

## **Detection of Local Recurrence After Breast Conserving Therapy**

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### **ABSTRACT**

The aim of this study is to evaluate the triple assessment (clinical examination, cytology and mammography), magnetic resonance imaging (MRI) in the differentiation of post-treatment changes from local recurrence of breast carcinoma following breast conservation therapy (BCT). Twenty-five patients treated previously by breast conservation surgery and radiotherapy with clinical suspicion of local recurrence were evaluated prospectively by triple assessment, MRI and open surgical biopsy. Local recurrence was confirmed histologically in 9 patients. Of these, mammography identified seven (sensitivity 77.8%), cytology 6 (sensitivity 66%) and breast MRI 9 (sensitivity 100%). False positive contrast enhancement was seen in two patients (Specificity 87.5%) in whom histopathology revealed inflammatory changes only. When triple assessment is inconclusive, MRI is a more accurate technique in diagnosis of recurrence versus scar formation. However, during the first postoperative year, due to the increased microvascular fragility and fat necrosis, the interpretation has to be guarded to reduce the number of biopsies and hence the false negative results.

**Key Words:** BCT - Local recurrence detection.

### **INTRODUCTION**

Breast conserving therapy differs from primary radical surgical treatment principally in the preservation of the affected breast and the requirement for breast irradiation. Although local control rates appear to be similar for both forms of treatment, concern about the continued risk of recurrence in the retained breast remains [10,11,26]. The differentiation of recurrent cancer from benign changes attributable to surgical excision and radiation treatment is a dilemma both on clinical examination and mammography [1,22,30]. Post-treatment changes are non-specific and may mimic or obscure recurrent tumors [29]. Diagnostic problems are also encoun-

tered with ultrasonography because of hypoechoic areas and shadowing within scar tissue [2].

Surgical biopsy based on the results of clinical and mammographic assessment alone have a poor positive predictive value of approximately 50% [31,32]. Mammography tend to underestimate the recurrence size and about 5-15% of recurrences are not visualized at all, with the resultant delay in diagnosis [20]. Ultrasonography is of limited value in the detection of small recurrence (< 1 cm), multifocal or intraductal disease [3]. Biopsy wounds are prone to postoperative complications as healing of the irradiated breast is suboptimal. Many studies with contrast-enhanced magnetic resonance imaging (MRI) have shown its usefulness in the distinction between benign post-treatment changes and recurrent tumors.

This study has been designed to compare breast MRI and triple assessment in the diagnosis of local tumor recurrence in patients with suspicious of local recurrence following BCT.

### **PATIENTS AND METHODS**

The study population consisted of 25 follow-up patients with suspected local recurrence after BCT. During the period from January 1999 to December 2000 at the National Cancer Institute, Kasr El-Aini Hospital Cairo University and Kobri El-Kobba Military Hospital. The original eligibility criteria for including these patients for BCT were: - clinical stage (T<sub>1</sub>-T<sub>2</sub>-N<sub>0</sub>-N<sub>1</sub>), tumor size up to 3 cm, M<sub>0</sub> by clinical examination and imaging studies, intraduct

component ( $0 - \leq 25\%$ ) and favorable tumor / breast size ratio. Briefly, the surgical treatment of all patients involved wide local excision and axillary dissection. Radiotherapy involved treatment to the entire breast and the draining lymph node areas, generally applying 4500-5000 rad in 5 weeks. Follow-up was done on a bimonthly basis in the outpatient with four monthly tumor marker estimation and six monthly radiological investigations, except when circumstances otherwise indicated. Upon suspicion of local recurrence the initial assessment included:

- Mammography and complementary ultrasonography.
- FNAC from the suspected radiological or clinical region.
- MRI breast.
- Metastatic work-up and patients with evidence of distant metastasis were excluded.
- Open surgical biopsy for histopathological examination.

Statistical analysis of the qualitative data was done using the chi-square test.

## RESULTS

Table (1) summarizes the results of the study. The median age at diagnosis of local recurrence was 49 (35-62) years.

The median interval from the original surgery to suspected local recurrence was 26 (range 3-90) months. The clinical presentation of the 25 patients were: no symptoms (radiologic diagnosis)  $n=14$ , mass at the site of the scar  $n=8$ , skin changes  $n=2$  and diffuse breast retraction  $n=1$ .

A total of 16 patients had benign lesions including 3 patients with cysts, one patient with fat necrosis and one patient with fibroadenosis. Eleven patients had benign scars. Recurrent cancer cases ( $n=9$ ) were localized to the previously treated breast quadrant in all except one patient. The histologic types of recurrent tumor were infiltrating duct carcinoma ( $n=6$ ), invasive lobular carcinoma ( $n=2$ ) and ductal carcinoma in situ ( $n=1$ ). Recurrent tumor was unifocal in 6, multifocal in one and diffuse in 2 patients.

Diffuse recurrence was evident on microscopic examination as scattered cancer cells present within a fibrotic stroma. The sizes of recurrent tumor within the conserved breast ranged from 15-3.5 cm.

Fine needle aspiration cytology from the suspicious region revealed malignant cells in 6 patients, suspicious but probably benign in 3 and benign ductal cells in 14 patients. FNAC was diagnostic in only 19 patients giving an accuracy of 76%, 66% sensitivity and 81% specificity.

Mammography identified 7 out of 9 patients with histologically proven recurrent cancer. Serial mammographic examination showed that the area of abnormality was present one year before diagnosis in 2 out of the seven patients, but had earlier been interpreted as suggestive of postoperative scar tissue rather than recurrent cancer. The mammographic appearance of the recurrent tumors was a speculated mass ( $n=6$ ) and new microcalcification ( $n=3$ ). Mammography underestimated tumor size in 3 patients. The two false negative mammograms were technically inadequate due to the fibrosed and dense nature of the breast. The sensitivity and specificity of mammographic findings for the presence of local recurrence in the conserved breast was 77.8% and 43.7%, respectively with an overall accuracy 56%.

Breast MRI identified correctly the 9 patients with true local recurrence. Precontrast  $T_1$  weighted images were not on their own diagnostic of recurrent tumor (Fig. 1C, 2B). On the postcontrast images recurrent tumor was seen as an enhancing region of a high signal intensity compared with the adjacent irradiated breast tissue (Fig. 1D, 2C). Table (2) shows the MRI findings and diagnosis in the studied patients. Contrast enhancement suggestive of tumor recurrence was found on MRI in 2 patients with suspicious mammographic findings (Fig. 3); however the diagnostic biopsy of these 2 patients showed intense areas of inflammation and postradiation fibrosis.

The sensitivity and specificity of MRI for detection of local recurrence within the conserved breast were 100% and 87.5% respectively; with an overall accuracy 92%.

Table (1): Results of the study.

	FNAC	Mammo- graphy	Sono- graphy	Breast MRI
True positive	6	7	8	9
True negative	13	7	12	14
False positive	3	9	4	2
False negative	3	2	1	0
Sensitivity	66%	77.8%	88.9%	100%
Specificity	81%	43.7%	75%	87.5%
Accuracy	76%	56%	80%	92%

FNAC: Fine needle aspiration cytology.  
MRI : Magnetic rsonance imaging.

Table (2): Distribution of lesions within the breast on contrast enhanced MR imaging.

Appearance of the lesion	Total number	Enhancement	No enhancement
Unifocal lesion	7	4	3
Diffuse lesions	3	3	-
Multifocal lesions	2	2	-
No lesion	13	2 (along the scar)	11

Fig. (1,A,B,C,DE,F): Imaging of 39 years old women with suspected local recurrence 36 months after left BCT: Histopathologic examination revealed old benign scar with fat necrosis.

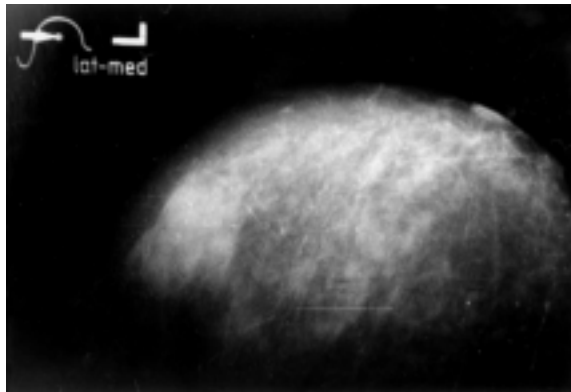


Fig. (1-A): Mammography cranio-caudal view revealed distorted anatomy of the left breast with globular radio-density at the upper outer aspect of the breast.

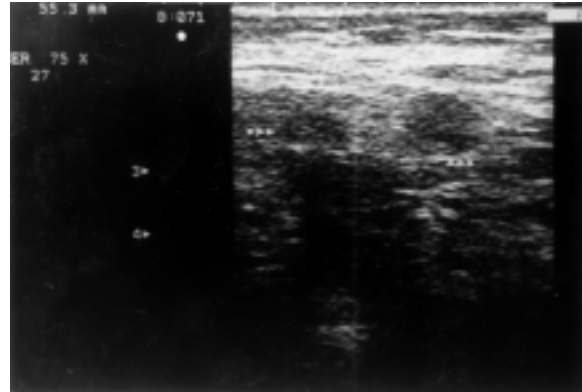


Fig. (1-B): Ultrasonography revealed a clean scar with no definite focal lesion.

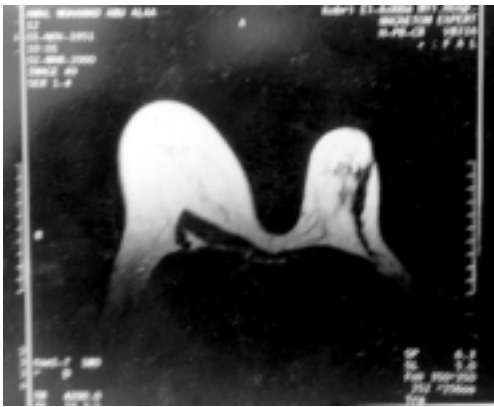


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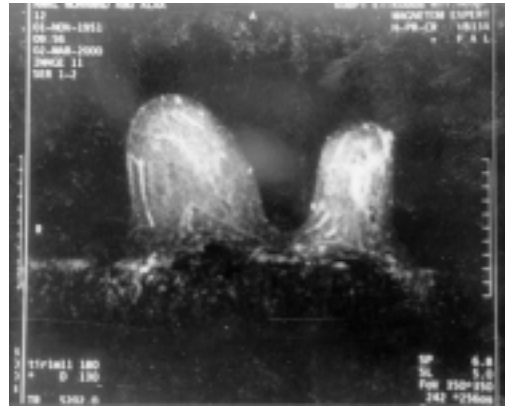


D

Fig. (1 C & D): T1 W-MRI picture without and with contrast revealed skin thickening in left breast with normal breasts tissue.



E



F

Fig. (1 E & F): T2 W1 MRI showed an old clean scar with skin thickening of the left breast with no suspicious lesions.

Fig. (2 A,B,C): Imaging of 63 years old female. She underwent right BCT-2 years ago for invasive lobular carcinoma. Follow-up examination showed a mass in the left breast. Mammography was confusing because of huge breast size. Histopathologic examination revealed recurrent tumor in the right breast and left metastasis.

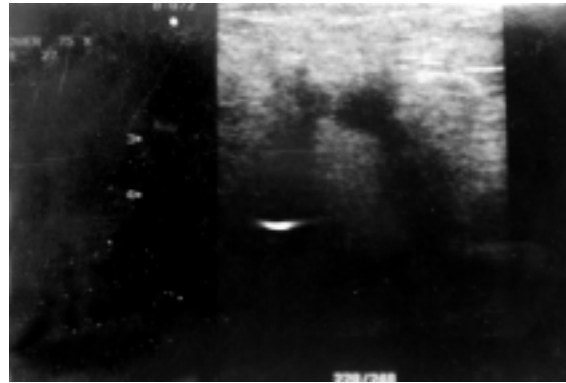
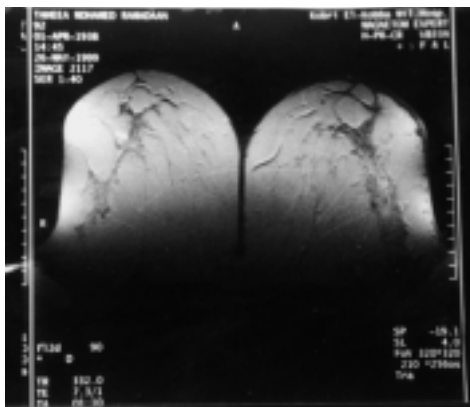
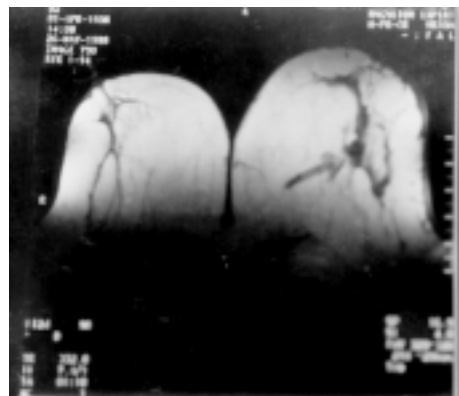


Fig. (2-A): Ultrasound examination showed irregular hypo-echoic mass in the left breast.



B



C

Fig. (2-B & C): T1 W-axial 3D MRI without and with contrast showed an irregular ring enhancement in right breast and another larger lesion with ring enhancement in the left breast.

Fig. (3): Imaging of 41 years female underwent left upper outer quadrant lumpectomy for fibroadenoma 3 years ago and right BCT for invasive duct carcinoma since 12 months. Follow-up mammography showed bilateral dense breast. Ultrasonography revealed hypo-echoic lesions in both breasts. MRI showed T1 W-axial 3D MRI with contrast showed enhanced right scar edge and adjacent area with no enhancement of the left breast scar. Histopathologic examination confirmed the MRI examination which was benign scar in both breasts.

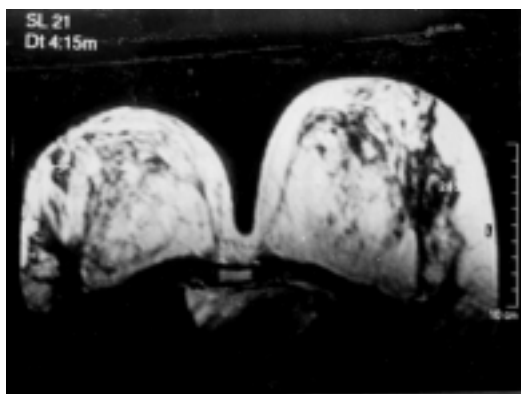


Fig. (3): T1 W-axial 3D MRI with contrast showed enhanced right scar edge and adjacent area with no enhancement of the left breast scar. Histopathologic examination confirmed the MRI examination which was benign scar in both breasts.

## DISCUSSION

Breast conserving therapy has become an established treatment modality for early breast cancer, with long-term survival equal to that with more radical surgery. Nevertheless, local recurrence remains a problem, although by combining radiotherapy with local excision the incidence has been reduced to 1 to 2% per year with the majority of recurrence occurring in the first 40 months [7].

Physical examination after BCT is usually more difficult due to the more pronounced local scarring, skin thickening, increased generalized fibrosis caused by radiation and some times fat necrosis which can obscure or mimic malignancy [3]. In addition, the findings associated with disease recurrence may be subtle producing only minimal thickening or retraction at the biopsy site [27,28] or may be diffuse breast retraction [14]. In the present study 14 patients were identified with asymptomatic lesions discovered only during follow-up mammography, eight patients presented with a clinically felt lump, 2 patients presented with skin thickening

and one patient with diffuse breast retraction. The anticipated radiologic changes in the treated breast are highly variable but usually include skin thickening, increased density of the fibroglandular and suspensory ligaments [25] and a mass or distortion in the tumor bed due to scarring with substantial overlap in radiologic appearance between benign and malignant lesions [14,32]. Recurrences of infiltrating lobular carcinoma are particularly likely to be radiologically occult [6]. In relation to these facts, there were 6 patients in the current study presenting with a mass in mammography which proved later by histopathology as a benign scar and 3 other patients were found to have cysts with an old scar presenting in mammography as suspicious lobulated lesions.

Ultrasonography at regular intervals has proven helpful in evaluation of post-treatment breasts [4]. Nevertheless, unless regular follow-up studies exist, the differential diagnosis of shadowing and hypoechoic areas, which might be caused by either scarring or malignancy, proves quite difficult. In addition, ultrasonography has limited capabilities in excluding early malignancy [3]. Similarly, according to our results there were 3 patients proved by U/S as cysts and other 6 benign scars, whom later were proven by histopathology. On the other hand there were 4 patients with false positive results giving 88.9% sensitivity and 75% specificity.

Including MRI as part of the initial assessment after BCT would have increased the sensitivity for detecting local recurrence to 100% in the present and other studies [8,16,18]. However, false positive contrast enhancement was noted in 2 patients and in both cases the surgical procedure had been performed within 12 months of MR imaging leading to specificity 87.5%. This false positive results were explained by the increased microvascular fragility and presence of fresh fat necroses leading to variable enhancement within or around the scar [15]. The identification of mammographically occult disease recurrence on MR imaging has necessitated the development of MR guided biopsy devices.

Currently, prototype biopsy systems have been developed at a number of academic sites [17,19]. However, considerable progress is required in the development of a reliable system that can routinely guide needle localization and biopsy.

Recent review [9] of the FNAC from palpable breast masses showed a range of sensitivity from 65% to 98% and specificity from 34% to 100% which is not out of keeping with our results sensitivity 66% and specificity 81%. The addition of U/S or stereotactic guidance to FNAC has been reported to improve the sensitivity to 95% and specificity to 99% [21]. However, these studies must be interpreted with caution because inadequate samples are generally not included in the analysis and histological correlation is not available for benign lesions. In addition, it is sometimes difficult to distinguish between radiation induced cellular atypia and malignant disease [9,27].

Wound complications were rare in two series when the volume of removed tissue was less than 10 cc [24,31] although in another series 4 out of 16 of such biopsies resulted in a wound infection [23]. Complication rates were higher when larger biopsies were performed or in patients with larger breasts or when skin was removed [23]. In the current series, 7 patients suffered wound complications which were infection (n=4), wound gapping (n=2) and hematoma formation (n=1).

#### Conclusion:

Triple assessment has been considered the standard method for early detection of recurrence following BCT. MRI is more accurate in diagnosing recurrence versus scars and this image technique may be considered when triple assessment is inconclusive. However, its interpretation during first year after treatment must be taken cautiously to avoid false positive results. It can reduce the number of inappropriate surgical biopsies with their attendant cost and complications.

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