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Breast Conservation Versus Mastectomy in Patients With T3 Breast Cancers (>5 cm): An Analysis of 37,268 patients from the National Cancer Database

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Abstract

Purpose—Breast conservation therapy (BCT) is standard for T1-T2 tumors, but early trials excluded breast cancers >5 cm. This study was performed to assess patterns and outcomes of BCT for T3 tumors.

Methods—We reviewed the National Cancer Database (NCDB) for noninflammatory breast cancers >5 cm, between 2004–2011 who underwent BCT or mastectomy (Mtx) with nodal evaluation. Patients with skin or chest wall involvement were excluded. Patients having clinical T3 tumors were analyzed to determine outcomes based upon presentation, with those having pathologic T3 tumors, subsequently assessed, irrespective of presentation. Overall survival (OS) was analyzed using multivariable Cox proportional hazards models, with adjusted survival curves estimated using inverse probability weighting.

Results—After exclusions, 37,268 patients remained. Median age and tumor size for BCT vs Mtx was 53 vs 54 years ($p < 0.001$), and 6.0 vs 6.7 cm ($p < 0.001$), respectively. Predictors of BCT included age, race, location, facility type, year of diagnosis, tumor size, grade, histology, nodes

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Compliance with Ethical Standards:

Ethical approval: This research was comprised of de-identified database records thus maintaining confidentiality and posing negligible or no risks to the participants within the dataset.

Informed consent: IRB review declared NCDB database review as exempt

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examined and positive, and administration of chemotherapy and radiotherapy. OS was similar between Mtx and BCT ($p=0.36$). This held true when neoadjuvant chemotherapy patients were excluded ($p=0.39$). BCT percentages declined over time ($p<0.001$) while tumor sizes remained the same ($p=0.77$). Median follow up was 51.4 months.

Conclusions—OS for patients with T3 breast cancers is similar whether patients received Mtx or BCT, confirming that tumor size should not be an absolute BCT exclusion. Declining use of BCT for tumors >5 cm in younger patients may be accounted for by recent trends towards mastectomy.

Keywords

Breast conservation; locally advanced breast cancer; mastectomy

Introduction

Breast conservation therapy (BCT) has become a desirable alternative to mastectomy (Mtx) for women with early breast cancer since the 1980s. These procedures have become standard of care [1] and provide equivalent outcomes to mastectomy when accompanied by radiotherapy [2]. Breast conservation surgery is typically a shorter procedure, can be scheduled more quickly for operation [3], and has psychological benefits over mastectomy [4]. These advantages have made this the standard of care, and rates of breast conservation are even now a quality measure for women having early stage breast cancer [5].

Early studies only included tumors up to 5 cm [6–9], out of an abundance of caution because it has long been known that as tumor sizes increase, so do local recurrence rates [7]. Breast conservation also spares the breast, but disfigurement caused by an unfavorable breast-to-tumor ratio when treating larger tumors is felt to obviate any benefit of BCT. Because of this, tumor size greater than 5 cm has remained a relative contraindication to BCT as suggested by NCCN guidelines [1]. There are, however, data to suggest that BCT is feasible and safe for tumors >5 cm.

Previous data has shown that there is no difference in disease-specific survival between BCT and mastectomy for tumors over 5 cm in the Medicare population [10]. That cohort of 5,685 patients was limited to those over 65, however, and we are not aware of any published literature that attempts to reproduce this analysis in a broader population of women. We therefore proceeded with this current study, using a larger, more diverse patient population from the National Cancer Database (NCDB). This investigation was performed to determine whether the overall survival (OS) conferred by BCT was similar to Mtx for noninflammatory T3 breast cancer primaries. This study was also performed to assess trends in the United States for performance of breast conservation in this group where it has traditionally been considered contraindicated.

Materials and Methods

We queried the National Cancer Database (NCDB) for breast cancers >5 cm diagnosed between 2004–2011, to provide adequate follow up, who underwent BCT or Mtx. Male

patients were excluded, as BCT is still not considered standard in this patient population. Histology codes were utilized to exclude Paget's disease and in-situ carcinomas. Patients with unknown tumor size, carcinomas labeled as "diffuse," inflammatory cancers, and patients with distant metastases were also excluded. Patients who received neoadjuvant chemotherapy were included, although neoadjuvant endocrine therapy or preoperative radiation therapy was excluded.

Clinical T3 (cT3) and pathologic T3 (pT3) tumors were reviewed to assess different objectives. cT3 tumors were used to determine predictors of BCT for tumors >5 cm as clinical stage determines treatment options. pT3 stage was utilized for survival analysis as final pathology is related to outcomes.

We excluded patients who did not undergo nodal evaluation, or for whom nodal status was not recorded, as this information is critical for survival analysis. Intervals >365 days from the time of diagnosis to surgery, which can affect survival [11], and patients who did not undergo surgery were also excluded. (Figure 1).

Sensitivity analyses were performed to determine overall survival of BCT vs. Mtx with patients receiving neoadjuvant chemotherapy excluded to eliminate any possible selection bias and confounding on survival. An additional sensitivity analysis was also performed by including pathologic T3 cases that were also clinically T3, to assess clinically accurate T3 lesions.

Age, tumor size, and nodal status were treated as continuous variables, while all others were categorical. Chi-squared and Wilcoxon rank sum tests were used to compare groups. Multivariable logistic regression was used to identify predictors of BCT based on patient, tumor, and treatment characteristics in patients with clinical T3 stage. The Cochran-Armitage test was used to analyze trends in BCT and Mtx over time, and Spearman's correlation assessed tumor size over time. OS was analyzed using Kaplan Meier methods and multivariable Cox proportional hazards models and adjusted survival curves were estimated using inverse probability weighting.

Results

After all exclusions, there were 37,268 patients fulfilling criteria for analysis (Figure 1). There were a total of 19,429 cT3 patients, among whom 16,502 (85%) underwent mastectomy versus 2,927 (15%) who received BCT. Median age was 54 for mastectomy patients versus 53 for BCT patients ($p<0.001$). Median tumor size for BCT versus Mtx was 6.0 cm versus 6.7 cm, respectively ($p<0.001$). Primaries >10 cm comprised only 4.5% of tumors in the BCT group but 8.2% of the Mtx group. Average number of lymph nodes examined was 9.2 for the BCT group and 13.2 for the Mtx group ($p<0.001$), while the average number of lymph nodes positive was 1.9 and 4.5 for BCT and Mtx, respectively ($p<0.001$). Fewer patients in the BCT group were >65 (16.3%) as versus <45 years of age (26.7%). Blacks having T3 tumors were more likely to have breast conservation (20.9% vs. 13.9%) than whites. Radiotherapy was administered to 86.9% and 66.5% of the patients having breast conservation and mastectomy, respectively (Table 1).

Overall predictors of BCT based on clinical T stage included age, race, Charlson comorbidity score, geographical location, facility type, year of diagnosis, tumor size, number of lymph nodes examined and positive, nuclear grade, histology, and chemotherapy and radiation therapy administration (Table 2). The largest predictors of BCT use included neoadjuvant chemotherapy administration (odds ratio [OR] 1.687, 95% confidence interval [95% CI], 1.499–1.898, $p<0.001$), black race (OR 1.471, 95% CI, 1.310–1.652, $p<0.001$), and grade III tumors (OR 1.542, 95% CI, 1.275–1.866, $p<0.001$). Patients less likely to undergo BCT included those who had a second cancer (OR 0.715, 95% CI, 0.600–0.852, $p=0.001$), and those who did not receive adjuvant radiation (OR 0.259, 95% CI, 0.228–0.294, $p<0.001$). Age <45 , greater number of lymph nodes examined and positive, geographic location outside of New England, lobular histology, year of diagnosis, and treatment at a comprehensive cancer center program were also less likely to receive BCT (Table 2).

The year of diagnosis predicted whether patients underwent BCT, declining from 17.5% in 2004 to 15% in 2011 ($p=0.001$) with 2010 having the lowest overall proportion of patients (13.5%) (Supplemental Table 1). However, the mean tumor size did not significantly change from 2004 to 2011 (trend $p=0.22$) (Figure 2). Over time, the use of BCT decreased in the <65 age group ($p<0.001$), whereas in the >65 age group, it was not significantly different over time (trend $p=0.288$) (Figure 3).

There was no significant difference in OS of pT3 patients when comparing BCT to Mtx ($p=0.163$). When adjusting for all of the characteristics listed in Table 2, OS of pT3 patients was still equivalent (HR 0.963, 95% CI, 0.889–1.043, $p=0.357$) between BCT and Mtx (Supplemental Table 2). The 5-year adjusted OS for BCT was 68% (95% CI 0.652 to 0.709), and 69% for Mtx (95% CI 0.686 to 0.700), $p=0.163$ (Figure 4).

When restricting the analysis to patients who were both clinically and pathologically T3, OS again remained unchanged (HR 0.963, 95% CI, 0.850–1.090, $p=0.551$). Finally, when removing patients who received neoadjuvant chemotherapy (a total of 6,424 patients) from the analysis, the survival for pT3 patients who received either Mtx or BCT still did not differ (HR 1.039, 95% CI, 0.951–1.136, $p=0.393$) (Supplemental Table 2, Figure 5).

Discussion

As the current standard of care for early stage breast cancer, breast conservation has gained wide acceptance since its introduction in the early 1970s [12]. Its application has been cautioned for tumors >5 cm because early trials, while widely varied, only included tumors 5 cm or smaller. Nevertheless, all of these studies found BCT equivalent to mastectomy, such as NSABP B-06, which limited patients to tumors >2 and <4 cm [13], as versus EORTC 10801, which included tumors up to 5 cm [9]. The Danish Cooperative Group included primaries >3 cm in 7% of the cohort, and found an 18% locoregional recurrence rate overall with no difference in OS [14]. Obedian and Haffty did not exclude T3 tumors, but these comprised only 1% of their patients. Still, they also found equivalent relapse-free and OS with negative or close margins [15]. These studies suggested that there is no difference in how larger tumors should be treated, but with none of these analyses powered to evaluate the

T3 subgroup, no conclusion can be gleaned from these data. We have now shown, in a large diverse cohort, that BCT confers similar survival to that of Mtx for tumors not previously considered amenable to breast conservation.

Large retrospective series have found that overall survival is inversely proportional to tumor size, which likely impelled exclusion of large tumors in breast conservation trials [16]. We now know that survival is equivalent for smaller tumors treated by BCT versus Mtx, and there is no biological basis for the arbitrary cutoff of 5 cm. Similarly, several small studies have shown the feasibility of BCT for large tumors in terms of overall and disease free survival, with neoadjuvant chemotherapy excluded from those analyses [17,18]. These findings are consistent with ours here, showing equivalent OS between the two treatment approaches, even when controlling for neoadjuvant chemotherapy, although these studies were small retrospective reviews [18,17]. A study by Khanna and colleagues, for example, found actuarial five year OS of 76% and actuarial disease free survival rates of 68% in tumors >4 cm, and no recurrences in patients with negative margins achieved. This coincides with our findings of an adjusted 5 year OS in pT3 patients of 68%.

Although our data show that breast conservation for larger tumors is safe, there was a trend towards mastectomy in younger women over time. Recent studies have similarly found that mastectomy rates in BCT-eligible patients have been increasing since at least 2004 [19–21]. Additionally, rates of bilateral mastectomy for unilateral disease have increased in the absence of factors increasing oncologic risk, with young age as an independent predictor of mastectomy use [22]. This trend may be related to a greater recognition of higher recurrence in younger age groups and its influence on clinical decision-making [23], but it should be noted that survival in young women (<40) is not different when treated via BCT versus Mtx [23]. This is also likely to be driven by increasing patient involvement and changing patient preferences [24].

Although the trend for BCT rates for tumors >5 cm in patients >65 years of age visually appears to decline over time in Figure 2, this was not statistically significant. It remains unknown why this differs from previously published SEER-Medicare data for women 65 showing a steady increase in BCT procedures for T3 lesions over time [10]. Meanwhile, women 65, who were not previously analyzed, had a significant decrease in BCT procedures for T3 primaries in this study. It is impossible to determine what factors would cause these variations, but both datasets do consistently find that the majority of patients with T3 tumors still undergo mastectomy [10] as expected based upon current guidelines, such as the NCCN [1], and the previous paucity of data supporting its safety.

Our data also suggest a selection bias towards Mtx for more aggressive tumors, shown here by a higher number of lymph nodes examined, greater numbers of positive nodes, and larger tumor sizes in the Mtx group. Although we do not provide benefit when varying the breast procedure based upon nodal status, this may reflect clinicians' underlying desire to be more "aggressive" in the setting of negative independent predictors of survival [16].

Also consistent with the SEER-Medicare published data on this topic, neoadjuvant chemotherapy use predicted BCT in patients having T3 tumors [10]. While we know that use

of neoadjuvant chemotherapy (as versus adjuvant chemotherapy) does not affect overall survival, it does potentially downstage the primary tumor and increase the likelihood of breast conservation [25]. This study indicates that the majority of tumors >5 cm continue to be treated with chemotherapy prior to surgery, with 66% of BCT patients having received chemotherapy in the neoadjuvant setting. Still, our sensitivity analysis removing patients receiving neoadjuvant chemotherapy confirmed the equivalence and safety of BCT versus Mtx.

Although we were unable to evaluate recurrence rates because the NCDB does not include such data, we know from the Early Breast Cancer Trialists' Collaborative Group meta-analysis that recurrence and survival are linked [26]. The similar OS found here therefore suggests that if any disease-specific survival (DSS) difference exists between BCT and Mtx for T3 tumors, the difference should be small. Moreover, a prior in a different large dataset (SEER-Medicare) has confirmed in that sizable, but smaller national cohort, there is no difference in DSS for T3 tumors undergoing BCT as versus Mtx [10].

Although this was not the focus of this study, a limitation of large datasets, like the NCDB, is the inability to judge cosmetic outcomes. There is some evidence to show that a good cosmetic appearance is feasible in BCT for T3 primaries, and recent oncoplastic techniques may provide more opportunities for cosmetically pleasing local resection of larger tumors. One such study evaluated 540 patients who underwent breast conservation for large tumor-to-breast ratio, and found that oncoplastics provided a "good" cosmetic outcome based on a five point grading scale in 97.7% of patients. The study patients' disease free survival and OS were also 87.9% and 92.9%, respectively, showing that safety was not compromised for cosmesis [27]. Another small study utilizing oncoplastic surgery with contralateral reduction mammoplasty found that these enabled larger resections, good cosmetic outcomes, and acceptable 5-year survival and local recurrence rates. Oncoplastic techniques have gained refinement and popularity, and may even allow patients having T3 lesions and smaller or borderline breast sizes to undergo breast conservation successfully.

In conclusion, BCT for tumors >5 cm is safe and has an equivalent OS to that of mastectomy. Although this study shows slightly declining use of breast conservation for larger tumors in recent years, practitioners should consider BCT based upon projected cosmetic outcome and patient desires, and no longer consider BCT contraindicated solely based upon an arbitrary size cutoff.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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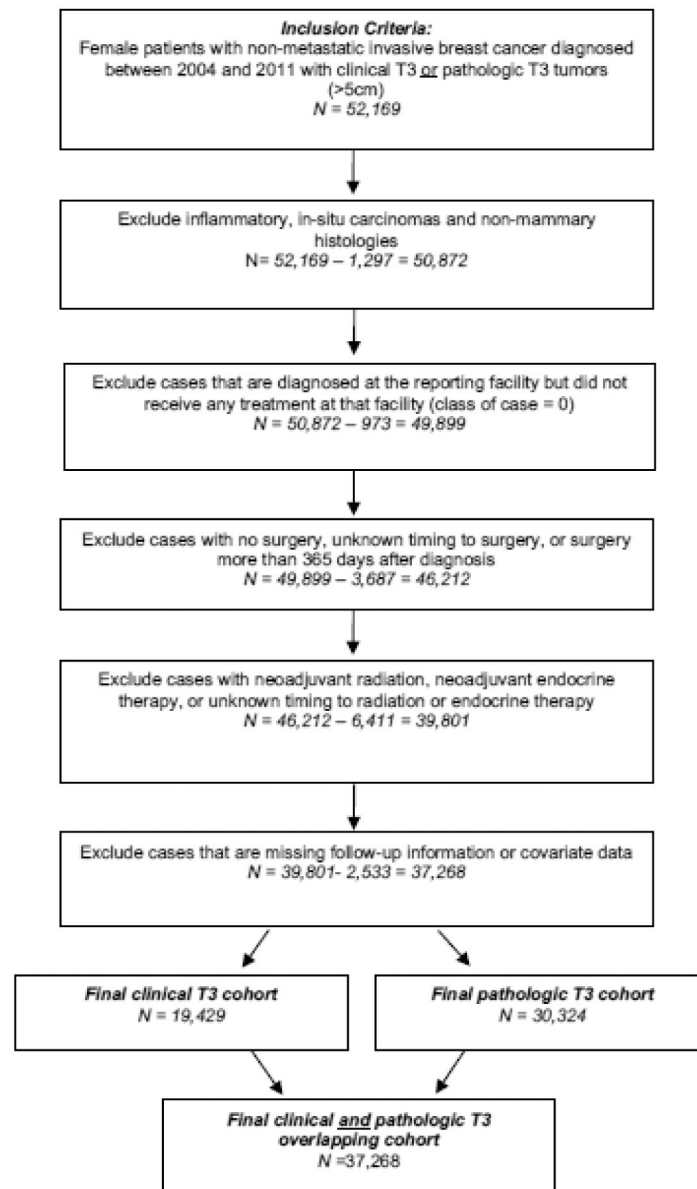


Figure 1.
Cohort exclusion diagram

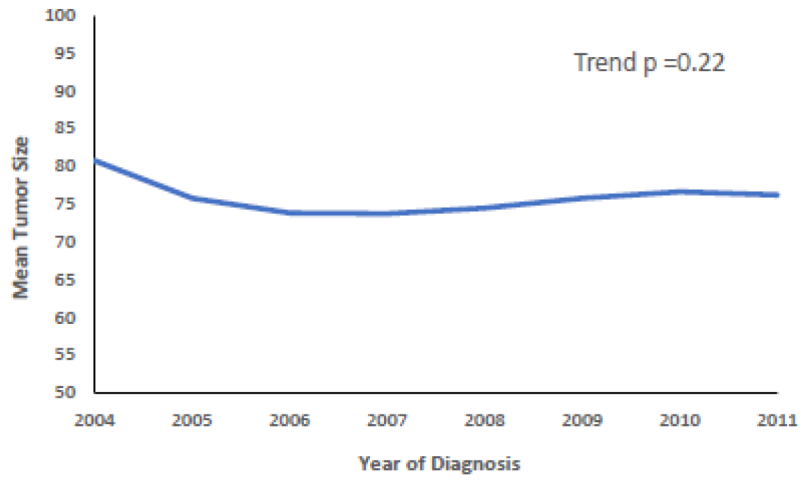


Figure 2.
Trend in tumor size over time.

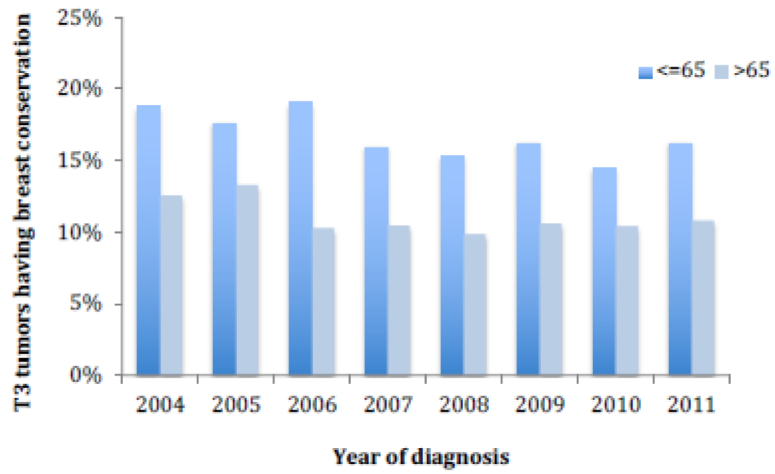


Figure 3. Unadjusted use of breast conservation over time. P for decreasing trend <0.001 for all ages; $p<0.001$ for ≤ 65 , $p=0.144$ for >65 .

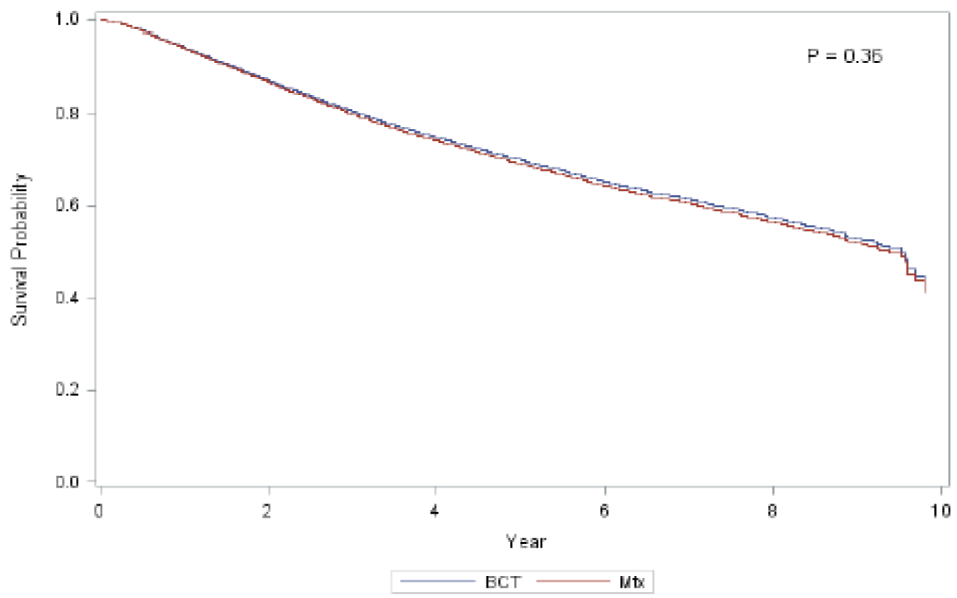
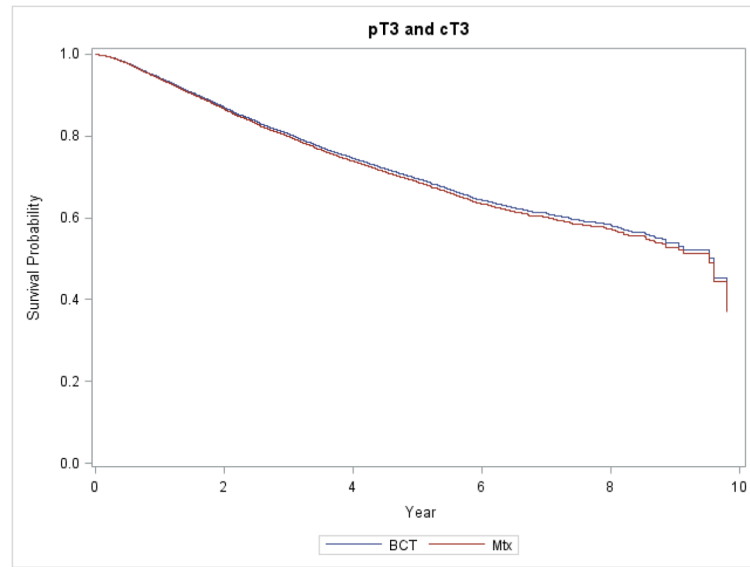


Figure 4.
Adjusted Overall Survival Breast Conservation vs. Mastectomy

a.



b.

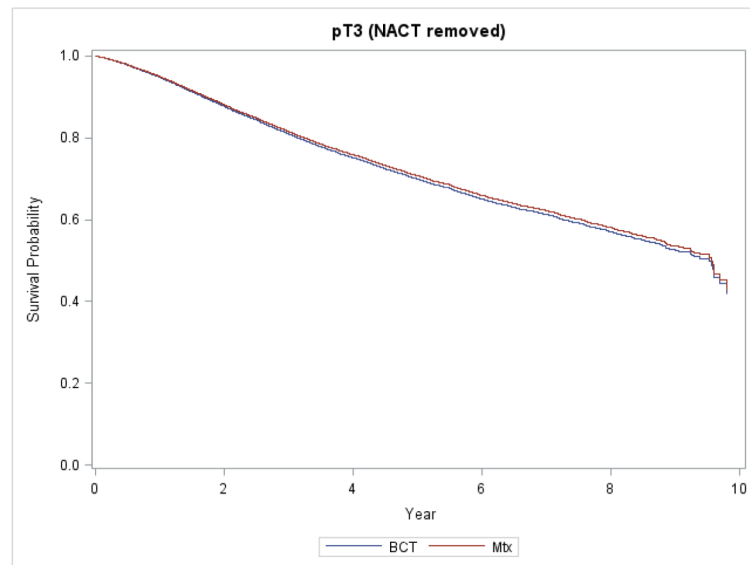


Figure 5. Kaplan-Meier Curves for Adjusted Overall Survival of (A) Combined pT3 and cT3 cohort and (B) pT3 with NACT removed.

Table 1.Characteristics by Surgical Treatment - Clinical T3 patients^a n(%)

		BCT (N =2,927)	Mtx (N = 16,502)	Total (N = 19,429)	P-value*
Age at Diagnosis	45	781 (16.2)	4048 (83.8)	4829	<0.001
	46–55	965 (16.9)	4751 (83.1)	5716	
	56–65	703 (15.8)	3742 (84.2)	4445	
	65	478 (10.8)	3961 (89.2)	4439	
Mean Age at Diagnosis (±SD)^b		53.7 (±12.56)	55.8 (±14.20)	55.5 (±13.98)	<0.001
Race	White	2093 (13.9)	13011 (86.1)	15104	<0.001
	Black	698 (20.9)	2635 (79.1)	3333	
	Other/Unknown	136 (13.7)	856 (86.3)	992	
Hispanic	No	2489 (14.9)	14175 (85.1)	16664	0.456
	Yes	214 (16.0)	1123 (84.0)	1337	
	Unknown	224 (15.7)	1204 (84.3)	1428	
Charlson Comorbidity Score	0	2609 (15.6)	14123 (84.4)	16732	<0.001
	1	258 (11.7)	1955 (88.3)	2213	
	2+	60 (12.4)	424 (87.6)	484	
	21% or more	546 (15.6)	2943 (84.4)	3489	
Education^c	13% - 20.9%	750 (15.4)	4117 (84.6)	4867	
	7% - 12.9%	903 (15.1)	5063 (84.9)	5966	
	Less than 7%	662 (14.0)	4059 (86.0)	4721	
	Missing	66 (17.1)	320 (82.9)	386	
	Less than \$38,000	570 (16.1)	2965 (83.9)	3535	
Income	\$38,000 - \$47,999	619 (14.4)	3691 (85.6)	4310	
	\$48,000 - \$62,999	755 (15.0)	4291 (85.0)	5046	
	\$63,000 +	916 (14.9)	5226 (85.1)	6142	
	Missing	67 (16.9)	329 (83.1)	396	
	Medicaid	374 (17.5)	1768 (82.5)	2142	
Insurance Status	Medicare	534 (11.2)	4229 (88.8)	4763	
	Not Insured	133 (17.2)	642 (82.8)	775	
	Other Government	35 (16.1)	182 (83.9)	217	
	Private Insurance	1785 (15.9)	9422 (84.1)	11207	
	Unknown	66 (20.3)	259 (79.7)	325	
Urban setting^d	Large metropolitan	1656 (16.0)	8708 (84.0)	10364	<0.001
	Small metropolitan	784 (14.1)	4789 (85.9)	5573	
	Suburban	255 (14.3)	1530 (85.7)	1785	
	Rural	118 (11.8)	879 (88.2)	997	
	Unknown	114 (16.1)	596 (83.9)	710	
Distance to reporting facility^e	10	1639 (15.5)	8907 (84.5)	10546	0.01
	11 – 20	626 (14.4)	3727 (85.6)	4353	
	21 – 50	447 (15.3)	2468 (84.7)	2915	

		BCT (N =2,927)	Mtx (N = 16,502)	Total (N = 19,429)	P-value*
Geographic location ^f	>50	150 (12.1)	1087 (87.9)	1237	<0.001
	Unknown	65 (17.2)	313 (82.8)	378	
	New England	188 (18.8)	810 (81.2)	998	
	Middle Atlantic	396 (16.3)	2037 (83.7)	2433	
	South Atlantic	755 (15.9)	3979 (84.1)	4734	
	East North Central	533 (14.9)	3050 (85.1)	3583	
	East South Central	143 (11.5)	1100 (88.5)	1243	
	West North Central	157 (11.6)	1195 (88.4)	1352	
	West South Central	221 (14.2)	1336 (85.8)	1557	
	Mountain	120 (11.9)	887 (88.1)	1007	
	Pacific	414 (16.4)	2108 (83.6)	2522	
	Facility Type ^g	Community Cancer Program	**	1790 (84.6)	
Comprehensive Community Cancer Program		1557 (14.0)	9598 (86.0)	11155	
Academic/Research Program		1038 (16.9)	5088 (83.1)	6126	
Other/Missing		**	26 (83.9)	**	
Year of Diagnosis	2004	248 (17.5)	1166 (82.5)	1414	0.001
	2005	265 (16.7)	1321 (83.3)	1586	
	2006	292 (17.2)	1410 (82.8)	1702	
	2007	303 (14.9)	1731 (85.1)	2034	
	2008	404 (14.0)	2488 (86.0)	2892	
	2009	461 (14.9)	2636 (85.1)	3097	
	2010	447 (13.5)	2876 (86.5)	3323	
	2011	507 (15.0)	2874 (85.0)	3381	
Cancer Sequence ^h	1st	2761 (15.6)	14967 (84.4)	17728	<0.001
	2+	166 (9.8)	1535 (90.2)	1701	
Tumor Size	1 – 7 cm	2186 (17.6)	10221 (82.4)	12407	<0.001
	7.1 – 10 cm	609 (11.0)	4925 (89.0)	5534	
	>10cm	132 (8.9)	1356(91.1)	1488	
Mean Tumor Size (±SD) ^b		74.1 (±74.25)	78.8 (±71.16)	78.1 (±71.65)	<0.001
No. of Nodes examined	1 – 5	1318 (28.7)	3274(71.3)	4592	<0.001
	6 – 10	504 (13.2)	3313 (86.8)	3817	
	11 – 15	490 (10.7)	4094 (89.3)	4584	
	16 – 20	330 (9.9)	3011 (90.1)	3341	
	>20	285 (9.2)	2810 (90.8)	3095	
Mean No. of Nodes Examined (±SD) ^b		9.2 (±7.94)	13.2 (±8.33)	12.6 (±8.39)	<0.001
No. of Nodes Positive	0	1524 (24.3)	4748 (75.7)	6272	<0.001
	1 – 3	919 (14.5)	5401 (85.5)	6320	
	4 – 6	212 (8.5)	2291 (91.5)	2503	
	7 – 9	112 (7.6)	1371 (92.4)	1483	
	10	160 (5.6)	2691 (94.4)	2851	

		BCT (N =2,927)	Mtx (N = 16,502)	Total (N = 19,429)	P-value*
Mean No. of Nodes positive		1.9 (±3.93)	4.5 (±6.06)	4.1 (±5.86)	<0.001
	(±SD) ^b				
	1	162 (10.3)	1410 (89.7)	1572	<0.001
	2	795 (11.9)	5875 (88.1)	6670	
Grade	3	1719 (17.7)	7971 (82.3)	9690	
	Undifferentiated	24 (16.3)	123 (83.7)	147	
	Unknown	227 (16.8)	1123 (83.2)	1350	
	Ductal	2449 (16.5)	12359 (83.5)	14808	<0.001
Histology	Lobular	306 (8.1)	3466 (91.9)	3772	
	Other	172 (20.3)	677 (79.7)	849	
	Administered	2545 (18.8)	10976 (81.2)	13521	<0.001
Radiation	Not administered	382 (6.5)	5526 (93.5)	5908	
	Neoadjuvant	1934 (19.8)	7842 (80.2)	9776	<0.001
	Adjuvant	664 (10.1)	5914 (89.9)	6578	
Chemotherapy	None	316 (10.7)	2641 (89.3)	2957	
	Unknown	13 (11.0)	105 (89.0)	118	

Abbreviations: SD- standard deviation

* Chi-square test (categorical variables) or Wilcoxon rank sum test (continuous variables)

** Cells have been censored in accordance with NCDB privacy requirements to do so for any cell <11 or for any cell that makes those cells calculable.

^a Numbers shown as number (row %) unless otherwise indicated.

^b Age and size analyses are shown here as continuous variables to illustrate cohort compositions.

^c Education represents the percentage of individuals within a ZIP code from census data having <12 years of education.

^d Setting definitions: Large metropolitan indicates counties of metropolitan areas of >1,000,000; Small metropolitan, counties in metropolitan areas of <250,000 to 1,000,000; Suburban, urban population of >20,000 adjacent to a metropolitan area or 2500 to 19,999 adjacent to a metropolitan area; rural, completely rural or <2500 or >20,000 urban population nonadjacent to a metropolitan area.

^e Miles between patient's residence and the hospital that reported the case

^f Region groupings: New England (CT, MA, ME, NH, RI, VT), Middle Atlantic (NJ, NY, PA), South Atlantic (DC, DE, FL, GA, MD, NC, SC, VA, WV), East North Central (IL, IN, MI, OH, WI), East South Central (AL, KY, MS, TN), West North Central (IA, KS, MN, MO, ND, NE, SD), West South Central (AR, LA, OK, TX), Mountain (AZ, CO, ID, MT, NM, NV, UT, WY), Pacific (AK, CA, HI, OR, WA).

^g Community Cancer program: >100 but <500 newly diagnosed cancer cases each year; Comprehensive community cancer program: 500 or more new cases for three consecutive years; Academic/Research program: participates in postgraduate medical education in at least four program areas, and >500 newly diagnosed cancer cases each year.

^h The number of the cancer that the breast cancer represents, among cancers of any type, if they had >1 cancer of any type during their lifetime.

Table 2:

Predictors of BCT (cT3 patients)

	OR	95% CI		p-value	Overall Significance
Age					
45	0.928	0.760	1.133	0.462	
46 – 55	1.145	0.954	1.376	0.147	<0.001
56 – 65	1.211	1.014	1.447	0.035	
>65	Referent				
Race					
White	Referent				
Black	1.471	1.310	1.652	<0.001	<0.001
Unknown	0.766	0.616	0.953	0.017	
Hispanic					
No	Referent				
Yes	1.077	0.897	1.293	0.426	0.297
Unknown	1.140	0.952	1.365	0.155	
Charlson Comorbidity Score					
0	Referent				
1	0.836	0.716	0.975	0.022	0.051
2	1.049	0.770	1.428	0.764	
Insurance					
Private Insurance	Referent				
Medicaid	1.086	0.944	1.250	0.249	
Medicare	0.948	0.798	1.126	0.544	0.060
Not Insured	1.023	0.813	1.288	0.844	
Other	1.052	0.694	1.593	0.813	
Unknown	1.762	1.272	2.440	0.001	
Education^a					
21% or more	Referent				
13% - 20.9%	1.139	0.983	1.319	0.084	0.318
7% - 12.9%	1.153	0.972	1.369	0.103	
Less than 7%	1.063	0.872	1.296	0.547	
Missing	1.912	0.055	66.780	0.721	
Income					
< \$38,000	Referent				
\$38,000 - \$47,999	0.907	0.783	1.050	0.190	0.755
\$48,000 - \$62,999	0.921	0.786	1.078	0.306	
\$63,000 +	0.896	0.740	1.084	0.259	
Missing	0.706	0.026	19.254	0.836	
Urban setting^b					
Large Metropolitan	Referent				0.330
Small metropolitan	0.912	0.805	1.033	0.148	

	OR	95% CI		p-value	Overall Significance
Suburban	0.832	0.677	1.022	0.079	
Rural	0.991	0.736	1.335	0.955	
Unknown	0.964	0.719	1.291	0.804	
Distance to reporting facility (miles)^c					
10	Referent				
11 – 20	0.944	0.848	1.050	0.288	0.236
21 – 50	1.108	0.964	1.274	0.148	
>50	0.952	0.750	1.209	0.688	
Unknown	0.857	0.226	3.242	0.820	
Geographic location^d					
New England	Referent				
Middle Atlantic	0.816	0.639	1.043	0.105	
South Atlantic	0.778	0.619	0.978	0.032	
East North Central	0.728	0.566	0.937	0.008	<0.001
East South Central	0.558	0.413	0.755	0.000	
West North Central	0.539	0.399	0.729	<0.001	
West South Central	0.757	0.561	1.023	0.070	
Mountain	0.641	0.4773	0.869	0.004	
Pacific	0.925	0.724	1.183	0.536	
Facility Type^e					
Community Program	Referent				
Comprehensive Community	0.797	0.676	0.939	0.007	0.005
Academic/Research	0.963	0.801	1.158	0.687	
Other/Missing	0.911	0.704	1.179	0.478	
Year of diagnosis	0.951	0.932	0.970	<0.001	<0.001
Cancer Sequence^f					
First	Referent				<0.001
2+	0.715	0.600	0.852	0.001	
Tumor size					
5.1 to 7 cm	Referent				<0.001
7.1 to 10 cm	0.576	0.521	0.637	<0.001	
>10 cm	0.457	0.367	0.568	<0.001	
No. nodes examined	0.948	0.941	0.975	<0.001	<0.001
No. nodes positive	0.928	0.914	0.943	<0.001	<0.001
Grade					
1	Referent				
2	1.123	0.930	1.356	0.252	<0.001
3	1.542	1.275	1.866	<0.001	
Undifferentiated	1.250	0.790	1.979	0.355	
Unknown	1.416	1.114	1.801	0.005	
Histology					<0.001

	OR	95% CI		p-value	Overall Significance
Ductal	Referent				
Lobular	0.604	0.524	0.696	<0.001	
Other	1.264	1.056	1.513	0.011	
Chemotherapy					
Adjuvant	Referent				
Neoadjuvant	1.687	1.499	1.898	<0.001	<0.001
None	1.533	1.283	1.832	<0.001	
Unknown	1.841	0.969	3.499	0.062	
Radiotherapy					
Administered	Referent				<0.001
Not administered	0.259	0.228	0.294	<0.001	

Abbreviations: BCT, breast conservation therapy; cT3, clinical T3 patients

^a Education represents the percentage of individuals within a ZIP code from census data having <12 years of education.

^b Setting definitions: Large metropolitan indicates counties of metropolitan areas of >1,000,000; Small metropolitan, counties in metropolitan areas of <250,000 to 1,000,000; Suburban, urban population of >20,000 adjacent to a metropolitan area or 2500 to 19,999 adjacent to a metropolitan area; rural, completely rural or <2500 or >20,000 urban population nonadjacent to a metropolitan area.

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