

# Electron Arc Irradiation of the Postmastectomy Chest Wall in Locally Recurrent and Metastatic Breast Cancer

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The purpose of this study was to evaluate local–regional control and overall survival in women with locally recurrent and metastatic breast cancer (MBC) treated with postmastectomy electron arc therapy. Postmastectomy electron arc irradiation was used to treat 39 women with isolated local–regional recurrence of breast cancer following mastectomy, and 14 patients with MBC who had, or who were at high risk of, local–regional recurrence. After computed tomography treatment planning, patients were treated with electron arc radiotherapy to a median dose of 59.3 Gy. The median follow-up for alive patients was 45.4 months. For patients with local–regional recurrence, the 5-year local–regional control and overall survival rates were 74% and 43%, respectively. The 2-year overall survival was greater for those patients with a disease-free interval greater than 24 months when compared to patients with a disease-free interval less than 24 months (83% vs. 60%, respectively); however, the median survival was not significantly different (57.6 and 58.6 months, respectively). Patients with a solitary nodule at recurrence had an improved 5-year overall survival of 58% compared with 40% for patients with multiple lesions. For patients with metastatic disease, the 5-year local–regional control and overall survival rates were 76% and 31%, respectively. Local–regional control can be achieved in the majority of patients with local–regionally recurrent breast cancer (74%) or MBC (76%) who had, or who were, at high risk of local–regional recurrence treated with postmastectomy electron arc irradiation.

**Key Words:** Breast cancer—Electron arc—Rotational therapy—Chest wall—Recurrence—Metastasis.

Local–regional recurrence after mastectomy with or without adjuvant chemotherapy is found to have a prevalence of 10% to 46%.<sup>1–5</sup> Previous convention was that chest wall and/or regional recurrences meant a uniformly poor prognosis for these patients.<sup>6–8</sup> Several studies have examined the survival of various subsets of patients with local–regional recurrence of disease after mastectomy and found that prognosis is not uniform.<sup>9–12</sup> Ret-

rospective studies have revealed that patients with small chest wall recurrences (<2-cm diameter) or disease-free intervals of at least 2 years have a higher overall and disease-free survival.<sup>10,12</sup>

For patients with a local or regional recurrence from breast cancer, irradiation of the postmastectomy chest wall and regional lymphatics has been demonstrated to contribute to local control.<sup>6–21</sup> Substantial morbidity can be caused by local–regional recurrence in those patients with uncontrolled disease.<sup>12</sup>

Since 1980, we have used computed tomography (CT) treatment planning and electron arc irradiation for postoperative treatment of patients who have undergone mastectomy.<sup>15</sup> This technique of conformal electron arc therapy was designed to diminish problems with irradiating curved surfaces, overdosing or underdosing tissues at risk, and incidental overdosing of critical normal structures. Other institutions successfully use fixed field techniques with photons, electrons, or combinations for treating this complex volume.<sup>6–21</sup> However, treatment-related morbidity and mortality may limit efficacy.<sup>22–27</sup> Our results from 140 patients who were treated with the electron arc technique showed that locoregional control of the postmastectomy chest wall is comparable to photon techniques. The radiation dose to heart and lung is minimized without compromise to local control, and the acute radiation reactions were well tolerated and of limited extent.<sup>15,28</sup> Presented here are the first 39 consecutive patients treated with electron arc therapy for local–regional recurrence of disease after mastectomy. We have also analyzed and compared the outcome of 14 consecutive women who had metastatic disease, were treated by mastectomy, and received electron arc therapy to the postmastectomy chest wall for high-risk features.

## PATIENTS AND MATERIALS

Patients were treated from February 1980 through September 1998. Clinical endpoints were evaluated through September 2000. The total population studied comprised 53 women who were separated in 2 groups for analysis. Group I comprised 39 women who presented to the University of Utah, Department of Radiation Oncol-

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TABLE 1. Patient characteristics at initial diagnosis of breast cancer

	Group I (N = 39) number	%	Group II (N = 14) number	%
Age				
Median, yrs	63 (range 34–82)		56.5 (range 41–79)	
Initial T stage				
T1	10	26	3	21
T2	14	36	3	21
T3	5	13	1	7
T4	4	10	7	50
TX	6	15	0	0
No. of involved nodes				
Median	0 (range 0–21)		13 (range 0–27)	
Mean	3.73		12.33	
0	18	46	1	7
1–3	3	8	1	7
4–9	8	21	2	14
>10	4	10	5	36
Unknown	6	15	5	36
No. of nodes examined				
Median	16 (range 2–39)		17 (range 3–30)	
Mean	16.63		17.44	
<10	7	18	2	14
>10	23	59	7	50
Unknown	9	23	5	36
ER status				
ER+	12	31	0	0
ER and PR+	7	18	9	64
ER and PR–	7	18	2	14
Unknown	13	33	3	21
Histology				
Ductal/mixed	32	82	12	86
Lobular	4	10	0	0
Adenocarcinoma NOS	2	5	1	7
Unknown	1	3	1	7
Grade				
Well diff.	0	0	1	7
Moderately diff.	12	31	5	36
Poorly diff.	10	26	5	36
Unknown	17	44	3	21
Chemotherapy				
Yes	32	82	12	86
Adriamycin	12	31	10	71
5-Flourouracil	19	49	8	57
Cytosoxan	25	64	10	71
Methotrexate	15	38	2	14
Hormonal treatment				
Yes	23	59	10	71
No	14	36	3	21
Unknown	2	5	1	7

ogy with isolated locoregional recurrence of breast cancer following mastectomy combined with or without chemotherapy and/or hormonal therapy. Group II comprised 14 women who were treated with a mastectomy and were found to have metastatic disease. Patients in group II were treated with electron arc radiotherapy to promote local control in conjunction with high-dose chemotherapy followed by stem cell support (n = 3), or because of synchronous disease on the chest wall and distantly (n = 11). In group II, five patients had a local-regional recurrence, and were found to have metastatic disease.

The technique of postmastectomy electron arc irradi-

ation has been described in detail in previous reports.<sup>15,28–32</sup> Briefly, all patients underwent a treatment-planning CT scan on the day of simulation. This permits calculation of the internal mammary chain nodal depth, thickness of the chest wall (skin–pleural surface), and change in the source-to-skin distance in the cephalad/caudad dimension. To promote dose uniformity, secondary collimators were customized for each patient.<sup>29</sup> The treatment volume on the chest wall was outlined by the radiation oncologist and frequently included an irregular-shaped contour to encompass surgical scars and drain sites as needed. For each patient, a plaster cast was constructed that rested on the treatment table and was

**TABLE 2.** Group I characteristics at time of recurrence (N = 39)

	No. of patients	%
Disease-free interval		
<24 mos	15	38
>24 mos	24	62
Biopsy		
Excisional	19	49
Incisional	17	44
Unknown	3	8
Recurrence involvement		
Solitary <3-cm chest wall (CW) nodule	11	28
Solitary >3-cm CW nodule	3	8
Solitary axillary lymph node (LN)	2	5
Solitary low posterior cervical LN	1	3
Multiple CW nodules	11	28
Multiple CW nodules + axillary or supraclavicular LN	3	8
Solitary CW nodule + axillary or supraclavicular LN	2	5
Multiple axillary LN	2	5
Unknown	4	10
Chest wall treated		
Right	15	38
Left	23	59
Bilateral	1	3
Treated lymph node areas		
Axillary	30	77
Supraclavicular	31	79
Internal mammary	37	95
Posterior axillary boost	7	18
Radiotherapy		
Median dose	5940 cGy (range 4,006–7,050 cGy)	
Median no. of fields	2 (range 1–4)	
Patient status at time of analysis		
Alive	13	33
Dead	26	67

subsequently covered with lead alloy to provide tertiary collimation. Wax bolus was frequently customized to each patient to provide a smooth contour and compensate for lack of tissue in the axial plan. In the first 3 years of the study (1980–1983), the standard fraction for chest wall irradiation was 225 cGy 4 days per week. In 1984, a five fraction per week regimen was adopted and most patients were treated at 1.8 Gy daily, 5 days a week to a dose of 50.4 Gy. In the setting of microscopic or gross residual disease, a portion of chest wall was frequently boosted to a higher dose.

Isodose plots were obtained at multiple levels for all patients. The rotational therapy was divided in three segments of approximately 40° each. For each rotational segment, a customized secondary collimator was used.<sup>29</sup> The treatments were designed by selecting electron energies and placement of customized wax bolus to have the 80% isodose surface conform to the curved, pleural surface. Typically 9-, 12-, or 16-MeV electrons were used on the medial segment to ensure coverage of the internal mammary nodes, and 6- or 9-MeV electrons were used on the lateral segments.

**TABLE 3.** Group II characteristics at time of radiation therapy

	Median or number	%
Margin status		
Negative	5	36
Microscopic involvement	2	14
Gross involvement	7	50
Patients with local regional recurrence	5	36
Site(s) of metastatic disease		
Bone	9	64
Lymph nodes	2	14
Skin	1	7
Bone and lymph nodes	1	7
Lung and lymph nodes	1	7
Number of metastatic sites	2	
Radiotherapy dose (Gy)	57.1	

Local–regional failure was defined as the reappearance of disease on the chest wall and/or regional nodes and was biopsy proven in all cases. The time to treatment failure or death was measured from the first day of radiotherapy. The Kaplan-Meier method was used to evaluate and compare locoregional control (LRC) and overall survival (OS).<sup>33</sup> Statistical comparisons between groups were calculated by the log-rank test.

Statistical analysis was performed in October 2000, at which time 13 patients were alive from group I and 6 patients from group II. The median follow-up for alive patients was 59.2 and 35.1 months for groups I and II, respectively. Follow-up information was obtained from the medical records, referring physicians, and from the University of Utah Hospital Tumor Registry.

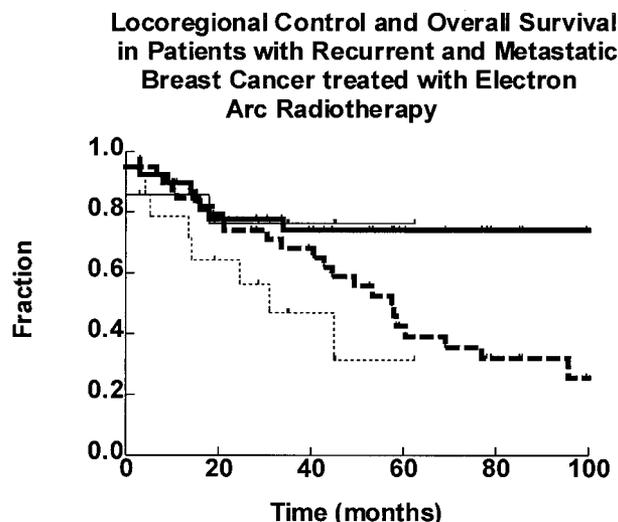
## RESULTS

### Patient Characteristics

Table 1 presents patient characteristics at initial diagnosis for patients with locoregional recurrent disease (group I) and for patients with metastatic disease (group II). The median age of patients in group I and group II were 63 (range: 34–82) and 56 (range: 41–79) years, respectively. Many patients (18/39) with recurrent breast cancer (group I) were initially lymph node negative. The group II patients had ominous prognostic factors including a median of 13 involved axillary lymph. The characteristics of the patients at the time of radiation therapy are shown in Tables 2 and 3.

Most patients received adjuvant systemic therapy. In groups I and II, 82% and 86% received chemotherapy, respectively. Hormonal therapy was a component of treatment in 59% and 71% of group I and group II patients, respectively. In group II, three patients received high-dose chemotherapy in preparation for stem cell transplant.

For patients with local–regional recurrence (group I), the 5-year LRC and OS rates were 74% and 43%, respectively (Fig. 1). For patients with metastatic disease (group II), the 5-year LRC and OS rates were 76% and

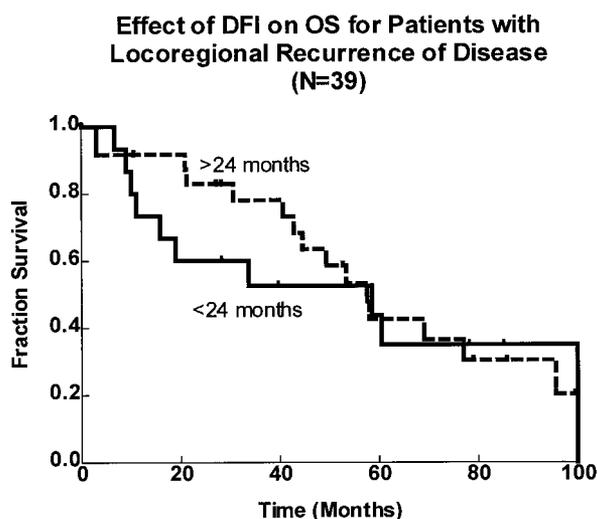


**FIG. 1.** Local-regional control (solid lines) and overall survival (dashed lines) in patients with recurrent breast cancer (group I, thick lines) and metastatic breast cancer (group II, thin lines).

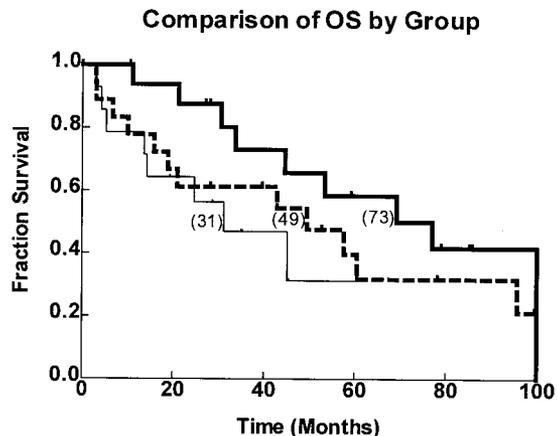
31%, respectively. Median OS times for group I and group II patients were 57.6 and 31.1 months, respectively.

The median disease-free interval (DFI) from original diagnosis to recurrence for group I patients was 30 months. The 2-year OS was greater for those group I patients with a DFI greater than 24 months when compared with the group with DFI less than 24 months (83% vs. 60%, respectively, Fig. 2); however, the median survival was not significantly different (57.6 and 58.6 months, respectively).

Figure 3 shows a comparison of survival curves be-



**FIG. 2.** Effect of disease-free interval on overall survival for patients with locoregional recurrence of breast cancer (group I).



**FIG. 3.** Comparison of overall survival for patients with a solitary recurrence (solid line), multiple lesions (dashed line), or metastatic disease (thin line). The median survivals are inset, adjacent to each curve, and were 73, 49, and 31 months, respectively.

tween groups of patients distinguished by their disease features at time of recurrence, or presence of metastatic disease. Group I is separated in solitary or multiple lesions. Seventeen patients had a solitary lesion with 11 patients having a single, smaller than 3-cm nodule confined to the chest wall. Multiple lesions at the time of recurrence were noted in 18 patients, with 11 of these patients having multiple lesions confined to the chest wall only. There was insufficient data to allow us to clarify the extent of involvement at time of recurrence for four patients. The patients with a solitary recurrence had a 5-year OS of 58% and a median survival of 73.1 months, whereas the patients with multiple recurrent lesions had a 5-year OS of 40% and a median survival of 49.4 months. In contrast, the group II patients demonstrated a 5-year OS of 31% and a median survival of 31.1 months. These survival curves did not achieve statistical significance by log rank comparison.

#### Morbidity from Radiation Therapy

Acute and chronic morbidity are described in Table 4. By Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer criteria, the most common reaction was a grade II skin reaction, which occurred in 58% of patients. Specifically, brisk erythema developed in 40% of patients and moist desquamation was observed in 30%. The development of moist desquamation was not strictly related to placement of wax bolus on the chest (as a missing tissue compensator). No patients experienced necrosis. The two incidences of esophagitis were likely secondary to use of a supraclavicular field. The most frequent chronic toxicity was a grade I skin reaction due to hyperpigmentation, which subsequently resolved in all patients. Telangiectasias formed in three patients. One patient with a history

**TABLE 4.** Incidence of acute and chronic radiotherapy toxicity

	RTOG/EORTC scoring				
	0 Number (%)	1 Number (%)	2 Number (%)	3 Number (%)	4 Number (%)
Acute					
Skin	5 (9)	17 (32)	31 (58)	0 (0)	0 (0)
Upper GI	51 (96)	2 (4)	0 (0)	0 (0)	0 (0)
Lung	100 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Chronic					
Skin	37 (70)	13 (24)	3 (6)	0 (0)	0 (0)
Upper GI	100 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Lung	52 (98)	1 (2)	0 (0)	0 (0)	0 (0)
Subcutaneous tissue	52 (98)	1 (2)	0 (0)	0 (0)	0 (0)
Bone	52 (98)	0 (0)	0 (0)	0 (0)	1 (2)

EORTC, European Organization for Research and Treatment of Cancer; GI, gastrointestinal; RTOG, Radiation Therapy Oncology Group.

of poor lung function developed a transient radiation pneumonitis, and one patient experienced a rib fracture.

## DISCUSSION

The University of Utah has used electron arc therapy for treatment of the post mastectomy chest wall since 1980.<sup>15</sup> Herbolsheimer et al. have published the only other large series describing electron arc irradiation of the postmastectomy chest wall.<sup>34</sup> As adjuvant therapy, the rates of local control appear promising with minimal rates of morbidity.<sup>15,34</sup>

Many groups have achieved favorable results of irradiation of the postmastectomy chest wall following locoregional recurrence.<sup>7-21</sup> A comparison of the LRC and OS rates with conventional irradiation techniques (fixed field approaches with photons, electrons, or combinations of both) and our results from electron arc therapy are shown in Table 5. Although the number of patients in each group is small, groups I and II had 5-year LRC rates of 74% and 76%, respectively. These values compare favorably with 5-year LRC rates for locoregionally recurrent disease following conventional radiation therapy ranging between 42% and 69%.<sup>5-14,16-21</sup>

Halverson et al. found in their analysis that those patients with a DFI greater than 24 months had a 50% 5-year OS following locoregional relapse, and that those patients with a DFI less than 24 months had 5-year OS of 35%.<sup>10</sup> Our study was too small to corroborate their observation.

We stratified patients in distinct groups based on the extent of their disease at time of recurrence. We found that the group who presented with a solitary lesion had a 58% 5-year OS in comparison with a 40% 5-year OS for patients who presented with multiple lesions.

Group II patients who were treated with known metastatic disease were included as a separate population at high risk of uncontrolled local-regional breast cancer. It is notable that LRC rates are not different for groups I

and II. In addition, 50% of the group II patients were treated with gross disease on the chest wall. Although long-term survival was limited in group II patients, a majority survived more than 30 months, more than sufficient time for local-regional recurrence to manifest. Since morbidity with this technique was not great, and recognizing the attendant problems of uncontrolled disease on the chest wall, we continue to advocate local-regional radiation in selected patients with metastatic disease to promote LRC.

A principal limitation of our study is the small number of patients analyzed. For patients with a local-regional recurrence, the prognosis is dependent on the extent of disease at recurrence. In our study, the patients with a solitary recurrence had a median survival of 73 months. This highlights the importance of minimizing morbidity in these patients, who may live for an extended period

**TABLE 5.** Overall survival and locoregional control after therapy for locoregional recurrence

Source	Number	OS (%)	LRC (%)	Interval (y)
Univ. of Utah	39	43	74	5
	39	25	74	10
Halverson <sup>9</sup>	224	43	57	5
	224	26		10
Halverson <sup>10</sup>	230	44-49		5
Toonkel <sup>21</sup>	124	38	58	5
	124	26	46	10
Aberizk <sup>6</sup>	90	50	42	5
	90	26	35	10
Beck <sup>13</sup>	121	37		5
	121	23		10
Deutsch <sup>19</sup>	107	35		5
Stadler <sup>17</sup>	149	22	49-69	5
Magno <sup>20</sup>	162	34	45	5
Schwaibold <sup>11</sup>	128	49	43	5

LRC, local-regional control; OS, overall survival.

after radiotherapy. To optimize the therapeutic benefit, morbidity of treatment must be minimized.<sup>22</sup> The importance of LRC in all subsets of patients with breast cancer is increasing as the options for systemic therapy increases. The advantages of electron arc radiation therapy in the postmastectomy setting include 1) good local control, comparable to photon techniques; 2) reasonable acute and late toxicity; 3) decreased dose to lung as demonstrated by dose-volume histogram analyses; 4) obviation of match line problem over the chest wall; 5) intramuscular nodes included without difficulty; and 6) relative ease of treatment with reproducible execution once planned. ©

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