__Original Research Article__

Accuracy of Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI) in Detecting Breast Tumors

ABSTRACT

Aims: To evaluate the accuracy of dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) in characterizing 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 medical centers in Khartoum, Sudan between June 2014 and July 2016.
Methodology: Patients were examined using two sequences of MRI; routine-MRI and 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 DCE-MRI were (82.6%) and (73.2%) respectively. In addition, breast cancer was more enhanced with fat suppression images. Image subtraction technique showed that breast cancer has heterogeneous features (89.9%), and ring enhancement was clearly seen on (8.7%).
Conclusion: The accuracy of MRI in this study was more than other imaging modalities in characterizing breast tumors. Therefore, it offers a new method to detect breast cancer in its early stage, and help improve the survival rate.

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

1. INTRODUCTION

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 [2].
Different methods have been used in the diagnosis of breast cancer, including self-examination and clinical examination, mammography, ultrasound, magnetic resonance imaging (MRI) modality, follow up methods and biopsy [2]. In certain situation, clinical examination, mammography, and ultrasonography have some limitations, either due to factors in the breast parenchyma such as dense breast in young females, post-operative changes or effect of irradiation or factors in modality itself, such as the inability of mammography to demonstrate deep part of the breast and operator dependency of ultrasound [3].
In the last few years, MRI has been introduced as a promising method for diagnosis of breast neoplasms particularly when dynamic contrast gadolinium (Gd) enhancement studies are used [4]. Dynamic contrast enhanced MRI (DCE-MRI) and diffusion weighted MRI (DW-MRI) have shown potential for improving the early assessment of tumor response to therapy. DW-MRI is a high sensitive and DCE-MRI is a high specific modality in predicting pathological response to neoadjuvant chemotherapy (NAC) in breast cancer. The combined use of DW-MRI and DCE-MRI has the potential to improve the diagnostic performance in monitoring NAC [5].
This study aimed to evaluate the accuracy of DCE-MRI in characterizing breast tumors, and to compare the findings with the other diagnostic modalities and histopathological findings.

2. MATERIAL AND METHODS

2.1 Patient samples

The study was conducted in 254 patients, 250 were females (98.4%) and 4 were males (1.6%).The mean age of all patients was 47 years, age range between 15-78 years. All patients were examined by DCE-MRI. Clinical examination and full history were taken as well as written informed consent was obtained. Sudanese patients who were 15 years old or older, with proven breast cancer were eligible for recruitment. Exclusion criteria were absolute contraindications to MRI, pregnancy or breast feeding, severe renal failure, known hypersensitivity to gadolinium chelates, inclusion in other clinical trials during the month before enrollment, and clinical status that would limit data reliability.

2.2 Breast mammography procedure

Mammography was performed with at least two views per breast (medio-lateral oblique and cranio-caudal views) using a low radiation dose digital mammography system (Mammomat, Siemens, Germany). Additional views or spot compression views were obtained where appropriate.

2.3 Breast ultrasound procedure

Breast ultrasound was performed using 7.5-13 MHz probes (high resolution General electric (GE) medical system, logic 5 expert, Sony Corporation, Japan); the entire breast was systematically examined by the physician who interpreted the study.

2.4 Breast biopsy procedure

Breast fine needle aspiration biopsy under the guidance of ultrasound, was performed while the patient lying on back on the examination bed in the ultrasound room. The patient's upper body undressed, with one arm above the head on the pillow in a comfortable position. One physician applied ultrasound gel on the breast and the ultrasound transducer (7.5-13 MHz) slowly moved across the breast to show and identify the lesion. The needle passed through the skin and into the lesion guided by the ultrasound images. Both local anesthetic and antiseptic liquids were used as the needle is inserted. Less than 1cm forward and backward, gentle movements with the needle to collect cells or, if the lesion is a cystic in nature, fluid may be collected. Two or three separate samples are usually taken in this way to ensure a good sample has been obtained.

2.5 Breast MRI protocols

The breast MRI examination was performed using 1.5 Tesla (General Electric, Milwaukee, WIS, USA) MRI scanner using phased-array breast surface coil, with patients lying in prone position. The MRI protocol included an echo-planar diffusion weighted (DW) sequence; for imaging with this sequence the phased-array breast coil was converted to operate in a linear mode to accommodate the high acquisition speeds (~ 80 kHz).

The MRI protocol consisted of the following sequences: 1) Coronal T_1-weighted spin echo sequence was carried out for localization purpose and followed by plain sequences using T_1-weighted fast spin echo sequence (TR=125msec, TE=5.3msec), in addition to T_2-weighted fast spin echo sequence (TR=3740msec, TE=90msec) in axial orientation. A bolus of gadolinium (Gd-DTPA) (Magnevist, Schering AG Berlin. Germany) was injected manually and intravenously at a dose of (0.1 mmol/kg) followed by a saline flush to ensure that contrast enhanced images could be obtained immediately after contrast agent injection, 2) Dynamic contrast T_1-weighted images, then performed using gradient echo T_1-weighted image with fat suppression at the following time point at 1 min, 2 min, 4 min, and 7 min, 3) Post processing subtraction for the MRI image was obtained between the post contrast imaging showing maximum enhancement and pre-contrast images (in the same axial plane), using the software subtraction function, and 4) Quantitative analysis was done by placing the region of interest (ROI) at the most enhanced part with the lesion result in automatically created time/signal curve. The type of curve (type 1, type 11, type 111), determine the type of tumors. Qualitative analysis of mammography, ultrasound, and breast MRI was done by three radiologists who were blinded to the clinical, operational and histopathological examination.

2.6 Statistical analysis

In this prospective cohort study, data were initially summarized in a form of comparison tables and graphs. Accuracy was represented using the terms sensitivity, specificity, and overall accuracy. All statistical calculations were done using a computer program of the standard Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 20 for windows. As *P*-value is a function of the observed sample results relative to a statistical model, which measures how extreme the observation is, a *P*-value ≤0.0001 was considered to be significant.

3. RESULTS

The results of this study were obtained from 254 patients; 4 (1.6%) males and 250 (98.4%) female, aged between 15-78 years old as presented in Figure 1 below. Table 1 demonstrates MRI findings and histopathological results cross tabulation. The histopathological findings in 74 (29%) benign breast lesions were 55 (21.7%) cases of fibroadenoma, post operative scar presents in 16 (6.3%) women, while the incidence of diabetic mastopathy was found in 3 (1%) out of the 74 (29%) benign cases. In addition, histopathology manages to detect 6 (2.4%) cases of tubular carcinoma, invasive lobular carcinoma of 18 (7.1%) cases, 5 (2%) women present with medullary carcinoma, and ductal carcinoma in situ (DCIS) incidence was about 107 (42.1%%) conditions, out of 136 (54%) malignant conditions as demonstrated in Table 1.

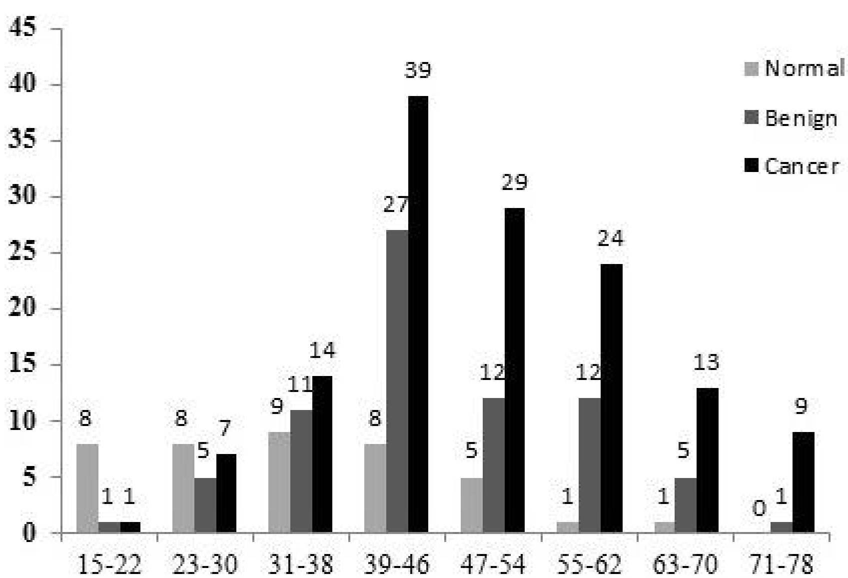

Fig. 1. The distribution of females' age, according to tumors count.

Table 1. MRI findings and histopathology result cross-tabulation

Histopathology	MRI examination finding			Total
	Normal	Benign tumors	Irregular/Suspected Cancers	
Normal	44 (17%)	0 (0%)	0 (0%)	44 (17%)
Benign	0 (0%)	74 (29%)	0 (0%)	74 (29%)
Malignant	0 (0%)	0 (0%)	136 (54%)	136 (54%)
Total	44 (17%)	74 (29%)	136 (54%)	254 (100%)

The sensitivity of DCE-MRI in detecting breast lesions was (82.7%) and the accuracy was (81.1%), when compared to other diagnostic modalities as mammography or ultrasonography as shown in Table 2.

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

Modality	Specificity (%)	Sensitivity (%)		Accuracy (%)
		Benign	Malignant	
DCE-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%)

In Table 3, T_1 with contrast presented a high signal in malignant breast lesions (97.8%). This signal increased after contrast administration. In addition, there was an increase in the signal, when the images that subtracted the tumors were isolated from normal tissues. Such findings were presented in Table 4, and Figure 2. Also, it was found that T_2 has high signal in some benign tumors such as cyst, and duct ectasia (95.1%).

Table 3. T_1-weighted with contrast and histopathology result cross-tabulation

Histopathology	T_1 with contrast			Total
	Hyper-signal	Hypo-signal	Iso-signal	
Normal	6	15	23	44
Benign	17	38	19	74
Cancer	114	16	6	136
Total	137	69	48	254

Table 4. 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 enhances	0	4	12	16
Total	41	75	138	254

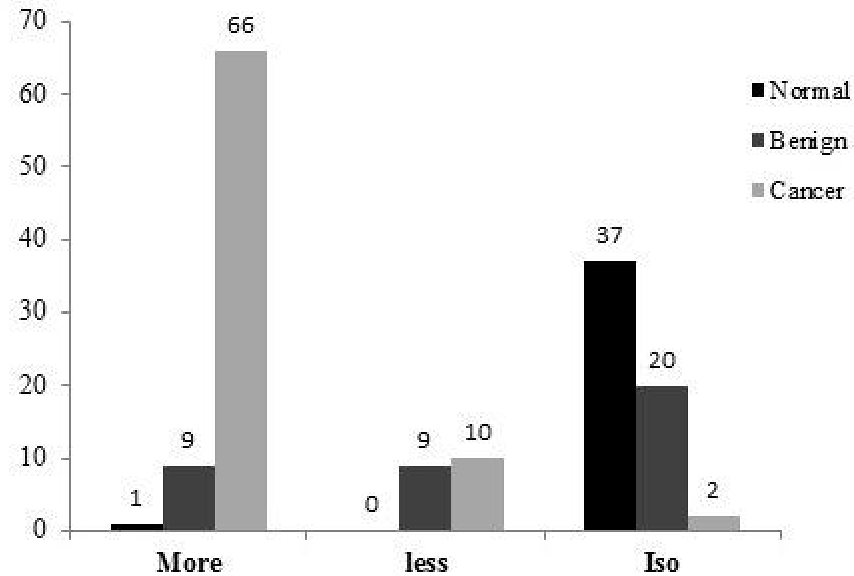

Fig. 2. Signal intensity in fat suppression images.

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

Table 5. Shows curve type in 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

A highly statistically significant difference (*P* <0.0001) was found between routine-MRI and DCE-MRI in the detection of benign breast lesions as shown in Table 6. Where routine-MRI manages to detect 55 (21.7%) of benign breast lesions, in contrast DCE-MRI help effectively in a diagnoses of 74 (29.1%) of benign breast masses. While in the detection of malignant breast lesions, DCE-MRI manage to diagnose 136 (53.5%) of malignant breast lesions in the sample, compare to 87 (34.3%) malignant breast lesions diagnosed by the aid of routine-MRI (*P* <0.0001) as presented in Table 6.

Table 6. Shows the difference in the outcome of routine-MRI and DCE-MRI in breast lesions

Benign lesion diagnosed by routine-MRI	**Benign lesions diagnosed by DCE-MRI**	**Total No. of cases**	***P*-value**
55 (21.7%)	74 (29.1%)	254 (100%)	<0.0001
Malignant lesion diagnosed by routine-MRI	**Malignant lesions diagnosed by DCE-MRI**	**Total No. of cases**	***P*-value**
87 (34.3%)	136 (53.5%)	254 (100%)	<0.0001

4. DISCUSSION

This study consisted of 254 patients, and it was designed with an aim of evaluating the accuracy of DCE-MRI in characterizing breast abnormalities and tumors, in comparing to other diagnostic modalities and histopathological findings. The result of this study revealed that the incidence of breast cancer increased in all ages, especially in women belong to the group (39-47) years (Figure 1). Risk factors for incident include older age and family history. The sensitivity and specificity of DCE-MRI were (82.6%) and (73.2%) respectively (Table 2). This result was in line with a previous study conducted in ductal carcinoma, which also reveals the high sensitivity of MRI over mammography in detecting breast tumors [6].
The results 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 [7]. Regarding signal intensity, the study showed that breast cancer has high signal intensity on T_1 image (Table 3), while it has hypo or iso-signal intensity on T_2 images. On T_2 weighted images, fat has intermediate signal intensity. The signal intensity of remaining tissue depends on their water contents, increase of fibrous element which have low signal compared to glandular, ductal element, and cystic lesions which have a very high signal intensity [8].
Also, this study showed that most breast cancer cases have been enhanced, such result was in line with the study of Wiener et al, 2004 [9], where it showed that in 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 sonography [9].
The image subtraction technique was performed, and it showed that the cancer has heterogeneous features (89.9%), and ring enhancement was clearly seen on (8.7%) of cases. This result in line with the previous studies as a speculated or irregular margin is suspicious for carcinoma, while a smooth margin is more suggestive of benign lesion [10].
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 [11]. 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 all 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 significantly higher diagnostic performance and increasing specificity of MRI.
It was stated that DCE-MRI imaging has high negative predictive value in excluding breast cancer, so it plays a role in the evaluation of selected clinical and imaging findings of the breast, especially when biopsy is not technically feasible. Case selection is very important in ensuring the efficacy of this use of MR imaging because of potential false-positive and false-negative results [12]. In our study the overall sensitivity of DCE-MRI, ultrasound, and mammography was 82.7%; 82.6%, 68.0%; 30.4% and 60.0%; 37.7% of both benign and malignant breast lesions respectively (Table 2). Their specificity was 73.2%, 75.6%, and 73.2%, respectively (Table 2). DCE-MRI was the most sensitive imaging method for detection breast cancer, but with limited specificity due to overlap in features of benign and malignant lesions.
The main additional diagnostic value of DCE-MRI relies on detecting foci of multifocal, multicentric or contra-lateral disease unrecognized on conventional assessment (physical examination, mammography and ultrasound); recognition of invasive components in DCIS; assessing the response to NAC; detecting an occult primary breast cancer in patients presenting with metastatic cancer in axillary nodes; and detection of cancer in dense breast tissue [13].
DCE-MRI is an emerging imaging method to enable the depiction of physiologic alterations and to assess tumor angiogenesis [14]. Some of the most powerful diagnostic criteria for the differentiation of benign and malignant tumors belong to internal enhancement of a focal mass [8]. The evaluation of the enhancement from the quantitative and qualitative points of view is in fact the assessment of vascularization of the lesion. The attribute of angiogenesis is used in malignant lesions which are often too small to be proved by another imaging method [14]. In this study non enhancing internal septations were only found in benign lesions proved to be fibroadenomas by histopathology. Kuhl et al, 1999 [8] reported that dark septation if present within a lobular or oval mass are typical of fibroadenomas. Imamura et al, 2010 [15] found that malignant non mass lesions tended to show either segmental or branching ductal distribution, he also reported that using the enhancement pattern in differentiation

between benign and malignant lesions is often difficult with non mass like enhancement as there is no standarized method for interpreting them. In this study authors encountered 18 lesions of non mass like enhancement, all of them proved to be malignant and proved pathologically to be invasive lobular carcinoma.

There are, however, limitations to DCE-MRI evaluation of residual disease after NAC. MRI tends to overestimate the size of residual disease and, because of the antiangiogenic effects of certain chemotherapeutic agents on tumor, the ability of DCE-MRI to evaluate lesion enhancement can be significantly decreased [15]. Among the limitations of breast MRI are its higher cost, longer examination time, and lower availability compared with mammography and ultrasound.

5. CONCLUSION

In 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.

CONSENT

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.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee.

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