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Trends and Patterns of Utilization of Hypofractionated Post-Mastectomy Radiotherapy: A National Cancer Database Analysis

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Abstract

Background—The acceptance of hypofractionated radiotherapy in treating breast cancer in the breast conservation therapy setting has stimulated interest in hypofractionated post-mastectomy radiotherapy (PMRT). We assessed national trends and patterns of utilization of hypofractionated PMRT.

Patients and Methods—Women 18 years with breast cancer treated with mastectomy and PMRT to the chest wall with or without regional lymph nodes from 2004–2014 were identified from the National Cancer Database. A standard fractionation cohort was defined as patients receiving 180–200 cGy per fraction to a total dose of 4500–7000 cGy over 5–7 weeks, and a hypofractionation cohort was defined as those receiving 250–400 cGy per fraction to a total dose of 3000–6000 cGy over 2–5 weeks. Multivariable logistic regression was used to determine factors associated with hypofractionated PMRT use.

Results—113,981 patients met study criteria. Overall, hypofractionated PMRT use was low (1.1%) though utilization increased over time ($p < 0.001$). Older age, greater comorbidity, further distance from treatment facility, treatment at academic facilities, less extensive disease, and recent treatment year were statistically significant predictors of hypofractionation use compared to standard fractionation. Conversely, breast reconstruction and receipt of chemotherapy were negative predictors.

Conclusions—Given the absence of high-level evidence to support its use, hypofractionated PMRT was uncommonly utilized in the US from 2004–2014, though a small increase in use was

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noted over time. Findings from this study may be useful in designing future studies, and may serve as a baseline for evaluation of future changes in practice patterns.

Keywords

Breast Cancer; Radiotherapy; Mastectomy; Post-Mastectomy Radiotherapy

Introduction

It is well established that post-mastectomy radiotherapy (PMRT) improves long-term outcomes by reducing the risk of breast cancer recurrence in patients with high-risk features.^{1–3} PMRT is typically delivered to the chest wall and regional lymph nodes using standard fractionation regimens consisting of 180–200 cGy per fraction over 5–7 weeks.⁴ However, there is a growing interest in delivering PMRT with hypofractionated regimens, which consist of a larger dose per fraction but fewer total fractions, possibly spurred by the successful adoption of such regimens in the breast conservation setting.^{4,5}

The rationale for treating breast cancer with hypofractionated radiotherapy is primarily twofold. First, the overall treatment course is shortened without sacrificing treatment efficacy which may result in greater patient convenience and lower cost to health-systems.^{6,7} Second, radiobiological data suggest that breast cancer cells may be more susceptible to larger radiation doses per fraction compared to standard doses.⁸ However, these considerations must be balanced by the potential for increased long-term toxicities such as poor cosmesis, lymphedema, cardiopulmonary injury, brachial plexopathy, and rib fracture.

While multiple trials with extensive follow-up have convincingly demonstrated equivalent disease control and toxicity between hypofractionated and standard radiotherapy in the breast conservation setting,^{9–13} there is a paucity of such data for chest wall and regional lymph node irradiation in the post-mastectomy setting. The best long-term evidence supporting hypofractionated PMRT comes from the UK START trials,^{9,10} in which approximately 12% of patients (513 of 4451) were treated with PMRT to the chest wall and regional lymph nodes. 10-year results of these trials demonstrate no significant differences in shoulder stiffness and arm edema between patients receiving hypofractionation versus standard fractionation radiotherapy, and the incidence of symptomatic pneumonitis or brachial plexopathy was rare (<1%) – only one patient in the Start A trial treated with hypofractionated PMRT developed brachial plexopathy.^{9,14} More recently, results from a Phase II trial of 69 patients treated with hypofractionated PMRT in the US demonstrated that hypofractionated PMRT may be safe and effective.¹⁵ The favorable results from this trial have provided the impetus for the development of a Phase III randomized trial – Alliance A221505 – which seeks to compare outcomes following hypofractionated PMRT versus standard fractionation PMRT in a large cohort of women.

Given the growing interest in hypofractionated PMRT and the limited data regarding its use in the US, we conducted an observational study using a national cancer registry to assess temporal trends and patterns of utilization of hypofractionated PMRT in women treated for breast cancer between 2004 and 2014. Findings from this study may aid in the design of future studies and may serve as a basis for comparison of future changes in practice patterns

with regards to hypofractionated PMRT. We hypothesized that use of hypofractionated PMRT would be uncommon overall, but that there may be an increase in use over time, perhaps owing to the increased acceptance of hypofractionation in the breast conservation setting during the same time period.

Patients and Methods

Data Source

The study cohort was identified from the National Cancer Database (NCDB),¹⁶ a national cancer registry that is jointly sponsored by the American College of Surgeons and the American Cancer Society, which collects hospital registry data from more than 1,500 Commission on Cancer (CoC) accredited facilities in the United States and Puerto Rico. The database captures approximately 70% of incident cancers in these regions and contains more than 34 million unique cancer cases.

Study Population

Inclusion criteria (Figure 1) consisted of women ≥ 18 years with invasive, non-metastatic breast carcinoma treated with mastectomy followed by adjuvant external beam radiotherapy directed to the chestwall with or without inclusion of regional lymph nodes. From this population, a standard fractionation cohort and a hypofractionation cohort were identified. The standard fractionation cohort consisted of patients who received 180–200 cGy per fraction to a total dose of 4500–7000 cGy over 5–7 weeks while the hypofractionation cohort consisted of patients who received 250–400 cGy per fraction to a total dose of 3000–6000 cGy over 2–5 weeks. As initial and boost doses of radiotherapy were not robustly delineated in the NCDB, the aforementioned dose ranges may or may not be inclusive of a boost. Patients who did not meet criteria for either cohort, or those who received radiotherapy as part of palliative care, were excluded from the analysis.

Variables

Covariates examined included age, race, population density of patient residence (classified as metropolitan, urban, or rural), facility type (community or academic), patient distance to facility, geographic location of facility, primary insurance coverage, level of educational attainment (defined as percentage of the population in the patient's home ZIP code not achieving a high school degree), income (median income in the patient's home ZIP code), Charlson/Deyo comorbidity score,^{17,18} laterality of tumor, tumor histology, estrogen receptor (ER) status, HER-2 receptor status, American Joint Committee on Cancer (AJCC) 7th edition¹⁹ pathologic T stage, pathologic N stage, tumor grade, type of mastectomy, receipt of breast reconstruction, receipt of chemotherapy, and year of treatment.

Aims

The primary aim was to assess nationwide temporal trends and patterns of utilization of hypofractionated PMRT in women treated for breast cancer from 2004–2014. We also sought to identify patient, facility, and tumor related factors that predicted for receipt of hypofractionation relative to standard fractionation.

Statistical Analysis

Baseline characteristics of patients receiving hypofractionated and standard fractionation PMRT were compared using the Pearson χ^2 test. A multivariable logistic regression model, that included all covariates meeting a threshold significance of $p < 0.1$ on univariable regression analysis, was created to assess the independent effect of each covariate on the odds of receiving hypofractionated versus standard fractionation PMRT.

A two-sided p-value of less than 0.05 was used to determine statistical significance. All analyses were performed using Stata SE, version 14.0 (Stata Corp, College Station, TX).

Results

Characteristics of the Overall Cohort

Baseline characteristics of the overall cohort are described in Table 1. Of the 113,981 patients who met study criteria, 1305 (1.1%) were treated with hypofractionated PMRT while 112,676 (98.9%) were treated with a standard fractionation regimen. The median age of the entire cohort was 54 years (interquartile range (IQR): 46–64).

In the hypofractionation cohort, the median total dose delivered was 5000 cGy (IQR: 4256–5090 cGy) in 16 fractions (IQR: 15–20); in the standard fractionation cohort, the median total dose delivered was 6000 cGy (IQR: 5040–6040 cGy) in 30 fractions (IQR: 28–33). The most commonly utilized dose-fractionation regimen in the hypofractionated cohort was 4,256 cGy in 16 fractions (266 cGy per fraction) which was utilized in 20% of the cohort, while the most common regimen in the standard fractionation cohort was 5,040 cGy in 28 fractions (180 cGy per fraction) which was utilized in 52% of the cohort.

As demonstrated in Table 1, most patients were white (76%), treated at community centers (63%), presented with invasive ductal carcinoma (76%), and ER-positive disease (75%). The majority of patients underwent a modified radical mastectomy (56%) and received chemotherapy (87%).

Temporal Trends

The utilization of hypofractionated PMRT increased over time from 0.8% of patients receiving such treatment in 2004 to 1.7% of patients receiving it in 2014 (p-trend < 0.001) (Table 1 and Figure 2). Receipt of PMRT from 2008–2011 or 2012–2014 was associated with a statistically significantly increased likelihood of receipt of hypofractionation compared to treatment from 2004–2007 (Table 2). Over the study period, there was a more rapid increase in the utilization of hypofractionation at academic facilities compared to community facilities (Figure 2).

Factors Associated with Receipt of Hypofractionated PMRT

On multivariable analysis (Table 2), notable factors associated with receipt of hypofractionated PMRT relative to standard fractionation were treatment at academic facilities compared to community facilities (OR = 1.84, 95% CI: 1.62–2.09, $p < 0.001$), greater degree of comorbidity (Charlson Deyo score 2 vs 0, OR = 1.38, 95% CI: 1.04–1.82,

$p = 0.024$), older age (≥ 70 years vs < 50 years, OR = 1.85, 95% CI: 1.47–2.32, $p < 0.001$), black race relative to white race (OR = 1.21, 95% CI: 1.02–1.43, $p = 0.028$), and greater distance from treatment facility (> 50 miles vs ≤ 50 miles, OR = 1.37, 95% CI: 1.10–1.71, $p = 0.005$).

Factors predictive of a decreased likelihood of receipt of hypofractionation compared to standard fractionation were aggressive disease features such as high pathologic T stage (T3 vs T1, OR = 0.67, 95% CI: 0.56–0.79, $p < 0.001$) and node positivity (N3 vs N0, OR = 0.51, 95% CI: 0.41–0.63, $p < 0.001$). In addition, more extensive treatment such as receipt of a modified radical mastectomy compared to a simple mastectomy (OR = 0.87, 95% CI: 0.77–0.98, $p = 0.022$), receipt of breast reconstruction (OR = 0.78, 95% CI: 0.67–0.91, $p = 0.001$), and receipt of chemotherapy (OR = 0.31, 95% CI: 0.26–0.35, $p < 0.001$) were negative predictors of receipt of hypofractionation. Other notable pathologic features such as tumor receptor status, tumor grade, and surgical margin status were not significant predictors.

Discussion

We examined temporal trends and patterns of utilization of hypofractionated PMRT in 113,981 women treated for breast cancer from 2004–2014. Our results show that the overall use of hypofractionation was low, as would be expected based upon slow acceptance of hypofractionation after lumpectomy during this period,^{7,20} and the paucity of data showing safety and efficacy after mastectomy. Hypofractionation was utilized predominantly at academic centers, in patients with less extensive disease, and in patients more likely to find a prolonged course of treatment challenging such as the elderly, those with greater comorbidities, and those living far from treatment.

National utilization of hypofractionated radiotherapy following breast conservation surgery has been increasing^{7,20} owing to randomized evidence that demonstrated equivalency in outcomes between hypofractionation and standard fractionation regimens.^{9–14} These data have led to the adoption of hypofractionated radiotherapy by national guidelines^{4,5} as a standard treatment option in the breast conservation setting. Given this success, there is a growing global interest in utilizing hypofractionation in the post-mastectomy setting. At the present time, high quality data regarding hypofractionated PMRT are scarce, though this approach is the subject of multiple ongoing Phase II trials in the US (ClinicalTrials.gov identifiers: NCT02515110, NCT02700386, NCT02912312), and at least 2 ongoing Phase III trials internationally (ClinicalTrials.gov identifiers: NCT02690636, NCT00793962).

Prior work on hypofractionated PMRT is heterogeneous.^{21–34} In a prospective study from Egypt, Ali et al.³¹ reported on 47 patients randomized to either conventional (50 Gy in 25 fractions) or hypofractionated PMRT (42 Gy in 16 fractions); with a median follow-up time of 34 months, the authors reported equivalent disease control and cosmesis between study arms. In a prospective trial of 112 patients from Greece treated with hypofractionated PMRT consisting of 3.5 Gy fractions to a total dose of 35 Gy followed by a boost dose of 8 Gy in 2 fractions, Koukourakis et al.²⁹ reported high rates of acute skin desquamation but good disease control at a median follow-up of 44 months. Shahid et al.²⁶ retrospectively reviewed outcomes of 300 patients treated with PMRT with 2700 cGy in 5 fractions, 3500 cGy in 10

fractions, or 4000 cGy in 15 fractions using Cobalt-60 units in Pakistan; almost 40% of patients developed acute Grade 3 or 4 skin toxicity in the 2700 cGy arm, and approximately 5% of patients developed radiation pneumonitis following treatment. These examples highlight some shortcomings of the currently available data, which include: (1) use of outdated radiotherapy techniques, (2) use of variable hypofractionation schedules, (3) limited follow-up times, and (4) uncertain generalizability to practice in the US. Results from the first dedicated North American trial of hypofractionated PMRT were recently reported by Khan et al.¹⁵ who treated 69 patients with 36.63 Gy in 11 fractions followed by an optional boost using modern radiation techniques; with a median follow-up of 32 months, local recurrence-free survival was 89.2% and toxicity rates were acceptable and in line with previously published reports. These promising results have prompted the development of a Phase III trial, Alliance A221505, which will aim to provide additional high level evidence regarding the long term efficacy and toxicity in patients treated with hypofractionated PMRT.

As there has been no clear evidence guiding the optimal use of hypofractionated PMRT, our study findings may reflect some of the complex forces that drive medical care in the US. The significant increase in hypofractionated PMRT over the study period mirrors the uptake of hypofractionated treatment in the breast-conservation setting,^{7,20} though on a smaller scale, and may indicate extrapolation of data by providers from one setting to another. Increased utilization of hypofractionation at academic centers compared to community centers may suggest a greater familiarity and comfort with hypofractionated radiotherapy at academic centers, perhaps stemming from their more frequent use in the breast-conservation setting,²⁰ or a greater ease with deviating from guideline based care.

The greater use of hypofractionated PMRT in the elderly, those with greater comorbidities, and those who lived far from treatment demonstrate an inclination towards increasing patient convenience and alleviating the challenges associated with a long course of treatment. Prior work suggests that increasing patient convenience with hypofractionated radiotherapy improves patient compliance with treatment.³⁵ The greater likelihood of treating elderly patients may also reflect concerns about treating younger patients with hypofractionation given the potential for increased long-term side effects when using larger doses per fraction, particularly with regards to cosmesis. It is worth noting, however, that such concerns have not materialized in the breast conservation setting with 15 year follow-up of the Canadian randomized trial.¹²

Our results also demonstrate that the overall use of hypofractionation was selective, likely reflecting a lack of clarity regarding optimal patient selection. The decreased likelihood of treating patients with node-positive disease with hypofractionation may reflect a concern that treating the regional lymph nodes with hypofractionation may increase the risk of lymphedema.³⁶ Our findings also suggest a reluctance to use hypofractionated PMRT in the setting of a breast reconstruction and prior chemotherapy use, both of which are settings where further research is warranted to allay concerns regarding both acute and chronic side effects. These questions, particularly those regarding outcomes following breast reconstruction, will be informed by the results of Alliance A221505 which will exclusively enroll patients with breast reconstruction following mastectomy.

Our findings should be interpreted in light of certain limitations. First, there are a number of important variables that are not recorded by the NCDB. For instance, we do not have data regarding disease control outcomes or treatment toxicity, which are important endpoints to consider when evaluating hypofractionated radiotherapy. Additionally, we are also unable to directly assess other patient-, provider-, and facility-level variables such as patient and provider preferences, institutional practice patterns, or reimbursement patterns, which could have further informed our results. Secondly, there were certain variables, such as HER-2 receptor status, that contained a significant proportion of missing information; therefore, findings regarding their association with hypofractionation should be interpreted cautiously. These limitations are offset by strengths of this study which include a large patient population, and the wide array of patient, facility, and treatment level variables that were included in the analysis.

Conclusion

In the absence of high-level evidence to support its use, utilization of hypofractionated PMRT was low in patients with breast cancer identified from the NCDB from 2004–2014. There was, however, a small trend towards increased use over time. Older age, greater comorbidity, further distance to treatment, treatment at academic facilities, and less extensive disease were independent predictors of receipt of hypofractionated treatment. These data may serve as a baseline upon which to evaluate future changes in practice patterns that may occur with accrual of high quality evidence regarding hypofractionated PMRT.

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Microabstract

There is growing interest in treating breast cancer with hypofractionated post-mastectomy radiotherapy (PMRT). National patterns of hypofractionated PMRT utilization were assessed using the National Cancer Database. Overall, hypofractionated PMRT use was uncommon though it increased over time. Hypofractionated PMRT was used in patients more likely to gain convenience from shorter treatment schedules.

Clinical Practice Points

- There is growing global interest in treating breast cancer with hypofractionated PMRT. However, data to guide optimal practice are limited by several factors including use of outdated radiotherapy techniques, use of variable hypofractionation schedules, limited follow-up times, and uncertain generalizability to practice in the US.
- This study was performed to assess national trends and patterns of utilization of PMRT in the United States. Patients with non-metastatic breast cancer who were treated with a mastectomy and PMRT were identified from the National Cancer Database.
- The use of hypofractionated PMRT was very low (1.1%) but there was a significant increase in utilization over the study period. Factors associated with hypofractionated PMRT use were older age, greater comorbidity, further distance from treatment facility, treatment at academic facilities, less extensive disease, and more recent treatment year. Receipt of breast reconstruction surgery and chemotherapy were negative predictors.
- Promising results from the first dedicated North American hypofractionated PMRT study, a Phase II trial, were recently published. These results have spurred the development of a Phase III randomized controlled trial – Alliance A221505 – which will assess the efficacy and safety of hypofractionated PMRT in a larger cohort of women.
- Results from this study provide an overview of recent patterns of care. This information may aid in designing future studies and may serve as a baseline upon which future changes in practice patterns with regards to hypofractionated PMRT are evaluated.

Figure 1.
Consolidated Standards of Reporting Trials (CONSORT) diagram. *PMRT*: Post-mastectomy radiotherapy.

Figure 2. Receipt of hypofractionated post-mastectomy radiotherapy from 2004–2014 (p-trend < 0.001). *PMRT*: Post-mastectomy radiotherapy.

Table 1

Patient Characteristics

	Standard Fractionation	Hypofractionation	Total	p-value (chi2)
Total no.	112676 (98.9)	1305 (1.1)	113981 (100)	
Age (years)				<0.001
49	41107 (36)	303 (23)	41410 (36)	
50–69	54715 (49)	573 (44)	55288 (49)	
70	16854 (15)	429 (33)	17283 (15)	
Race				0.032
Non-Hispanic White	86169 (76)	964 (74)	87133 (76)	
Non-Hispanic Black	14169 (13)	199 (15)	14368 (13)	
Hispanic	6547 (6)	72 (6)	6619 (6)	
Other	5791 (5)	70 (5)	5861 (5)	
County size				0.057
Metropolitan	93290 (82)	1070 (82)	94360 (82)	
Urban	14340 (13)	179 (14)	14519 (13)	
Rural	1862 (2)	30 (2)	1892 (2)	
Unknown	3184 (3)	26 (2)	3210 (3)	
Facility Location				<0.001
East	19011 (17)	204 (16)	19215 (17)	
South	34272 (30)	469 (36)	34741 (30)	
Central	29205 (26)	263 (20)	29468 (26)	
West	17649 (16)	274 (21)	17923 (16)	
Unknown	12539 (11)	95 (7)	12634 (11)	
Facility type				<0.001
Community	71214 (63)	739 (57)	71953 (63)	
Academic	28923 (26)	471 (36)	29394 (26)	
Unknown	12539 (11)	95 (7)	12634 (11)	
Distance to Treatment				<0.001
50 miles	105052 (93)	1183 (90)	106235 (93)	
>50 miles	6730 (6)	116 (9)	6846 (6)	
Unknown	894 (1)	6 (1)	900 (1)	
Insurance status				<0.001
Medicare	26815 (24)	521 (40)	27336 (24)	
Commercial Insurance	68855 (61)	589 (45)	69444 (61)	
Medicaid	10742 (10)	125 (10)	10867 (10)	
Uninsured	3490 (3)	38 (3)	3528 (3)	
Other Government/Unknown	2774 (2)	32 (2)	2806 (2)	
Education				0.03
21%	17062 (15)	222 (17)	17284 (15)	

	Standard Fractionation	Hypofractionation	Total	p-value (chi2)
13%–20.9%	27281 (24)	344 (26)	27625 (24)	
7%–12.9%	36424 (32)	410 (31)	36834 (32)	
<7%	31003 (28)	322 (25)	31325 (28)	
Unknown	906 (1)	7 (1)	913 (1)	
Income (\$)				0.158
<38,000	17612 (16)	230 (18)	17842 (16)	
38,000–47,999	24387 (22)	293 (22)	24680 (22)	
48,000–62,999	30396 (27)	344 (26)	30740 (27)	
>63,000	39330 (34)	431 (33)	39761 (34)	
Unknown	951 (1)	7 (1)	958 (1)	
Charlson/Deyo Comorbidity Score				<0.001
0	97016 (86)	1067 (82)	98083 (86)	
1	13134 (12)	182 (14)	13316 (12)	
2	2526 (2)	56 (4)	2582 (2)	
Laterality				0.194
Right	56036 (50)	675 (52)	56711 (50)	
Left	56525 (50)	630 (48)	57155 (50)	
Unknown	115 (0)	0 (0)	115 (0)	
Histology				0.171
Invasive Ductal Carcinoma	85440 (76)	991 (76)	86431 (76)	
Invasive Lobular Carcinoma	25075 (22)	280 (21)	25355 (22)	
Adenocarcinoma NOS	2161 (2)	34 (3)	2195 (2)	
ER-receptor status				0.715
Positive	84667 (75)	988 (76)	85655 (75)	
Negative	26649 (24)	299 (23)	26948 (24)	
Unknown	1360 (1)	18 (1)	1378 (1)	
Her2-receptor status				<0.001
Positive	12940 (12)	141 (11)	13081 (12)	
Negative	49746 (44)	705 (54)	50451 (44)	
Unknown	49990 (44)	459 (35)	50449 (44)	
Pathologic T Stage				<0.001
T1	28661 (25)	473 (36)	29134 (26)	
T2	45316 (40)	432 (33)	45748 (40)	
T3	21647 (19)	205 (16)	21852 (19)	
T4	5427 (5)	86 (7)	5513 (5)	
Other/Unknown	11625 (10)	109 (8)	11734 (10)	
Pathologic N Stage				<0.001
N0	23577 (21)	522 (40)	24099 (21)	
N1	41076 (36)	368 (28)	41444 (36)	

	Standard Fractionation	Hypofractionation	Total	p-value (chi2)
N2	27945 (25)	208 (16)	28153 (25)	
N3	14184 (13)	114 (9)	14298 (13)	
Unknown	5894 (5)	93 (7)	5987 (5)	
Grade				<0.001
1	10622 (9)	182 (14)	10804 (9)	
2	45153 (40)	518 (40)	45671 (40)	
3	49177 (44)	529 (40)	49706 (44)	
Unknown	7724 (7)	76 (6)	7800 (7)	
Type of Mastectomy				<0.001
Simple	46383 (41)	685 (53)	47068 (41)	
Modified Radical	63641 (56)	576 (44)	64217 (56)	
Radical	1995 (2)	29 (2)	2024 (2)	
Mastectomy NOS	657 (1)	15 (1)	672 (1)	
Surgical Margin Status				<0.001
Negative	103254 (92)	1137 (87)	104391 (92)	
Positive	7883 (7)	143 (11)	8026 (7)	
Unknown	1539 (1)	25 (2)	1564 (1)	
Receipt of Breast Reconstruction				<0.001
No	82386 (73)	1043 (80)	83429 (73)	
Yes	30290 (27)	262 (20)	30552 (27)	
Receipt of Chemotherapy				<0.001
No	13690 (12)	539 (41)	14229 (12)	
Yes	98485 (87)	748 (57)	99233 (87)	
Unknown	501 (1)	18 (2)	519 (1)	
Year of Treatment				<0.001
2004	6566 (6)	51 (4)	6617 (6)	
2005	6953 (6)	43 (3)	6996 (6)	
2006	7741 (7)	63 (5)	7804 (7)	
2007	8632 (8)	77 (6)	8709 (7)	
2008	9329 (8)	101 (8)	9430 (8)	
2009	10419 (9)	102 (8)	10521 (9)	
2010	11435 (10)	129 (10)	11564 (10)	
2011	12506 (11)	150 (10)	12656 (11)	
2012	13074 (12)	167 (13)	13241 (12)	
2013	13415 (12)	206 (16)	13621 (12)	
2014	12606 (11)	216 (17)	12822 (11)	

NOS – Not otherwise specified.

Table 2

Factors associated with receipt of hypofractionated PMRT

	Univariable		Multivariable	
	OR [95% CI]	p-value	OR [95% CI]	p-value
Age (years)				
49	–	–	–	–
50–69	1.42 [1.24, 1.63]	<0.001	1.27 [1.07, 1.50]	0.005
70	3.45 [2.98, 4.00]	<0.001	1.85 [1.47, 2.32]	<0.001
Race				
Non-Hispanic White	–	–	–	–
Non-Hispanic Black	1.26 [1.08, 1.46]	0.004	1.21 [1.02, 1.43]	0.028
Hispanic	0.98 [0.77, 1.25]	0.89	0.98 [0.75, 1.26]	0.85
Other	1.08 [0.85, 1.38]	0.53	1.00 [0.77, 1.29]	0.99
County size				
Metropolitan	–	–	–	–
Urban	1.09 [0.93, 1.28]	0.30	1.10 [0.92, 1.32]	0.31
Rural	1.40 [0.97, 2.02]	0.069	1.44 [0.97, 2.13]	0.068
Unknown	0.71 [0.48, 1.05]	0.088	0.73 [0.48, 1.11]	0.14
Facility Location				
East	–	–	–	–
South	1.28 [1.08, 1.50]	0.004	1.40 [1.17, 1.67]	<0.001
Central	0.84 [0.70, 1.01]	0.062	0.90 [0.75, 1.09]	0.29
West	1.45 [1.21, 1.74]	<0.001	1.68 [1.39, 2.04]	<0.001
Unknown	0.71 [0.55, 0.90]	0.005	1.63 [1.22, 2.17]	0.001
Facility type				
Community	–	–	–	–
Academic	1.57 [1.40, 1.76]	<0.001	1.84 [1.62, 2.09]	<0.001
Unknown	0.73 [0.59, 0.90]	0.004	omitted	–
Distance to Treatment				
50 miles	–	–	–	–
>50 miles	1.53 [1.26, 1.86]	<0.001	1.37 [1.10, 1.71]	0.005
Unknown	0.60 [0.27, 1.33]	0.21	0.54 [0.10, 3.04]	0.49
Insurance status				
Medicare	–	–	–	–
Commercial Insurance	0.44 [0.39, 0.40]	<0.001	0.88 [0.75, 1.04]	0.14
Medicaid	0.60 [0.49, 0.73]	<0.001	1.10 [0.87, 1.39]	0.42
Uninsured	0.56 [0.40, 0.78]	0.001	0.99 [0.69, 1.41]	0.94
Other Government/Unknown	0.59 [0.41, 0.85]	0.004	0.93 [0.64, 1.36]	0.72
Education				
21%	–	–	–	–

	Univariable		Multivariable	
	OR [95% CI]	p-value	OR [95% CI]	p-value
13%–20.9%	0.97 [0.82, 1.15]	0.72	1.04 [0.87, 1.25]	0.66
7%–12.9%	0.87 [0.73, 1.02]	0.084	1.00 [0.81, 1.23]	0.99
<7%	0.80 [0.67, 0.95]	0.010	0.91 [0.72, 1.16]	0.45
Unknown	0.59 [0.28, 1.26]	0.18	omitted	–
Income (\$)				
<38,000	–	–	–	–
38,000–47,999	0.92 [0.77, 1.09]	0.35	1.05 [0.87, 1.28]	0.58
48,000–62,999	0.87 [0.73, 1.03]	0.095	1.07 [0.87, 1.30]	0.54
>63,000	0.84 [0.71, 0.99]	0.033	1.16 [0.92, 1.46]	0.21
Unknown	0.56 [0.26, 1.20]	0.14	omitted	–
Charlson/Deyo Comorbidity Score				
0	–	–	–	–
1	1.26 [1.08, 1.48]	0.004	1.00 [0.85, 1.18]	0.98
2	2.02 [1.54, 2.64]	<0.001	1.38 [1.04, 1.82]	0.024
Laterality				
Right	–	–	–	–
Left	0.93 [0.83, 1.03]	0.16	–	–
Unknown	omitted	–	–	–
Histology				
Invasive Ductal Carcinoma	–	–	–	–
Invasive Lobular Carcinoma	0.96 [0.84, 1.10]	0.58	0.85 [0.73, 0.99]	0.033
Adenocarcinoma NOS	1.36 [0.96, 1.91]	0.083	1.01 [0.71, 1.44]	0.94
ER-receptor status				
Positive	–	–	–	–
Negative	0.96 [0.84, 1.10]	0.55	–	–
Unknown	1.13 [0.71, 1.81]	0.60	–	–
Her2-receptor status				
Positive	–	–	–	–
Negative	1.30 [1.08, 1.56]	0.005	1.03 [0.85, 1.25]	0.77
Unknown	0.84 [0.70, 1.02]	0.077	0.95 [0.75, 1.20]	0.67
Pathologic T Stage				
T1	–	–	–	–
T2	1.05 [0.76, 1.46]	0.77	0.73 [0.63, 0.84]	<0.001
T3	1.04 [0.74, 1.47]	0.81	0.67 [0.56, 0.79]	<0.001
T4	1.75 [1.19, 2.56]	0.004	0.94 [0.74, 1.20]	0.62
Unknown	1.13 [0.75, 1.68]	0.56	0.51 [0.40, 0.66]	<0.001
Pathologic N Stage				
N0	–	–	–	–

	Univariable		Multivariable	
	OR [95% CI]	p-value	OR [95% CI]	p-value
N1	0.40 [0.35, 0.46]	<0.001	0.50 [0.43, 0.57]	<0.001
N2	0.34 [0.29, 0.40]	<0.001	0.46 [0.39, 0.55]	<0.001
N3	0.36 [0.30, 0.45]	<0.001	0.51 [0.41, 0.63]	<0.001
Unknown	0.71 [0.57, 0.89]	0.003	1.18 [0.91, 1.53]	0.20
Grade				
1	–	–	–	–
2	0.67 [0.56, 0.79]	<0.001	0.92 [0.77, 1.09]	0.33
3	0.63 [0.53, 0.74]	<0.001	1.08 [0.90, 1.30]	0.41
Unknown	0.57 [0.44, 0.75]	<0.001	0.80 [0.61, 1.06]	0.12
Type of Mastectomy				
Simple	–	–	–	–
Modified Radical	0.61 [0.55, 0.69]	<0.001	0.87 [0.77, 0.98]	0.022
Radical	0.98 [0.68, 1.43]	0.93	1.31 [0.89, 1.91]	0.17
Mastectomy NOS	1.55 [0.92, 2.59]	0.099	1.52 [0.89, 2.59]	0.12
Surgical Margin Status				
Negative	–	–	–	–
Positive	1.65 [1.38, 1.96]	<0.001	1.15 [0.96, 1.38]	0.13
Unknown	1.48 [0.99, 2.20]	0.056	1.52 [1.01, 2.29]	0.044
Receipt of Breast Reconstruction				
No	–	–	–	–
Yes	0.68 [0.60, 0.78]	<0.001	0.78 [0.67, 0.91]	0.002
Receipt of Chemotherapy				
No	–	–	–	–
Yes	0.19 [0.17, 0.22]	<0.001	0.31 [0.26, 0.35]	<0.001
Unknown	0.91 [0.57, 1.47]	0.71	1.04 [0.64, 1.68]	0.88
Year of Treatment				
2004 – 2007	–	–	–	–
2008 – 2011	1.41 [1.20, 1.65]	<0.001	1.37 [1.14, 1.65]	0.001
2012 – 2014	1.92 [1.65, 2.24]	<0.001	1.81 [1.45, 2.26]	<0.001

PMRT – Post Mastectomy Radiotherapy; NOS – Not otherwise specified