

# Comparative Study between <sup>18</sup>F FDG-PET/CT and Whole Body MRI DWIBS in Assessment of Recurrent Breast Cancer (Prospective, Comparative, Cross-sectional Study Design)

## Abstract

**Aim:** This study aims to assess the diagnostic performance of <sup>18</sup>F-fluorodeoxyglucose-positron emission tomography/computerized tomography (<sup>18</sup>FDG-PET/CT) compared to whole body (WB) magnetic resonance diffusion-weighted imaging (DWI) with background body signal suppression (MR/DWIBS) in lesions detection in patients with recurrent breast cancer. **Materials and Methods:** Twenty-three female patients with suspected breast cancer recurrence by clinical, laboratory, or conventional imaging underwent both <sup>18</sup>FDG-PET/CT and WB MR/DWIBS. WB <sup>18</sup>FDG-PET/CT was performed using the standard technique. WB MR/DWIBS acquired sequences were WB DWI with short tau inversion recovery (STIR), coronal T1, and coronal STIR. Both <sup>18</sup>FDG-PET/CT and WB-magnetic resonance imaging/DWIBS were independently interpreted using visual qualitative and quantitative analysis. Pathological findings and combined clinical/radiological follow-up data were used as a reference standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated for both techniques. **Results:** PET/CT demonstrated higher specificity and sensitivity indices than MR/DWIBS in the detection of the nodal and distant lesions, while the latter displayed higher sensitivity in the detection of local breast lesions. The overall sensitivity, specificity, NPV, PPV, and accuracy of PET/CT were 84.8%, 86.3%, 90.4%, 78.7%, and 85.4% versus 82.1%, 78.0%, 85.2%, 74.0%, and 80.5% for MR/DWIBS. A high degree of agreement existed between PET/CT and MR-DWIBS. **Conclusion:** <sup>18</sup>FDG-PET/CT is more sensitive and has superiority in the assessment of nodal and distant lesions than DWIBS that has a potential superior role in the assessment of local breast lesions. DWIBS has a promising and helpful complementary tool for <sup>18</sup>FDG-PET/CT in the evaluation of patients with proven malignancies.

**Keywords:** <sup>18</sup>Fluorodeoxyglucose-positron emission tomography/computerized tomography, breast cancer, whole body magnetic resonance imaging-diffusion weighted imaging with background body signal suppression

## Introduction

The second leading cause of death in developed countries is cancer. In developing countries, it is also, among the three leading causes of death for adults, and is responsible for 12.5% of all deaths worldwide. Once a malignant tumor is detected, staging is important for treatment planning and determining prognosis. Imaging plays a pivotal role in cancer staging. It is also of great importance in monitoring response to therapy and the detection of tumor recurrence.<sup>[1]</sup>

Advances and ongoing improvements in imaging technologies have improved the sensitivity of breast cancer detection and diagnosis. However, it is still the case that

no single imaging modality can identify and characterize all breast abnormalities and a combined modality approach will continue to be necessary.<sup>[2]</sup>

As the survival time of patients is now longer, accurate detection, and diagnosis of metastatic diseases by whole body (WB) imaging becomes more important. <sup>18</sup>Fluorodeoxyglucose-positron emission tomography/computerized tomography (<sup>18</sup>FDG-PET/CT) is the usual modality for the assessment of metastatic diseases.<sup>[3]</sup>

The visualization and measurement of the diffusivity of water molecules in the human body by diffusion-weighted imaging (DWI) actually represents a fingerprint of the

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cellular characteristics of the tissue. This is because biological tissues are composed of barriers that restrict-free diffusion of water molecules such as cell membranes, fibers, and macromolecules.<sup>[4]</sup>

The major role of DWI in clinical routine is in the early detection of cerebral ischaemia, but changes in tissue water diffusion properties can be helpful for the detection and characterisation of pathological processes, including cancer, in any part of the body.<sup>[5]</sup> DWIBS allows acquisition of volumetric diffusion-weighted images of the entire body and also has unique features different from conventional DWI.<sup>[1,3,6]</sup> The fact that MR/DWIBS does not require the use of ionizing radiation or contrast agents had advantages; because it means that it is less invasive and more widely available compared to <sup>18</sup>F-DG-PET/CT.<sup>[6]</sup>

DWIBS gives functional information and can be used for the detection and characterization of pathologic processes, including malignant tumors; it may, therefore, be of value in staging and follow-up imaging of malignant tumors.<sup>[7]</sup> DWIBS techniques coupled with anatomic conventional morphologic techniques allow greater lesion conspicuity and characterization compared with other functional and anatomic imaging modalities.<sup>[8]</sup>

### Aim of the work

The aim of the study is to assess the diagnostic performance of <sup>18</sup>F-DG-PET/CT compared to WB MR/DWIBS in patients with recurrent breast cancer.

### Materials and Methods

We used a prospective, comparative, cross-sectional study design with a purposeful convenience sample collected from the National Cancer Institute (NCI) and Zagazig University Hospitals. This study included a total of 23 treated breast cancer women with suspected recurrence by clinical, laboratory, or conventional imaging. Patients who had double primary malignancy, fulminant infectious disease, those who were diabetics and those with an estimated life expectancy <6 months were excluded from the study.

Patients who met the eligibility criteria underwent full clinical examination, laboratory tests and conventional imaging (including sonomammography, ultrasonography, CT scans of the chest, abdomen, and pelvis as well as bone scan), <sup>18</sup>F-DG-PET/CT, and WB-MRI/DWIBS that were performed with maximum 1 month time interval in-between. All patients were followed up from 6 months to 1 year for the evaluation of lesions behavior over time. Malignant lesions included lesions documented pathologically or those that progressed with time and/or lesions that regressed or cured after specific therapy. Benign lesions included lesions documented pathologically or those that regressed spontaneously or remain stationary without therapy.

### Lesion definition

- a. A lesion on <sup>18</sup>F-DG-PET was defined as: An area with increased <sup>18</sup>F-DG uptake regardless of size by using a five-point grading system in which the area of uptake was compared to liver uptake (or blood pool in patients with liver disease) as follows: Score 0 (no uptake): The lesion was definitely negative, Score 1 (lesion uptake <liver uptake): The lesion was probably negative, Score 2 (lesion uptake = liver uptake): The lesion was equivocal, Score 3 (lesion uptake slightly higher than liver): The lesion was probably positive, and Score 4 (intense lesion uptake that is significantly higher than liver): The lesion was definitely positive
- b. On CT, the lesion was considered according to its morphological appearance. Lymph nodes (LNs) were suggested if increased size more than 1 cm on the coronal short axis diameter, loss of normal oval configuration, loss of the fatty hilum as well as the presence of bulky nodes or amalgamated nodal mass
- c. On WB-MR/DWIBS, lesion was defined as: An area with signal intensity equal or higher than the signal intensity from the organ with the highest signal intensity. LNs larger than 10 mm in short-axis diameter were considered positive. LN size was measured in the coronal plane on T1-weighted and short tau inversion recovery (STIR) images. LNs and masses were not measured on diffusion-weighted images. For each distant region, any areas with altered signal in T1-weighted (T1WI) or STIR, showing signal intensity in DWIBS higher than surrounding tissues.

<sup>18</sup>F-DG-PET/CT scan was done at the Nuclear Medicine Unit of NCI. Ethical approval was granted by the Institutional Review Board before the study started. Informed consent was obtained from all patients before they were enrolled in the study.

<sup>18</sup>F-DG-PET/CT scan was performed on an integrated PET/CT system with 16-slice CT (GE Medical Systems). All patients were asked to fast for 6 h before scan. The patients were instructed to avoid any kind of strenuous activity before the examination and following injection of the radioisotope to avoid physiologic muscle uptake of FDG. <sup>18</sup>F-FDG administered in a standard dose of 5.5 MBq/Kg, 60 min before scanning. Patients were asked to rest in a quiet room, devoid of distractions, and they were also asked to keep their movements, including talking, at an absolute minimum. The patients were positioned in a comfortable head fixation with arms up. The PET emission scan was performed over several bed positions (5–7) for 2 min per bed position with an axial field of view of approximately 21.6 cm per bed position and in-plane spatial resolution of 2 mm covering the same field of view as with CT. Transaxial PET and CT images were first acquired. These are then reformatted into coronal and sagittal images. For each of these sets of PET and CT images, corresponding “fusion” images, combining the two types of data, also were generated. PET image data sets were reconstructed using CT

data for attenuation correction, and coregistered images were displayed using special software. PET/CT scan was interpreted by an expert nuclear medicine physician.

Whole-body MRI DWIBS protocol design was conducted on MRI Achieva, Philips 1.5 T scanner. Q-body coil used, with the patient positioned feet first on an extended anatomical coverage table, based on the rolling-table technology (MobiTrak, Philips). The used sequences were: Coronal T1-weighted Turbo Spin Echo (TSE), Coronal STIR from the head to the mid-thigh, and axial DWIBS single-shot echoplanar imaging (ss-EPI). The coronal T1WI was with Q body coil with parameters: slice thickness 6 mm, gap 1 mm, number of slices for station, 39, field of view 530 × 265, acquisition matrix × 208 × 287, and reconstruction matrix × 512. The coronal STIR sequence was acquired with the same parameters as coronal T1WI except TR/TE 64; inversion time, 165 ms; acquisition matrix, 336 × 12; both T1WI and STIR images were acquired in free breathing. DWIBS was acquired in free breathing and the axial plane, using Q body coil with the following parameters: Ss-EPI; TR/TE, shortest; inversion time, 180 ms; slice thickness, 6 mm; gap, 0 mm; EPI factor, 61; b values 0–1000 s/mm<sup>2</sup>. The total examination time was average about 40 min for WB DWIBS. No contrast agent applied. Reconstructed DWIBS images from axial plane (in coronal, sagittal planes as well as maximum intensity projection (MIP), and volumetric view), were obtained and merged with T1 and STIR to form fused T1/DWIBS and STIR/DWIBS fused images.

Color-coded fused T1-DWIBS images were generated at Philips workstation. Apparent diffusion coefficient (ADC) maps were automatically generated from DW images by the MR software.

### Statistical analysis

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 22. Data were summarized using mean, standard deviation, median, minimum, and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Receiver operator characteristic (ROC) curves were derived and area under the curve (AUC) analysis performed to get the best cutoff values for detecting malignant lesions. Accuracy measures (sensitivity, specificity, positive predictive value [PPV], and negative predictive value [NPV]) with their 95% confidence intervals were calculated for PET CT and DWIBS.  $P < 0.05$  was considered statistically significant.

### Results

Twenty-three female patients with mean age 56 and age range 47–65 years old were included in the current study out of them 15 (65.2%) were premenopausal. Overall clinicopathological and or follow-up data results analysis demonstrated a total of 185 lesions as standard lesions (73 benign and 112 malignant).

Out of the 185 total lesions, only 14 (7.5%) were local breast lesions, 5 benign and 9 malignant. However, high frequency of both locoregional ( $n = 30$ ) and distant nodal lesions ( $n = 54$ ) was noted with more malignant than benign LNs ( $n = 48$  vs. 36). The axillary and the mediastinal LNs were most commonly encountered among the locoregional and the distant metastatic LNs ( $n = 12$  for each) respectively [the sites and distribution of the locoregional and distant LNs is displayed in Figure 1]. Furthermore, a high frequency of distant lesions ( $n = 87$ ) was seen with higher number of malignant lesions ( $n = 55$ ) than benign ( $n = 32$ ). Bone and lungs were the most common organs of distant lesions (40 and 27 respectively) while other organs were less frequently involved, such as liver, peritoneum, pleura, suprarenal gland, and adnexa. A statistically significant difference ( $P > 0.005$ ) was found between malignant and benign osseous and LNs lesions [Table 1].

PET/CT characterized 105 lesions as malignant (8 breast, 19 regional LNs, 27 distant LNs, and 51 distant metastatic lesions) and 80 lesions as benign (6 breast, 11 regional LNs, 27 distant LNs, and 36 distant lesions), while MRI-DWIBS characterized 108 lesions as malignant (10 breast, 19 regional LNs, 29 distant LNs, and 50 distant metastatic lesions) and 77 as benign (4 breast, 11 regional LNs, 25 distant LNs, and 37 distant lesions) [Table 2].

PET/CT correctly diagnosed 158 lesions 63 benign (4 breast, 9 regional LNs, 23 distant LNs, and 27 distant lesions) and 95 malignant (7 breast, 17 regional LNs, 25 distant LNs, and 46 distant lesions) versus 149 lesions for MRI-DWIBS 57 benign (3 breast, 8 regional LNs, 20 distant LNs, and 26 distant lesions) and 92 malignant lesions (8 breast, 16 regional LNs, 24 distant LNs, and 44 distant lesions).

Of the 14 breast lesions DWIBS characterized 10 as malignant and 4 as benign with one false negative (88.9% sensitivity) and 2 false positive (60.0% specificity) while PET/CT characterized 8 lesions as malignant and 6 as benign with 2 false negative (77.8% sensitivity) and 1 false positive (80.0% specificity). PET/CT has comparable results to MRI-DWIBS in the diagnosis of benign and malignant locoregional LNs; both modalities characterized 19 as malignant and 11 lesions as benign. MRI-DWIBS had 3 false negative (84.2% sensitivity) and 3 false positive (72.7% specificity), while PET/CT had 2 false negative (89.5% sensitivity) and 2 false positive (81.8% specificity). In respect to distant LNs, DWIBS characterized 29 as malignant and 25 as benign with 5 false negative (82.8% sensitivity) and 5 false positive (80.0% specificity) while PET/CT characterized 27 as malignant and 27 as benign with 4 false negative (86.2% sensitivity) and 2 false positive (92.0% specificity) [Table 3].

PET/CT had 10 false-positive and 17 false-negative lesions [lesions distribution was illustrated in Table 3]. The reported findings for the false-positive results include; subcutaneous-infected breast nodule, lymphadenitis,

postoperative sequelae, pulmonary granulomatous nodule, spondylodiscitis, and osteomyelitis. Other causes such as benign suprarenal adenoma, fibroadenoma, and hepatic regeneration nodules with increased FDG uptake were also detected.

The false-negative PET/CT results for local breast lesions were demonstrated in two lesions, one missed lesion was seen as isodense lesion in the operative bed infiltrating the pectoralis muscle, while the other was diagnosed as hard subcutaneous nodule with no significant metabolic activity (sclerosed recurrent malignant nodule). Four small-sized metastatic nodal lesions with insignificant <sup>18</sup>F PET uptake were recorded as false-negative lesions; these nodal lesions progressed with time. Early bone marrow-based lesions, sclerotic osseous lesions and subcentimetric pulmonary nodules that lack FDG uptake are the main contributing factor for false-negative PET/CT results at distant lesions. However, 16 false-positive MRI-DWIBS lesions were noted [their distribution was also illustrated at Table 3]. Infections or Inflammation were the most common causes for false-positive local lesions as well as nodal and pulmonary lesions (>1 cm). Osseous spondylodegenerative, osteomyelitis, and porotic changes as well as imperfect monitoring to therapy response were the main contributing factors for false-positive bone lesions. A single instant of suprarenal adenoma, as well as hepatic atypical posterior hemangioma, were false-positive lesions in DWIBS.

On the other hand, a total of 20 false-negative lesions were demonstrated in DWIBS; the local breast lesions were missed due to overlapping pathology (fibrocystic changes, mastitis and/or postoperative sequelae). The false-negative

nodal and pulmonary lesions are related to operative bed or posteriorly located isointense lesion infiltrating the chest wall muscles. Moreover, motion artifacts, poor yield in thoracic and around diaphragmatic regions, cortical based lesions, the overlapping spondylodegenerative, and porotic changes were the main factor in false-negative results.

The overall sensitivity, specificity, PPV, and NPV of PET/CT were 84.8%, 86.3%, 90.4%, and 78.7% versus 82.1%, 78.0%, 85.2%, and 74.0% for MRI-DWIBS, respectively [Table 3].

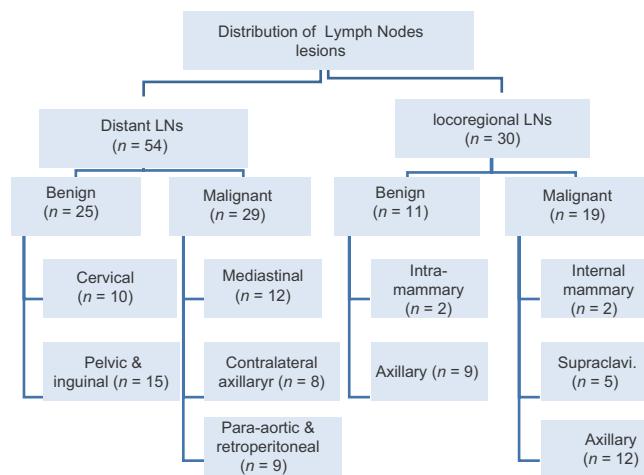
Table 4 shows a comparison by site between PET/CT and DWIBS using different parameters of sensitivity and specificity indices in the assessment of local, nodal, and distant lesions. The overall results showed the superiority of <sup>18</sup>F PET/CT over DWIBS in specificity indices in all sites. On the other hand, the sensitivity and NPV indices for DWIBS were only significantly higher in local breast lesions. In contrast, PET/CT was significantly higher than DWIBS in sensitivity and specificity indices in distant lesions.

ROC curves were derived and AUC analysis performed to determine a cutoff value for both maximum standardized uptake value (SUV max) (A) and ADC mean (B) that discriminate between malignant and benign breast lesions

**Table 1: Results of Clinico-pathological and/or follow up data (standard lesions)**

	Total (n=185)	Benign (n=73)	Malignant (n=112)
Local breast lesions	14	5	9
Loco-regional LNs	30	11	19
Distant LNs	54	25	29
Distant lesions	87	32	55

LNs: Lymph nodes



**Figure 1: The sites and distribution of the locoregional and distant lymph nodes according to clinicopathology and/or follow-up data**

**Table 2: Results of lesions detection for positron emission tomography/computerized tomography and magnetic resonance diffusion weighted imaging with background body signal suppression**

	PET-CT			MR DWIBS		
	Total (n=185)	Benign (n=80)	Malignant (n=105)	Total (n=185)	Benign (n=77)	Malignant (n=108)
Local breast lesions	14	6	8	14	4	10
Loco-regional LNs	30	11	19	30	11	19
Distant LNs	54	27	27	54	25	29
Distant lesions	87	36	51	87	37	50

NB: For each site <sup>18</sup>F PET/CT and MRI-DWIBS results were correlated to the reference standard, PET/CT: Positron emission tomography/computerized tomography, MR DWIBS: Magnetic resonance diffusion weighted imaging with background body signal suppression, MRI: Magnetic resonance imaging, LNs: Lymph nodes, <sup>18</sup>F: <sup>18</sup>fluoro-2-deoxy-d-glucose

and yield the best compromise between sensitivity and specificity for PET/CT and MRI-DWIBS respectively for the assessment of local breast lesions [Figure 2] and locoregional LNs lesions [Figure 3]. For local breast lesions, the ROC curve determined SUV cutoff value 2.050 with 97.3% sensitivity and 75.0% specificity. On the other hand, the ROC curve determined ADC cutoff value  $0.9415 \times 10^{-3}$  mm<sup>2</sup>/s with 100% sensitivity and 84.2% specificity. Both have statistically significant difference ( $P < 0.0001$ ).

Regarding the locoregional nodal lesions, the ROC curve determined SUV cutoff value 2.250 with 94.7% sensitivity and 85.0% specificity, and ADC cutoff value  $1.150 \times 10^{-3}$  mm<sup>2</sup>/s with 91.7% sensitivity and 68.4% specificity. Both have statistically significant difference ( $P < 0.0001$ ).

### Discussion

This current prospective study is a trial to illustrate the efficacy of DWIBS in comparison with <sup>18</sup>FDG-PET/CT in the assessment of patients with recurrent cancer breast. This comparison entails local breast lesions, locoregional and distant LNs as well as distant lesions including osseous and pulmonary in addition to other miscellaneous distant sites.

To the best of our knowledge, no prior studies using DWIBS in comparison with <sup>18</sup>FDG-PET/CT in the assessment of breast cancer patients exist in the literature. However, DWIBS has been reported related to other pathologies.

The overall results showed a comparable yield of both techniques with the tendency of PET/CT to have better sensitivity and specificity indices with no significant difference ( $P > 0.005$ ). On the other hand, the significant site related difference was occasionally noted between both techniques. This is in agreement with Takenaka *et al.* and Madueño who showed MR-DWIBS could be effective WB imaging technique in detection and evaluation of metastasis compared to PET/CT.<sup>[4,9]</sup>

Our results showed overall accuracy 80.5% that is comparable to Sushil *et al.* study, yet the authors focused in general metastatic lesions.<sup>[10]</sup> Gu *et al.* reported that DWIBS provides satisfactory diagnostic accuracy compared with PET/CT also, Goudarzi *et al.* suggested that the addition of T1WI and T2WI MRI together with DWIBS should improve accuracy (similar to what we did in our study).<sup>[11,12]</sup>

The differentiation between benign and malignant multicentric breast lesions is critical issues in local assessment of breast cancer. <sup>18</sup>FDG-PET/CT as a

**Table 3: Results of positron emission tomography/computerized tomography and diffusion weighted imaging with background body signal suppression focusing on true and false lesions**

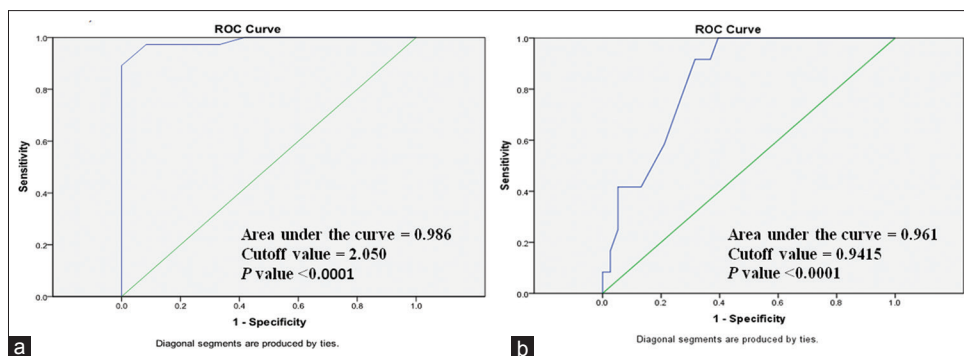
	PET-CT					DWIBS				
	Total (n=185)	Local breast lesion (n=14)	Loco-regional LNs (n=30)	Distant LNs (n=54)	Distant lesions (n=87)	Total (n=185)	Local breast lesions (n=14)	Loco-regional LNs (n=30)	Distant LNs (n=54)	Distant lesion (n=87)
TP	95	7	17	25	46	92	8	16	24	44
TN	63	4	9	23	27	57	3	8	20	26
FP	10	1	2	2	5	16	2	3	5	6
FN	17	2	2	4	9	20	1	3	5	11
SN (%)	84.8	77.8	89.5	86.2	83.6	82.1	88.9	84.2	82.8	80.0
SP (%)	86.3	80.0	81.8	92.0	84.4	78.0	60.0	72.7	80.0	81.2
PPV (%)	90.4	87.5	89.5	92.6	90.2	85.2	80.0	84.2	82.8	88.0
NPV (%)	78.7	66.7	81.8	85.2	75.0	74.0	75.0	72.7	80.0	70.3

TP: True positive, TN: True negative, FP: False positive, FN: False negative, SN: Sensitivity, SP: Specificity, PPV: Positive predictive value, NPV: Negative predictive value, PET/CT: Positron emission tomography/computerized tomography, DWIBS: Diffusion-weighted imaging with background body signal suppression, LNs: Lymph nodes

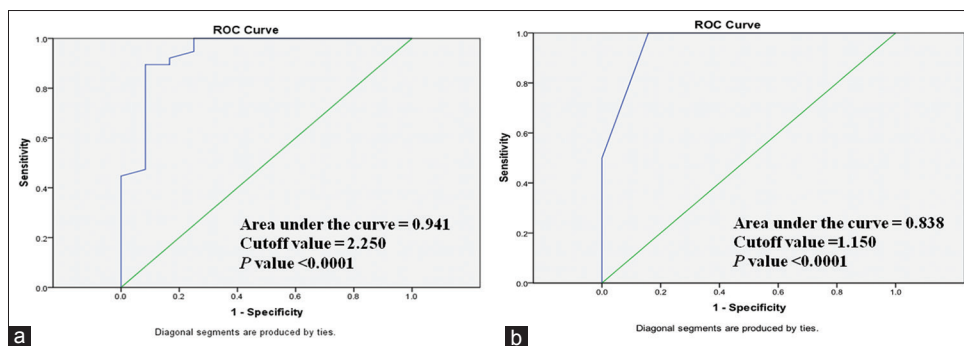
**Table 4: Overall comparison between <sup>18</sup>fluoro-2-deoxy-d-glucose positron emission tomography/computerized tomography and diffusion-weighted imaging with background body signal suppression for lesions detection of the involved sites**

	PPV		NPV		SN		P	SP		Overall accuracy
	PET/CT	DW	PET/CT	DW	PET/CT	DW		PET/CT	DW	
Local breast (%)	87.5	80.0	66.7	75.0	77.8	88.9	0.32	80.0	60.0	P=0.66
Nodal (%)	89.5	84.2	81.8	72.7	89.5	84.2	0.59	81.8	72.7	
Distant nodal (%)	92.6	82.8	85.2	80.0	86.2	82.8	0.75	92.0	80.0	
Distant lesions (%)	90.2	88.0	75.0	70.3	83.6	80.0	0.75	84.4	81.2	
Total	90.4	85.2	78.7	74.0	84.8	82.1	0.62	86.3	78.0	

DW: DWIBS, SN: Sensitivity, SP: Specificity, PPV: Positive predictive value, NPV: Negative predictive value, CI: Confidence interval, PET/CT: Positron emission tomography/computerized tomography, DWIBS: Diffusion-weighted imaging with background body signal suppression



**Figure 2: (a and b) Comparison between standardized uptake value of fluorodeoxyglucose positron emission tomography/computerized tomography and apparent diffusion coefficient of diffusion weighted imaging with background body signal suppression for the best cutoff value in quantitative assessment of breast lesions**



**Figure 3: (a and b) Comparison between standardized uptake value of positron emission tomography/computerized tomography and apparent diffusion coefficient of diffusion weighted imaging with background body signal suppression for the best cut off value in quantitative assessment of loco-regional lymph nodes**

multimodality imaging technique is required to help in solving questionable or indeterminate breast lesions either initially or posttherapy. Furthermore, DWIBS recently introduced as a multimodality technique that showed better soft-tissue differentiation, contrast resolution, provide a better sensitivity, and acceptable specificity.<sup>[13]</sup>

Many studies illustrated the role of <sup>18</sup>FDG-PET/CT in the evaluation of suspicious breast lesions, and also support our PET-CT results with variable sensitivity values ranging between 80 and 90% and specificity values between 71% and 95%.<sup>[2]</sup> Better tissue differentiation and higher spatial resolution of DWIBS were the main contributing factors in a better yield of DWIBS results in the locoregional assessment of breast cancer lesions compared to PET/CT [Figure 4]. Stadlbauer *et al.* have similar yet with high sensitivity indices results as they performed a full quantitative and qualitative interpretation of DWIBS and found that DWIBS is a superior technique than the conventional DWI with accuracy of 96.5%.<sup>[5]</sup>

In the current study, DWIBS had a relatively lower specificity; this is attributed to much more false-positive results of MR DWIBS compared to PET/CT. Many reasons were postulated for the more frequent false-positive results with DWIBS. First, the presence of dual pathology such as nonmalignant lesions with restricted diffusion (fibrocystic

disease/fibro-adenomas, inflammatory lesions, and postoperative sequelae) is a main factor. Second, many artifacts that disturbed the homogeneity of the magnetic field.<sup>[4,5,14]</sup>

Nodal (regional and distant) assessment is a crucial issue for all diagnostic modalities. The current imaging techniques are mainly based on morphological criteria in the assessment of nodal lesions either locoregional or distant and do not have enough accuracy to characterize the normal size involved LNs. Furthermore, exclusion of malignancy from benign nodal lesions larger than 1 cm is considered still questionable.<sup>[15]</sup>

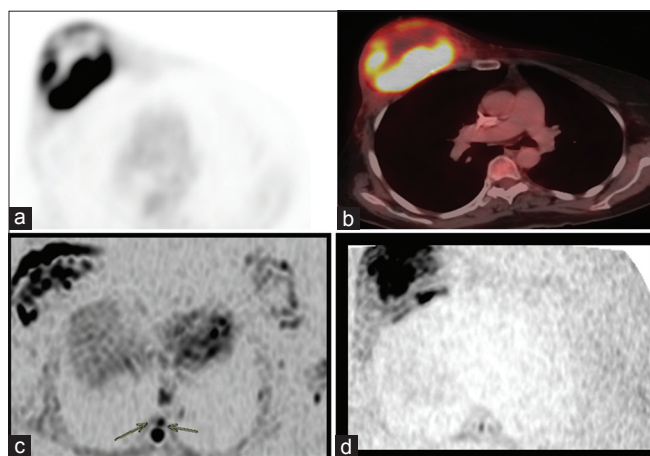
In this study, more or less similar number of false-negative results was demonstrated in both techniques. Both techniques have acceptable power to detect malignancy in normal size nodes with better scale for PET/CT in sensitivity (87.5% compared to 83.3% of DWIBS) and specificity (88.9% compared to 77.8% of DWIBS). On the other hand, significant higher false-positive nodal lesions were demonstrated by DWIBS that were metabolically inactive in PET/CT [Figure 5]. The disagreement mainly concerned in the mediastinal and hilar areas where DWIBS-MRI has a lower performance, partly due to respiratory and cardiac motions. The addition of quantification assessment by ADC may help in attaining better specificity, in particular, the

locoregional LNs (cutoff value was  $1.150 \times 10^{-3} \text{ mm}^2/\text{s}$  with 91.7% sensitivity and 68.4% specificity). The added value of ADC value in DWIBS quantification try to add in solving these false-positive results; however, artifacts and native restriction pattern of normal nodes of DWIBS play a central role in such inferiority of its results compared to PET/CT.<sup>[15]</sup>

Chemotherapy effect may produce false-negative results on DWIBS, as anticancer therapy may produce cell membrane rupture and cause cell necrosis, resulting in decreasing cell density, which increases the mobility of water molecules accompanied with low signal intensity on DWIBS.<sup>[16]</sup>

Comparable sensitivity and specificity was noted among both techniques for detection of bone deposits with the <sup>18</sup>FDG-PET/CT showed slightly better sensitivity 86.96% versus 84.62% and DWIBS better specificity 90.0% compared to 85.0%. This was attributed to slightly lower DWIBS false-positive results compared to PET-CT. Both techniques were sharing some difficulties in the specification of the bone marrow lesions within severe spondylodegenerative and porotic changes; however, this was more obvious with DWIBS rather than <sup>18</sup>FDG-PET/CT.<sup>[12,17]</sup>

However, others demonstrated that DWIBS is superior to PET/CT and bone scan in the detection of bone metastases especially in pelvic cavity with the advantage of no ionizing radiation and the many false-negative results of PET/CT overlapped by degenerative changes.<sup>[12]</sup>



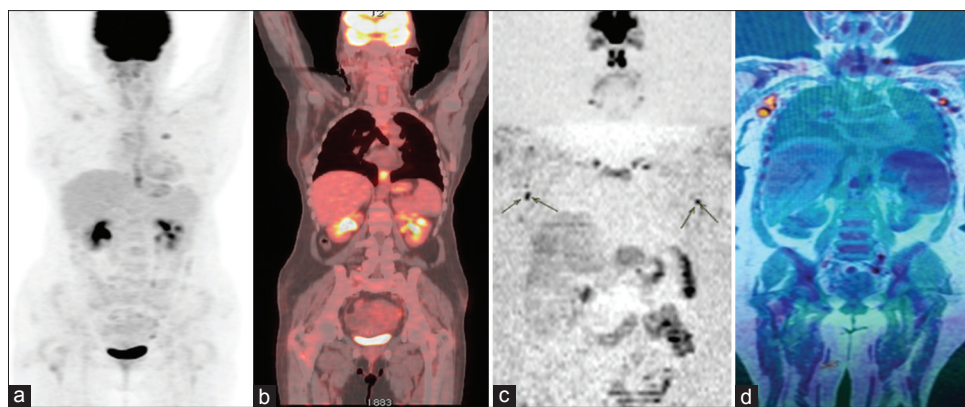
**Figure 4: Case 1 – A 45-year-old female patient with recurrent right breast cancer. positron emission tomography/computerized tomography images (a) axial positron emission tomography and (b) fused axial positron emission tomography/computerized tomography images demonstrating metabolically active (fluorodeoxyglucose avid) right breast neoplasm. whole body Magnetic resonance imaging/diffusion weighted imaging with background body signal suppression axial images (c and d) showing restricted diffusion pattern of the right breast multi focal mass. Note the chest wall affection better appreciated in diffusion weighted imaging with background body signal suppression. Note also the marrow infiltrative lesion (arrow) at the axial diffusion weighted imaging with background body signal suppression**

Our results showed clearly higher specificity for <sup>18</sup>FDG-PET/CT (81.82%) in the characterization of pulmonary lesions compared to MR DWIBS (63.64%). Moreover, the sensitivity indices were also significantly higher (90.0%) than that of DWIBS (65.0%). Technical difficulties and motion artifacts in thoracic region are the main reasons for relatively high false-positive and false-negative DWIBS results.

Wenkel *et al.* and Stadlbauer *et al.* focused on ADC cutoff values for benign and malignant lesions which ranged between  $1.1 \times 10^{-3} \text{ mm}^2/\text{s}$  and  $1.6 \times 10^{-3} \text{ mm}^2/\text{s}$ . In the current study, a relatively lower ADC cutoff value was obtained ( $0.9415 \times 10^{-3} \text{ mm}^2/\text{s}$ ) with 100% sensitivity and 84.2% specificity. This finding may be attributed firstly to the inclusion of more frequent malignant breast lesions, and second, that other studies with higher cutoff value were using conventional DWI and not the newly introduced DWIBS. The addition of fat signal suppression in the technique of DWIBS may produce more diffusion restriction results.<sup>[5,18]</sup>

The current work suffered from several limitations: This study included a limited number of patients with different pathology, age and duration of disease; therefore, no significant difference was achieved between DWIBS and PET/CT in overall results. The reference of standard lesions in the current study was partially based and not fully on histopathological data, as multiple biopsies from several lesions is not ethically or clinically applicable. Instead, clinical outcome data obtained through clinical follow-up, multiple laboratory and radiological imaging evaluation were satisfactory and used as a reference. The limited number of benign lesions particularly in local assessment interfered with the achievement of a conclusive result in differentiation between benign and malignant lesions in both techniques. Accurate comparative quantification using ADC and SUV was not done during the current study as technical and motion artifacts in DWIBS interfere with performing such comparative quantification. Finally, the availability and cost stay behind this limitation.

On the other hand, the strength of the current study relies on its novel prospective nature in comparing <sup>18</sup>FDG-PET/CT and DWIBS in different regions (e.g., local, nodal, and distant). Second, all patients in this work performed <sup>18</sup>FDG-PET/CT and DWIBS within a short time interval (one month) without therapy in-between to avoid change in disease status. Technical precautions that permit satisfactory imaging yield by DWIBS were strictly followed. One of the advantages is the fusion technique that we used in this study and mentioned by other authors as Tsushima *et al.* which illustrated that DWIBS/anatomical MRI fusion had a potential role in high sensitivity and specificity indices, in addition, the postprocessed MIPs, and PET-like images which are very attractive for demonstration purposes; however, the source images should always be



**Figure 5:** Case 2 – A 43-year-old female patient with history of old operated breast Cancer. positron emission tomography-computerized tomography images (a) coronal positron emission tomography images and (b) fused positron emission tomography/computerized tomography demonstrating negative study for metabolically active infiltrative nodal or distant lesions whole body Magnetic resonance imaging/diffusion weighted imaging with background body signal suppression: (c and d) coronal diffusion weighted imaging with background body signal suppression and fused T1 diffusion weighted imaging with background body signal suppression showing restricted diffusion pattern of the bilateral axillary lymph nodes (arrows). Histopathological analysis revealed their inflammatory nature. In this case; diffusion weighted imaging with background body signal suppression have frequent false-positive nodal lesions

consulted, because subtle lesions may be missed or obscured in projected images.<sup>[1,19,20]</sup>

Considering its safety and patient tolerance, the future alternative role of DWIBS technique compared to PET/CT has to be determined. Although diffusion images are a powerful new tool that improves the sensitivity and specificity of classical anatomical image but not providing metabolic information, it is really unlikely to completely exclude PET/CT.

## Conclusion

<sup>18</sup>F-DG-PET/CT is more sensitive and has superiority in the assessment of nodal and distant lesions in patients with recurrent breast cancer than DWIBS that have a potential superior role in the assessment of local breast lesions. DWIBS has a promising complementary tool for <sup>18</sup>F-DG-PET/CT in the evaluation of patients with malignancies. Further studies should be recommended to minimize its artifacts and improve its feasibility for diagnosis.

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## Conflicts of interest

There are no conflicts of interest.

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