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Role of Diffusion Weighted Magnetic Resonance Imaging in Post-Operative Breast Cancer Patients

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Abstract

Breast cancer is the chief reason of cancer death in women, the second most common cancer worldwide, and the fifth most common cause of cancer-related deaths. Following surgical management of breast neoplasm and radiotherapy, the incidence of local recurrence ranges from 1 to 2 percent yearly, with most of the recurrence rates was occurred in the 1st five years. The objective of our study was to evaluate role of Diffusion Weighted MR Imaging (DWI) and Apparent Diffusion Coefficient (ADC) in differentiated between tumor recurrences and benign changes in breast Cancer patients after surgery, so early detection and proper treatment of recurrent disease is of foremost importance. Thirty breast cancer patients with suspicious breast lesions after surgical intervention. After giving informed consent, all patients subjected to sono-mammography, Diffusion Weighted MR Imaging (DWI) and Apparent Diffusion Coefficient (ADC), and their findings compared to histopathology results. This study showed that Sensitivity of sono-mammography was 70% and its specificity was 66.67%. Conventional MRI sensitivity was 85% and specificity was 90%. Regarding sensitivity of ADC&DWI, it was 92.23%while its specificity was 94.51%. The cut off ADC value was 0.95-x 10−3 mm2/s. DWI&ADC are noninvasive techniques that can easily inserted into routine clinical breast MRI protocols. Detection of restricted diffusion can accurately discriminate benign from malignant breast lesions with high sensitivity and specificity. These results confirm the importance of the combined use of both sono-mammography and magnetic resonance image (MRI) for proper differentiation between local tumor recurrence and benign breast changes in breast cancer patients following different surgical procedures.

Keywords: DWI, ADC, Breast cancer recurrence.

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1. Introduction

Number of women who are seeking evaluation for detected breast abnormalities after surgery is increasing. More women with breast cancer are living with the consequences of treatment. Improved technologies have helped to individualize diagnostic evaluation and treatment, improve efficacy and minimize morbidity [1]. Surgery as well as radiotherapy might lead to scarring with architectural distortion of the breast that causes the evaluation of local recurrence difficult via clinical examination, mammography, and US. Alterations in management may simulate neoplasm or obscure locally recurrent breast neoplasm [2].

Diffusion-weighted imaging (DWI) is an unenhanced MRI sequence that evaluate the mobility of water molecules in vivo and offers various and efficiently complementary data to DCE-MRI. DWI is sensitive to biophysical criteria of tissues, including cell density, membrane integrity, and microstructure [3]. Promising findings from preliminary DWI studies of the breast revealed markedly lower ADC values for breast carcinomas than for benign breast lesions or normal tissue. The lower ADC in tumors is mainly due to high cell density that cause more limitation of the ECM and higher fraction of signal coming from intracellular water [4].

2. Patients and Methods

Our study was a prospective, approved by the Faculty of Medicine Ethics committee of the Beni-Suef University; cases had given informed consents for their used data. The study performed at least six months after the operation on thirty breast cancer female patients who underwent surgical intervention. The study conducted at radiology department of Beni-Suef University. The study done from May-2020 until September 2022. The patients underwent full history taking and clinical examination. Mammography, US and MRI examinations performed for cases.

2.1. Imaging protocol: Techniques

2.1.1. Sono-mammographic examination

All patients underwent ultrasound examination using a high frequency probe (10 MHZ). While only 20 patients underwent mammography by semi digital machine. Medio-lateral oblique and cranio-caudal views done. Then detected pathology classified according to BIRADS lexicon (Breast Imaging Reporting and Data System) fifth edition, last updated in 2015.

2.1.2. Magnetic Resonance imaging (MRI)

All patients underwent Magnetic Resonance imaging of the breast. The following protocols used: MRI done by field strength 1.5 Tesla on Siemens machine while the patient was lying prone using double breast coil.

- ***MRI Sequences***

Coronal T1-weighted spin echo sequence was done for localization. Axial T1-weighted and T2-weighted fast spin echo sequences. Axial STIR weighted sequences.

- ***DW-MRI Protocol***

DW-MRI technique done using single-shot echo planar imaging with fat suppression. The following parameters were used; 5700 msec/72 msec (repetition time/echo time), 4mm (section thickness), 50% (matrix), 346mm (field of view) and 25% (section gap). Three b-values used, trying to get more accurate values of ADC (apparent diffusion coefficient). B-values obtained at zero, 500 and 1000s/mm2.

- ***ADC value calculation***

For ADC value calculation, it calculated automatically as the ROI (region of interest) drawn manually on the ADC maps within the regions corresponded to high signal lesions on DWI.

- ***MRI interpretation***

Two radiology consultants reported MRI images in consensus. Then detected pathology classified according to ACR (American College of Radiology) BIRADS lexicon published in 2013.

The lesions assessed according to the following

Presence or absence of the lesions. Morphology and signal of each lesion in pre-contrast T1 and T2 weighted imaging and STIR.

2.2. Statistical analysis

Data statistically described in terms of mean ± standard deviation (± SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups done using Kruskal Wallis test. For comparing categorical data, Chi-square ($\chi 2$) test performed. Exact test used instead when the expected frequency is less than five. Accuracy represented using the terms sensitivity, specificity, +ve predictive value, -ve predictive value, and overall accuracy. Two-sided p values less than 0.05 considered statistically significant. All statistical calculations done using computer program IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

2.3. Image interpretation

Two radiology consultants (with experience (20&10 years) reported MRI images in consensus. To analyze and assess a breast lesion we used ACR (American College of Radiology) BIRADS lexicon published in 2015. The lesions assessed according to the following

- The signal pattern and morphological features of the lesions (shape, site, size and margins) at T1, T2 and STIR weighted images.
- Signal appearance at DWIs (free or restricted diffusion) and quantitative ADC map as well as the value of the ADC.

We considered 0.95×10^{-3} mm^2/s to be our cutoff ADC. Findings correlated with histopathological results.

3. Results and discussion

3.1. Results

Thirty female patients were included in our final statistical analysis. Mean of age was 47 with range from 29 to 70. Our results showed that (12(40%)) patients were malignant cases. Benign cases (18(60%)): Diffuse skin thickening and Edema were found in 4 patients, fat necrosis 3 patients, fibro adenoma in 4 patients, post-operative scar at 4 patients and seroma at 3 patients.

3.1.1. Case 1

Thirty-eight years old female patient presented with left breast lump after right breast MRM. (Figure 2)

- Sono-mammographic BIRADS classification: BIRADS III.
- Dynamic MRI BI-RADS classification: BI-RADS IV.
- Pathology: fibro adenoma

3.1.2. Case 2

Fifty-four years old female came for follow up after right breast MRM. (Figure 3)

- Sono -mammographic BIRADS classification: BIRADS II.
- Dynamic MRI BI-RADS classification: BI-RADS IV.
- Pathology: invasive duct carcinoma.

3.2. Discussion

Breast cancer is the second foremost cause of tumor mortality among females accounting for 6.5% of mortalities worldwide [5]. Early determination in addition to appropriate management of recurrent disease is highly necessary for long-term survival. However, breast conservative surgeries and radiation treatment make the treated breast susceptible to various modifications that result in complicated interpretation of ultrasound and mammographic images, particularly if local recurrence is anticipated [6]. To evaluate the role of Diffusion Weighted MR Imaging (DWI) and Apparent Diffusion Coefficient (ADC) in differentiation between tumor recurrence and benign changes in breast Cancer patients following surgical intervention. Sono-mammography is the most common and available imaging modality for breast lesions diagnosis. Depending on the sono-mammographic breast imaging reporting and data system (BI-RADS), the present results showed that all cases of BIRADS II&III were benign. Cases categorized as BIRADS V were malignant cases. With a statistically significant increase in category II and III sono-mammographic BIRADS among the benign cases (P value<0.001) and a statistically significant increase in category V among the malignant cases (P value<0.001). This result is consistent with Sherif et al. [7] study indicated that

BI-RADS II, III denoting non-suspicious breast lesions while BI-RADS IV, V denoting suspicious breast lesions.

Regarding the margin of the lesion, our results showed that margin of the lesion was irregular in five patients, speculated in 7patients among malignant cases, but in benign cases was irregular in six patients, regular in 10 patients and speculated in 2 patients. With a statistically significant increase in regular margin among the benign cases and a statistically significant increase in speculated margin among the malignant cases (P value<0.001). These findings are in coherence with the results made by Sherif et al. [7] that exhibited irregular & speculated margins in 3 & 4 mass lesions respectively, 5 of them proved to be malignant, 1 of them were grade I carcinoma, 2 of them were grade II while 2 of them were grade III.

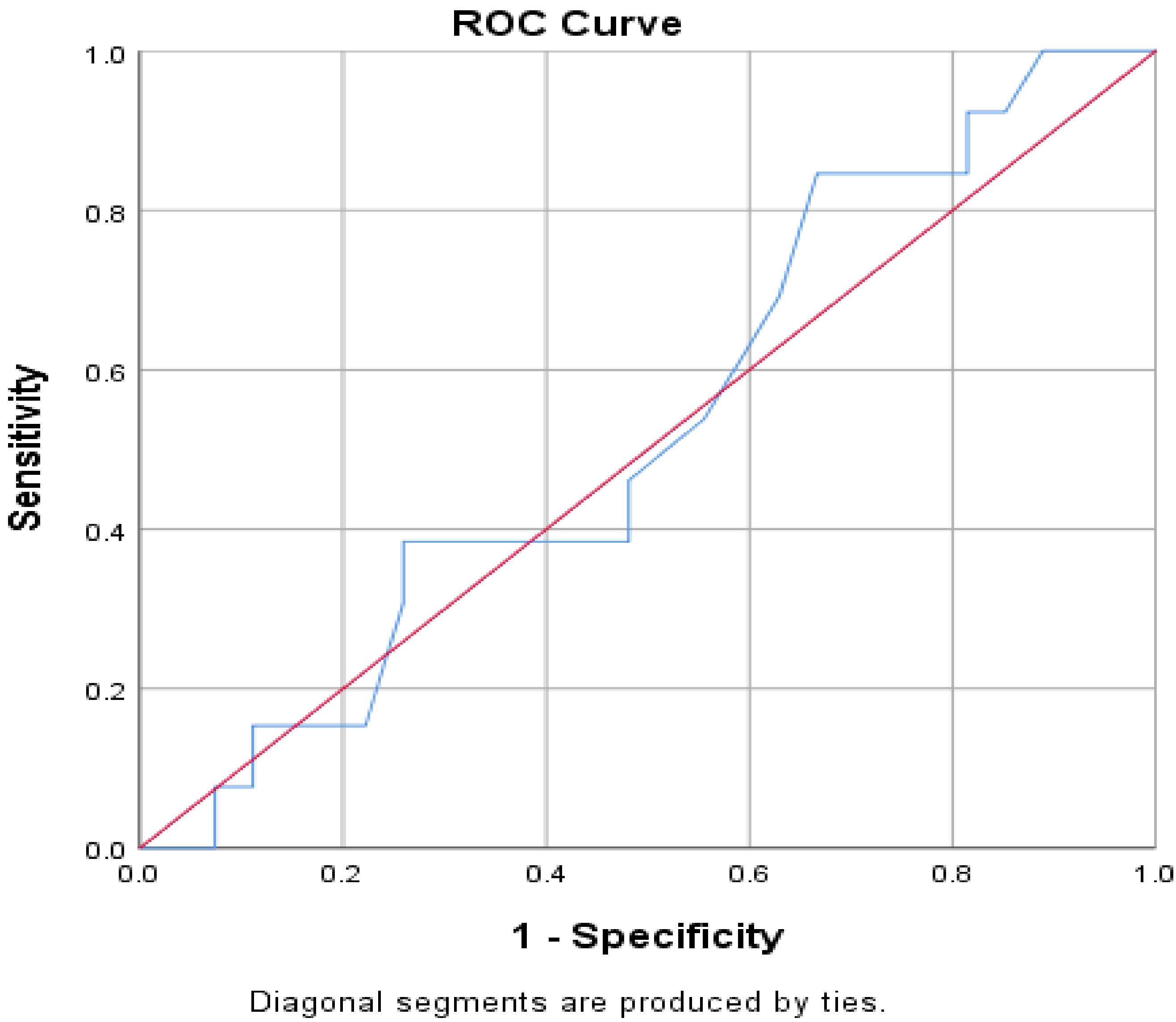

Figure 1. ROC (Receiver operating characteristic) curve for ADC value: showed that the recommended cut off ADC value was 0.95x 10−3 mm2/s. (Area under the curve 0.531), (Specificity 94.5100%), (Sensitivity 92.23%).

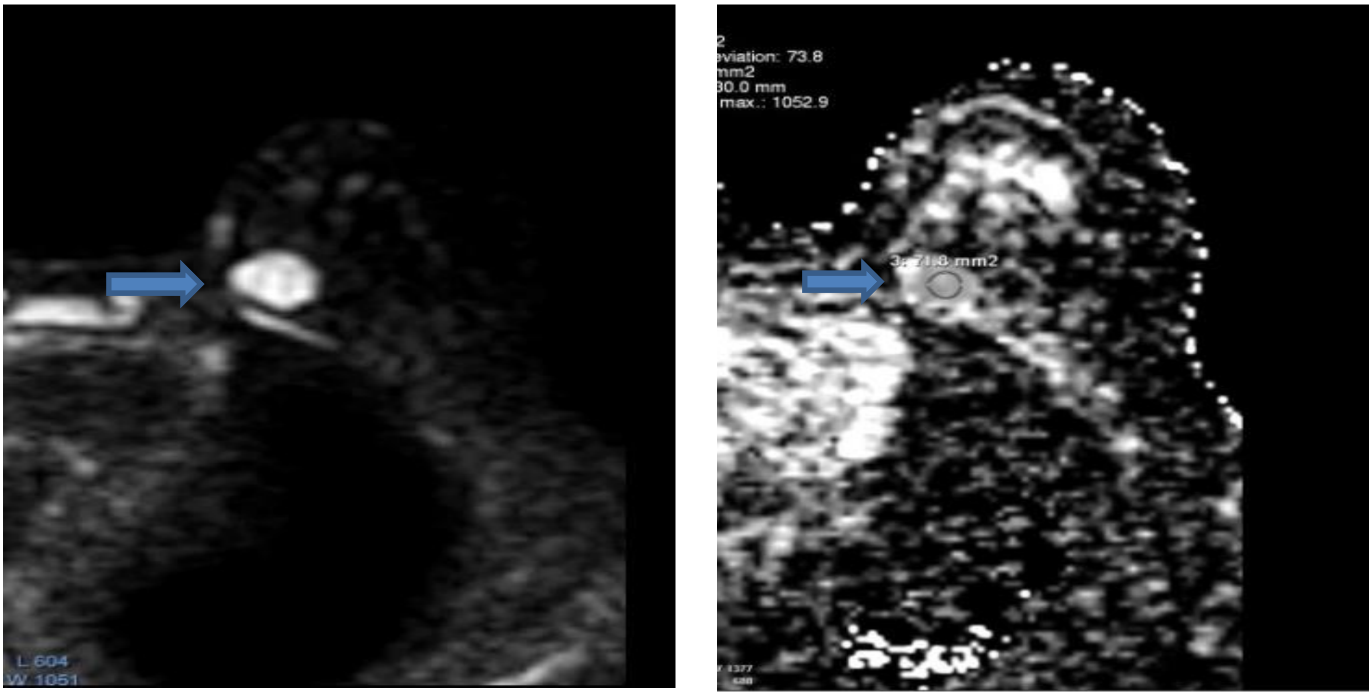

Figure 2. MRI axial images: Diffusion sequence and post processing ADC map showing restricted diffusion of the left breast upper inner quadrant mass. ADC value for ROI was 0,9x 10 -3 mm 2.

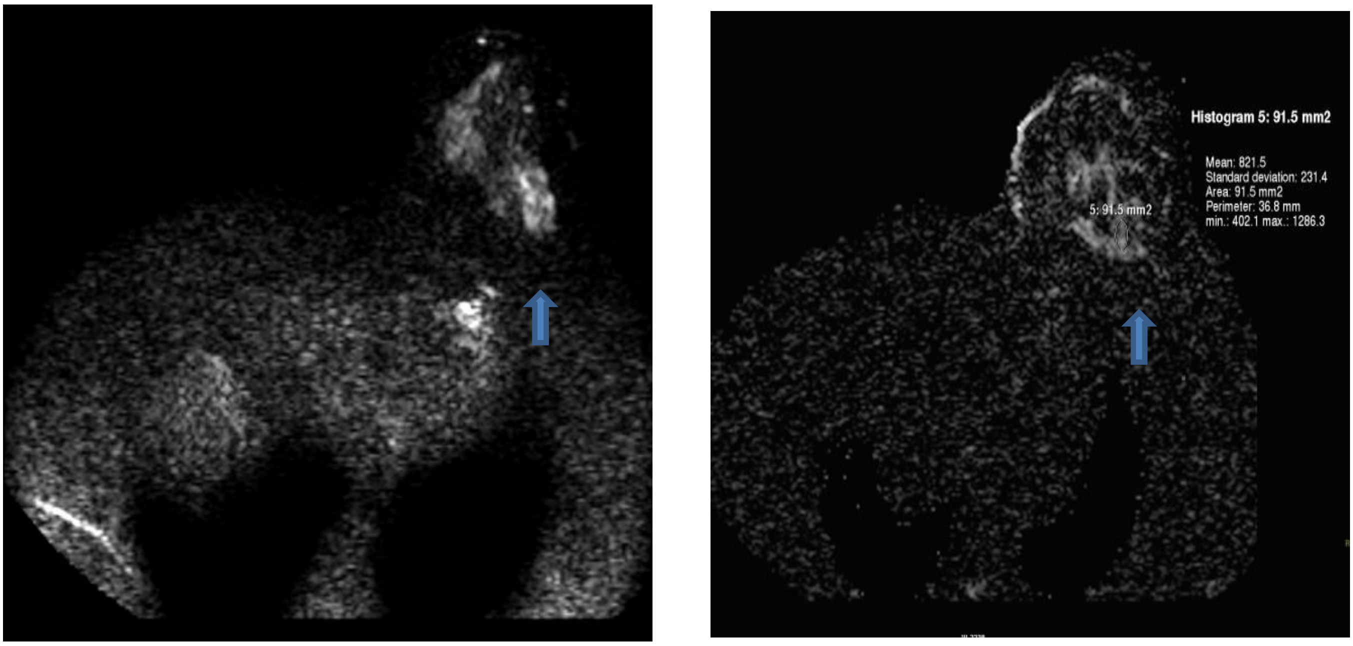

Figure 3. MRI axial images: Diffusion sequence and post processing ADC map showing restricted diffusion of the left breast upper central quadrant mass. ADC value for ROI was 0.8 x 10 -3 mm 2.

Findings of sono-mammography:

Table 1. Correlation between the histopathological diagnosis and sonomammographic BIRADS classification

		Classification regarding final diagnosis				
		Malignant(No.=12)		Benign(No.=18)		Chi square test
		No	%	No	%	P value
Sono mammographic BIRADS	II	0	0.0%	10	55.5%	<0.001
	III	0	0.0%	4	22.2%	
	IV	4	33.33%	4	22.2%	
	V	8	66.66%	0	0.0%	

P value <0.001(significant result)

Findings of MRI:

Table 2. Margin of the lesion

		Classification regarding Final diagnosis				
		Malignant No.=12)		Benign (No.=18)		Chi square test
		No	%	No	%	P value
Margin of the lesion	Irregular	5	41.66%	6	33.33%	0.002
	Regular	0	0.0%	10	55.55%	
	Spiculated	7	58.33%	2	11.11%	

Table 3. MRI BIRADS classifications

		Classification regarding Final diagnosis				
		Malignant (No.=12)		Benign (No.=18)		Chi square test
		No	%	No	%	P value
MRI BIRADS Classifications	II	0	0.0%	13	72.22%	<0.001
	III	0	0.0%	3	16.66%	
	IV	7	58.33%	2	11.11%	
	V	5	41.66%	0	0.0%	

Table 4. ADC values

		Classification Regarding final diagnosis			
		Malignant No.=12)	Benign (No.=18)	Independent t test	
				t	P value
ADC	Mean± SD	0.72± 0.21	1.41± 0.44	-0.012	<0.001
	Range	0.93-1.34	0.92-1.64		

Table 5. Diffusion weighted image

		Classification regarding Final diagnosis				
		Malignant (No.=12)		Benign (No.=18)		Chi square test
		No	%	No	%	P value
Diffusion Weighted Image	Free Diffusion	2	16.66%	16	88.88%	<0.001
	Restricted Diffusion	10	83.33%	2	11.11%	

Table 6. Comparison of the diagnostic indices of different imaging modalities

Item	Sensitivity	Specificity	PPV	NPV
Sono-mammography	70.00	66.67	43.18	80.96
conventional MRI	85.00	90.00	71.00	96.00
ADC&DWI	92.23	94.51	79.8	95.55

Regarding MRI BI-RADS classifications, the present study revealed that all cases of BIRADS V were malignant. All cases of BIRADS II &III were benign. With a statistically significant increase in categories II and III among the benign cases and a statistically significant increase in category IV and V among the malignant cases (P value<0.001). Such findings were in agreement with Choi et al. [8] study on the utility of abbreviated breast MRI screening for females having a history of BC operation that indicated that the rates of malignancies of categories I, II, III, and IV of the BI-RADS were 0, 0, 4.8, and 57.1%, respectively. In addition, Ramírez-Galván et al. [9] indicated that BI-RADS MRI lexicon is a helpful and clinically pertinent classification for the categorizing lesions according to the morphological criteria, enhancement patterns, and kinetic curves. However, imaging participates of some benign & malignant lesions remain overlapping that result in false +ve or false -ve results.

Regarding ADC, the current study revealed that there was statistically significant difference between malignant (mean=0.72± 0.21) and benign lesions (mean=1.41± 0.44) (P value< 0.001). The recommended cut off ADC value was 0.95 x 10−3 mm2/s. Such finding was in agree with Rinaldi et al. [10] that exhibited that the average ADC value of recurrence statistically decreased in comparison with scar tissue postoperatively. Moreover, agree with El-nasr et al. [11] that indicated that the mean ADC value of benign lesions (1.50 ± 0.45 Standard Deviation) was statistically elevated in comparison with the mean ADC value of neoplastic lesions (0.81 ± 0.23 Standard Deviation). As regard the lesion signal observed in DWI, our results revealed that free diffusion found in 2 malignant lesions& 16 benign lesions.

Restricted diffusion was found in 10 malignant lesions &2 benign lesions, with statistically significant increase in free diffusion among the benign cases (P value<0.001). Such findings were in agreement with Osman et al. [12] that showed that all the neoplastic lesions revealed restricted diffusion. Additionally, six benign lesions revealed restricted diffusion indicated that benign lesions have the criteria of being of low cellularity that explain the low signal on DWI because of increased water motion high causing elevated ADC value. In addition, comparable study done by Yadav et al. [13] showed rather nearby results as 29 (87%) of the benign lesions showed free diffusion, with corresponding high ADC values 33 (89 percent) of the neoplastic lesions revealed restricted diffusion, that corresponded low ADC values.

4. Conclusion

DWI&ADC are noninvasive techniques that can easily inserted into routine clinical breast MRI protocols. Detection of restricted diffusion can accurately differentiate benign from malignant breast lesions with high sensitivity and specificity to early diagnosis & stages of post-operative breast cancer patients.

Conflict of interest

The authors declare that there is no conflict of interests.

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