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The Impact of Post-Mastectomy Chest-Wall Radiation on Overall Survival for Intermediate Risk Breast Cancer Patients: A National Cancer Data Base Analysis

By

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Master of Public Health

Biostatistics and Bioinformatics

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2017

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Abstract

Background:

The recommendation of post-mastectomy radiation therapy (PMRT) to breast cancer women with intermediate-risk disease requires clinical judgment without a single, validated formula. We assessed the impact of PMRT on overall survival (OS) among breast cancer patients considered intermediate risk for local recurrence by querying the National Cancer Data Base (NCDB) 2004-2014.

Methods:

We replicated the SUPREMO phase III clinical trial by including patients with pT1-2N1 (or pT2N0 with either histologic Grade = 3 or presence of lymph vascular invasion) who underwent total mastectomy and did not receive neoadjuvant therapy. PMRT had a total radiation dose 40-70 Gy given within 6 months after surgery. OS was defined as survival duration in months from surgery date. Logistic regression assessed the pattern of PMRT utilization. Cox proportional hazard model was used for the association with OS. Propensity score (PS) overlap weighting was implemented to balance observed baseline characteristics. The effect of PMRT in subgroups was estimated through a multivariable model (MVA) with interactions.

Results:

We obtained 35,244 eligible subjects with a median follow up of 65.5 months. The median age was 57, 82.6% were white, the median tumor size was 2.4 cm, 38.4% had Grade III-IV, 96.2% had a negative surgical margin, and 68.3% received adjuvant chemotherapy. 4841 (13.7%) received PMRT while 30,403 (86.3%) without. Factors associated with a higher probability of PMRT usage include 3 PLN, present of LVI, younger age, and larger tumor size. The 10-year survival rate was 72.1% (PMRT+) vs. 68.7% (PMRT-). According to MVA, the hazard ratio (HR) for PMRT+ vs. PMRT- was 0.82 (95%CI: 0.75-0.89), and it was 0.84 (95%CI: 0.74-0.95) by the PS weighting approach. In the subgroups, compared to PMRT- group, PMRT increased the OS among patients with age > 60 (HR=0.68, 95%CI: 0.60-0.77) and ER positive (HR = 0.75, 95% CI: 0.67-0.84).

Conclusion:

In this large respective study based on NCDB, PMRT provided significant long-term survival benefits among intermediate-risk breast cancer patients, with larger survival benefits noted amongst patients age > 60 and ER positive. Additional guidance for PMRT may require information such as disease-specific survival or recurrence, which is unavailable in NCDB.

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Contents

Introduction:

An estimated number of 252,710 new cases of invasive breast cancer is expected to be diagnosed among female patients in 2017 and about 1 in 8 women living in the US has a lifetime risk of breast cancer [1]. Post mastectomy radiation therapy (PMRT) is the radiation therapy given to patients after surgery to kill residue cancer cells. Reasons for PMRT includes: reduction in local-regional failure risk, potential physical and psychologic morbidity and distant relapse and death risk [2]. The optimal approach to PMRT remains in question. According to the National Comprehensive Cancer Network, patients with more than four positive lymph nodes and tumor size >5 cm is strongly recommended for PMRT and patients with one to three positive lymph node and tumor size ≤ 5cm should "strongly consider radiation" [3].

Randomized clinical trials have confirmed the PMRT can reduce the mortality rate in high-risk breast cancer women for a tumor size ≥ 5cm and with equal or more than 4 histologically involved axillary nodes [4-5]. However, both long and short term side effects of radiation therapy after mastectomy includes infection, implant removal, increasing the risk of breast reconstruction failure and wound healing complications which may affect the overall survival rate and the quality of life for patients [6-9]. The effect of chest wall radiation after mastectomy on overall survival remains unclear on intermediate risk breast cancer patients with one to three axillary lymph nodes involved [10]. There is no clear formula to decide whether to recommend the use of PMRT or not from previous studies. A closed Phase III randomized clinical trial (Selective Use of Postoperative Radiation aftEr MastectOmy, SUPREMO) studied the role of adjuvant

chest wall radiation following mastectomy for patients with intermediated risk of breast cancer (one to three positive lymph nodes involved or with T2 stage tumor, grade 3 histology conformation and/ or with lymph vascular invasion) [11]. In this 10-year clinical trial from 2007-2017 held by chief investigator Dr. Ian Kunkler in the UK, more than 1600 female patients went to mastectomy first followed by randomization to +/- adjuvant chest wall radiation [10, 12]. While the primary endpoint of 10-yr OS is pending, the differences between groups for quality of life measures up to two years' post-randomization were found to be small [13].

In this retrospective study, we replicated the eligibility and design of the SUPREMO trial using the data from the National Cancer Database (NCDB) from 2004 to 2014. Samples were selected based on the instruction of SUPREMO protocol. The primary outcome of interest is the overall survival rate comparison between patients with or without PMRT. The goal of this study includes 1) the usage pattern of PMRT by patients' socioeconomic status; 2) the overall impact of PMRT on OS in all eligible patients, as well as in the subgroups of patients. This is a timely topic that will peek into utility of PMRT and its impact in a real-life setting, and the results will guide the clinicians and patients to use PRMT more wisely.

Method:

Data Source:

NCDB is a clinical oncology database sponsored by the American College of Surgeons and the American Cancer Society. The sources of NCDB are hospital registry data which are collected from more than 1,500 Commission on Cancer (CoC) accredited facilities. About 70 percent of newly diagnosed cancer cases in the US are included in NCDB. The dataset includes patient's characteristics, tumor histological characteristics, cancer staging, and outcome data which are investigable in this study [14].

Sample Selection Criteria:

NCDB data were queried for breast cancer patients diagnosed from 2004 -2014. According to the SUPREMO protocol, female patients were enrolled if they have the following inclusion criteria: diagnosis of unilateral pT1-2, pN1, M0 invasive breast cancer or unilateral pT2, pN0 invasive breast cancer with grade III histology and/or lymph-vascular invasion, with 1-3 pathological involved lymph nodes, and treated with total mastectomy (simple mastectomy, radical mastectomy or modified radical mastectomy). Patients who have undergone neoadjuvant systematic therapy or had a previous or concurrent malignancy diagnosis were excluded. The remaining patients were separated into two groups: with or without PMRT. For the chest wall radiation cohort, the time lag between surgery date and first radiation date was within 6 months and the total radiation dose (boost dose + regional dose) was between 40 to 70 Gy. Complete selection and exclusion criteria and sample size are in Table 1.

Variable Descriptions:

The overall survival is defined as the months between the surgery date and the last follow up or death date. Study cohorts were patients who received either a PMRT or not. The following patients' characteristics were examined: race (white, black or others/ unknown), primary payer (private, Medicare and others), median household income from 2000 based on patient's zip code matching (< $30,000, $30,000 - $35,999, $36,000 - $45,999 and $46,000 +), county of residence from 2013 (urban, rural and metro), percent of residents without high school diploma based on patient's zip code matching(>=21%, 13-20%, 7.0-12.9% and <7%), year of diagnosis (2004-2007, 2008-2011, 2012-2014). The others group in primary payer variable was made by combination of four groups: non-insured, unknown, Medicaid and other government due to the small sample size.

The tumor characteristics were evaluated: tumor grade (well differentiated, moderately differentiated, poorly differentiated/ undifferentiated and cell type not determined), comorbidity is presented using Charlson-Deyo Score (1, 2, and 2+)[15], estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), number of regional lymph nodes positive, present of lymph-vascular invasion (LVI), AJCC pathologic T (pT1 and pT2), AJCC pathologic N (p0, p1, p1A, p1B, p1C, p1MI), multigene signature results (low risk of recurrence, intermediate risk of recurrence and high risk of recurrence), tumor size in cm, and Nottingham Prognostic Index (NPI, NPI= 0.2* tumor size in cm + node status + tumor grade)[16].

The treatment characteristics were also examined: facility type (community cancer program, comprehensive community cancer program, academic/ research program, integrated network cancer program), region to receive treatment (Chest wall, Chest wall/Lymph nodes or No radiation treatment), surgical procedure (simple mastectomy,

modified radical mastectomy and radical mastectomy and, mastectomy, NOS), weeks between surgery and diagnosis, and whether or not the patient receive chemotherapy after surgery.

Statistical Analysis

All the statistical analysis was performed using SAS (version 9.4) with SAS Macros developed by Biostatistics and Bioinformatics Shared Resource at Winship Cancer Institute in Atlanta, Georgia [17]. The descriptive statistics for each variable of interest were generated, and in bivariate association with the study cohort, the parametric p-value was calculated based on the Chi-square test for categorical covariates while ANOVA was used for numeric covariates. The univariate association (UVA) between covariates and the use of PMRT was also conducted using the logistic regression. Cox proportional hazard regression was performed to examine association of covariates with OS in the univariate analysis. For the MVA model, a backward selection approach was used with significant level 0.01 to analyze the multivariable association between OS and covariates. Covariates lymph-vascular invasion and Her2 were removed from the MVA due to the high rate of the missing values. Kaplan-Meier (KM) plots were generated to compare the 10-year survival rate of PMRT groups. For the subgroup analyses, the interaction term between PMRT and the stratified variable entered the multivariable model that is subject for a backward elimination procedure, and the hazard ratio of PMRT+ vs. PMRT- at each level of the stratified variable were reported with the 95% confidence interval along with the p-value for the interaction.

Propensity score (PS) overlapping weighting method was used to mimic the randomized clinical trial where the baseline covariates balance between the two cohorts and hence

control potential selection bias [18]. The propensity score was estimated as the probability of a patient having been treated by PMRT given her baseline characteristics. This is done using a logistic regression model with the binary study cohort as an outcome and all baseline covariates as predictors. The patients who received PMRT, the weight assigned is 1-PS, while for patients in the other cohort, the weight assigned is PS. The covariate balance is evaluated by the standardized difference (SD) [19], and an SD < 0.1 is considered as sufficiently balanced. The covariate balance was assessed in all baseline variables in both the original study sample and final PS weighted sample.

Results

35244 patients met the study eligibility criteria (Table 2). The mean follow up time was 65.5 months after mastectomy. The median age of patients was 57 years ranging from 19 to 90. Among these patients, 29112 (82.6%) were white and 4104 (11.6%) were black. For the study cohort, 30403 (86.3%) of patients did not receive PMRT while 4841 (13.7%) received PMRT. The median tumor size was 2.2 cm (range, 0.10-85.0 cm). 19598 (55.6%) of patients had one positive lymph node, 10339 (29.3%) had two and 5307 (15.1%) had three positive lymph nodes involved. 6896 (19.6%) of patients had a lymph vascular invasion presented. In these patients, 15390 (43.7%) of tumors were pT1, while 19854 (56.3%) were pT2. For the tumor grade, 4566 (13.0%) of these patient's tumor was well differentiated, 15540 (44.1%) were moderately differentiated and 13545 (38.4%) was poorly differentiated or not differentiated. 33913 (96.2%) of patients had a negative surgical margin. 24066 (68.3%) of patients received adjuvant chemotherapy while 10328 (29.3%) did not.

Table 2 demonstrates the univariate association and multivariate association with utilization of PMRT. The use of PMRT was associated with patient's characteristics of being younger, white race, higher median county income, residing in urban area, private primary insurance carrier, higher county educational status (<7% of residence without a high school diploma), being diagnosed between year 2012-2014 compare to previous years, comorbidity score of 0. The use of PMRT was also associated with tumor characteristics: larger tumor size, ER, PR and Her2 positive tumors, well differentiated tumors, three regional lymph nodes positive, LVI presented, low risk of recurrence, T2 stage, NPI III, positive surgical margin. Treatment factors associated with PMRT use were: unknown facility type (for patients' age < 40), undergone chemotherapy, and undergone modified radical mastectomy was also associated with utilization of PMRT (p-value <0.01).

Adjusting for multiple covariates, PMRT was statistically significantly ($p<0.05$) associated with patient's characteristics: younger age at diagnosis, residing in urban area, private primary insurance carrier, higher county educational status with <7% of residence without a high school diploma, being diagnosed between year 2012-2014, larger tumor size, positive PR tumor, three regional lymph nodes positive, LVI presented, NPI II, Comprehensive Community Cancer Programs, undergone chemotherapy, and undergone modified radical mastectomy There is a trend of greater PMRT use with more recent year (Cochran-Armitage Trend Test $p<0.01$, Appendix Figure 1).

The 10-year survival rate was 72.1% (PMRT) vs. 68.7% (NR) by KM method (p-value < 0.01, Figure 1). According to UVA, the use of PMRT can significantly improve the OS (hazard ratio [HR] = 0.72, 95% CI = 0.66-0.78, p <0.01, Table 3). According to UVA, improvement of OS is associated with patient's characteristics: younger age at diagnosis, other race (non-white and non-black), patient's county median income > $63,000, residing in urban area, private insurance coverage, higher education level with <7% county residence without high school degree, year of diagnosis between 2012-2014 compared to earlier years, 0 Charlson-Deyo comorbidity score (p<0.05). OS was also effected by tumor characteristics: smaller tumor size, ER, PR positive tumor, Her2 negative tumor, well-differentiated tumor grade, 1 regional lymph nodes positive, LVI not presented, low risk of recurrence, T1 tumor stage, NPI I, negative surgical margin. Patient in academic/ research program facility, undergone chemotherapy and undergone simple mastectomy also had statistically significant association with improvement of OS (p<0.05). Adjusting for multiple covariates simultaneously, the result was similar on the utilization of PMRT (HR = 0.82, 95% CI = 0.75-0.89, Table 4). Longer survival was seen among those younger at diagnosis, other race(non-black and non-white), county median income > $63,000, private primary insurance payer, ER, PR positive tumor, well differentiated tumor grade, one regional lymph nodes positive, LVI not present, NPI I, academic/ research program facility, undergone chemotherapy and simple mastectomy (all p<0,05).

In subgroup analysis, we examined whether the relationship between PMRT and OS was modified by other health traits (Table 5). There were significant interactions between PMRT and covariates including: age at diagnosis, ER, and county of residence (p<0.05).

Patients whose age at diagnosis >60 (HR =0.68 95% CI =0.60-0.77, p<0.001), with ER positive tumor (HR= 0.75, 95% CI =0.67-0.84, p< 0.001), and living in rural area (HR=0.51, 95% CI=0.26-1.00, p=0.049) can benefit more from PMRT.

Besides those covariates, there is evidence of improvement of OS with PMRT use among patients in academic/ research program (HR = 0.67, 95% CI= 0.55-0.81, p<0.001), with three RLN positive (HR=0.75 95% CI =0.64-0.88), tumor size ≤ 5cm (HR =0.83 95% CI =0.76-0.91, p<0.01), without receiving chemotherapy (HR= 0.70 95% CI =0.60-0.82, p<0.01), with 2+ Charlson- Deyo Score (HR=0.59 95% CI =0.40-0.88, p =0.009), with well differentiated tumor grade (HR=0.72, 95% CI =0.53-0.98, p=0.037), tumor in T2 stage (HR=0.80, 95% CI =0.72-0.88, p<0.001).

According to the PS weighting approach, 3476 samples were selected with PMRT treatment without PMRT respectively. The samples were well balanced with covariates compared to the unbalanced result (all standard difference <0.1, see Appendix Table 1). With the average treatment effect for the overlap (ATO) weighted sample, the 10-year OS with PMRT is 72.1% compared to the 10-year OS without PMRT is 68.7% (Figure 2). The result of UVA with ATO weighted sample had a similar association with PMRT compared to the unweighted sample (HR =0.84 95% CI =0.74-0.95, p =0.006, Appendix Table 2).

Discussion and Conclusion

From this respective observational study based on breast NCDB from 2004-2014, we found that PMRT plays an important role in improving the long-term OS for patients with

intermediate risk of breast cancer recurrence. The survival benefit of PMRT for patients age over 60 years, with 3 involved PLN involved and tumor size ≤ 5cm, treated in Academic/ research program, with 2+ Charlson- Deyo Score, T2 stage, or had well-differentiated tumor grade was larger compared to other subgroups.

From previous meta- analysis performed by Early Breast Cancer Trialists' Collaborative Group (EBCTCG) with subjects selected from 22 clinical trials with 1-3 positive lymph nodes involved, PMRT reduced locoregional recurrence rate (LRR) (RR=0.68, 95% CI=0.57–0.82, 2p=0.00006) as well as the breast cancer mortality (RR= 0.80, 95% CI= 0.67–0.95, 2p=0.01). The radiotherapy can further reduce the rate of breast cancer mortality by one fifth (RR=0.78, 95% CI= 0.64–0.94, 2p=0.01) when subjects also received systematic therapy [20]. The analysis also discussed the impact of adjuvant chest wall radiation with patients after mastectomy compare to PMRT given to the regional nodes only since the most common site for LRR is chest wall [21]. According to eight clinical trial, chest wall radiation can reduce the LRR rate (RR=0.30, 95% CI =0.20-0.44, 2p <0.001) while had no effect on breast cancer mortality rate (RR=1.00, 95% CI = 0.82–1.20, 2p>0.1) [20]. The effect of chest wall radiation compared to radiation on regional nodes only on specific patients with intermediated risk breast cancer was unavailable. Other studies also implied that PMRT has a beneficial effect on reducing LRR rate for patients with T1-2 tumor and 1-3 positive lymph nodes [22-24]. However, the sample size in these studies was relatively small.

The strength of this study was that it includes a large number of subjects for analysis with long follow up time (median follow up time = 62 months). Since the sample size was very large, the p-value is less informative and we focus on the 95% CI and hazard ratio.

The current study has many limitations. Firstly, since the analysis was based on NCDB data, some additional information such as recurrence rate, locoregional failure rate, cancer-specific mortality rate and quality of life were unavailable. The result from this study may not provide a comprehensive view from a different angle. Some result from this study is inconsistent with the postmastectomy radiotherapy guideline generated by American Society for Radiation Oncology (ASTRO) [25]. According to ASTRO, for patient's age > 40 to 45 years old, PMRT is not recommended considering to patients' limited life expectancy and potential complications. However, based on the current study, patients with age> 60 will benefit more regarding long-term survival with PMRT. Since the NCDB only provides information on OS, OS is the only outcome we consider in this study.

Moreover, this study could not completely follow the protocol of the SUPREMO clinical trial due to some unavailable covariates in NCDB. For example, in the SUPREMO protocol, pregnant females or females with BRACA 1 or 2 should be excluded while those variables were unavailable in NCDB. Furthermore, the recommended dose from the SUPREMO protocol was 50 Gy TAD in 25 daily fractions over 5 weeks, 45 Gy TAD in 20 daily fractions over 4 weeks 40 Gy TAD in 15 daily fractions over 3 weeks. These doses could not be reached with the NCDB data since the dose received by NCDB patients was quite larger (mean = 60.4 Gy). In order to keep as much data with PMRT as possible, the patients with radiotherapy dose from 40-70 Gy were included in this study.

Lastly, some unobserved confounders or missing values in prognostic factors may bring in bias and imbalance in the final estimation. For instance, variable facility type was only available for patient's age over 40 years old. LVI was only available after 2010.

Covariates such as ER, PR, Her2, multigene signature results, and radiation dose also includes a large number of missing values. Subgroup analysis and propensity score approach were used to deal with confounders, and the benefit of using of PMRT was cross-verified according to both methods.

The result of the study may be helpful for patients with intermediate-risk breast cancer who received total mastectomy to decide on the usage of PMRT. Also, we are still looking forward to the SUPREMO results.

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Table 1. Selection and Exclusion Criteria for Study Design

Selection and Exclusion Criteria	Sample Size	Excluded
NCDB Breast PUF Cancer Cases	2445870	-
Exclude previous or concurrent malignancy	2022217	423653
Include Behavior = Invasive	1630831	391386
Include cases with positive histology diagnostic confirmation	1617983	12848
Include patients who have 1 to 3 pathologically involved axillary nodes	302788	1315195
Include pT1, pN1, M0 patients and pT2, pN1, M0 patients and pT2, pN0, grade III histology patients	207641	95147
Include patients undergone total mastectomy	103132	104509
Exclude patients who have undergone neoadjuvant radiation therapy	102851	281
Exclude patients who have undergone neoadjuvant systemic therapy	90764	12087
Exclude Male Patients	88755	2009
Exclude bilateral breast cancer	88703	52
Include patients who have 10 to 90 pathologically involved lymph nodes removed and examined	51300	37403
Include Chest Wall Radiation Only	45057	6243
Exclude patients< 18	45057	0
Exclude metastasis case	44803	254
Exclude cases were not treated at reporting facility	44110	693
Exclude OS<0 or missing values	40897	3213
Include 6 month time lag between surgery and radiation therapy	35779	5118
Total radiation dose between 40-70 Gy	35244	535

Table 2. Descriptive Statistics for Variables of Interest, Overall and by PMRT status.

	Overall 35244		PMRT- No N=30403		PMRT+ Yes N=4841		Parametric P-value*
	% N , Mean (SD)						
Demographics							
Age at Diagnosis	58	(14)	58	(14)	55	(13)	**<.001**
Race							
White	83	29112	83	25091	83	4021	
Black	12	4104	12	3596	11	508	**0.004**
Others/Unknown	6	2028	6	1716	6	312	
Median Income Quartiles 2008-2012							
<$38,000	17	5891	17	5169	15	722	
$38,000-$47,999	22	7634	22	6606	21	1028	**<.001**
$48,000-$62,999	27	9300	27	8018	27	1282	
$63,000 +	35	12102	34	10327	37	1775	
County of Residence 2013							
Metro	85	29000	85	25086	83	3914	
Urban	13	4595	13	3900	15	695	**0.012**
Rural	2	686	0	593	2	93	
Primary Payer							
Private	57	20038	56	16934	64	3104	
Medicare	31	10845	32	9718	23	1127	**<.001**
Others	31	10845	32	9718	23	1127	
Percentage of County Residence without High School Degree 2008-2012							
>=21%	17	5783	17	5128	14	654	
13-20%	25	8797	25	7654	24	1142	**<.001**
7.0-12.9%	32	11141	32	9565	33	1575	
<7%	26	9232	26	7794	30	1437	
Year of Diagnosis							
2004-2007	33	11573	35	10552	21	1021	
2008-2011	38	13542	39	11738	37	1804	**<.001**
2012-2014	29	10129	27	8113	42	2016	
Charlson-Deyo Score							
0	82	29045	82	24952	85	4093	
1	14	5001	14	4386	13	615	**<.001**
2+	3	1198	4	1065	3	133	
Tumor Characteristics							
Tumor Size (cm)	2.40	(1.33)	2.34	(1.30)	2.81	(1.45)	**<.001**
ER							
Negative	18	6434	18	5599	17	835	
Positive	80	28071	79	24090	82	3981	**<.001**
Unknown	2	739	2	714	1	25	
PR							
Negative	28	9766	2	714	27	1304	
Positive	70	24601	28	8462	73	3511	**<.001**
Unknown	3	877	69	21090	1	26	
HER2							
Negative	40	14234	38	11698	52	2536	
Positive	9	3027	8	2431	12	596	**<.001**
Unknown	51	17983	54	16274	35	1709	
Grade							
Well Differentiated	13	4566	13	4071	10	495	
Moderately Differentiated	44	15540	44	13418	44	2122	
Poorly Differentiated/Undifferentiated	38	13545	38	11573	41	1972	**<.001**
Cell Type Not Determined	5	1593	4	1341	5	252	
Number of PLN							
1	56	19598	59	17795	37	1803	
2	29	10339	28	8644	35	1695	**<.001**
3	15	5307	13	3964	28	1343	
LVI							

Not present	25	8825	24	7446	28	1379	
Present	20	6896	18	5446	30	1450	**<.001**
Unknown	55	19523	58	17511	42	2012	
Multigene Signature Results							
Low Risk of Recurrence	64	2090	62	1693	70	397	
Intermediate Risk of Recurrence	27	877	28	753	22	124	**0.003**
High Risk of Recurrence	10	315	10	269	8	46	
AJCC Pathologic T							
T1	44	15390	45	13634	36	1756	**<.001**
T2	56	19854	55	16769	64	3085	
AJCC Pathologic N							
p0	0	120	0	99	0	21	
p1	29	10029	29	8927	23	1102	
p1A	62	21970	61	18526	71	3444	**<.001**
p1B	1	171	0	148	0	23	
p1C	1	246	1	191	1	55	
p1MI	8	2708	8	2512	4	196	
Nottingham Prognostic Index							
NPI I	8	2637	8	2422	5	215	
NPI II	66	22046	66	19146	64	2900	**<.001**
NPI III	26	8865	26	7419	32	1446	
Surgical Margin							
Negative	96	33913	97	29351	94	4562	
Positive	3	1068	3	822	5	246	**<.001**
Unknown	1	263	1	230	1	33	
Treatment Characteristics							
Facility Type							
Community or Integrated Network Cancer Program	19	6724	19	5903	17	821	
Comprehensive Community Cancer Program	43	15107	43	13052	42	2055	**<.001**
Academic/Research Program	30	10588	30	9195	29	1393	
Unknown (patient's age<40)	8	2825	7	2253	12	572	
Chemotherapy							
No	29	10328	31	9415	19	913	
Yes	68	24066	66	20159	81	3907	**<.001**
Unknown	2	850	3	829	0	21	
Surgical procedure							
Simple Mastectomy	39	13832	40	12102	36	1730	
Modified Radical Mastectomy	59	20689	58	17683	62	3006	**<.001**
Radical Mastectomy and Mastectomy, NOS	2	723	2	618	2	105	
Definitive Surgical Procedure, Weeks from Diagnosis	6.81	(7.00)	6.50	(6.53)	8.73	(9.18)	**<.001**

* The parametric p value is calculated by ANOVA for numerical covariates and Chi-Square test for categorical covariates.

Table 3. Univariate and Multivariate Analysis of Factors Associated with Utilization of PMRT

Covariate	UVA OR (95% CI)	UVA OR P-value	MVA OR (95% CI)	MVA OR P-value
Demographics				
Age at Diagnosis	0.98 (0.98-0.98)	**<.001**	0.98 (0.98-0.98)	**<.001**
Race				
Black	0.88 (0.80-0.97)	**0.012**		
Others/Unknown	1.13 (1.00-1.29)	**0.048**	-	-
White	-	-		
Median Income Quartiles 2008-2012				
<$38,000	0.81 (0.74-0.89)	**<.001**		
$38,000-$47,999	0.91 (0.83-0.98)	**0.019**	-	-
$48,000-$62,999	0.93 (0.86-1.01)	0.068		
$63,000 +	-	-		
County of Residence 2013				
Rural	1.01 (0.81-1.25)	0.964	1.21 (0.95-1.54)	0.117
Urban	1.14 (1.05-1.25)	**0.003**	1.28 (1.16-1.41)	**<.001**
Metro	-	-	-	-
Primary Payer				
Others	0.89 (0.81-0.97)	**0.012**	0.83 (0.75-0.92)	**<.001**
Medicare	0.63 (0.59-0.68)	**<.001**	0.88 (0.79-0.97)	**0.013**
Private	-	-	-	-
Percentage of County Residence without High School Degree 2008-2012				
>=21%	0.69 (0.63-0.76)	**<.001**	0.64 (0.57-0.72)	**<.001**
13-20%	0.81 (0.74-0.88)	**<.001**	0.76 (0.69-0.83)	**<.001**
7.0-12.9%	0.89 (0.83-0.97)	**0.004**	0.88 (0.81-0.96)	**0.004**
<7%	-	-	-	-
Year of Diagnosis				
2004-2007	0.39 (0.36-0.42)	**<.001**	0.55 (0.48-0.63)	**<.001**
2008-2011	0.62 (0.58-0.66)	**<.001**	0.74 (0.68-0.80)	**<.001**
2012-2014	-	-	-	-
Charlson-Deyo Score				
2+	0.76 (0.63-0.91)	**0.004**		
1	0.85 (0.78-0.94)	**<.001**	-	-
0	-	-		
Tumor Characteristics				
Tumor Size (cm)	1.30 (1.27-1.34)	**<.001**	1.29 (1.25-1.33)	**<.001**
ER				
Negative	0.90 (0.83-0.98)	**0.012**		
Unknown	0.21 (0.14-0.32)	**<.001**	-	-
Positive	-	-		
PR				
Negative	0.93 (0.86-0.99)	**0.027**	0.98 (0.90-1.06)	0.594
Unknown	0.18 (0.12-0.27)	**<.001**	0.30 (0.20-0.45)	**<.001**
Positive	-	-	-	-
HER2				
Negative	0.88 (0.80-0.98)	**0.015**	1.03 (0.92-1.16)	0.561
Unknown	0.43 (0.39-0.47)	**<.001**	0.69 (0.59-0.82)	**<.001**
Positive	-	-	-	-
Grade				
Moderately Differentiated	1.30 (1.17-1.44)	**<.001**		
Poorly Differentiated/Undifferentiated	1.40 (1.26-1.56)	**<.001**	-	-
Well Differentiated	1.55 (1.31-1.82)	**<.001**		
Number of PLN				
3	3.34 (3.09-3.62)	**<.001**	3.31 (3.04-3.61)	**<.001**
2	1.94 (1.80-2.08)	**<.001**	1.88 (1.74-2.03)	**<.001**
1	-	-	-	-
LVI				
Unknown	0.62 (0.58-0.67)	**<.001**	1.05 (0.93-1.19)	0.441
Present	1.44 (1.33-1.56)	**<.001**	1.18 (1.08-1.29)	**<.001**

Not present	-	-	-	-
Multigene Signature Results				
high risk of recurrence	0.73 (0.52-1.02)	0.062		
intermediate risk of recurrence	0.70 (0.56-0.87)	**0.002**	-	-
low risk of recurrence	-	-		
AJCC Pathologic T				
T1	0.70 (0.66-0.75)	**<.001**	-	-
T2	-	-		
Nottingham Prognostic Index				
NPI III	2.20 (1.89-2.55)	**<.001**	1.21 (1.02-1.44)	**0.028**
NPI II	1.71 (1.48-1.97)	**<.001**	1.26 (1.08-1.48)	**0.003**
NPI I	-	-	-	-
Surgical Margin				
Unknown	1.08 (0.75-1.56)	0.668	-	-
Positive	2.09 (1.41-3.09)	**<.001**		
Negative	-	-		
Treatment Characteristics				
Facility Type				
Community or Integrated Network Cancer Program	0.92 (0.84-1.01)	0.069	0.93(0.82-1.07)	0.318
Comprehensive Community Cancer Program	1.04 (0.97-1.12)	0.301	1.17(1.08-1.27)	**<.001**
Unknown (patient's age<40)	1.68 (1.50-1.87)	**<.001**	1.11(0.98-1.25)	0.112
Academic/Research Program	-	-	-	-
Chemotherapy				
Unknown	0.26 (0.17-0.41)	**<.001**	0.33(0.21-0.51)	**<.001**
Yes	2.00 (1.85-2.16)	**<.001**	1.58(1.44-1.74)	**<.001**
No	-	-	-	-
Surgical procedure				
Radical Mastectomy and Mastectomy, NOS	1.19 (0.96-1.47)	0.112	1.12 (0.87-1.43)	0.372
Modified Radical Mastectomy	1.19 (1.12-1.27)	**<.001**	1.28 (1.19-1.37)	**<001**
Simple Mastectomy	-			-

* Number of observations in the original data set = 35244. Number of observations used = 32594.
** Backward selection with an alpha level of removal of .01 was used. The following variables were removed from the model: Charlson- Deyo Score, ER, Facility Type, Grade, Median Income Quartiles 2008-2012, and Race.

Table 4. Univariate and Multivariate Analysis of Factors Associated with OS

Covariate	UVA HR (95% CI)	UVA HR P-value	MVA HR (95% CI)	MVA HR P-value
PMRT				
Yes	0.72 (0.66-0.78)	**<.001**	0.82 (0.75-0.89)	**<.001**
No	-	**-**	-	-
Demographic				
Age at Diagnosis	1.05 (1.05-1.06)	**<.001**	1.04 (1.04-1.04)	**<.001**
Race				
Black	1.26 (1.17-1.35)	**<.001**	1.10 (1.02-1.19)	**0.019**
Others/Unknown	0.64 (0.56-0.73)	**<.001**	0.76 (0.66-0.88)	**<.001**
White	-	**-**	-	-
Median Income Quartiles 2008-2012				
<$38,000	1.71 (1.59-1.84)	**<.001**	1.24 (1.15-1.33)	**<.001**
$38,000-$47,999	1.48 (1.38-1.58)	**<.001**	1.12 (1.05-1.20)	**0.001**
$48,000-$62,999	1.31 (1.22-1.40)	**<.001**	1.08 (1.01-1.16)	**0.021**
$63,000 +	-	**-**	-	-
County of Residence 2013				
Rural	1.16 (0.98-1.37)	0.087		
Urban	1.16 (1.09-1.25)	**<.001**	**-**	**-**
Metro	-	**-**		
Primary Payer				
Others	1.69 (1.56-1.84)	**<.001**	1.46 (1.34-1.60)	**<.001**
Medicare	3.59 (3.40-3.79)	**<.001**	1.29 (1.20-1.39)	**<.001**
Private	-	**-**	-	-
Percentage of County Residence without High School Degree 2008-2012				
>=21%	1.49 (1.38-1.62)	**<.001**		
13-20%	1.47 (1.37-1.58)	**<.001**		
7.0-12.9%	1.30 (1.22-1.40)	**<.001**	-	-
<7%	-	**-**		
Year of Diagnosis				
2004-2007	1.43 (1.30-1.56)	**<.001**		
2008-2011	1.18 (1.07-1.29)	**<.001**	**-**	**-**
2012-2014	-	**-**		
Charlson-Deyo Score				
2+	3.59 (3.27-3.95)	**<.001**	2.29 (2.08-2.52)	**<.001**
1	1.97 (1.86-2.10)	**<.001**	1.41 (1.32-1.50)	**<.001**
0	-	**-**	-	-
Tumor Characteristics				
Tumor Size (cm)	1.07 (1.06-1.08)	**<.001**	1.10 (1.08-1.11)	**<.001**
ER				
Negative	1.77 (1.67-1.87)	**<.001**	1.37 (1.26-1.48)	**<.001**
Unknown	1.47 (1.28-1.68)	**<.001**	0.88 (0.65-1.18)	0.391
Positive	-	**-**	-	-
PR				
Negative	1.76 (1.67-1.85)	**<.001**	1.28 (1.19-1.38)	**<.001**
Unknown	1.61 (1.42-1.82)	**<.001**	1.45 (1.11-1.91)	**0.007**
Positive	-	**-**	-	-
HER2				
Negative	0.89 (0.78-1.02)	0.084		
Unknown	1.44 (1.27-1.63)	**<.001**	**-**	**-**
Positive	-	**-**		
Grade				
Moderately Differentiated	1.19 (1.09-1.30)	**<.001**	1.09 (0.97-1.23)	0.149
Poorly Differentiated/Undifferentiated	1.79 (1.64-1.95)	**<.001**	1.24 (1.08-1.43)	**0.002**
Well Differentiated	-	**-**	-	-
Number of PLN				
3	1.36 (1.27-1.45)	**<.001**	1.32 (1.23-1.41)	**<.001**
2	1.11 (1.05-1.17)	**<.001**	1.11 (1.05-1.18)	**<.001**
1	-	**-**	-	-

LVI				
Unknown	1.68 (1.54-1.82)	**<.001**	1.53 (1.40-1.66)	**<.001**
Present	1.27 (1.15-1.42)	**<.001**	1.20 (1.08-1.34)	**<.001**
Not present	-	-	-	-
Multigene Signature Results				
High Risk of Recurrence	2.68 (1.69-4.25)	**<.001**		
Intermediate Risk of Recurrence	1.06 (0.68-1.64)	0.793	-	-
Low Risk of Recurrence	-	-		
AJCC Pathologic T				
T1	0.57 (0.54-0.60)	**<.001**	-	-
T2	-	-		
Nottingham Prognostic Index				
NPI III	2.53 (2.25-2.85)	**<.001**	1.55 (1.28-1.87)	**<.001**
NPI II	1.43 (1.27-1.60)	**<.001**	1.19 (1.01-1.40)	**0.036**
NPI I	-	-	-	-
Surgical Margin				
Unknown	0.92 (0.64-1.33)	0.668		
Positive	1.93 (1.66-2.23)	**<.001**	-	-
Negative	-	-		
Treatment Characteristics				
Facility Type				
Community or Integrated Network Cancer Program	0.92 (0.84-1.01)	0.069	1.23 (1.14-1.32)	**<.001**
Comprehensive Community Cancer Program	1.04 (0.97-1.12)	0.301	1.14 (1.07-1.22)	**<.001**
Unknown (patient's age<40)	1.68 (1.50-1.87)	**<.001**	2.25 (1.95-2.60)	**<.001**
Academic/Research Program	-	-	-	-
Chemotherapy				
Unknown	0.26 (0.17-0.41)	**<.001**	0.67 (0.57-0.78)	**<.001**
Yes	2.00 (1.85-2.16)	**<.001**	0.60 (0.57-0.64)	**<.001**
No	-	-	-	-
Surgical Procedure				
Radical Mastectomy and Mastectomy, NOS	1.19 (0.96-1.47)	0.112	0.94 (0.78-1.13)	0.498
Modified Radical Mastectomy	1.19 (1.12-1.27)	**<.001**	1.09 (1.03-1.15)	**0.004**
Simple Mastectomy	-	-	-	-

* Number of observations in the original data set = 35244. Number of observations used = 33245.

** Backward selection with an alpha level of removal of .01 was used. The following variables were removed from the model: Percent No High School Degree 2008-2012, Surgical Margin, County of Residence 2013, and Year of Diagnosis.

Table 5. HR of PMRT+ vs. PMRT- to OS in Stratified Selected Health-related Covariates

Covariate	N	HR (95% CI)	HR P-value	P-value for interaction
Age at Diagnosis :		-	-	**<.001**
≤60	3031 vs. 16481	0.97 (0.86-1.11)	0.698	-
>60	1498 vs. 12235	0.68 (0.60-0.77)	**<.001**	-
County of Residence 2013 :		-	-	**0.033**
Metro	3684 vs. 23901	0.87 (0.79-0.95)	**0.004**	-
Urban	647 vs. 3697	0.65 (0.51-0.82)	**<.001**	-
Rural	87 vs. 560	0.52 (0.26-1.02)	0.055	-
Charlson-Deyo Score :		-	-	0.181
0	3824 vs. 23532	0.85 (0.77-0.94)	**0.002**	-
1	580 vs. 4166	0.77 (0.63-0.94)	**0.011**	-
2+	125 vs. 1018	0.59 (0.40-0.88)	**0.009**	-
Tumor Size :		-	-	0.052
≤5cm	4399 vs. 28603	0.83 (0.76-0.91)	**<.001**	-
>5cm	130 vs. 113	1.49 (0.83-2.67)	0.185	-
ER :		-	-	**0.016**
Negative	791 vs. 5335	0.98 (0.84-1.15)	0.847	-
Positive	3715 vs. 22760	0.75 (0.67-0.84)	**<.001**	-
Unknown	23 vs. 621	0.92 (0.43-1.96)	0.833	-
Grade :		-	-	0.469
Well Differentiated	485 vs. 4035	0.72 (0.53-0.98)	**0.037**	-
Moderately Differentiated	2106 vs. 13263	0.78 (0.68-0.91)	**0.001**	-
Poorly Differentiated/Undifferentiated	1938 vs. 11418	0.85 (0.76-0.96)	**0.008**	-
Number of PLN:		-	-	0.255
1	1684 vs. 16826	0.90 (0.77-1.04)	0.146	-
2	1579 vs. 8163	0.80 (0.69-0.93)	**0.004**	-
3	1266 vs. 3727	0.75 (0.64-0.88)	**<.001**	-
Comparisons Stratified by LVI :		-	-	0.467
Not present	1285 vs. 7070	0.84 (0.66-1.07)	0.153	-
Present	1361 vs. 5241	0.72 (0.57-0.90)	**0.004**	-
Unknown	1883 vs. 16405	0.84 (0.75-0.93)	**<.001**	-
Pathologic T stage :		-	-	0.081
T1	1743 vs. 13517	0.94 (0.80-1.11)	0.48	-
T2	3064 vs. 16603	0.80 (0.72-0.88)	**<.001**	-
Facility Type :		-	-	0.055
Community or Integrated Network Cancer Program	781 vs. 5578	0.79 (0.65-0.95)	**0.013**	-
Comprehensive Community Cancer Program	1948 vs. 12360	0.87 (0.77-0.99)	**0.034**	-
Academic/Research Program	1271 vs. 8640	0.67 (0.55-0.81)	**<.001**	-
Unknown (age<40)	529 vs. 2138	1.03 (0.77-1.38)	0.852	-
Chemotherapy :		-	-	0.058
No	845 vs. 8891	0.70 (0.60-0.82)	**<.001**	-
Yes	3664 vs. 19052	0.88 (0.79-0.98)	**0.024**	-
Unknown	20 vs. 773	0.94 (0.38-2.28)	0.883	-

* Number of observations in the original data set = 35244. Number of observations used = 34927.
** Backward selection with an alpha level of removal of .01 was used. The following variables were removed from the model: Percent No High School Degree 2008-2012, Nottingham Prognostic Index, and County of Residence 2013.
*** The estimated stratified treatment effect was controlled by: Age at Diagnosis, Charlson-Deyo Score, Chemotherapy, ER, Facility Type, Grade, LVI, Median Income Quartiles 2008-2012, Number of Regional Lymph Nodes Positive, PR, Primary Payer, Race, Surgical procedure

Figure 1. Kaplan Meier Curve of 10- year OS with original sample

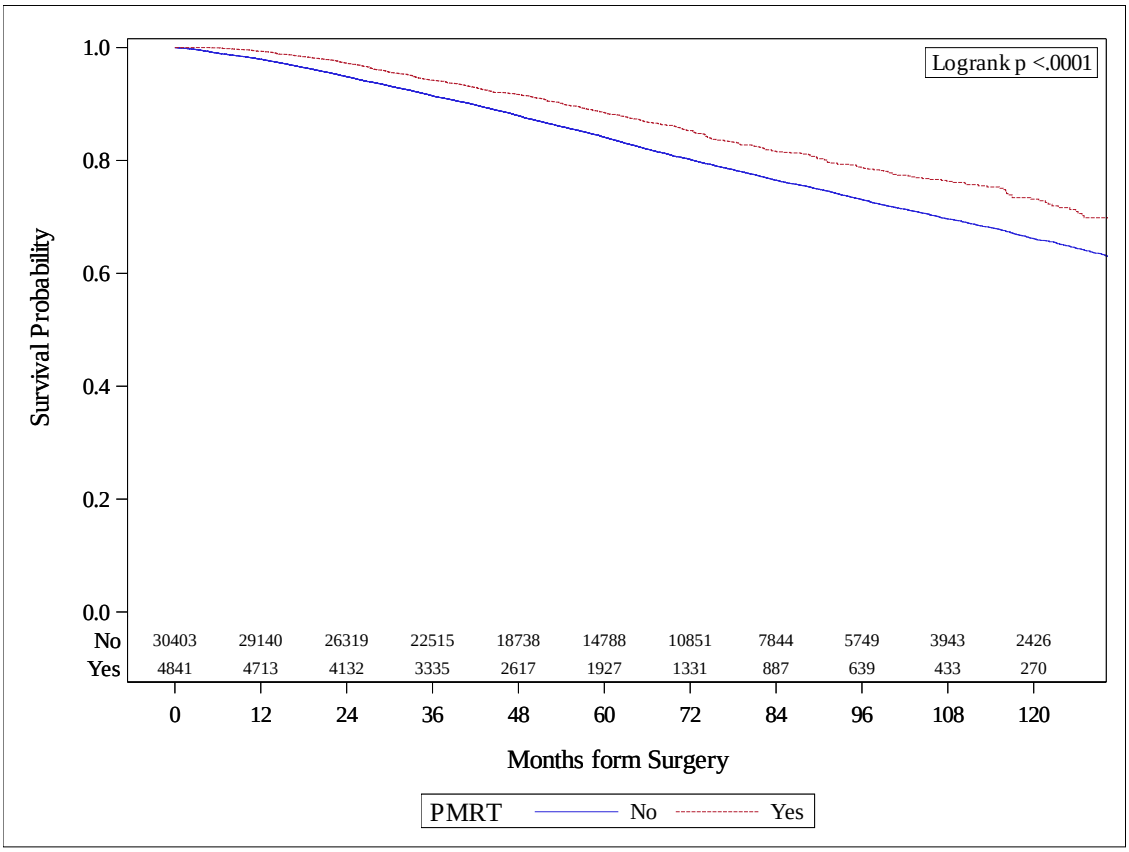
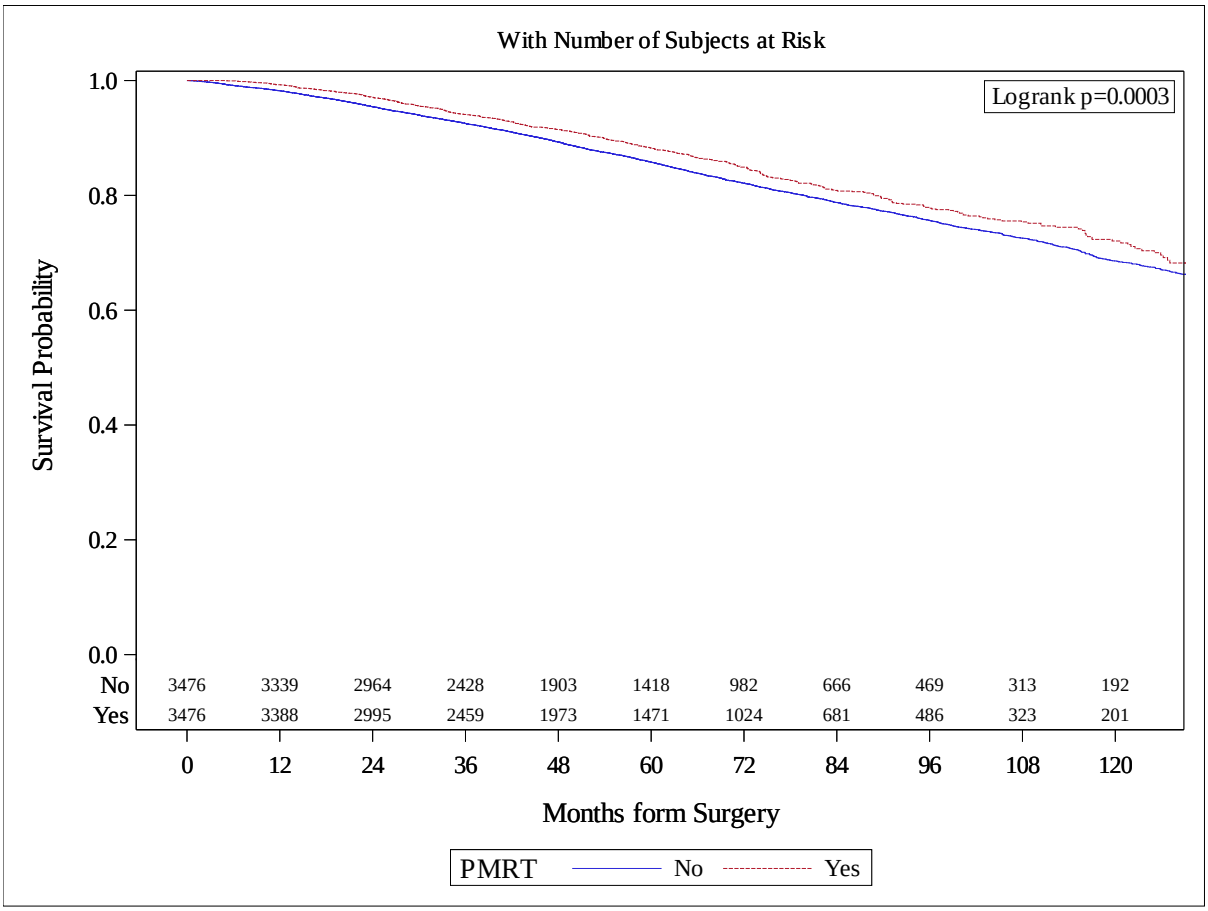


Figure 2. Kaplan Meier Curve of 10- year OS with weighted sample



Appendix:

Table 1. Balance of Covariates between Two Cohorts after PS Weighting

Covariate	Level	PMRT		Standardized Difference
		No N=3476	Yes N=3476	
Race	White	2884 (82.97)	2884 (82.97)	0
	Black	373 (10.74)	373 (10.74)	0
	Others/Unknown	219 (6.29)	219 (6.29)	0
Facility Type	Community or Integrated Network Cancer Program	622 (17.9)	622 (17.9)	0
	Comprehensive Community Cancer Program	1498 (43.1)	1498 (43.1)	0
	Academic/Research Program	986 (28.36)	986 (28.36)	0
	Unknown (age<40)	370 (10.64)	370 (10.64)	0
Median Income Quartiles 2008-2012	<$38,000	537 (15.44)	537 (15.44)	0
	$38,000-$47,999	759 (21.85)	759 (21.85)	0
	$48,000-$62,999	929 (26.73)	929 (26.73)	0
	$63,000 +	1251 (35.98)	1250 (35.98)	0
Percentage of County Residence without High School Degree 2008-2012	>=21%	495 (14.25)	495 (14.25)	0
	13-20%	836 (24.05)	836 (24.05)	0
	7.0-12.9%	1141 (32.83)	1141 (32.83)	0
	<7%	1004 (28.87)	1003 (28.87)	0
County of Residence 2013	Metro	2904 (83.55)	2904 (83.55)	0
	Urban	502 (14.45)	502 (14.45)	0
	Rural	70 (2)	70 (2)	0
Primary Payer	Not Insured/Unknown and Medicaid/Other Government	433 (12.45)	433 (12.45)	0
	Private	2183 (62.8)	2183 (62.8)	0
	Medicare	860 (24.76)	860 (24.75)	0
Year of Diagnosis	2004-2007	790 (22.72)	790 (22.72)	0
	2008-2011	1360 (39.11)	1360 (39.11)	0
	2012-2014	1327 (38.17)	1327 (38.17)	0
Charlson-Deyo Score	0	2915 (83.86)	2915 (83.86)	0
	1	458 (13.17)	458 (13.17)	0
	2+	103 (2.98)	103 (2.98)	0
Grade	Well Differentiated	386 (11.11)	386 (11.11)	0
	Moderately Differentiated	1620 (46.6)	1620 (46.6)	0

	Poorly Differentiated/Undifferentiated	1470 (42.29)	1470 (42.29)	0
ER	Negative	626 (18)	626 (18)	0
	Positive	2830 (81.42)	2830 (81.42)	0
	Unknown	20 (0.58)	20 (0.58)	0
PR	Negative	963 (27.72)	963 (27.72)	0
	Positive	2489 (71.6)	2489 (71.6)	0
	Unknown	24 (0.69)	24 (0.69)	0
Number of PLN	1	1420 (40.85)	1420 (40.85)	0
	2	1205 (34.67)	1205 (34.67)	0
	3	851 (24.48)	851 (24.48)	0
LVI	Not present	974 (28.03)	974 (28.03)	0
	Present	969 (27.89)	969 (27.89)	0
	Unknown	1532 (44.08)	1532 (44.08)	0
Nottingham Prognostic Index	NPI I	178 (5.13)	178 (5.13)	0
	NPI II	2245 (64.58)	2245 (64.58)	0
	NPI III	1053 (30.29)	1053 (30.29)	0
Surgical procedure	Simple Mastectomy	1285 (36.97)	1285 (36.97)	0
	Modified Radical Mastectomy	2123 (61.09)	2123 (61.09)	0
	Radical Mastectomy and Mastectomy, NOS	67 (1.94)	67 (1.94)	0
Surgical Margin	Negative	3296 (94.82)	3296 (94.82)	0
	Positive	155 (4.47)	155 (4.47)	0
	Unknown	25 (0.71)	25 (0.71)	0
Chemotherapy	No	716 (20.59)	716 (20.59)	0
	Yes	2741 (78.85)	2741 (78.86)	0
	Unknown	19 (0.56)	19 (0.56)	0
Age at Diagnosis		55.4 (4.66)	55.4 (11.77)	0
Tumor Size (cm)		2.69 (0.65)	2.69 (1.17)	0
Definitive Surgical Procedure, Days from Diagnosis		46.21 (16.24)	58.5 (54.87)	**0.363**

* The parametric p value is calculated by ANOVA for numerical covariates and Chi-Square test for categorical covariates.

Table 2. Univariate Analysis of Weighted Sample Associated with OS

Covariate	Level	Months form Surgery Hazard Ratio (95% CI)	HR P-value
PMRT	Yes	0.84 (0.74-0.95)	**0.006**
	No	-	-
Race	Black	1.38 (1.15-1.66)	**<.001**
	Others/Unknown	0.72 (0.52-0.99)	**0.04**
	White	-	-
Facility Type	Community or Integrated Network Cancer Program	1.59 (1.31-1.92)	**<.001**
	Comprehensive Community Cancer Program	1.45 (1.24-1.71)	**<.001**
	Unknown (age<40)	0.93 (0.72-1.20)	0.59
	Academic/Research Program	-	-
Median Income Quartiles 2008-2012	<$38,000	1.79 (1.50-2.15)	**<.001**
	$38,000-$47,999	1.43 (1.20-1.70)	**<.001**
	$48,000-$62,999	1.26 (1.07-1.50)	**0.006**
	$63,000 +	-	-
Percent No High School Degree 2008-2012	>=21%	1.64 (1.34-2.00)	**<.001**
	13-20%	1.54 (1.29-1.83)	**<.001**
	7.0-12.9%	1.25 (1.06-1.49)	**0.008**
	<7%	-	-
County of Residence 2013	Rural	1.01 (0.65-1.57)	0.974
	Urban	1.10 (0.92-1.30)	0.302
	Metro	-	-
Primary Payer	Others	1.77 (1.45-2.16)	**<.001**
	Medicare	3.26 (2.85-3.73)	**<.001**
	Private	-	-
Year of Diagnosis	2004-2007	1.28 (1.04-1.58)	**0.021**
	2008-2011	1.04 (0.85-1.27)	0.689
	2012-2014	-	-
Charlson-Deyo Score	2+	3.16 (2.42-4.11)	**<.001**
	1	1.99 (1.70-2.32)	**<.001**
	0	-	-
Grade	Moderately Differentiated	1.14 (0.89-1.46)	0.301
	Poorly Differentiated/Undifferentiated	1.90 (1.50-2.42)	**<.001**
	Well Differentiated	-	-
	Cell Type Not Determined	-	-
ER	Negative	2.02 (1.76-2.31)	**<.001**
	Unknown	1.73 (0.97-3.11)	0.065
	Positive	-	-
PR	Negative	1.88 (1.65-2.13)	**<.001**
	Unknown	2.09 (1.27-3.45)	**0.004**
	Positive	-	-
Number of Regional Lymph Nodes Positive	3	1.35 (1.15-1.57)	**<.001**
	2	1.11 (0.96-1.29)	0.171
	1	-	-
LVI	Unknown	1.61 (1.32-1.96)	**<.001**
	Present	1.20 (0.95-1.52)	0.125
	Not present	-	-
AJCC Pathologic T	T1	0.58 (0.50-0.67)	**<.001**

	T2	-	-
	NPI III	2.58 (1.78-3.76)	**<.001**
Nottingham Prognostic Index	NPI II	1.35 (0.93-1.97)	0.11
	NPI I	-	-
Surgical procedure	Radical Mastectomy and Mastectomy, NOS	1.30 (0.83-2.05)	0.252
	Modified Radical Mastectomy	1.38 (1.20-1.59)	**<.001**
	Simple Mastectomy	-	-
	Negative	1.13 (0.58-2.19)	0.727
Surgical Margin	Positive	1.12 (0.54-2.32)	0.755
	Unknown	-	-
	Unknown	0.72 (0.36-1.42)	0.34
Chemotherapy	Yes	0.39 (0.34-0.44)	**<.001**
	No	-	-
Age at Diagnosis		1.05 (1.04-1.05)	**<.001**
Tumor Size (cm)		1.07 (1.05-1.09)	**<.001**

Analysis was weighted by variable: ATO weighted sample.

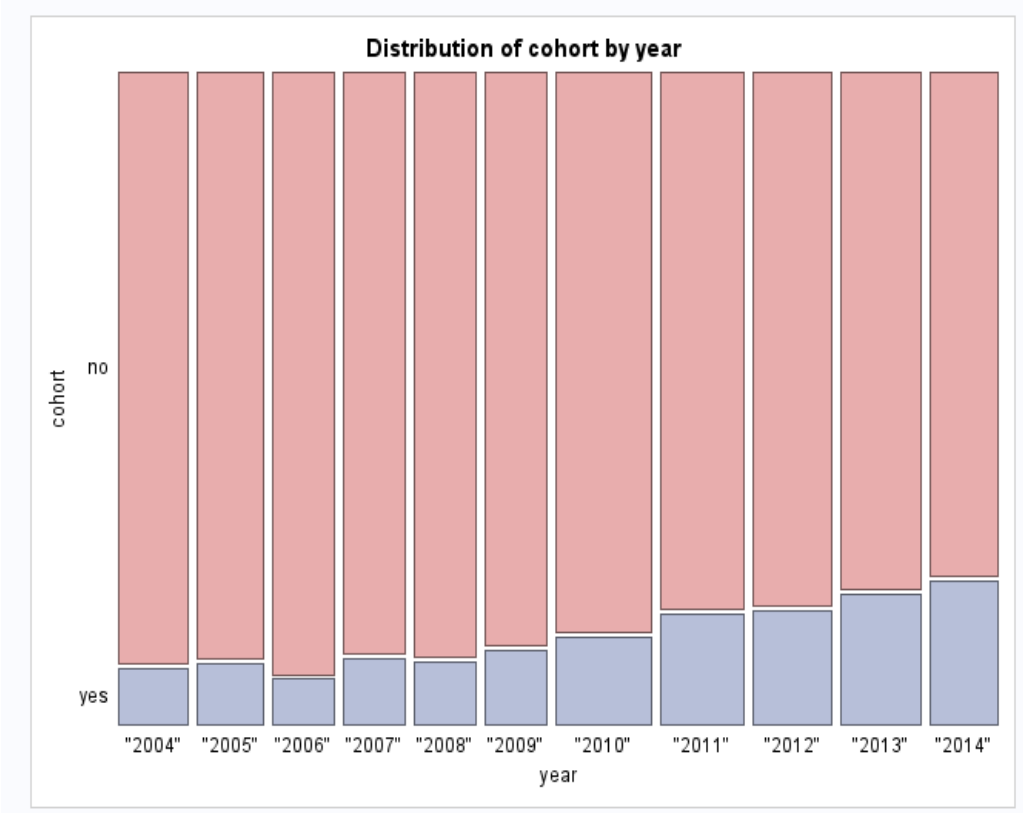


Figure 1. Trend between Utilization of PMRT and Year of Diagnosis