THE DIAGNOSTIC ACCURACY OF UN-ENHANCED BREAST MRI (STIR, T2W-TSE AND DWIBS) COMPARED TO CONTRAST ENHANCED MRI IN DETECTION AND CHARACTERIZATION OF SUSPICIOUS BREAST LESIONS

Mai Eid A. El Ghannam 1, Sahar Mohammed El Feky 2, Mona Ali Abdel-Wahed 3, Asmaa Magdy M. Salama 4

1Radio-diagnosis specialist, Department of Diagnostic and Interventional Radiology, Faculty of medicine, Ain Shams University, Cairo, Egypt.
2Professor of Radio-diagnosis, Department of Diagnostic and Interventional Radiology, Faculty of medicine, Ain Shams University, Cairo, Egypt.
3Lecturer of Radio-diagnosis, Department of Diagnostic and Interventional Radiology, Faculty of medicine, Ain Shams University, Cairo, Egypt.
4lecturer of Radio-diagnosis, Department of Diagnostic and Interventional Radiology, Faculty of medicine, Ain Shams University, Cairo, Egypt.

ABSTRACT

Background: The aim of this retrospective study is to assess the role of STIR, T2-weighted TSE and DWIBS sequences for detecting and characterizing breast lesions and to compare unenhanced (UE)-MRI results with dynamic contrast-enhanced (DCE)-MRI. Diffusion weighted imaging with background suppression MR mammography (DWIBS-MRM) is a new MRI technique, which requires no contrast, may provide a safe, non-invasive method for resolving suspicious breast lesions.

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 95% and 97% respectively.

Conclusion: DWIBS sequence is a safe (no ionizing radiation, no contrast media), rapid and highly sensitive imaging technique for detection and characterization of breast lesions. DWIBS is recommended as an alternative to DCE-MRI in patients who cannot tolerate the contrast and as an adjunct to improve the specificity in patients with no contraindications to intra-venous contrast administration.

Keywords: Breast cancer-DWIBS- Suspicious breast lesions-Accuracy.

I. BACKGROUND

Breast cancer is the most common neoplasm in women worldwide and one of the leading causes of cancer-related death in women. Early detection of breast cancer is considered to be an essential milestone in controlling breast cancer, with early diagnosis being crucial in determining the choice of therapy, as well as disease prognosis (Vercher et al., 2015).

Conventional X-ray mammogram has been widely used for screening of breast cancer, resulting in many unnecessary breast biopsies. Since almost 50% of these biopsies were found to be negative, the need for more informative imaging techniques become necessary (Jens and Daniel, 2014).

Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI) represents the most sensitive technique for breast cancer detection. However, major limitations are represented by its specificity and by the injection of contrast material which increases examination time, costs and may lead to various reactions as well as nephrogenic systemic fibrosis syndrome in patients with impaired renal function (Telegrafo et al., 2015).
Efforts have been made for further improvement of the diagnostic accuracy of DCE-MRI in characterization of breast masses by the introduction of Diffusion weighted imaging (DWI). DWI is a non-contrast MRI technique, sensitive to the random motion of water molecules in tissues. Using the apparent diffusion coefficient (ADC) as a quantitative imaging biomarker to differentiate malignant from benign lesions with high sensitivity and specificity (Horvat et al., 2018).

In 2004, Takahara et al. developed and introduced a DWI technique that used a short TI inversion recovery (STIR)–echo planar imaging (EPI) sequence and free breathing to screen for malignancies in the whole body. This technique was named DWIBS, which stands for diffusion-weighted whole body imaging with background body signal suppression.

DWI potential has been improved by diffusion-weighted imaging with background body signal suppression (DWIBS) which has proven to be more accurate than DWI in detecting breast lesions. Besides, fat suppression allows increasing the detection rate of glandular lesions by using free-breathing scans (Moschette et al., 2014).

The biologic information provided by DWI and DWIBS images combined with morphological and signal intensity data of STIR (Short TI Inversion Recovery) and T2W TSE (T2weighted Turbo Spin Echo) can be used for characterization of breast lesions without the injection of contrast material (Telegrafo et al., 2015).

The use of DWIBS approach is thought to decrease the rate of unnecessary biopsies from false mammographic results without the need for a lengthy MRI procedure or the need for IV contrast administration (Bickelhaupt et al., 2016).

AIM OF THE WORK: is to assess the role of STIR, T2-weighted TSE and DWIBS sequences for detecting and characterizing breast lesions and to compare unenhanced (UE)-MRI results with contrast-enhanced (CE)-MRI and histological findings, having the latter as the reference standard.

II. METHODS

Participants:
The study included 43 patients with suspicious breast masses diagnosed by clinical examination or by sonomammography. All included patients were recruited from the outpatient clinic and surgical department, they subjected to the following:

- Full history taking.
- Full clinical examination by the referring clinician.
- Laboratory: serum creatinine assay.
- MRI examination using dedicated breast coil. In all patients both DWIBS and DEC MRI sequences are going to be taken.
- Correlation with histopathological results obtained from ultrasound guided core needle biopsy.

Inclusion criteria: Adult females more than 18 years old, with suspicious breast masses detected either clinically or by sonomammography (BI-RADS III, IV and V).

Exclusion criteria: MRI examination contraindications (e.g. presence of pacemakers, ferromagnetic vascular clips, and ocular implants), people who are not suitable for prone positioning (e.g. obese and claustrophobic patients), and patients with elevated serum creatinine level more than 1.8 mg/dl.

Methods:
This study was conducted in MRI unit on Philips machine Achieva 1.5 Tesla during the period from 2017 and January 2020 after the approval of the institute ethics committee.

Patient preparation:
- Pre-procedural assessment of serum creatinine.
- Detailed explanation of imaging procedure.
- Obtaining an informed consent.
Procedure:
- Patients are placed prone on MRI coil.
- Bilateral breast images will be acquired.
- Field of view: AP 325.
- Slice thickness: 2 mm.
- Morphological sequences were 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°.
- Axial echo-planner DWI study was performed for all cases with 2 b-values. ADC values were measured for all lesions.
- Gadolinium (0.1 mmol/kg) was administered by injector with flow rate 2-3 ml/sec followed by saline injection of 15 ml. The post contrast images was T1 fat suppressed, and subtracted images were added.
- In addition to the routine protocol, axial echo-planner DWIBS images were taken after the Contrast-enhanced magnetic resonance imaging (CE-MRI).
- After MR examination, histological examination provided by US-guided core needle biopsy was performed for the suspicious lesion.

Reference standard:
The final diagnosis was based on the histopathological examination results of surgically excised specimens and needle biopsy specimens and the follow up in benign cases.

In our study
- The main idea was to assess possibility for developing improved non-contrast method of breast MR screening.
- We assessed the sensitivity and specificity of DWIBS as a stand-alone tool without the benefit of DCE-MRI images.

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.
4. The probability of error at 0.05 was considered significant, while at 0.01 and 0.001 are highly significant.
5. 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.

III. RESULTS
- Forty-three female patients were included in the study, in the period from 2017 till 2020. Their age ranged from 30 to 68 years with mean±SD of 48.53 ± 10.61. There was no significant correlation between the patients age and the histopathology results.
- All the patients had suspicious breast lesions on sonomammography BI-RADS III: 12 (27.9%), BI-RADS IV: 21 (48.8%) and BI-RADS V: 10 (23.3%).
The sizes of the lesions largely varied between 0.9 cm$^3$ to 9.3 cm$^3$ (calculated as a volume: APxCCxOblique$^0.5$) with a median of 4.4 cm$^3$. The change in size shows no significant correlation with the histopathology results.

Out of the 43 patients, 30 were histo-pathologically proven to have malignant lesion (all of which were IDC) (69.8%) and 13 were proven to be benign (30.2 %) (Fig: 1).

On contrast enhanced images;

Breast lesions detected on DCE-MRI were interpreted according to the morphologic criteria and pattern of enhancement into heterogeneous enhancement mass (19 lesions) (44%), homogenous enhancement mass (13 lesions) (30%), non-mass like enhancement (4 lesions) (9.3%), peripheral enhancement (5 lesions) (11.6%) or no enhancement could be detected (2 lesions) (4.6%).

There was significant increase in the incidence of suspicious morphology and enhancement patterns with the malignant lesions.

Out of the 30 malignant lesions, 29 lesions showed suspicious enhancement kinetics (type II and type III kinetic curves) (96.6 %), this indicates a significant increase in the incidence of suspicious enhancement kinetic features with malignant lesions (p<0.05).

The results of DCE-MRI imaging were compared to the histopathology results, and then we calculated the overall sensitivity & specificity of DCE-MRI in characterization of the benign and malignant lesions when we considered BI-RADS 2 and 3 lesions as negative and BI-RADS 4 and 5 lesions as positive test result.

| Parameter | TP | TN | FP | FN | Accuracy | Sensitivity | Specificity | PPV | NPV | Accuracy | Sensitivity | Specificity | PPV | NPV |
|-----------|----|----|----|----|----------|-------------|-------------|------|-----|--|----------|-------------|-------------|------|-----|
| CE        | 29 | 13 | 0  | 1  | 97.7     | 96.7        | 100.0       | 100.0| 92.9|

The previous table shows that the DCE can predict pathological results with sensitivity of 96.7%, specificity of 100% and accuracy of 97.7%.

On DWIBS images:

Out of 30 patients with malignant lesions, 28 patients showed qualitative diffusion restriction and malignant criteria with ADC value< 1.28 (93.3 %) and two showed no restriction (6.7 %). Out of the 13 patients with benign histopathologies, five showed neither diffusion restriction nor any suspicious criteria (38.5 %) and 8 showed diffusion restriction and benign criteria with ADC value > 1.28 (61.5 %) (table:2).
There is highly significant increase in the incidence of diffusion restriction on DWIBS imaging in malignant lesions. (p<0.001).

**Table (2):** shows comparison between benign and malignant cases according to pathological results regarding DWIBS and its ADC value

<table>
<thead>
<tr>
<th></th>
<th>Benign</th>
<th>Malignant</th>
<th>test value</th>
<th>value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DWIBS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Restriction</td>
<td>5 (38.5%)</td>
<td>2 (6.7%)</td>
<td>9.677*</td>
<td>0.008</td>
<td>HS</td>
</tr>
<tr>
<td>Restriction</td>
<td>8 (61.5%)</td>
<td>28 (93.3%)</td>
<td>9.386*</td>
<td>0.000</td>
<td>HS</td>
</tr>
<tr>
<td><strong>ADC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>1.53 ± 0.17</td>
<td>0.80 ± 0.20</td>
<td>9.386*</td>
<td>0.000</td>
<td>HS</td>
</tr>
<tr>
<td>Range</td>
<td>1.3 – 1.8</td>
<td>0.4 – 1.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DWIBS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>13 (100.0%)</td>
<td>2 (6.7%)</td>
<td>34.782*</td>
<td>0.000</td>
<td>HS</td>
</tr>
<tr>
<td>Positive</td>
<td>0 (0.0%)</td>
<td>28 (93.3%)</td>
<td>34.782*</td>
<td>0.000</td>
<td>HS</td>
</tr>
</tbody>
</table>

- 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.
- The results of DWIBS imaging were compared to the histopathology results, and then we calculated the overall sensitivity & specificity of DWIBS in characterization of the benign and malignant lesions.

**Table (3):** Shows the sensitivity, specificity, PPV, NPV and accuracy of DWIBS in characterization of the benign and malignant breast lesions.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>DWIBS</td>
<td>28</td>
<td>13</td>
<td>0</td>
<td>2</td>
<td>95.3</td>
<td>93.3</td>
<td>100.0</td>
<td>100.0</td>
<td>86.7</td>
<td></td>
</tr>
</tbody>
</table>

The previous table shows that DWIBS results can predict pathological findings with sensitivity of 93.3%, specificity of 100% and accuracy of 95.3%.

**IV. DISCUSSION**

The biologic information provided by DWI and DWIBS images combined with morphological and signal intensity data of STIR (Short TI Inversion Recovery) and T2W TSE (T2weighted Turbo Spin Echo) can be used for characterization of breast lesions without the injection of contrast material (Telegrafo et al., 2015).

In our study 43 patients with suspicious breast lesions from sonomammography clinic has been selected and underwent MRI breast protocol which includes T1WI, T2WI, STIR, DCE-MRI, DWIs as well as DWIBS (with ADC maps).

Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) is a state-of-the-art in breast imaging diagnosis, it reported sensitivity rate as high as 89 to 100%, but with an inhomogeneous specificity ranging from 65% to 93% (Nechifor et al., 2013).

In our study, DCE MRI showed overall efficacy of 97.7 % when compared to histo-pathological results. It showed sensitivity of 96.7 %. However, Specificity was 100 %. It showed NPV of 92.9 % and PPV of 100%.

Bickelhaupt et al., 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% (Bickelhaupt et al., 2016).

The relatively high results could be explained by our pre selection of patients where we only included patients with BIRADS III-IV and V sonomammography results.

The false-negative result in one of the cases of our study occurs due to diffusely enhancing surrounding parenchyma that could obscure an abnormal enhancing lesion. One limitation of this study is that we did not take the hormonal status of our patients into account for scheduling the examinations.
DWIBS images were qualitatively evaluated searching for hyper-intense areas; then, quantitative examination was performed by calculating apparent diffusion coefficient (ADC) values (Telegrafo et al., 2015).

Kuroki-Suzuki et al. combined DWI and STIR imaging in order to evaluate the diagnostic capability of UE-MRI for detecting breast cancer. In particular, sensitivity and false negative values respectively of 97% and 2.9% were found (Suzuki et al., 2007).

The sensitivity and specificity of DWIBS in our study are comparable to the results of the study conducted by Bickelhaupt et al. that DWIBS showed sensitivity of 92% and specificity of 94% (Bickelhaupt et al., 2016).

Our study shows that DWIBS results can predict pathological findings with sensitivity of 93.3%, specificity of 100% and accuracy of 95.3% when compared to histo-pathological results. It showed false negative value of 6.7%.

The false-negative result in two of the cases of our study occurred in tumors with extensive necrosis.

Our results 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 1.28x10^-3.

Our cut-off ADC value was comparable to cut-off values present in literature. Bickelhaupt et al. had a cut-off value of 1.30 x 10-3mm2/s (Bickelhaupt et al., 2016).

In our study however, DWIBS did not have a superior result to DCE-MRI as regards the sensitivity or the overall efficacy. The DCE can predict pathological results with sensitivity of 96.7%, specificity of 100% and accuracy of 97.7% while the DWIBS results can predict pathological findings with sensitivity of 93.3%, specificity of 100% and accuracy of 95.3.

Though the sensitivity and specificity of DWIBS and DCE-MRI are comparable, the lower sensitivity is attributed to known fallacies of DW imaging and DWIBS discussed thoroughly in literature.

The sensitivity and specificity values obtained in our experience could suggest the possibility of applying UE-MR sequences for breast cancer screening. Besides, the very high negative predictive value could indicate the possibility of avoiding further investigations in patients with negative UE-MRI (Telegrafo et al., 2015).

Another potential benefit of UE-MRI could be represented by the reduction of the acquisition time excluding the 9 minutes necessary for CE-MRI and obtaining similar diagnostic accuracy. In fact, the overall duration of our MR protocol was of 18.16 minutes including both UE-MRI (9.16 minutes) and CE-MRI (9 minutes). By replacing dynamic sequences with morphological ones, the use of the only UE-MRI would allow to save 9 minutes with the same diagnostic results and without the need for gadolinium injection. However, in order to confirm our results, other experiences are needed also in this field (Telegrafo et al., 2015).

V. CONCLUSIONS

DWIBS sequence is a safe (no ionizing radiation, no contrast media), rapid and highly sensitive imaging technique for detection and characterization of breast lesions.

DWIBS can be used as an alternative to DCE-MRI in patients who cannot tolerate the contrast and as an adjunct to improve the specificity in patients with no contra-indications to intra-venous contrast administration.

It will relieve the cost of examination and could be a promising tool in screening for breast cancer without using contrast medium also it will reduce the acquisition time of the examination.

To achieve this non contrast screening, more work must be done to standardize breast DWIBS acquisition and interpretation approaches to facilitate multi-center trials that will evaluate and optimize the sensitivity and specificity of DWIBS as a stand-alone tool for cancer detection.
Our study has some limitations:

- Small sample size of the patients so our results need to be further evaluated on a larger sample.
- All of the histo-pathologies encountered in our study were infiltrative ductal carcinoma or fibro-adenoma so 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 evaluated adequately.
- The potential biases resulting from patient selection.

Further Recommendations:

- Further studies should be enrolled with a larger number of cases with a larger variety of pathologies.
- Comparison between the efficacy of conventional DWI's and DWIBS.
- Assessment of the efficacy of DWIBS in characterization of inflammatory breast lesions.
- Assessment of the efficacy of DWIBS in monitoring the response to neo-adjuvant therapies.

List of Abbreviations:

- DWIBS: diffusion weighted imaging with back-ground suppression
- (UE)-MRI: un enhanced MRI
- (DCE)-MRI: Dynamic contrast enhanced MRI
- ADC: apparent diffusion co-efficient
- DWI: Diffusion weighted imaging
- BI-RADS: The Breast Imaging Reporting and Data System
- T2W TSE: T2weighted Turbo Spin Echo
- STIR: Short TI Inversion Recovery
- IDC: invasive ductal carcinoma
- PPV: positive predictive value
- NPV: negative predictive value

Ethics approval and consent to participate

This study was approved by the research ethics committee of the faculty of medicine at Ain Shams University, in Egypt, on 11 July 2018, reference number of approval: FMASU MD 177/2018.

All patients included in this study is informed about the nature of the study and written consent to participate in this research is obtained.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Availability of data and material

The datasets used and/ or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors’ contributions

M.Gh was responsible for the data acquisition and analysis, M.Gh and A.MS were responsible for data interpretation and images analysis, and S.MF was responsible for final data revision.
All of the authors are responsible to the design and implementation of the research, to the analysis of the results, and to the writing of the manuscript. The authors read and approved the submitted manuscript version.

The authors agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved and the resolution documented in the literature.

REFERENCES


