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Comparison of Sensitivity and Specificity of DWIBS and Contrast Enhanced T1Wi Sequences in Characterization of Suspicious Mammography Lesions

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ABSTRACT

Background: Diffusion Weighted Imaging with Back-ground Suppression is a new technique which uses the same concept of diffusion weighted imaging yet has the privilege of back-ground suppression and acquisition at a wider range of b-values hence increasing sensitivity and specificity.

Objective: to determine the accuracy of DWIBS MR imaging in comparison to the DEC MR imaging in characterizing suspicious mammography lesions.

Patients and Methods: twenty patients were included in the study, all with suspicious breast lesions from Ain-Shams University mammography clinic. A cross-sectional study was held where all the patients under-went MRI breast protocol which included DCE and DWIBS sequences. The MRI of all the patients was read by two expert radiologists blinded to each other's opinion. Biopsy was then done for histo-pathological correlation. The results were statistically analyzed.

Results: seventy percent of the patients included in our study had malignant lesions and 30% had benign lesions. Both DWIBS and DCE showed comparable efficacy of 90% and 95% respectively.

Conclusion: DWIBS can be used as an adjunct to DCE breast MRI improving its sensitivity and specificity. It can as well be used instead of DCE sequences in cases of renal impairment.

Keywords: Invasive ductal carcinoma (IDC), Invasive lobular carcinoma (ILC), Ductal carcinoma insitu (DCIS), Lobular carcinoma insitu (LCIS), DWIBS (Diffusion weighted imaging with back-ground suppression), DCE (Dynamic contrast enhanced)

INTRODUCTION

Being the most common invasive cancer to affect females worldwide, screening aiming at early detection and thereby improving outcomes of breast cancer has always been an issue of concern [(1)].

For decades conventional X-ray mammograms have been widely used for this purpose. This however resulted in many unnecessary biopsies, since almost 50% of the biopsies following suspicious mammograms were found to be negative. The anticipation associated with waiting for unnecessary biopsies after query mammography findings has created a real need for more informative imaging techniques [(2,3,6)] .

To meet this growing need, MR imaging of the breast has become a region of interest for researchers worldwide [(3)].

Diffusion weighted MR imaging, which depends on the micro structural diffusivity of water between the cells, has been employed to help characterize different breast lesions. Diffusion weighted imaging has proved high sensitivity and specificity in this insight, yet it must be combined with administration of contrast enhanced imaging and the acquisition of dynamic contrast enhanced MR images for proper characterization [(2,4,5)] .

DCE-MR imaging of the breast helps depict malignant lesions by showing their pathological vascularization. The kinetics of contrast enhancement depends upon the capillary permeability, micro vascular density and diffusivity. These factors affect the rate of initial contrast uptake, wash-out as well as the heterogeneity of the lesion.

Combining the pattern of contrast enhancement with the morphologic features allows high sensitivity and specificity [(7,8)] .

The long examination times as well as the need for intravenous contrast were found to be practical limitations of the DCE-MRI of the breast. This is especially appreciated in patients with contra-indications to MR contrast material injection [(2,4,5)] .

A newly introduced MRI sequence DWIBS, which is the abbreviation of Diffusion Weighted Imaging with Background Suppression, allows the acquisition of volumetric diffusion weighted images with high lesion-to-background contrast, hence making the use of contrast material unnecessary. DWIBS is said to outweigh the conventional DW imaging due to its short time of acquisition as well [(2,4)] .

The use of DWIBS approach is thought to decrease the rate of unnecessary biopsies from false mammography results without the need for

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a lengthy MRI procedure or the need for IV contrast administration [(2)].

AIM OF THE STUDY

The purpose of this study was to determine the accuracy of DWIBS MR imaging in comparison to the DEC MR imaging in characterizing suspicious mammography lesions.

PATIENTS AND METHODS

The study will include 20 patients with query mammography findings referred from Ain Shams oncology hospital and outpatient breast clinics

1- Full history taking.
2- Full clinical examination.
3- Laboratory investigations including renal profile.
4- The selected patients with query mammography findings will be imaged a follows:

- After the mammography is done revealing query findings but before the biopsy is taken. In all patients both DWIBS and DEC MRI sequences are going to be taken.

5- The results of MRI imaging will be compared to the biopsy pathology.

Inclusion criteria

a. Patients with query mammography findings (BIRADs IV, V).
b. Females.
c. No age predilection.

Exclusion criteria

a. Patients known to have contraindications for MRI, e.g. an implanted magnetic device, pacemakers or claustrophobia.
b. Patients with bad general condition needing life support and those with severe hepato-renal disease.

Patient preparation:

a. Pre-procedural assessment of serum creatinine.
b. Detailed explanation of imaging procedure.
c. Obtaining an informed consent.
d. Administration of 1 ante-cubital intravenous catheter.

Machine used:

The study will be done in MRI unit at Ain shams university hospitals on Philips machine Achieva 1.5 Tesla.

Patient position: The patient is positioned prone, using a special breast coil, on the MRI table.

Procedure duration: The study takes about 30 – 40 minutes.

METHOD

a. MRI study will be performed on a 1.5 Tesla system.
b. Field of view: AP 325.
c. Slice thickness: 2 mm.
d. Morphological sequences will be performed in multiple projections, including pre-contrast axial T1 WIs (TE =10 ms, TR = 538 ms), axial T2 WIs (TE =120 ms, TR =4130 ms), axial T2 STIR (TR/TI = 6637/150, TE = 55 ms). All these sequences are single shot spin echo with flip angle 90^{o}.
e. Axial echo-planner DWI study will be performed for all cases with 3 b-values. ADC values will be measured for all lesions.
f. In addition, Gadolinum (0.1 mmol/kg) will be administered by injector with flow rate 2-3 ml/sec followed by saline injection of 15 ml. The post contrast images will be T1 fat suppressed, and subtracted images will be added.
g. Axial echo-planner DWIBS images will be taken in all patients.

Risks and complications:

Risks of developing complications from contrast media:

a. Nephrogenic systemic fibrosis (NSF).
b. Nausea, vomiting, headache, hives, itching (uncommon).
c. Treatment in cases of risks and complications:
d. Immediate dialysis for patients with NSF.
e. If allergy from contrast occurs (uncommon) it will be managed by using a plastic cannula for IV access & maintain IV access for 30 minutes. Emergency drugs (such as corticosteroids, antihistaminics and adrenaline) will be administered.

Statistical Analysis

IBM SPSS statistics (V. 24.0, IBM Corp., USA, 2016) was used for data analysis. Data were expressed as Mean± SD for quantitative parametric measures in addition to Median and Percentiles for quantitative non-parametric measures and both number and percentage for categorized data.

The following tests were done:

1. Comparison between two independent mean groups for parametric data using Student t test.

2. Comparison between two independent groups for non-parametric data using Wilcoxon Rank Sum test.
3. Chi-square test to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data.

The probability of error at 0.05 was considered significant, while at 0.01 and 0.001 are highly significant.

4. Diagnostic validity test: It includes:

a. The diagnostic sensitivity: It is the percentage of diseased cases truly diagnosed (TP) among total diseased cases (TP+FN).

b. The diagnostic specificity: It is the percentage of non-diseased truly excluded by the test (TN) among total non-diseased cases (TN+FP).

c. The predictive value for a +ve test: It is the percentage of cases truly diagnosed among total positive cases.

d. The predictive value for a -ve test: It is the percentage of cases truly negative among total negative cases.

e. The efficacy or the diagnostic accuracy of the test: It is the percentage of cases truly diseased plus truly non-diseased among total cases.

RESULTS

- 20 patients were included in the study, all of which were females (100%).
- Their ages ranged from 25 to 58 years with a median age of 38 years.
- All the patients had suspicious breast lesions on mammography (BI-RADS VI and BI-RADS V).
- The sizes of the lesions largely varied between 0.5 cm^3 to 30 cm^3 (calculated as a volume: APxCCxObliquex0.5) with a median of 7.4 cm^3.
- Out of the 20 patients, 14 were histo-pathologically proven to have malignant lesion (all of which were IDC) (70%) and 6 were proven to be benign (30%).

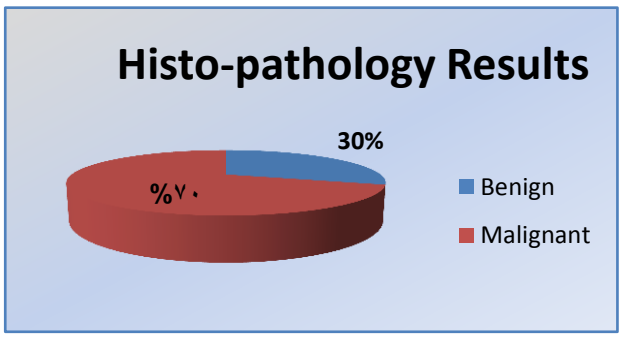

Fig.1 *Illustration of the percentage of benign and malignant lesions.*

- One of the patients visited the out-patient clinic complaining of discomfort (5%), one with nipple discharge (5%), one for heaviness (5%), six patients came for screening (30 %) and 11 complained of a palpable lump (55%).
- Out of the 20 patients, 8 (40%) had positive family history for breast cancer and 12 (60%) had negative family history of breast cancer in the first degree relative.

On contrast enhanced images, all the fourteen malignant lesions showed suspicious enhancement kinetics (type II and type III kinetic curves) and were labeled "positive" (100%), while 1 of the benign lesions showed suspicious enhancement kinetics (16.7%).

There is highly significant increase in the incidence of suspicious contrast enhancement patterns with malignant lesions ($p<0.001$)

DCE-MRI showed:

- Sensitivity: 100%.
- Specificity: 83.3 %.
- Positive predictive value (PPV): 100%.
- Negative predictive value (NPV):93.3%.
- Efficacy: 95%.

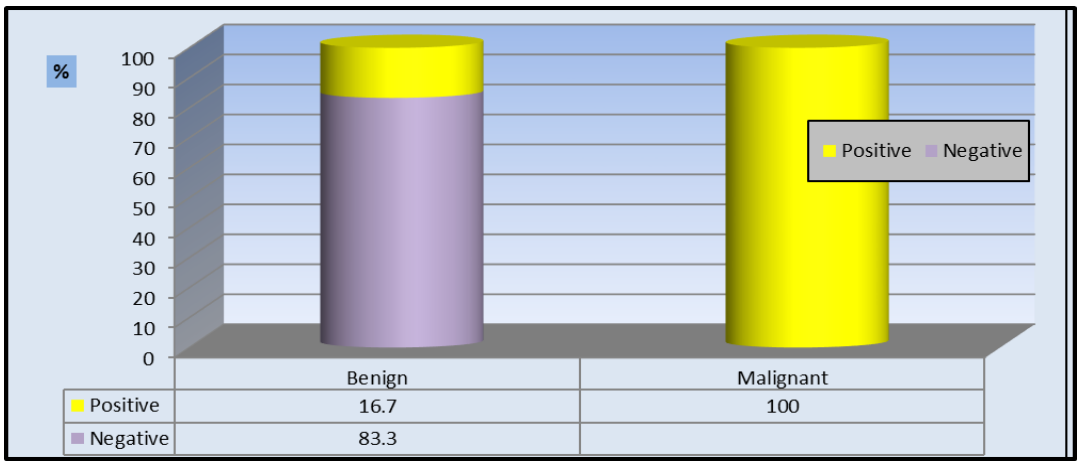

Fig. 2 *Illustration of the contrast enhancement patterns in relation to histo-pathology.*

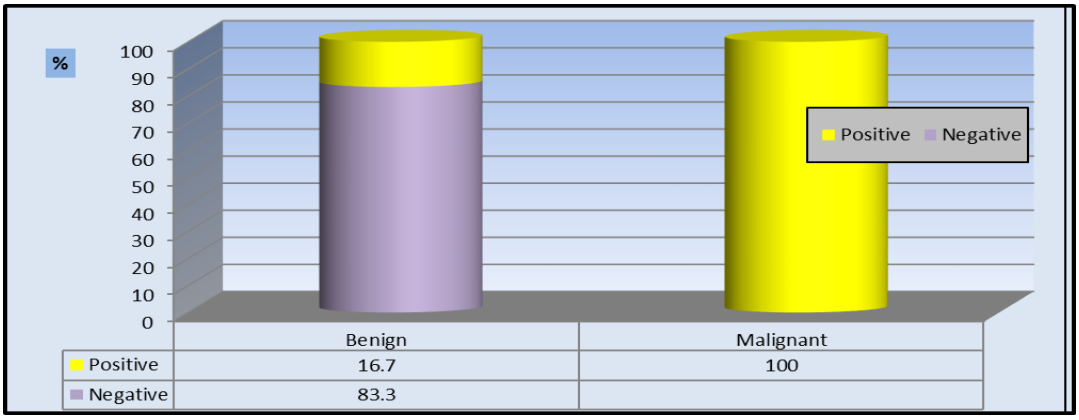

Fig. 2 Illustration of the contrast enhancement patterns in relation to histo-pathology

On DWIBS imaging, thirteen out of the fourteen patients showed qualitative diffusion restriction and malignant criteria (92.9%) and one showed no restriction (7.1%). Out of the 6 patients with benign histopathologies, five showed no diffusion restriction or any suspicious criteria (83.3 %) while only one showed diffusion restriction (16.7%). There is highly significant increase in the incidence of diffusion restriction on DWIBS imaging in malignant lesions. ($p<0.001$)

DWIBS showed:

- Sensitivity: 92.9%.
- Specificity: 83.3%.
- Positive predictive value: 92.9%.
- Negative predictive value: 83.3%.
- Efficacy: 90%.

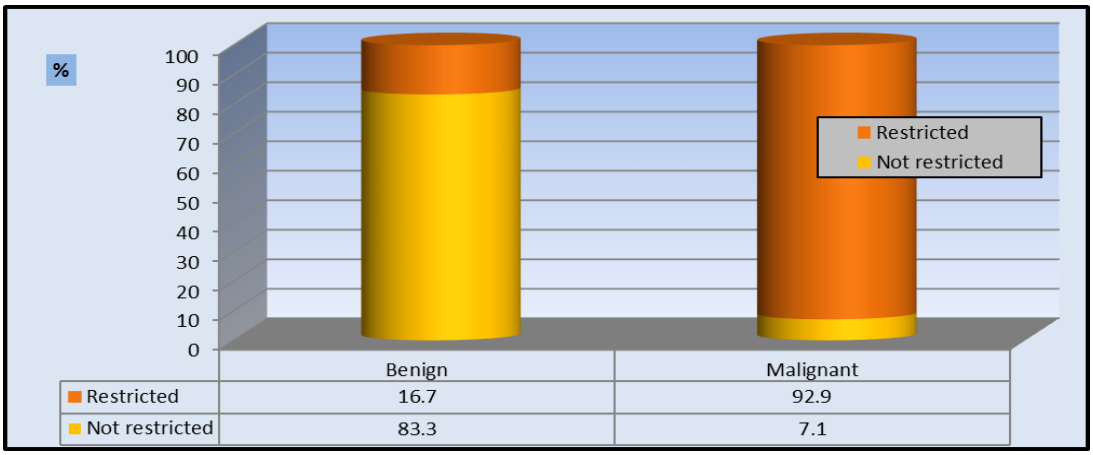

Fig. 3 Illustration of the relation-ship between restriction on DWIBS images and histo-pathology.

The ADC maps revealed highly significant decrease in the malignant lesions when compared with the benign ($P<0.001$). Diagnostic validity test showed that the best cut-off value to differentiate benign from malignant lesions was 1.28x 10^-3; at which:

- Sensitivity= 92.9%.
- Specificity= 83.3%.

DISCUSSION

To obtain DCE images, contrast material is injected through the venous system of the patient after which a series of images is taken over 2-3 minutes to monitor the kinetics of contrast uptake within a lesion. The rate of contrast uptake and wash-out as described before in the review of literature, largely depends on micro-vasculature and permeability of cell-membranes which vary greatly according to the nature of the lesions; malignant tumors being more vascular and there by showing rapid initial uptake and slow wash-out [(9)].

In our study, DCE MRI showed overall efficacy of 95% when compared to hito-pathological results. It showed sensitivity of 100%; ability to detect all malignant lesions. Specificity of the DEC-MRI however was 83.3 %; ability to distinguish non-malignant lesions was 83%. It showed NPV of 93 % and PPV of 100%. **Bickelhaupt *et al.*** [(2)], in a study published in 2016 conducted over 50 patients with

suspicious breast lesions reported results similar to ours with a sensitivity of 85% and specificity of 90%. Another study published in 2014 by Marco Moschetta ***et al.*** [(10)] showed comparable results with sensitivity of 100% and specificity of 80%.

The false-positive result we have in our study is a part of what has long been criticized about DCE-MRI. False-positive results commonly occur due to high back-ground enhancement of breast tissue in a special time of the menstrual cycle. Back-ground enhancement may give a mass like distribution and hence could be mistaken for a suspicious lesion [(9)].

In the study conducted by Sebastian Bickelhaupt ***et al.***[(2)], it has been suggested that by adding DWIBS to DCE-MRI sequences this will increase the rate of positive biopsies as it will increase the specificity. In their study, DWIBS showed sensitivity of 92% and specificity of 94%. If only DWIBS positive patients were biopsied they assume, biopsy positive for malignancies will increase.

In our study however, DWIBS did not have a superior result to DCE-MRI as regards the specificity or the sensitivity. DWIBS showed sensitivity of 93% and specificity of 83%, NPV of 83% and PPV of 93%. The over-all efficacy of DWIBS was about 90%.

Though the sensitivity and specificity of DWIBS and DCE-MRI are comparable, the lower sensitivity and specificity are attributed to known fallacies of DW imaging and DWIBS thoroughly discussed in literature. False negative results of DWIBS commonly occur due to lack of restriction in cystic tumors or necrotic tissue [(9)] which was the case in our study. The false positive results seen with DWIBS are attributed to benign fibro-adenomas with high fibrous tissue content restricting the process of free water molecule diffusion within the mass [(9)]. The DWIBS derived ADC map has shown a highly significant decrease in the mean ADC value associated with malignant lesions. The cut-off value obtained from our study was 1.28x10^-3 at which it showed sensitivity of 93% and specificity of 83%.

Our cut-off ADC value was comparable to cut-off values present in literature. Sebastian Bickelhaupt ***et al.*** [(2)], had a cut-off value of 1.30x 10^-3 and Moschetta ***et al.*** [(10)] had a cut-off value of 1.44x10^-3.

CONCLUSION

DWIBS can be used as an adjunct to DCE breast MRI improving its sensitivity and specificity. It can as well be used instead of DCE sequences in cases of renal impairment.

Limitations of The Study: Small sample size of the patients so our results need to be further assessed on a larger sample.

- All of the histo-pathologies encountered in our study were infiltrative ductal carcinoma or fibro-adenoma and hence the results cannot be generalized for other malignant or benign pathologies.
- Ratio of benign lesions to malignant lesions was relatively small so behavior of benign lesions on DWIBS was not adequately evaluated.

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