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Short Communication

Can 'boost' be avoided in pre-invasive and early breast cancer with free surgical margins after breast conservation surgery and irradiation?

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Abstract

Guidelines concerning early stage breast cancer do not clearly recommend tumour bed boost dose after breast conserving surgery and irradiation when the resection margins are negative. Because the number of these patients is expected to increase, we evaluated the results of our treatment scheme in which the additional tumour bed dose was omitted. One hundred consecutive individuals with ductal carcinoma in-situ or stage I or II cancer of the breast were identified for this retrospective analysis. The observed ipsilateral breast tumour recurrence and 10-year disease-free survival rates were 4% and 91% respectively. Univariate analysis indicated that triple receptor negative tumour is the most independent prognostic risk factor. In conclusion, the observed low rate of local recurrence and many long-term survivors in this study seem to legitimize the omission of the tumour bed boost dose after whole breast irradiation in women with early carcinoma of the breast and free breast conserving surgical margins.

Keywords

Breast cancer; breast conservation surgery; radiotherapy

Breast conservation therapy is an accepted standard of care for ductal carcinoma in-situ (DCIS) and early stage cancer of the breast. The goals of this approach are survival equivalent to mastectomy, a low ipsilateral breast tumour recurrence (IBTR) rate in the treated breast, and cosmesis.

Several randomized trials summarized in a recent review article[1] about pre-invasive or early breast cancer (BCa) have shown that IBTRs are significantly reduced when an additional 'boost' dose to the tumor bed is administered after whole breast irradiation (WBI). However, it should be noted that the possibility of reduced cosmesis exists[2] and an improvement in overall survival has yet to be demonstrated with the use of the supplemental dose. Moreover, several investigators[3–5] observed that such a tumour bed boost dose (TBBD) may not be required in patients with more favorable tumours, in which margins of resection are clearly negative and in which total WBI dose is at least 50 Gy.

BCa patients who receive less than definitive care are at excess risk for disease recurrence and mortality and, therefore, women with early stage disease should be treated in accordance with existing guidelines. National

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Comprehensive Cancer Network 2010 recommendations concerning invasive BCa indicate that WBI may be given with or without TBBD.

This retrospective study has two specific objectives: (1) to determine the frequency of IBTR and long-term prognosis when the TBBD is omitted after WBI: (2) to define the risk factors associated with IBTRs and decreased survival, which could confirm the decision to administer the additional dose especially in the younger population.

Approval to analyze our database was obtained from our Institutional Review Board. Between October 1992 and October 2005, 1,998 cases of BCa were diagnosed at the Louisiana State University Health Sciences Center in Shreveport. The 100 consecutive patients identified for this retrospective study shared a diagnosis of DCIS, stage I or II BCa, treatment by breast conservation surgery with WBI, and the omission of TBBD because of free resection margins. Free surgical margin was defined as the absence of tumour at least 2 mm away from the inked margin. Exclusion criteria consisted of stage III or IV BCa; failure to complete 50 Gy of WBI; referral elsewhere for radiotherapy; undergoing accelerated partial breast irradiation; and receiving tumour bed boost dose because of tumour-positive resection margins. WBI to a total dose of 50 Gy given in 25 fractions was administered using two tangential megavoltage (6 MV) photon beams. Adjuvant chemotherapy (usually given as four cycles of doxorubicin and cyclophosphamide in 53 patients) was administered prior to WBI or hormonal manipulative therapy (Tamoxifen in 36 patients) was applied after irradiation. Study endpoints were cancer recurrence and death from any cause. The overall median follow-up period was 97.5 months (17–215 months). Overall disease-free survival was assessed by the Kaplan-Meier method. Univariate analysis using the log-rank test was performed to identify variables that influenced overall survival.

The mean age was 58.5 years (28–80 years). Twenty-four patients were 45 years old or younger, whereas 76 women were older than 45 years. Eighty-eight cases were diagnosed with invasive ductal carcinoma; 3 were invasive lobular carcinoma; 7 were medullary, micropapillary, mucinous or tubular carcinomas; and 2 were invasive intraductal mixed with lobular carcinoma of the breast. Breast cancers graded according to the Scarff-Bloom-Richardson system were 4% grade 1, 54% grade 2, 27% grade 3, and 15% grade not known. The disease stages based on the American Joint Committee on Cancer system were Tis (9 cases), stage I (61 cases), IIA (17 cases) and IIB (13 cases). The status of the tumour receptors (estrogen, progesterone, and HER2-neu) was determined by immunohistochemistry; the known instances showed a positive result in 44%, 42%, and 19% of the cases, respectively.

Four people (4%) were disease-free with follow-up ranging from 48 to 93 months after salvage mastectomy for documented IBTRs (Table 1). IBTRs occurred in 2%, 6%, and 15% of patients with stage I, IIA, and IIB diseases, respectively; IBTRs appeared in 8% of patients who were 45 years of age or younger. Such an infrequent local relapse rate, in accord with the percentages from other accounts as summarized in a 2002 report,[6] could be attributed to the pre-WBI use of adjuvant chemotherapy or hormonal therapy. The very few IBTRs precluded a meaningful analysis of the associated risk factors. Regional relapse in the supraclavicular fossa, accompanied by visceral metastases in 4 women, was found in 5 individuals (5%); survival following chemotherapy ranged from 3 to 47 months. The locoregional relapse risk

Table 1. *Oncological outcome*

Alive*	
Without cancer[a]	(89)
With regional-distant disease	(2)
Died**	
Without cancer	(3)
With regional-distant disease	(2)
With second primary cancer[b]	(2)
Cancer status unknown	(2)

*Follow-up (range 46–215 months); **Survival (range 17–130 months).
[a]Included four patients with ipsilateral breast tumour recurrences and an individual with regional relapse who were rescued by salvage surgery; [b]Multiple myeloma, lung adenocarcinoma.

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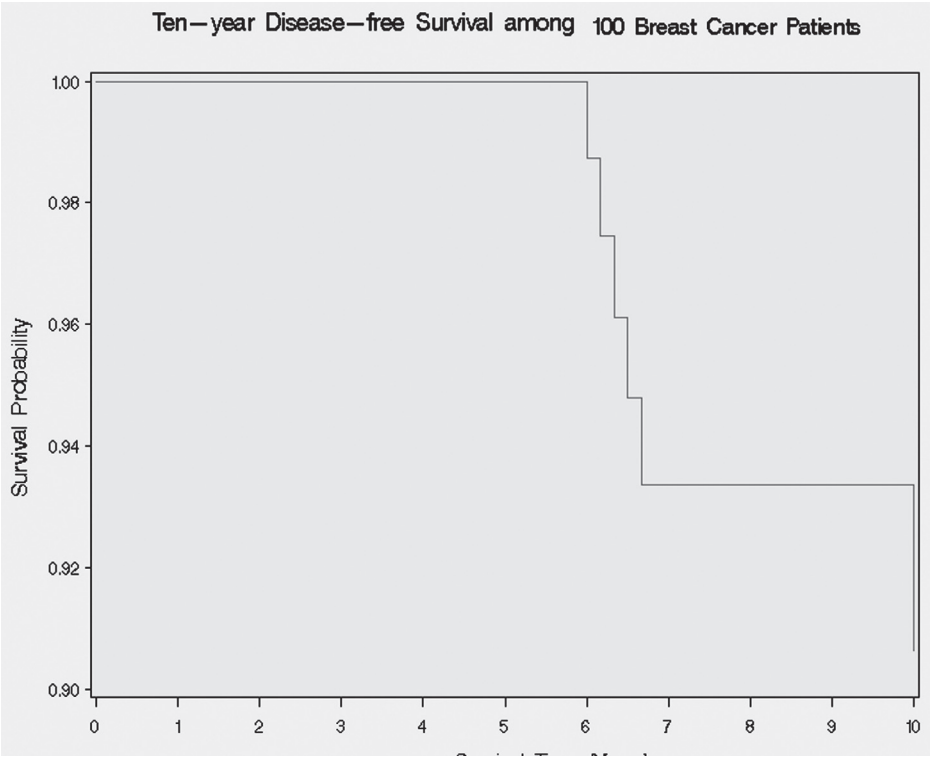

Figure 1. Kaplan-Meier overall disease-free survival at 10 years of patients with pre-invasive or early stage breast cancer managed by breast conserving surgery and irradiation without tumour bed boost dose.

Table 2. *Univariate analysis of survival*

Prognostic factors	10-year overall survival rate	*P* value
Age (≤45 years vs >45 yrs)[a]	91% vs 91%	0.98
Tumour grade* (grade 1–2 vs grade 3)[b]	96% vs 87%	0.12
Co-morbid illness** (absent vs present)[c]	97% vs 94%	0.22
Receptors (ER, PR or Her2-Neu+ vs triple negative)[d]	98% vs 80%	0.02

Evaluable patients ([a]$n = 24$ vs $n = 76$; [b]$n = 58$ vs $n = 27$; [c]$n = 31$ vs $n = 69$; [d]$n = 46$ vs $n = 22$).
*Scarff-Bloom-Richardson tumour grading classification.
**Illnesses (i.e., hypertension, diabetes mellitus, coronary artery disease, Parkinson's disease, multiple sclerosis).

factors present in 8 of these 9 patients were of a young age and had additional histopathology such as triple-receptor negative tumour, a micropapillary type of BCa, lymphovascular/perineural invasion, or more than 4 positive axillary nodes. Most of these recurrences appeared 4 years or more after the diagnosis of BCa. A second primary malignant tumour (stage IV lung adenocarcinoma or multiple myeloma) was detected in 2 people; both died with the disease. The overall 10-year disease-free survival rate was 91% (Figure 1). Analysis indicated the triple receptor negative tumour as the only independent prognostic risk factor (Table 2).

This review of cases emphasizes the importance of clinical audit, since 'IBTR rates in excess of 10% at 5 years are associated with increased BCa mortality at 15 years.'[7] In conclusion, despite the observed favorable results, the question of whether or not to administer TBBD in people with tumour-free margins of resection cannot be firmly answered considering

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the retrospective nature and non-randomized design of the investigation. We believe that the estimated IBTR risk based on patient age and additional histopathology (i.e., presence of lymphovascular invasion and high grade tumour) would better define the subgroup of individuals who will need TBBD.

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