women in the industrialized world. A woman's average lifetime risk for developing breast cancer in the United States is 1 in 8 [1]. In Sudan breast cancer is about (29%-34.5%) of all women's cancers, breast cancer cannot be prevented at the present time; however, early detection of breast cancer provides the best chance of survival and early treatment options [2]. Because early breast cancer is asymptomatic, the only way to detect it is through screening [3].

18 Different methods have been used in the diagnosis of breast cancer, including self examination, clinical 19 examination, mammography, ultrasound, and different type of Magnetic resonance imaging modalities 20 such as flow up method and biopsy [2]. Regular breast self examination can help to know how the breast 21 normally feels and look so one can notice any changes, but also provide evidence of harm. In spite of the 22 fact that breast is superficial organ which is amenable to clinical examination, may not reveal any 23 pathological problems, so that clinical examination would not easily detect sub centimeter lesions if they 24 are deeply situated within the breast and would not easily and confidently differentiate between benign 25 and malignant breast lesion [4]. In certain situation, clinical examination, mammography, and 26 ultrasonography have some limitations, either due to factors in the breast parenchyma such as dense 27 breast in young females, post operative changes or effect of irradiation or factors in modality itself, such 28 as the inability of mammography to demonstrate deep part of the breast and operator dependency of 29 ultrasound [5].

30 In diagnosing breast abnormalities -tumors- we need specific diagnostic procedures modalities to reach 31 an accurate diagnosis of these abnormalities, such as mammography, which is an effective means of 32 detecting and diagnosing breast tumors and breast cancer, it decreases breast cancer mortality by 1/3 33 when used as screening, however reported high false negative (-ve) from (4%-34%) [6]. Because an 34 abnormal screening mammogram requires a diagnostic test to confirm whether cancer is present, many 35 women who do not have cancer will undergo these unnecessary diagnostic tests [3]. In these difficult 36 situations, a biopsy may be restored to as a diagnostic method. In the last few years, magnetic resonance 37 (MR) imaging has been introduced as a promising method for diagnosis of breast neoplasms particularly 38 when dynamic contrast gadolinium (Gd) enhancement studies are used [7]. In addition, MRI of the breast 39 is a tool for detecting and staging breast cancer and other breast abnormalities, it is able to capture 40 multiple cross sectional image of the breast and combines them via computer to generate detailed two 41 dimensional and three dimensional imaging [8]. The potential role of MRI in the diagnosis of breast disease has been investigated since the late 1970s. Conventional MRI has not been reliable for diagnosis 42 43 of breast masses, so contrast MRI uses gadolinium diethylenetriamine penta-acetic acid (Gd-DTPA) has 44 been performed. Several studies have explored a multi-parametric approach to breast imaging that 45 combines analysis of traditional contrast enhancement patterns and lesion architecture with novel 46 methods such as diffusion, perfusion, and spectroscopy to increase the specificity of breast MRI studies 47 [9]. After the administration of an extracellular, gadolinium-based contrast medium, can be used to detect 48 and characterize human tumors. The success of DCE-MRI is dependent on its ability to demonstrate 49 intrinsic differences between varieties of issues that affect contrast medium behavior. Evidence is 50 mounting that DCE-MRI measurements correlate with immune histochemical surrogates of tumor 51 angiogenesis [9].

52 This study aimed to emphasize MRI protocols to characterize breast tumors by using different pulse 53 sequences, and compare the findings with the histopathological results.

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2. MATERIAL AND METHODS

57 2.1 Patient samples

The study was conducted in 254 patients, 250 were female (98.4%) and 4 male (1.6%). The mean age of all patients was 47 years, age range between 15-77 years. 154 patients (60.6%) examined by routine MRI technique and 100 patients (39.4%) examined by DCE-MRI. All patients referred to the MRI departments for examination of the breast. Clinical examination and full history were taken as well as written informed consent was assigned.

65 2.2 MRI machines used

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General Electric (Milwaukee, WIS, USA). The power of the magnet was 1.5 Tesla. Multiple array coils
were used; their length was 7 inches (12.7 cm).

70 2.3 Breast MRI protocols

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72 All patients were examined in prone position in double breast coil (multiple arrays). The localizer was 73 done into axial, sagittal and coronal, and all examinations done by using Gadolinium contrast materials, 74 routine and dynamic. T₁ weighted fast spin echo sequence (TR=125ms, TE=5.3 ms), in addition to T₂ weighted fast spin echo sequence (TR= 3740 ms, TE= 90 ms) in axial orientation. A bolus of gadolinium 75 76 (Gd-DTPA) (Magnevist, Schering AG Berlin, Germany) was injected manually and intravenously at a dose 77 of (0.1 mmol/kg) followed by a saline flush. Dynamic contrast T₁ weighted image, then performed using 78 gradient echo T₁ weighted image with fat suppression at the following time point at 1 min, 2 min, 4 min, 79 and 7 min. Post processing subtraction for the MRI image was obtained between the post contrast 80 imaging showing maximum enhancement and pre-contrast images (in the same axial plane), using the 81 software subtraction function. Quantitative analysis was done by placing the region of interest (ROI) at the 82 most enhanced part with the lesion result in automatically created time/ signal curve. The type of curve 83 (type 1, type 11, type 111), determine the type of tumors. Qualitative analysis of mammography and MRI 84 was done by three radiologists who were blinded to the clinical, operational and Histopathological 85 examination.

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87 2.4 MRI image interpretation and criteria for evaluating the presence of breast lesions

88 89 The shape of the mass smooth, irregular shape, crumpled, homogeneous or heterogeneous. In case of 90 lesion enhancement the corresponding non subtracted pre-contrast and post contrast images in each 91 time point was viewed together and lesions interpretation took place whether it is mass or non mass like 92 enhancement.

In case of mass enhancement evaluation was made in shape (regular or irregular), border (well defined,
 ill defined, speculated), pattern of enhancement (homogenous, heterogeneous, or ring enhancement),
 while in case of non-mass like enhancement, its distribution and enhancement were evaluated.

96 In DCE-MRI, the behavior of the mass was evaluated based on the percentage of the enhancement as

97 well as the shape of the time/signal curve and type of curve (type 1, type 11, and type 111).

98 3. RESULTS

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100 The results of this study were obtained from 254 patients 250 (98.4%) female and 4 male (1.6%), aged

- 101 between 15-78 years old as presented in Figure 1. Table 1 demonstrates MRI findings and
- 102 histopathological results cross tabulation.
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Fig. 1. Shows the female age group, according to tumors count.

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108 Table 1. Shows MRI findings and Histopathology result cross-tabulation

Histopathology	Normal Benign tumors		Irregular/Suspected Cancers.	Total
Normal	30	11	0	41
Benign	1	62	19	82
Malignant	0	17	114	131
Total	31	90	123	254

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110 Patients were examined by two types of magnetic resonance imaging; one was routine pulse sequences 111 and the other was dynamic contrast enhancement magnetic resonance imaging (DCE-MRI). The

sensitivity of MRI was (82.7%) and accuracy was (81.1%) as shown in Table 2.

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114 Table 2. The sensitivity, specificity and accuracy of MRI compared with other imaging modalities

Modality	Specificity (%)	Sensitivity (%)		Accuracy (%)
		Benign	Malignant	-
MRI	(73.2%)	(82.7%)	(82.6%)	(81.1%)
Ultrasound	(75.6%)	(68.0%)	(30.4%)	(48.8%)
Mammography	(73.2%)	(60.0%)	(37.7%)	(50.0%)

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116 T_1 and T_2 signal were same or no more different in normal breast tissue. In Table 3, T_1 with contrast, has 117 high signal in tumors, especially cancer (97.8%), this signal increase after contrast administration, and 118 when images subtracted the tumors is isolated from normal tissues, shape and other features so that 119 tumors can be diagnosed. Such findings are presented in Table 4, Figure 2, and Figure 3. Also, it was 120 found that T_2 has high signal in some benign tumors such as cyst, and duct ectasia (95.1%).

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122 Table 3. Shows T₁ with contrast and histopathology result cross-tabulation

Histopathology		Total		
	Hyper-signal	Hypo-signal	lso-signal	
Normal	3	15	23	41
Benign	17	39	19	75
Cancer	115	16	7	138
Total	135	70	49	254

123 124

125 Table 4. Shows image subtraction result and histopathology cross-tabulation

Subtraction	Histopathology			Total
	Normal	Benign	Malignant	
Normal	1	3	1	5
Homogeneous	40	42	12	94
Heterogeneous	0	26	113	139
ring enhance	0	4	12	16
Total	41	75	138	254

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UNDER PEER REVIEW



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Fig. 2. Shows signal intensity in fat suppression images.

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Quantitative measurement of kinetic curve type resulted in significantly higher diagnostic performance
 when compared with the qualitative assessment, that rapid wash (86.0%) is highly suggested of cancer,
 plateau (26.7%) cancer and persistent (1.6%) cancer as depicted in Table 5.



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 - Fig. 3. Shows signal intensity in Short T₁ inversion recovery (STIR) images.
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137 Table 5. Shows curve type in dynamic contrast enhancement MRI (DCE-MRI)

Curve type	Histopathology			Total
	Normal	Benign	Malignant	
Persistent	2	17	1	20
Plateau	1	13	16	30
Rapid	0	7	43	50
Total	3	37	60	100

138 4. DISCUSSION

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140 This study consisted of 254 patients with the aim to emphasis MRI protocols to characterize breast 141 tumors, using different pulse sequences, and compare it with histopathology findings in order to identify 142 the accuracy of MRI in detecting breast tumors. The result of this study revealed that the incidence of 143 breast cancer increased in all ages, but more so in women in the group (39-47) years (Figure 1). Risk 144 factors for incident include older age and family history. The sensitivity and specificity of MRI were 145 (82.6%) and (73.2%) respectively (Table 2). This result was in line with previous studies conducted in 146 ductal carcinoma, which also reveals the high sensitivity of MRI over mammography in detecting breast 147 tumors [10].

Fat suppression is commonly used in MR imaging to suppress the signal from adipose tissue or detect adipose tissue. However, this technique is not specific for fat, and the signal intensity of tissue with a long

- T_1 and tissue with a short T_1 may be ambiguous. Opposed-phase imaging is a fast and readily available technique [11]. The result of this study showed that breast cancer was more enhanced with fat suppression images (Figure 2), because this method suppressed the fat signal more potently and improved contrast and visibility of the breast lesions that embedded in fatty tissue [12].
- In short tau inversion recovery (STIR) sequences, T_2 and T_1 relaxation times additively contribute to the
- contrast; therefore, also considering the inherent fat suppression, contrast is extremely good, and tissue with long T_1 and long T_2 may appear very bright [13]. In this study breast cancer showed iso-signal intensity, this revealed the small contribution of short T_1 inversion recovery in enhancing breast cancer (Figure 2)
- 158 (Figure 3).

159 Regarding signal intensity, the study showed that breast cancer has high signal intensity on T_1 image 160 (Table 3), while it has hypo or iso-signal intensity on T_2 images. On T_2 weighted images, fat has 161 intermediate signal intensity. The signal intensity of remaining tissue depends on their water contents, 162 and increases from the fibrous element which very low signal to glandular and ductal element to cystic

163 lesions which have a very high signal intensity [14].

164 CE-MRI has been shown to be more sensitive than mammography in detecting DCIS. The study showed

- that most breast cancer cases have been enhanced, the result was in line with the study of Wiener et al, 2004 [15], it showed that the primary index lesions, the sensitivity of MRI was (100%) in predicting a breast malignancy and the specificity was (73.7%) in predicting benign lesions. MRI detected an additional 37 lesions, of which 23 were cancerous, beyond those suspected on mammography or
- 169 sonography [15].

170 The image subtraction technique was performed it showed that the cancer has heterogeneous features

(89.9%), and ring enhancement was clearly seen on (8.7%). This result in line with the previous studies
as speculated or irregular margin is suspicious for carcinoma where a smooth margin is more suggestive

173 of benign lesion [16].

DCE-MRI has been used to evaluate focal breast lesions (Table 5). Adding information derived from the kinetic curve type of the architectural features of a lesion, improves the specificity of breast MRI [17]. By categorizing the type of the enhancement curve either as an absolute change in percentage enhancement, significantly greater values were seen compared with the qualitative method. In this study only 100 patients were selected for DCE-MRI, it revealed that most cases of cancer represented on type 111 curve or rapid wash out. However, quantitative measurements of kinetic curve type resulted in

- 180 significantly higher diagnostic performance and increasing specificity of MRI.
- 181

182 **5. CONCLUSION**

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184 In conclusion, the accuracy of MRI in this study was more than other imaging modalities in characterizing 185 breast abnormalities and tumors. Therefore, it offers a new method to detect breast cancer in its early

- 186 stage, and help improve the survival rate.
- 187

188 CONSENT

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All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

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195 ETHICAL APPROVAL

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All authors hereby declare that all experiments have been examined and approved by the appropriate
 ethics committee and have therefore been performed in accordance with the ethical standards laid down
 in the 1964 Declaration of Helsinki.

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