

## Critical Review

# Radiation Therapy Practice Patterns for Treatment of Curative Breast Cancer in a Large Tertiary Health Care System



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**Purpose:** Disparities have been reported in women treated for breast cancer (BrCa). This study examines potential disparities in BrCa treatment offered based on race and age from a multicenter radiation department.

**Methods and Materials:** We identified 901 patients with early stage BrCa who received curative intent radiation therapy (RT) between 2004 and 2018. Data extracted included age, race, disease stage, treatment technique, treatment dates, and fractionation. Patient race was recorded as Asian, Black, Hispanic, and White. RT technique delivered was classified as a type of external beam radiation therapy or brachytherapy/intraoperative radiation therapy. Fractionation schema were defined as 1) standard fractionation, 1.8-2 Gy; 2) hypofractionation, 2.5-2.67 Gy; 3) accelerated partial breast irradiation (APBI), 3.4 Gy – 4.25 Gy, and 4) intraoperative radiation therapy, single dose of 20 Gy. Stage was recorded using TNM staging. The  $\chi^2$  test and a multivariable multinomial logistic regression model were used to assess whether patient characteristics, such as age, race, or stage influenced fractionation schemes. Results with 2-sided  $P$  values < .05 were considered statistically significant.

**Results:** Racial composition of the study was 13.8% Asian, 22% Black, 29%, White, and 35.1% Hispanic. Mean age was 61 and was divided into 4 age range groups: 30 to 49 (n = 160), 50 to 59 (n = 231), 60 to 69 (n = 294), and  $\geq 70$  years (n = 216). In addition, 501 patients (56%) received hypofractionation, 342 (38.8%) received standard fractionation, and 58 (7.1%) received APBI, respectively. For all groups, hypofractionation became more common over time. Age  $\geq 70$  years was associated with 9 times higher odds of APBI and 14 times higher odds of hypofractionation, compared with age 30 to 49 years. After adjusting for the other predictors in a multivariable multinomial logistic regression model, the race distribution differed among the 3 groups ( $P = .03$ ), with a smaller percentage of Hispanics and higher percentage of blacks in the standard group.

**Conclusions:** This study of a diverse cohort of patients with breast cancer failed to identify treatment differences associated by race. The study found an association between age and hypofractionation.

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## Introduction

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Breast Cancer (BrCa) is the most diagnosed form of cancer in women in the United States. It is estimated that 1 in 11 women in countries with a high social development index will develop BrCa during their life.

Postoperative radiation after breast conservation in early-stage breast cancer is the standard of care. Disparities in breast cancer occurrence and outcomes in terms of both race and age have been well documented.<sup>1</sup> Smith et al identified substantial racial disparities in the utilization of radiation therapy after breast conservation. After adjusting for demographics and socioeconomic variables, White women were still significantly more likely than Black women to have received RT after BCS. The disparities were found to be regional and more pronounced in the Northeast and Southern states, as well as persistent in young or older populations.<sup>2</sup> These disparities led our institution to ask the question as to whether race and/or age disparities existed in our early breast cancer population in terms of the therapeutic options patients were being offered.

Therapeutic options for patients with early BrCa are diverse, usually consisting of combinations of partial mastectomy followed by adjuvant treatment, such as chemotherapy/hormone therapy and radiation therapy (RT).<sup>3</sup> The use of RT reduces disease recurrence, and in early stage BrCa obviates the need for mastectomy, allowing for breast conserving surgery.<sup>4-10</sup> A variety of radiation therapy (RT) techniques and fractionation schemes are available, the rationale for using a particular technique is complex and depends on many variables, including; available technology, patient characteristics, tumor characteristics, and physician decision.

Fractionation schemes for radiation therapy range from a standard course of external beam radiation therapy (EBRT) for 5 to 6 weeks, an abbreviated course of 3 weeks (hypofractionation), to accelerated partial breast irradiation (APBI), which can be done using brachytherapy, EBRT, or intraoperative radiation therapy (IORT). In our multicenter academic radiation oncology department, all the RT techniques are available. We set out to assess the utilization of particular RT fractionation schemes, and whether patient characteristics such as race or age influenced the regimen chosen.

## Methods and Materials

This is a retrospective study of all patients with BrCa treated from 2004 to 2018. We used Oncora, a data extracting software program to identify patients from the department electronic medical records. We identified 1142 patients with nonmetastatic breast cancer who received curative intent RT after breast conservation between 2000 and 2018. We then selected patients with early-stage breast cancer defined here as patients with T1-T2N0 disease. Data extracted included date of the first fraction of RT, patient age at first fraction, race, fractionation, and disease stage. We attempted to acquire hormone receptor status, but too few patients had it documented, and this was not recorded.

Patient race was recorded as Asian, Black, Hispanic, or White. RT technique delivered was classified as a specific type of EBRT or brachytherapy/IORT. Fractionation schemas were defined based on dose per fraction as 1) standard fractionation, 1.8-2 Gy; 2) hypofractionation, 2.5-2.67 Gy; 3) APBI, 3.4-4.25 Gy, and 4) IORT, single dose of 20 Gy. Both standard and hypofractionation schemas were standard tangents delivered to the whole breast. Patients were recorded to receive boost or no boost to the lumpectomy cavity. Disease stages were recorded using TNM staging as T1N0M0, T2N0M0, or other.

## Statistical analysis

Patient baseline characteristics were compared among the 3 fractionation schemes using the  $\chi^2$  test. A multivariable multinomial logistic regression model was used to examine the associations of age group, race, stage, and treatment period with fractionation, using standard fractionation as the reference level. Associations were reported using odds ratios and 95% CIs. SAS 9.4 (SAS Institute Inc) was used for the statistical analyses. Two-sided *P* values <.05 were considered statistically significant.

## Results

Of 1142 total patients with nonmetastatic BrCa initially extracted for analysis, 901 early-stage BrCa patients were included in the final analysis of 3 fractionation schemes. We excluded 235 patients of stage category "other" given that patients with stage >T2N0 would not meet criteria for APBI. We excluded 6 patients treated with IORT because of the small sample size.

## Univariate analysis

Most patients (525/901) were between the ages of 50 to 69 years (*P* < .05). In addition, 762 patients had T1N0M0 disease, and 139 with T2N0M0 disease. Racial makeup of the cohort was 334 Hispanic patients, 269 White patients, 183 Black patients, and 130 Asian patients (*P* < .05).

On univariate analysis, 901 patients with early-stage breast cancer were divided into 4 age groups, stratified by fractionation scheme, with a mean age of 61.2 years (SD, 11.3). Younger patients received more standard fractionation (*P* < .05; Table 1). We also observed that a higher percentage of T2N0M0 patients received standard fractionation (*P* < .05). More than 50% of the use of standard and APBI fractionation occurred in the earliest period of 2004 to 2011, and hypofractionation was used more in the later periods (*P* < .05; Table 1).

Patient race distributions stratified by stage are shown in Table 2. A statistically significant association was found

**Table 1 Demographic and clinical characteristics by fractionation scheme**

Characteristics	Fractionation scheme			P value
	APBI (n = 58)	Hypofractionation (n = 501)	Standard (n = 342)	
Race				.0336
Asian	8 (13.8%)	71 (14.2%)	51 (14.9%)	
Black	6 (10.3%)	79 (15.8%)	83 (24.3%)	
Hispanic	24 (41.4%)	196 (39.1%)	114 (33.3%)	
White	20 (34.5%)	155 (30.9%)	94 (27.5%)	
Stage				<.0001
T1N0M0	53 (91.4%)	447 (89.2%)	262 (76.6%)	
T2N0M0	5 (8.6%)	54 (10.8%)	80 (23.4%)	
Age group, y				<.0001
30-49	5 (8.6%)	48 (9.6%)	107 (31.3%)	
50-59	10 (17.2%)	130 (25.9%)	91 (26.6%)	
60-69	22 (37.9%)	177 (35.3%)	95 (27.8%)	
70+	21 (36.2%)	146 (29.1%)	49 (14.3%)	
Period				<.0001
2004-2011	33 (56.9%)	63 (12.6%)	185 (54.1%)	
2012-2014	14 (24.1%)	125 (25%)	89 (26%)	
2015-2016	6 (10.3%)	168 (33.5%)	49 (14.3%)	
2017-2018	5 (8.6%)	145 (28.9%)	19 (5.6%)	

*Abbreviation:* APBI = accelerated partial breast irradiation.

between patient race and stage. Asian and Black patients were twice as likely to be diagnosed at T2N0M0 23.1% and 23.8%, respectively compared with Hispanic or White patients at 12.3% and 10.4%, respectively ( $P < .05$ ; Table 2). The race distribution differed among the 3 fractionation groups, with the standard fractionation group having smaller percentage of Hispanic patients, and higher percentage of Black patients ( $P < .05$ ; Table 1). A multivariate analysis was performed after the univariate analysis to assess which noted trends persisted, after adjusting for covariates.

### Multivariable analysis

A multivariable multinomial logistic regression model was used to examine the associations of age group, race, stage, and treatment period with the type of fractionation, using standard fractionation as a reference level. Overall, 58 (6.4%) patients received APBI, 501(55.6%) hypofractionation and 342 (38.0%) standard fractionation. Older age was associated with an increased likelihood of APBI or hypofractionation compared with standard fractionation after adjusting for covariates (Table 3). For example,

**Table 2 Stage of patients with BrCa by race**

Race, n (%)	Stage		P value*
	T1N0M0, (n = 762)	T2N0M0, (n = 139)	
Asian	100 (77%)	30 (23.1%)	<.0001
Black	128 (76.2%)	40 (23.8%)	
Hispanic	293 (87.8%)	41 (12.3%)	
White	241 (89.6%)	28 (10.4%)	

*Abbreviation:* BrCa = breast cancer.

**Table 3** Multivariable multinomial logistic regression model for fractionation scheme, using standard fractionation as a reference

Effect	APBI		Hypofract	
	APBI-OR (95% CI)	P value	Hypofract-OR (95% CI)	P value
Race				
White	Reference		Reference	
Asian	1.19 (0.46-3.04)	.7205	0.84 (0.48-1.48)	.5473
Black	0.48 (0.18-1.29)	.1447	0.88 (0.53-1.47)	.6244
Hispanic	1.07 (0.54-2.11)	.8549	1.14 (0.74-1.75)	.5572
Stage				
T1N0M0	Reference		Reference	
T2N0M0	0.32 (0.12-0.85)	.0218	0.29 (0.18-0.47)	<.0001
30-49	Reference		Reference	
50-59	2.25 (0.73-6.92)	.1566	4.40 (2.60-7.45)	<.0001
60-69	4.67 (1.68-13.01)	.0032	5.09 (3.06-8.47)	<.0001
70+	9.37 (3.23-27.18)	<.0001	14.79 (8.29-26.39)	<.0001
Period				
2004-2011	Reference		Reference	
2012-2014	1.01 (0.50-2.04)	.9817	4.99 (3.22-7.72)	<.0001
2015-2016	0.97 (0.37-2.55)	.9486	16.25 (9.87-26.77)	<.0001
2017-2018	2.18 (0.72-6.60)	.1671	38.93 (20.71-73.18)	<.0001

Abbreviations: APBI = accelerated partial breast irradiation; hypofract = hypofractionation.

age  $\geq 70$  years was associated with more than 9 times higher odds of receiving APBI and 14 times higher odds of receiving hypofractionation, compared with age 30 to 49 years. Stage T2N0M0 was associated with about 70% lower odds of using of APBI and hypofractionation compared with stage T1N0M0 (Table 3). Treatment delivered in later periods was associated with higher odds of receiving hypofractionation, but not APBI. For example, treatment during 2012 to 2014 was associated with 5 times higher odds of receiving hypofractionation compared with 2004 to 2011.

Race was not found to be associated ( $P = .57$ ) with the type of fractionation after adjusting for the other predictors. The estimated odds ratios for most differences were close to 1, indicating no differences in type of fractionation (Table 3). For example, the estimated odds of hypofractionation for Black patients was only 12% lower compared with White patients ( $P = .62$ ). The estimated odds of Black patients receiving APBI was half that of White patients (Table 3), but this trend did not reach a statistical significance ( $P = .14$ ) because of the small size of the APBI group.

## Discussion

There are a wide range of RT options for early-stage breast cancer, including different techniques, and

fractionation schemes. We examined the patterns of practice regarding selection of RT regimens in early-stage breast cancer from 2000 to 2018, and their potential correlation with age, race, and stage. Previous studies have conducted similar analyses regarding the use of hypofractionation.<sup>11-14</sup> In prior research, Gilbo et al demonstrated the underutilization of hypofractionation despite equivalent local control and superior toxicity profiles. Factors such as patient characteristics and individual practitioners' preferences as well as institutional bias were cited as potential reasons for the reluctance to use hypofractionation. To increase its use, our department instituted the use of clinical treatment directives to standardize the practice of multiple physicians from diverse backgrounds across multiple sites.<sup>15</sup> We appreciated an increase in the use of hypofractionation over time in our study population from 2004 to 2018. Our study, to the best of our knowledge was the first to examine the role of various regimens, including hypofractionation, APBI, and their potential association with age and or race. We did find that patients in the 70+ age group were more likely to receive hypofractionation and younger patients were more likely to receive standard fractionation.

We did not find a significant association between race and the choice of fractionation. Although the difference in fractionation between the race groups did not reach a statistical significance, we observed that the use of

hypofractionation in Black patients was lower. We found Asian and Black patients twice as likely to be diagnosed at T2N0M0 23.1% and 23.8%, respectively than Hispanic or White patients at 12.3% and 10.4%, respectively ( $P < .0001$ ). This finding was consistent with data demonstrating that Black women are likely to be diagnosed at a later stage.<sup>16,17</sup> Incidence rates of breast cancer are increasing significantly for certain Asian American subgroups,<sup>18</sup> but there have been very few studies comparing breast cancer in Asian women compared with White or Black women.<sup>19</sup> Yu et al recently examined breast cancer characteristics between Asian women and compared with other races. It was noted that Asian women are often studied as a single entity without acknowledging differences in country of origin, ancestry, socioeconomic status. Breast cancer characteristics and outcomes vary significantly for Asian women. To draw useful conclusions future studies will need to disaggregate Asian women by country or region.<sup>20</sup>

This large multisite retrospective review assessed the utilization of particular RT techniques, fractionation, and whether patient characteristics, such as race or age influenced the technique chosen. Patients in the  $\geq 70$  years age group were more likely to receive hypofractionation, and younger patients were more likely to receive standard fractionation. We did not find a significant association between race and the choice of fractionation. Limitations of our study included the retrospective nature and a change in patient population demographics after acquisition of new centers in our institution's health network. Lastly, individual physician bias may have also played a role in the use of hypofractionation.

## Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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