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Breast Cancer In Elderly Women (≥80 Years): Variation In Standard Of Care?

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Abstract

Objective—The study aim was to investigate the methods of breast cancer diagnosis and treatment for women at advanced ages.

Methods—We identified 134 patients ≥80 years old treated for breast cancer. Data included patient and tumor characteristics, treatment, and outcomes.

Results—Of 134 women ≥80 years old, 146 breast cancers were diagnosed. Sixty-five (45%) were detected by mammography. Surgical therapy included partial mastectomy in 50% and mastectomy in 50%. Although 12 (9%) women had no axillary staging, 22 (16%) underwent axillary lymph node dissection for node-negative disease. Of 73 patients undergoing partial mastectomy, 34 (47%) received adjuvant radiation. Of 113 cancers with known estrogen receptor (ER) status, 83% were ER positive; 95% received endocrine therapy. Fourteen (10%) received adjuvant chemotherapy. Eleven (8%) were Her-2neu-amplified; 1 patient received adjuvant trastuzumab. At follow-up, 87 (65%) patients were alive without evidence of disease, while 6 (4%) died of breast cancer.

Conclusions—Breast cancer in women ≥80 years is more likely to be early-stage with favorable tumor biology. While most women eligible for anti-estrogen therapy received it, adjuvant radiation, chemotherapy, and/or trastuzumab were utilized infrequently. Despite these variations, older women with breast cancer are unlikely to suffer breast cancer-related mortality.

Keywords

Breast cancer; Elderly; Adjuvant therapy

Introduction

Breast cancer incidence increases with age, peaking at age 80 [1]. Life expectancy has steadily increased. An 80 year old American woman has a life expectancy of 89 years, and a 90 year old woman has a life expectancy of 94.5 years [2]. With the aging “Baby Boomer” population, our health system is seeing a higher volume of elderly women with breast cancer. Unfortunately, large national trials include only small numbers of these older women, and the data that is available suggests that these women often receive less than the standard of care [3-6] and have worse outcomes because of it [1, 7-9]. Other data propose that older women may, in fact, do equally well without aggressive treatment [10-12] or that standard treatments cause more complications in elderly patients [13]. Much of the literature

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defines “elderly” very broadly, including women as young as 65 or even excluding women over 80 from studies focused on older breast cancer patients [10]. There is a paucity of data for the “oldest old” patients, or patients 80 years and over.

Our study aim was to review the treatment and outcomes for women 80 years and older treated for breast cancer at our institution. Specifically, we were interested in determining whether these elderly patients received treatments that were similar to what is typically administered for specific biologic tumor characteristics in younger patients, based on available literature. This indirect comparison is performed as a consequence of the infrequent inclusion of elderly patients in randomized trials. Further, we investigated the outcomes of the elderly breast cancer patients as a proxy for the impact of their prescribed treatment plan on overall longevity.

Methods

Institutional review board approval was obtained prior to the commencement of this retrospective study. Written informed consent of the patients was not required. Clinical, demographic, and pathologic data from all breast cancer patients treated at our institution are prospectively recorded in a database. We reviewed this database and identified 134 consecutive women aged 80 and older with a diagnosis of Stage 0-IV breast cancer who underwent surgical treatment at our institution between January 1, 1998 and June 30, 2009. This included a subset of women aged 90 and older. Patient and tumor characteristics and vital status were recorded. Specific data collected included mode of presentation, patient comorbidities, tumor pathology, receptor status, staging, methods of treatment, and outcomes. The first sentinel lymph node biopsy (SLNB) performed in this cohort of patients occurred in 2000. Axillary staging described as “axillary sampling” or as a “Level I dissection” was categorized as an axillary lymph node dissection (ALND).

All data were transferred to a single spreadsheet (Excel; Microsoft, Redmond, WA). Data analysis for this study was descriptive in nature. All statistical analyses were performed using a statistical package SAS (SAS Institutes, Cary, NC). Vital status outcomes of interest included alive without evidence of breast cancer, alive with evidence of breast cancer, death from breast cancer, and death from other causes.

Results

Patients and diagnoses

We identified 146 breast cancers in 134 women aged 80 or older (Table 1). The median age of the total cohort was 84 (range 80-96), including 9 women in their nineties. There were 104 (78%) Caucasian women and 30 (22%) African-American women. Of 134 women, 59 (44.0%) had concurrent co-morbidities, excluding hypertension. Common co-morbidities included diabetes mellitus, cerebrovascular disease, coronary artery disease, arrhythmia, dementia, pulmonary disease, deep venous thrombosis, and Parkinson's disease. Eleven (8.2%) women had prior non-breast malignancies, including cervical (n = 1), carcinoid (n = 1), bladder (n = 2), melanoma (n = 2), renal cell (n = 1), lung (n = 1), anal (n = 1), endometrial (n = 1), and colon (n = 1). Twelve women (8.9%) had two primary breast cancers, either synchronous contralateral (n = 3), metachronous contralateral (n = 1), synchronous ipsilateral (n = 4), or recurrent disease (n = 4). Because the two cancers of each of these twelve women had different presentations, biopsy methods, sizes, pathologies, receptor status, and treatments, they were counted separately in the analysis.

Nearly half of the cancers (65, 44.5%) were identified by an abnormal screening mammogram. Six (4.1%) were found during workup of a contralateral or separate ipsilateral

breast cancer or during surveillance following treatment of a prior cancer. One breast cancer was seen on computed tomography of the chest as part of a renal mass work-up, and one was diagnosed on a positron emission tomography scan performed for colorectal cancer staging. However, the majority of cancers presented symptomatically, either as a palpable mass (n = 60), bloody nipple discharge (n = 4), axillary mass (n = 3), skin changes (n = 1), breast pain (n = 1), or non-resolving cystic lesion (n = 1). Two presented in an unknown fashion. The majority of cancers (114, 78.1%) were biopsied percutaneously with or without imaging guidance. Twelve cancers (8.2%) were diagnosed by excisional biopsy. The remaining cancers were diagnosed by non-bloody cyst aspirate (n = 1), bloody cyst aspirate (n = 1), duct excision for bloody nipple discharge (n = 1), fine needle aspiration biopsy (FNAB) of an axillary mass (n = 1), and skin punch biopsy of a locally advanced cancer (n = 1). Four cancers were diagnosed by unknown means.

Tumor characteristics

Most of the cancers were diagnosed at early stages, including 16 ductal carcinoma in situ (DCIS) (10.9%), 3 Tmic cancers (2.1%), and 78 T1 cancers (53.4%). The majority of cancers were either invasive ductal cancer (IDC) (94, 64.4%) or invasive lobular cancer (ILC) (14, 9.6%). Other pathologies included tubular (n = 3), papillary (n = 3), mucinous (n = 5), medullary (n = 1), mixed IDC/ILC (n = 5), and carcinoma not otherwise specified (n = 4). One recurrence has not been resected. Forty-four (30.1%) of the breast cancers were classified as low grade, 63 (43.2%) as moderate grade, and 24 (16.4%) as high grade. Of the 146 tumors, hormone receptor status was known for 113, and 83.2% of these were estrogen receptor (ER) positive (64.4% of the entire cohort). Her-2neu status was known for 112 of the tumors, and 11 were noted to be Her-2neu-amplified (9.8%). Fourteen tumors were “triple negative” (12.4%). Tumor characteristics are summarized in Table 2.

Surgical treatment

Surgical therapies are summarized in Table 3. Less than half [72 (49.3%)] of the cancers were treated with partial mastectomy, while 70 cancers (47.9%) were treated with mastectomy. Four of the cancers treated with mastectomy occurred after failed partial mastectomy, including 2 which were performed for an in-breast disease recurrence. One breast tumor was resected with an unknown procedure and one chest wall recurrence was resected. One cancer was resected by mastectomy in the setting of an axillary breast cancer metastasis without an identified breast primary tumor. One recurrence has not yet been resected.

Of the 128 invasive cancers that were resected, 12 (9.4%) did not have concurrent axillary staging. Two additional cancers were not staged due to prior ALNDs and 2 invasive cancers had unknown axillary staging. Less than half of the DCIS cases had axillary staging: 3 (18.8%) with SLNB concurrent with mastectomy, 2 (12.5%) by ALND during modified radical mastectomy (MRM), and 1 (6.3%) with a SLNB concurrent with partial mastectomy. Of the total invasive tumor cohort (n = 128), 47 (36.7%) were staged with ALNDs, including 40 of 47 (85.1%) which were performed in the era of SLNB. Eighteen of the 47 cancers (38.3%) staged with ALND without prior SLNB had positive nodes found at dissection, but 22 (46.8%) had no evidence of nodal disease. One cancer (2.1%) had micrometastatic axillary disease only, and nodal pathology was unknown for 6 of the cancers (12.8%) staged with ALND. In cases with axillary metastases, the median number of involved lymph nodes was 2 (range 1-16). The remaining 65 invasive cancers were staged by SLNB, with or without completion ALND. Of those patients undergoing SLNB, 52 (80.0%) had negative SLNs and 13 (20.0%) had positive SLNs. Two cancers (3.2%) were associated with micrometastatic disease in the SLNs and ALND was not performed in either case.

Adjuvant treatment

Of the 72 cancers treated with partial mastectomy, 34 (47.2%) completed adjuvant radiation therapy (27 whole breast/unspecified radiation, 7 partial breast radiation). Of the cancers that were ER positive (n = 94), 89 (94.7%) received adjuvant endocrine therapy (35 tamoxifen, 54 aromatase inhibitors). We were unable to verify the total length of treatment. Of 14 cancers with "triple negative" immunostains, 5 (35.7%) were treated with chemotherapy. A total of 14 cancers in our cohort were treated with chemotherapy overall, including the 5 "triple negative" cancers. Only 1 of 11 (9.1%) Her-2neu-amplified cancers was treated with adjuvant trastuzumab therapy; all 11 patients were identified in the era of trastuzumab therapy.

Women aged 90 and older

Of the 9 women in their nineties at the time of diagnosis, 4 (44.4%) were diagnosed by screening mammography and the remainder were diagnosed by a palpable abnormality. Three (33.3%) cancers occurred in patients who had previous contralateral breast cancer. Of the 9 women, 8 were diagnosed at early stages (3 DCIS and 5 T1). Four (44.4%) of the tumors in the women aged 90 and older were treated with mastectomy while 5 (56.6%) were treated with partial mastectomy. Of the 6 invasive tumors, 4 (66.7%) underwent axillary staging (1 SLNB, 1 ALND, 2 unknown axillary staging), but 2 (33.3%) did not. Of the five cancers treated with partial mastectomy, none received adjuvant radiation therapy. With regards to ER status, 2 cancers were ER positive and were treated with tamoxifen, 1 cancer with an unreported ER status was treated with tamoxifen, 1 cancer was ER negative, and 5 cancers had unknown ER status.

Patient outcomes

The median follow-up for the overall cohort was 34 months (range 1-124 months, mean 36 months). Of the 134 patients included in the cohort, 6 (4.5%) developed systemic metastases and died during the follow-up period. There was no significant difference in survival according to patient race. In comparison, the breast cancer-specific mortality for women <80 years old at our institution during the same follow-up period was 16.8% ($p<0.001$). Of those elderly patients who did not die secondary to breast cancer, 87 (64.9%) are alive with no evidence of breast cancer, 4 (3.0%) are alive with evidence of breast cancer recurrence, and 37 (27.6%) are dead secondary to other causes. Thus, the overall recurrence rate was 7.5% (10 of 134 patients), including a locoregional recurrence rate of 3.0% (4 of 134 patients) and a distant recurrence rate of 4.5% (6 of 134 patients).

Discussion

Breast cancer incidence increases with age, peaking at age 80 [1]. Elderly women appear to be a unique subset of breast cancer patients, but there is no clear consensus in the literature regarding breast cancer pathology or optimal treatment for these patients. In fact, there is disagreement about the definition of elderly; studies focusing on "elderly" or "older" patients often include women 70 or older, but may include women as young as 65 or exclude women over 80 [10]. Further, older patients are rarely included in randomized clinical trials [14].

The literature reports that 45-80% of elderly patients present with T2 or greater or palpable tumors [5, 19-21]. Our results partially corroborate these reports in that 41% of the cancers in our cohort were palpable, and over 50% of our patients were symptomatic at diagnosis. However, only 25% of the cancers were T2 or larger. This is likely secondary to the fact that nearly 50% of the patients in our cohort were diagnosed by screening mammography, despite a lack of recommendation for screening mammography in this patient population.

One would hypothesize that the lack of standard screening guidelines for elderly women may translate to advanced disease at diagnosis. Some studies do report that elderly women over the age of 80 have a higher likelihood of presenting with advanced disease [18], with up to 44% axillary nodal involvement [20-22], or with breast cancers that have poor prognostic features [19]. Other studies, however, suggest that older women have less aggressive disease [15, 16], are less likely to have nodal involvement [17], and that at least 74% of patients have hormone receptor positive tumors [9, 19-22]. Our results are more consistent with these latter studies, in that the majority of our patients had early-stage disease, only 25% of the invasive cancers staged had nodal involvement, and 83% of the cancers were ER positive. Table 4 summarizes the current study and available literature.

The current study found that the main cause of death for our elderly patients were non-breast cancer causes, and only a small number of women (4%) died secondary to their breast cancer. We did not observe any significant difference in survival according to patient race, though the low breast cancer-specific mortality may have precluded any meaningful comparison. Previous studies have reported higher rates of breast cancer-specific mortality for the elderly population [23]. Rodriguez et al. [23] reported on a series of 100 patients aged 70 and older who underwent curative-intent surgical therapy for breast cancer and found that breast cancer was the principle cause of death, despite a 77% co-morbidity rate. Evron et al. [17] similarly identified breast cancer as the cause of death in one third of the deceased patients in their cohort of 135 women aged 80 and older. It is unclear why so few women in our study died secondary to breast cancer. This finding is consistent with the less aggressive tumor biology observed in our cohort. It is also possible that the co-morbidities of our patient population were more significant than those reported in other series.

The extent of surgical treatment performed in elderly breast cancer patients varies in previous reports. The combination of concomitant co-morbidities and the relative safety of endocrine therapy in elderly patients have prompted some limited data regarding primary endocrine therapy in the absence of surgical treatment [1, 7, 24]. The GRETA trial randomized patients to receive tamoxifen alone versus surgical removal of the breast cancer followed by adjuvant tamoxifen. Although patients in the tamoxifen alone group had increased local disease progression, there was no difference in overall or disease-specific survival [24]. In contrast, other studies have shown that replacement of surgical therapy with primary endocrine therapy in elderly patients is associated with a poorer survival [1, 7]. We do not have any data regarding the use of primary endocrine therapy in our surgical database. However, we did find that our elderly patients undergoing surgical treatment of their breast cancer were as likely to have mastectomy as partial mastectomy. In fact, previous reports also demonstrate this trend toward lower rates of breast-conserving therapy in elderly women [5, 9, 19, 20, 22, 25-27].

In contrast to the trends in breast surgical procedures, elderly women are less likely to undergo axillary staging procedures compared to younger women [3, 19, 21, 25]. This is despite previous studies demonstrating that nodal involvement retains prognostic significance in older breast cancer patients [12] and that adjuvant treatment decisions are altered in many elderly patients based on axillary staging results [28-30]. Whether the absence of axillary staging necessarily translates to less favorable outcomes is less clear. Martelli et al. [10] reported 5-year follow-up on a cohort of 219 women aged 65-80 with clinical T1N0 breast cancer who were randomized to ALND versus no axillary surgery. Two women who had no axillary surgery developed an axillary recurrence, but there was no difference in overall or disease-specific mortality between the two groups [10]. Mandelblatt et al. [13] found that women aged 67 and older who underwent axillary staging, either by SLNB or ALND, developed upper extremity complications three times that of younger women. These sequelae also had a larger impact on physical and mental function in the

older patients [13]. The risks of axillary procedures in elderly women must be weighed against the potential prognostic information and benefits obtained; this is true for women of all ages, but may be particularly relevant in the elderly population. Overall, 9% of the patients in our study had no axillary surgical staging procedures, consistent with the literature. However, we were surprised by the high rates of ALND usage in women who were clinically and pathologically node-negative. It is difficult to interpret the reasons retrospectively, but this does represent potential surgical over-treatment in our cohort.

Our results corroborate that older patients receive less adjuvant radiation therapy following breast-conserving procedures [5, 25]. A report from the Netherlands Cancer Registry found that women over 80 years old were 10 times less likely to receive adjuvant radiation therapy compared to women less than 80 years of age [31]. Hughes et al. [11] randomized 636 women aged 70 and older with ER positive, Stage I breast cancer who underwent partial mastectomy to receive tamoxifen alone or tamoxifen plus adjuvant radiation therapy. The locoregional recurrence rate was 1% in the group receiving both tamoxifen and radiation therapy and 4% in the group receiving tamoxifen only ($p < 0.001$), but there was no difference in overall survival or distant disease recurrence. In contrast, a study of over 1800 women found a higher rate of death in patients not receiving adjuvant radiation therapy following partial mastectomy [9]. This latter study, however, included women aged 65 and older with Stage I and II disease. Current National Comprehensive Cancer Network guidelines state that adjuvant radiation therapy may be omitted in selected older patients. At our institution, all women aged 70 and older who undergo partial mastectomy are seen by the radiation oncologists and a multidisciplinary decision is made.

Systemic chemotherapy appears to provide elderly women the same benefit as in younger women, and poorer outcomes have been reported for patients in whom chemotherapy is omitted [5, 20, 32, 33]. Despite this, most studies report that elderly patients receive less cytotoxic therapy than younger women [5, 20, 22, 25]. Few of our patients received systemic chemotherapy. With respect to tumors with high risk characteristics, only 36% of the patients with “triple negative” breast cancer received adjuvant chemotherapy, and only 1 patient with a Her-2neu-amplified cancer received trastuzumab. The reasons for low rates of systemic chemotherapy use are likely multifactorial. Standard chemotherapy regimens may expose elderly patients to increased morbidity with less benefit when compared to their younger counterparts [11, 34]. Deviation from standard treatment guidelines may be a result of patient co-morbidity and/or preferences as well [35]. Although we observed a low rate of systemic chemotherapy use in our elderly patients, only 4.5% developed metastatic disease. Thus, other patient factors not readily evident in the available patient and tumor data may have resulted in the omission of systemic chemotherapy and/or trastuzumab secondary to perceived lower risk of distant recurrence.

Limitations of this study include its retrospective nature and potential for selection bias. We included only patients who underwent surgical therapy and were recorded in our surgical database. We do not know how many elderly patients with significant or life-threatening co-morbidities were not treated. We also do not know how many elderly patients may have been treated with endocrine therapy alone. We also do not have information for many patients regarding the reasons various surgical or adjuvant treatment options were performed and/or omitted. The individual factors involved in these complex surgical-decision-making processes were not discernible in the existing data. In addition, the extended time period over which the patients were treated could contribute to the results, as improvements in chemotherapy and hormonal therapy have been observed over time. We were unable to control for changes in treatment recommendations that occurred during the study period, such as the use of SLNB for axillary staging and trastuzumab for Her-2 neu amplified

tumors. Finally, this represents a single institutional experience with a relatively small patient cohort and results are difficult to extrapolate to other population-based data.

In summary, there is disagreement within the literature regarding the biology, natural history, and optimal treatment of breast cancer in elderly women. Our data show that elderly women treated at our institution present with early-stage, ER- positive disease, even when the majority are symptomatic at diagnosis. For women undergoing surgical therapy, more extensive surgical resection was observed. Although endocrine therapy was utilized in nearly all eligible patients, a minority of eligible patients received adjuvant radiation, systemic chemotherapy, and/or trastuzumab. Overall, breast cancer-specific mortality was low in our elderly population. Future institutional research will focus on standardizing surgical treatment algorithms for elderly women with breast cancer. Randomized controlled trials are necessary to determine optimal multidisciplinary treatment strategies for women of advanced age.

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Synopsis

Breast cancer in elderly women (≥80 years) is associated with favorable tumor biology. Despite some differences in surgical and adjuvant treatment approaches, older women with breast cancer are unlikely to suffer breast cancer-related mortality.

Table 1
Presentation and Diagnosis of 146 Breast Cancers in 134 Women Aged 80 and Older

	Number	Percent
Presentation		
Routine mammography	65	44.5
Palpation	60	41.1
Breast disease follow-up	6	4.1
Axillary mass	3	2.0
Bloody nipple discharge	4	2.7
Unknown	2	1.4
Imaging an unrelated problem	2	1.4
Skin change	1	0.7
Breast pain	1	0.7
Incidental biopsy finding	1	0.7
Enlarging breast cyst	1	0.7
Diagnosis		
Ultrasound core	74	50.7
Stereotactic core	20	13.7
Excisional biopsy	12	8.2
Unspecified core	12	8.2
Fine needle aspiration	11	7.5
Palpation core	8	5.5
Unknown	4	2.7
Cyst aspiration	2	1.4
Skin punch biopsy	1	0.7
Duct excision	1	0.7
Axillary mass biopsy	1	0.7

Table 2
Tumor Characteristics of 146 Breast Cancers in 134 Women Aged 80 and Older

	Number	Percent
Tumor size		
In situ	16	10.9
Tmic	3	2.1
T1a	6	4.1
T1b	25	17.1
T1c	47	32.2
T2	25	17.1
T3	6	4.1
T4	3	2.1
Unknown	15	10.3
Grade		
I	44	30.1
II	63	43.2
III	24	16.4
Mixed	2	1.4
Unknown	13	8.9
Estrogen receptor status		
Positive	94	64.4
Negative	19	13.0
Unknown	33	22.6
Her-2neu status		
Amplified	11	7.5
Non-amplified	101	69.2
Unknown	34	23.3

Table 3
Surgical Treatment of 146 Breast Cancers in 134 Women Aged 80 and Older

	Number	Percent
Breast Procedure		
Partial mastectomy	72	49.3
Mastectomy	70	47.9
Other*	4	2.7
Axillary Procedure		
SLNB	54	42.2†
ALND	47	36.7†
SLNB + ALND	11	8.6†
No axillary staging	12	9.4†
Other‡	4	3.1†

MRM = modified radical mastectomy; SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection

*Includes 1 patient with unknown surgical resection, 1 excision of a chest wall recurrence, 1 patient who underwent mastectomy for an occult breast primary, and 1 recurrence not yet resected.

†Calculated as a percentage of invasive tumors.

‡Includes 2 patients with prior ALND and 2 patients with unknown axillary staging.

Table 4

Elderly breast cancer characteristics in the literature

	Current study	Evron [17]	Litvak [5]	Brunello [16]	Poltinnikov [18]	Laki [15]	Smith [25]	Yood [9]
N	134	135	354	260	106	538	56725	1837
Age	80+	80+	70+	70+	70+	70+	65+	65+
Median age	84	83	N/A	75.6 (mean)	76	N/A	76	N/A
Palpable	41%	80%	46%	N/A	N/A	N/A	N/A	N/A
T1	53%	90% T1 and T2	70% Stage I-II	53%	85%	41%	N/A	71%
T2	17%	90% T1 and T2	70% Stage I-II	43%	15%	49%	N/A	29%
T3	4%	N/A	N/A	3%	0%	N/A	N/A	N/A
IDC	64%	67%	71%	73%	90%	78%	N/A	N/A
ILC	10%	11%	12%	13%	10%	14%	N/A	N/A
ER positive	83%	76%	45%	80%	78%	84%	N/A	74%
Her-2 amplified	10%	N/A	N/A	N/A	22%	N/A	N/A	N/A
Partial mastectomy	49%	N/A	47%	55%	100%‡	72%	59%	47%
Radiation therapy*	47%	N/A	45%	65%	100%‡	100%	74%	74%
Antiestrogen therapy*	93%	N/A	67%	N/A	90%	N/A	N/A	N/A
Axillary staging performed	90%	N/A	N/A	90%	69%	89%	N/A	N/A
Nodal metastases⁄	25%	44%	N/A	36%	23%	31%	N/A	N/A
Median follow-up (months)	34	70	N/A	30	55	91	N/A	N/A
Recurrence	4%	13%	N/A	N/A	N/A	9%	N/A	N/A

Table 4 legend:

N = Number of patients in sample; N/A = not available; IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma; ER = estrogen receptor.

*Calculated as the percentage of patients eligible for therapy, rather than absolute numbers receiving therapy.

⁄Calculated as the percentage of patients undergoing nodal staging who were found to have nodal metastases .

‡This study examined only women undergoing partial mastectomy with adjuvant radiation therapy.