

# RADIOTHERAPEUTIC MANAGEMENT OF EARLY BREAST CANCER AFTER CONSERVATIVE SURGERY

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**Abstract** - Breast conservation surgery combined with radiation therapy is now an accepted option for the treatment of early breast cancer. So we decided to evaluate the results of such treatment in our first group of patients treated by this method. From 1992 to 1996, one hundred patients with Stage I and II breast cancer treated with breast conservative surgery (lumpectomy or quadrantectomy) were irradiated at Tehran Cancer Institute and Marie Curie Clinic. In stage II the whole breast and the draining lymph-node areas, and in stage I only the breast were irradiated to 50 Gray (Gy) in 5 weeks using cobalt 60. A booster dose of 10 Gy was given at the primary tumor site by photons in 1 week. Thirty-eight percent of patients received adjuvant chemotherapy. Tamoxifen was given to 96 %. With a mean and median follow-up time of more than 3 years, three local recurrences and eight distant metastases occurred. The estimated 5-year recurrence-free survival rate was 92 % and the metastasis-free survival rate was 81 %. Seventy-seven percent were disease-free with preserved breast. Young patients and those with positive margins had a higher risk for local failure. Nodal metastasis and the omission of adjuvant tamoxifen increased the distant failure rate. Complications were rare, except for mild telangiectasia in four patients. The cosmetic result was excellent or good in 90 % of patients and the only factor with a statistically significant effect on cosmetic result was the treatment of both tangential fields per day. *Acta Medica Iranica* 38 (3): 160-165; 2000

**Key Words:** Early breast cancer, breast conservation, radiotherapy

## INTRODUCTION

Breast conservation is now the preferable treatment for the majority of women with early breast cancer. It is defined as local excision of the primary tumor with an adequate margin and axillary dissection (level I and II), followed by radiotherapy. By using irradiation, this treatment not only provides local control and survival equivalent to mastectomy, but also improves the quality of life by preserving the breast. In Western countries, a large number of prospective randomized trials or retrospective analyses have established conservative surgery plus radiation as an alternative to mastectomy in terms of locoregional recurrence and overall survival for the treatment of early breast cancer (1-5). Also the

National Institute of Health Consensus Panel Conference (USA, 1990) concluded that breast preservation was the best treatment for appropriately selected patients (3). Nonetheless, a significant proportion of women who are candidates for conservative therapy continue to be treated with mastectomy.

In the present study, we have evaluated the result of such treatment in our first group of patients treated by this method.

## MATERIALS AND METHODS

Files of all patients with early breast cancer who were treated by conservative surgery plus radiation therapy during 1992 to 1996 at Tehran Cancer Institute and Marie Curie Clinic were retrospectively reviewed. A formal inquiry form was mailed to all patients who had not come back for follow-up.

Local relapse was defined as the appearance of carcinoma in the scar and the remaining breast tissue. Regional relapse was defined as the appearance of carcinoma in lymph node areas. All other relapse locations were assumed to be distant metastases.

The breast size, shape, consistency (texture) on palpation, edema and any discoloration of skin were evaluated and assigned a score of 1-20 (total 100). The overall cosmetic result was classified as "excellent" when the treated breast was virtually indistinguishable from the opposite one (score 100), "good" when there were small but noticeable changes (score  $\geq 80$ ), "fair" if there were significant variations (score  $\geq 60$ ) and poor if there were severe sequelae (score  $< 60$ , mastectomy would have been a better option in retrospect). The cosmetic outcome was evaluated by two physicians.

Age of 35 years has been chosen as a age cutoff for the young patients in many reports (1,3,6); we did so too in this study. The period of follow-up was calculated from the onset of definitive radiotherapy to the date of last follow-up visit. The influence of various characteristics on the number of local and distant recurrences was evaluated with the chi-square test (Fisher exact test for small subgroups) and logistic-regression. The latter was also used for the evaluation of factors influencing the cosmetic result. Proportions of patients surviving various periods of time

free of recurrence and / or metastasis were computed by the life-tables. The mean survival time was calculated by Kaplan-Meier method. The univariate and multivariate analysis of factors influencing the recurrence- and metastasis-free survival was performed by the log-rank test and Cox- regression analysis, respectively.

## RESULTS

A total of 100 patients with early breast cancer had been treated by irradiation after conservative surgery at Tehran Cancer Institute and Marie Curie Clinic in the study period.

The median age at diagnosis was 44 years (range: 28-75 y); sixty-four percent of patients were premenopausal and 36% were postmenopausal at diagnosis. Primary patient characteristics are shown (Table 1).

Table 1. Patient characteristics

Characteristic	n
Menopausal status	
pre.	64
post.	36
Age at diagnosis	
< = 34	14
> 34	86
Laterality	
right	58
left	42
Tumor size	
* T0	1
Tis (in-situ)	1
T1	55
T2	37
multifocal	6
Nodal status	
negative	61
positive	35
unknown	4
Estrogen receptor (Er) status	
Er <sup>+</sup>	48
Er <sup>-</sup>	23
unknown	29
Grade	
I	11
II	24
III	13
unknown	52
Margins	
involved	2
free	88
unknown	10

\* T0 : no evidence of primary tumor

The extent of primary surgery, consisting of a lumpectomy or a quadrantectomy, depended on the preference of the referring surgeon. Treated patients had a single lesion not exceeding 5 cm clinically with an adequate tumor-to-breast ratio that produced an acceptable cosmetic result and did not have any other palpable or mammographically suspicious areas and no evidence of metastatic disease. Axillary dissection had been performed in 96%. The primary tumor was located in upper outer quadrant in 63%; eighty-six percent were invasive ductal carcinoma. In pathologic examination, a total of 55 % of patients had a T<sub>1</sub> (<= 2cm) tumor, 37 % had a T<sub>2</sub> (>2, <= 5cm) tumor and 6 % had a multifocal tumor (defined as a separate aggregate of tumor cells, not > 5 cm altogether). The median interval between surgery and the beginning of radiation was 1.5 months (range: 0.5-11 m.) and the median duration of irradiation was 47 days (range: 33-57 d.). All patients received postoperative breast irradiation in a cobalt unit. Two opposed tangential portals were used to deliver a dose of 45 or 50 Gy in 25 fractions during 5 weeks to the whole breast and one reduced portal was used to boost the primary tumor site (10 Gy / 5 fractions). Ten patients had not received the booster and were recurrence-free at the last follow-up. Twenty-six patients had been treated with one tangential field per day because of the overloaded conditions in the department. If the axillary nodes were positive, the nodal areas received 50 Gy, using an anterior supraclavicular field and a posterior axillary one. The internal mammary nodes were included in the tangential portals. Adjuvant chemotherapy was given to node-positive patients and those with high-grade tumors (total 38 %). Ninety six percent of patients received adjuvant tamoxifen. Usually the patients were followed-up at 2-3 monthly intervals for the first 2 years, 3-4 monthly intervals for a further 3 years and every 6-12 months thereafter.

The follow-up study policy consisted of a clinical examination and annual mammography for the first 5 years after treatment. The mean and median follow-up time was more than 3 years. Three percent developed local recurrence either alone (2 patients) or with a metachronous distant metastasis (1 patient). The median time to recurrence was 36 months (range: 27-39 m). The mean recurrence-free survival time was 81 months (Kaplan- Meier). The estimated 5-year local recurrence-free survival rate was 92 % (life-tables). All patients who developed recurrent breast cancer did so in the region of the original primary site. Mastectomy was performed in all of them as salvage.

Factors likely to predict breast cancer recurrence were first evaluated by the chi-square test. Young patients (< 35 years of age at diagnosis) had significantly more breast recurrences (14.3%) than did

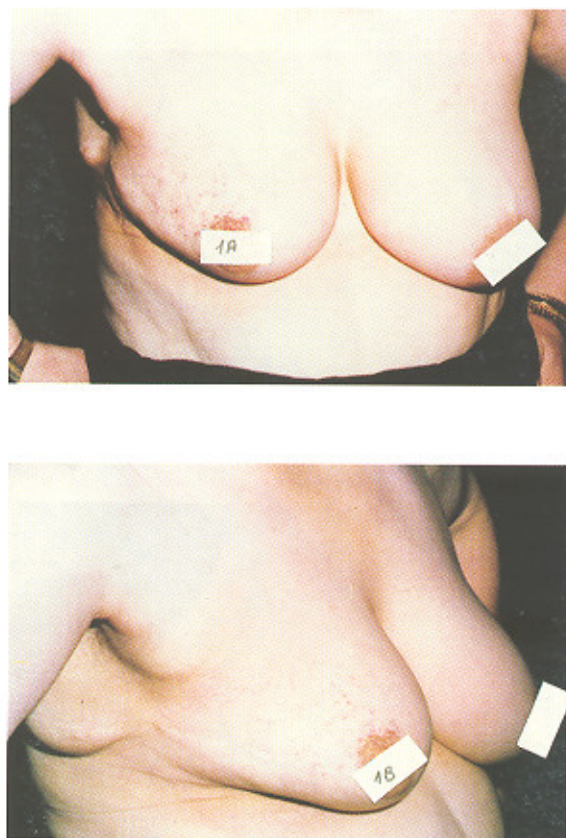


Fig. 1 (A,B). Telangiectasia 18 years after conservative surgery plus radiotherapy, right breast. This is one of our oldest cases in conservative therapy, not included in this study.

patients who were older than 34 years (1.2%;  $P=0.05$ ). One patient out of two with positive margins had a breast recurrence ( $P=0.06$ , nearly significant). When the influence of the tumor size and margin status was evaluated by logistic-regression, only the margin status was significant ( $P=0.02$ ). In univariate analysis (log-rank test), young patients ( $P=0.03$ ) and those with involved margins ( $P=0.0001$ ) had lower local recurrence-free survival; but these findings were not confirmed by multivariate Cox-regression. None of the other factors examined, including age, tumor size, grade, lymph-nodes involvement and the number involved, significantly influenced the local recurrence rate.

Eight patients developed distant metastasis with a median time of 27 months (range: 15-50 m). The mean metastasis-free survival time was 76 months (Kaplan-Meier). The estimated 5-year metastasis-free survival rate was 81 % (life-tables). Seventy-seven percent were disease-free with preserved breast (recurrence- and metastasis-free; life-tables).

The factors influencing the occurrence of distant metastasis (chi-square test) were nodal status ( $P=0.03$ ) and adjuvant tamoxifen ( $P=0.03$ ). Tamoxifen ( $P=0.025$ ) and lymph-nodes involvement ( $P=0.03$ ) remained statistically significant when the impact of young / old grouping, chemotherapy, tamoxifen, lymph-nodes involvement and the number involved were assessed by logistic-regression. In univariate analysis (log-rank test), tamoxifen ( $P=0.02$ ), lymph-nodes involvement ( $P=0.04$ ) and the number of involved nodes ( $P=0.0015$ ) significantly influenced the metastasis-free survival. When the impact of tamoxifen, chemotherapy, young / old grouping, lymph-nodes involvement and the number involved were evaluated by multivariate Cox-regression analysis, lymph-nodes involvement ( $P=0.02$ ) and tamoxifen ( $P=0.01$ ) remained significant. None of the other factors significantly influenced the metastasis-free survival ( $P>0.05$ ). None of the patients developed regional relapse. Complications were infrequent. Four patients developed mild telangiectasia (Fig. 1). Five patients developed mild breast parenchymal induration on palpation (treated with one field per day) and 3 patients (treated with axillary dissection and regional irradiation) developed arm lymphedema. Cosmetic results (Fig. 2-4) were excellent or good in 90 % (score: 80-100) and fair in 10 % (score: 60-79). None of patients had poor cosmetic result. When the impact of tamoxifen, chemotherapy, tumor size, age, young / old grouping and treatment of one field per day on cosmetic result were assessed, only the last factor was associated with a worse cosmetic outcome (logistic-regression,  $P=0.003$ ).

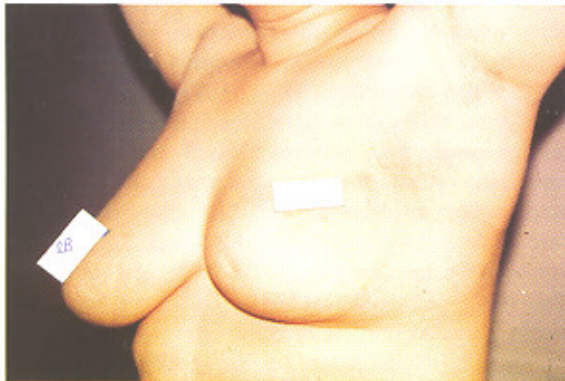
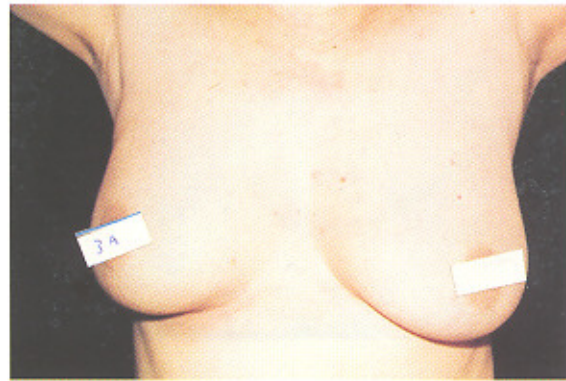
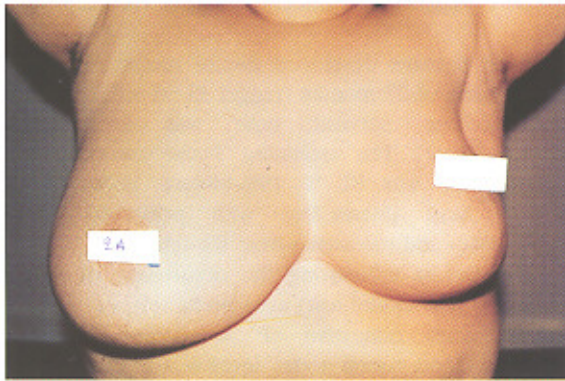


Fig. 2 (A,B) Conservative surgery plus radiotherapy, large breast (left), tumor located in tail.

Fig. 3 (A,B) Lumpectomy plus radiotherapy, normal sized breast, right.

## DISCUSSION

In recent years, the combination of conservative surgery and radiation has gained acceptance as an alternative to mastectomy with reconstruction. Women generally prefer their own breast with intact sensation and tend to score their cosmetic results more favorably than do their physicians. Many patients with breast cancer have problems with self-esteem and body image. The potential psychological, sexual and physical dysfunction caused by both the diagnosis and treatment can deteriorate the quality of a woman's life. Conservation of the breast is associated with improved psychoemotional adjustment of the patient to her own life and social functioning, in addition to excellent tumor control. The local recurrence and disease-free survival rate in our patients is comparable to those obtained in other series treated by similar techniques (1-5). In fact, the survival of women treated with breast conservation is comparable to that obtained when mastectomy is used. This trend is related to the prevention of local recurrence by systematic irradiation of the breast. Most local recurrences develop at or near the primary site (1-5). The incidence is higher during the first 5 years after treatment. Surgical salvage is possible in most patients. Early local relapses (within 5 years from initial treatment) and invasive pathology (in contrast to in-situ pathology) adversely affect survival (1). In our study, patients aged 34 years or younger were found to have a higher number of breast recurrence. There is considerable controversy in the literature regarding the importance of young age as a risk factor for local recurrence, probably due to the small number of young patients (under 35 years) and the confounding influence of unfavorable histopathological risk factors. These patients have a higher incidence of extensive intraductal component and high-grade tumors (1-4, 6). The status of margins of resection has proven to be a significant indicator of local tumor control. In addition to the present report, several other investigators have shown that in those patients with microscopic involvement there is an increased risk for local recurrence (7,8). One may speculate that if local tumor progression occurs, then it could provide a source for distant metastases. Radiotherapy can reduce the incidence of local recurrence, but cannot compensate for inadequate surgery. To ensure adequate tumor control, a negative margin is essential in breast conservation therapy. Distant failure as the first sign of relapse is related to nodal status, and this was a statistically significant finding in our study too. Patients with lymph-nodes involvement have a decreased survival rate and warrant the use of adjuvant chemotherapy (1). Because of limited use of chemotherapy in early years, we have not found any significant influence of such treatment on

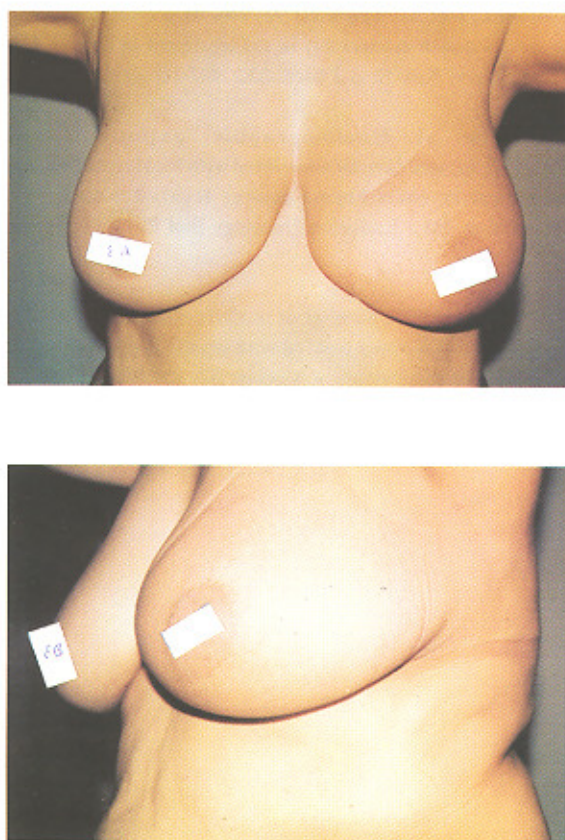


Fig. 4(A,B) Lumpectomy plus radiotherapy, large breast, left.

survival of our patients. Breast cancer is estrogen dependent and adjuvant hormonal manipulation seems to be beneficial in all patients, even in those with estrogen-receptor negative tumors. Tamoxifen has been shown to decrease not only the local and distant recurrence rate, but also the de novo cancer in contralateral breast (1). This is confirmed in part by our study too. In our patients, the cosmetic result was generally good and was influenced only by the treatment of both tangential fields per day. Delivering a homogeneous dose is essential in radiotherapy. This is accomplished by treating both tangential fields in each radiotherapy session and is accompanied with better consistency of breast parenchyma and cosmetic result (specially in large breasts).

In conclusion, the results of the present report offer a safe basis for conservative management of early breast cancers with limited surgery and irradiation in our centers. We recommend such treatment for appropriately selected women with early breast cancer and an acceptable tumor-to-breast ratio, and emphasize again the standard practice of treating all radiation fields per day.

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