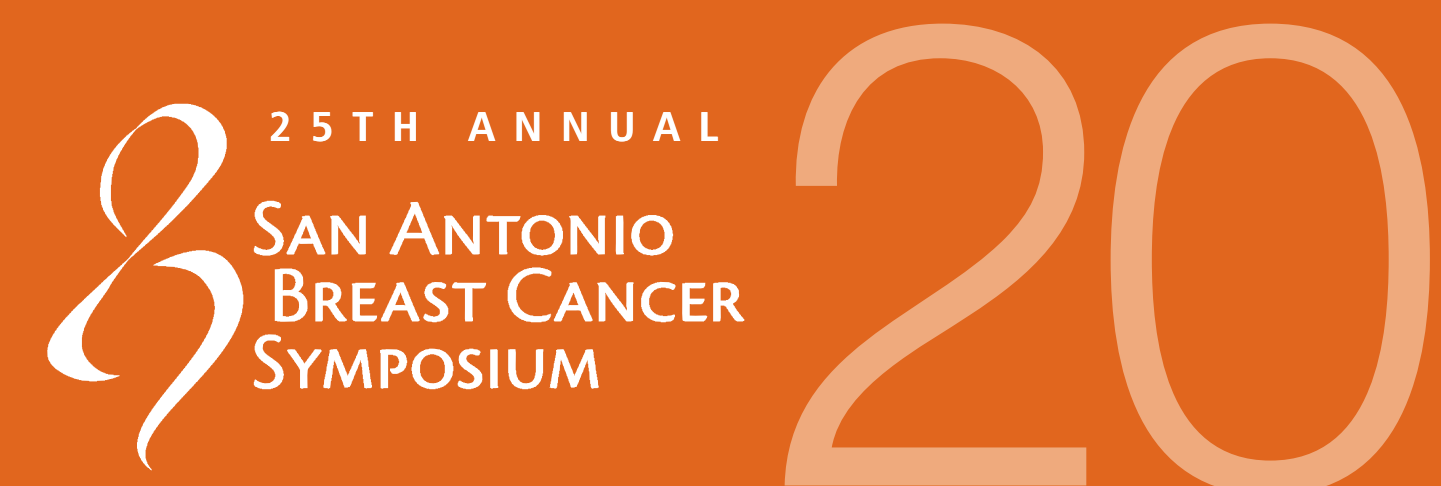


# Radiation Therapy for Primary Breast Cancer



A number of important questions about the role of radiation therapy in primary breast cancer are being evaluated in current clinical trials. One of the few local therapy questions addressed by the 2000 NIH Consensus Conference was postmastectomy radiation therapy. The panel endorsed treatment in women with four or more positive nodes and supported trials in patients with one to three nodes. A major Intergroup trial is currently addressing this question. Many researchers believe that the benefits of postmastectomy radiation therapy — like adjuvant systemic therapy — exist in a continuum, with the greatest absolute benefit occurring in patients with the greatest risk for recurrence.

## PHASE III COOPERATIVE GROUP TRIALS OF RADIATION THERAPY IN PRIMARY BREAST CANCER

Protocol	Eligibility	Randomization Arms
SWOG-S9927, RTOG-9915	Stage II breast cancer, postmastectomy, 1-3 nodes +	5 weeks radiotherapy or observation
EORTC-10981	Sentinel node-positive, operable invasive cancer	Axillary lymph node dissection or axillary radiotherapy
CAN-NCIC-MA20	Resected, early stage, invasive breast cancer Node-positive or high-risk node-negative	Adjuvant breast radiotherapy alone or with regional radiotherapy
RTOG-9804	Ductal Carcinoma <i>In Situ</i> (DCIS)	Observation or whole breast radiotherapy (tamoxifen optional for both arms)
EORTC-10925	Resected stage I/II/III breast cancer	No further therapy or internal mammary and medial supraclavicular lymph node chain radiotherapy

## DANISH BREAST CANCER COOPERATIVE GROUP (DBCG) 82B RANDOMIZED TRIAL: POSTMASTECTOMY RADIOTHERAPY IN HIGH-RISK PREMENOPAUSAL BREAST CANCER PATIENTS GIVEN ADJUVANT CHEMOTHERAPY

Eligibility	Premenopausal, high-risk stage II or III breast cancer after mastectomy	10-YEAR RESULTS			
		N	CMF	CMF + RT	
ARM 1	Radiotherapy + CMF x 8				
ARM 2	CMF x 9				
		DFS			
N 1-3+	1061	39%		54%	
N 4+	510	14%		27%	
		OS			
N 1-3+	1061	54%		62%	
N 4+	510	20%		32%	

Overgaard M et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. *N Engl J Med* 1997;337:949-955.

## DANISH BREAST CANCER COOPERATIVE GROUP RANDOMIZED (DBCG) 82C TRIAL: POSTMASTECTOMY RADIOTHERAPY IN HIGH-RISK POSTMENOPAUSAL BREAST CANCER PATIENTS GIVEN ADJUVANT TAMOXIFEN

Eligibility	Postmenopausal, high-risk stage II or III breast cancer after mastectomy	10-YEAR RESULTS			
		N	TAM	TAM + RT	
ARM 1	Adjuvant tamoxifen (30 mg po qd x 1 yr)				
ARM 2	Tamoxifen + regional XRT				
		DFS			
N 1-3+	794	31%		44%	
N 4+	448	6%		18%	
		OS			
N 1-3+	794	44%		55%	
N 4+	448	17%		24%	

Overgaard M et al. Postoperative radiotherapy in high-risk postmenopausal breast cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. *Lancet* 1999;353:1641-1648.

## BRITISH COLUMBIA RANDOMIZED TRIAL: POSTMASTECTOMY RADIOTHERAPY AND CHEMOTHERAPY IN NODE-POSITIVE PREMENOPAUSAL WOMEN WITH BREAST CANCER

Eligibility	Premenopausal, node-positive breast cancer after modified radical mastectomy	17-YEAR RESULTS				
		N	CMF	CMF + RT	RR	P
ARM 1	CMF					
ARM 2	CMF + postmastectomy XRT (between 4th and 5th cycles)					
		Local DFS				
N 1-3+	183	80%	92%	0.44	0.066	
N 4+	112	49%	83%	0.32	0.004	
		OS				
N 1-3+	183	53%	64%	0.65	0.07	
N 4+	112	28%	35%	0.74	0.2	

Ragaz J et al. Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. *N Engl J Med* 1997;337:956-962.  
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Bartelink H et al. Recurrence rates after treatment of breast cancer with standard radiotherapy with or without additional radiation. *N Engl J Med* 2001;345:1378-1387.

Cuzick J. Overview: Postmastectomy radiotherapy. NIH Consensus Conference on Early Breast Cancer. 2000.

Pierce LJ. Treatment guidelines and techniques in delivery of postmastectomy radiotherapy in management of operable breast cancer. *J Natl Cancer Inst Monogr* 2001;30:117-124.

Recht A et al. Locoregional failure 10 years after mastectomy and adjuvant chemotherapy with or without tamoxifen without irradiation: Experience of the Eastern Cooperative Oncology Group. *J Clin Oncol* 1999;17:1689-1700.

Recht A et al. Postmastectomy radiotherapy: Clinical practice guidelines of the American Society of Clinical Oncology. *J Clin Oncol* 2001;19:1539-1569.

Whelan TJ et al. Does locoregional radiation therapy improve survival in breast cancer? A meta-analysis. *J Clin Oncol* 2000;18:1220-1229.

## POSTMASTECTOMY RADIATION THERAPY

"Recent trials have shown a survival benefit following radiotherapy in all node-positive women, but the degree of benefit is unclear in patients with one to three positive nodes. Part of the dilemma is based upon the discrepancy in the rates of locoregional failure without radiotherapy in those trials, in comparison to failure rates reported in American series. The recent report by Recht and colleagues, of the patterns of failure found in studies conducted by the Eastern Cooperative Oncology Group, notes that the risk of locoregional failure was 13% at 10 years in patients with one to three positive nodes. Although this is comparable to the 16% actuarial rate seen in the British Columbia trial at 10 years, it is strikingly different from the Danish studies, where the crude rates of locoregional recurrence were approximately 30%. Based upon these results, the statement produced from the Consensus Conference, convened by the American Society for Therapeutic Radiology and Oncology to address the controversies regarding patient selection for postmastectomy radiotherapy, stated that, while there was a consensus that patients with four or more positive lymph nodes should receive radiation therapy, the data were less clear for patients with one to three positive nodes."

—Lori Pierce, MD  
Abstract, 2000 NIH Consensus Conference

## INDIVIDUALIZING TREATMENT

The ongoing Intergroup trial is very important. This study is using modern radiotherapy techniques, and one would hope that the incidence of late cardiac morbidity is going to be very low. In a nonprotocol setting, we evaluate these one to three node-positive cases individually and discuss radiation therapy in patients with large nodal metastases, extracapsular extension and large primary tumors, particularly with lots of lymphatic invasion in the breast. We also discuss this option in a woman who is very anxious to minimize her risk of failure and wants to opt for treatments that may give very little benefit. Node-positive disease is a continuum. I suspect that this will also be true of the benefits of postmastectomy radiation therapy.

—Monica Morrow, MD

## CONTINUUM OF BENEFITS

Some of the controversy in the one to three node subset is akin to what happened in adjuvant chemotherapy early in its development. Initially we thought that patients with large numbers of nodes benefited, but patients with small numbers of nodes did not. Then we recognized that patients with small numbers of nodes benefited, but we thought patients with no nodes did not. Now we recognize that even patients with no nodes in certain subsets can benefit. This principle applies across the spectrum of disease that systemic chemotherapy reduces risk of failure; however, the absolute benefit is harder and harder to see as the absolute risk of failure gets smaller. The same must be true in postmastectomy radiation. It almost certainly must help patients with one to three positive nodes. The question is, what is their absolute risk of failure, and, is the benefit of the reduction conferred by postmastectomy radiation worth taking? With the uncertainty surrounding the one to three node-positive group, we have designed a trial to assess this. This trial — sponsored through SWOG — is being run through the Intergroup. There is a huge subgroup of women out there who fit into this category, and we hope clinicians will enroll their patients in this study.

—Allen Lichter, MD  
2001 Lynn Sage Breast Cancer Symposium