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Clinical Investigation

The Role of Facility Variation on Racial Disparities in Use of Hypofractionated Whole Breast Radiation Therapy

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Purpose: Hypofractionated radiation therapy is a less burdensome and less costly approach that is efficacious for most patients with early-stage breast cancer. Concerns about racial disparities in adoption of medical advances motivate investigation of the use of hypofractionated radiation in diverse populations. The goal of our study was to determine whether hypofractionated whole breast radiation therapy after breast-conserving surgery was being similarly used across racial groups in the state of Michigan.

Methods and Materials: A prospectively collected statewide quality consortium database from 25 institutions was queried for patients with breast cancer who completed hypofractionated (HF) or conventionally fractionated whole breast radiation therapy from January 2012 to December 2018. We used patient-level multivariable modeling to evaluate associations between HF use and race, controlling for patient and facility factors, and multilevel modeling to account for patient clustering within facilities.

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Results: Of 9634 patients analyzed, 81% self-reported race as white, 17% as black, and 2% as Asian, similar to statewide and national distributions. In addition, 31.7% of whites were treated at teaching centers compared with 66.7% of blacks and 64.8% of Asians. In 2018, HF was used in 72.7% of whites versus 56.7% of blacks and 67.6% of Asians ($P = .0411$). On patient-level multivariable analysis, black and Asian races were significantly associated with a lower likelihood of HF receipt ($P < .001$), despite accounting for treatment year, age, laterality, body mass index, breast volume, comorbidities, stage, triple-negative status, intensity modulated radiation therapy use, teaching center treatment, and 2011 American Society for Radiation Oncology Hypofractionation Guideline eligibility. On multilevel analysis, race was no longer significantly associated with HF receipt.

Conclusions: We observed that black and Asian patients receive hypofractionated whole breast radiation therapy less often than whites, despite more frequent treatment at teaching centers. Multilevel modeling eliminated this disparity, suggesting that differences in facility-specific HF use appear to have contributed. Further inquiry is needed to determine whether reduction of facility-level variation may reduce disparities in accessing HF treatment.

Introduction

Breast cancer mortality rates have been declining over the past several decades, but a breast cancer mortality disparity still exists for black women compared with white women. For example, one study reported a 33.4% 10-year cumulative incidence of breast cancer death in black women compared with 21.5% in white women.[1] A patterns-of-failure analysis by Pierce et al also showed worse overall survival in a population of black women with early stage breast cancer compared with similarly staged white patients.[2] Breast cancer has been purported to be more biologically aggressive in subsets of black women, and social barriers to care may also disproportionately affect women of color.[3] In addition to genetic, biologic, and environmental factors, treatment factors may also contribute to disparities in outcomes.

Whole breast radiation therapy (RT) is an important part of breast conservation therapy and has been shown to improve survival.[4] However, black women are less likely to receive breast RT to appropriately complete local therapy. Multiple Surveillance, Epidemiology, and End Results (SEER) studies have shown that black women were significantly less likely than white women to receive RT after breast conserving surgery (BCS).[5-8] Analysis of a national sample of older women (age ≥65) also found that black women were significantly less likely than white women to receive RT after lumpectomy.[9] It is imperative that women of all races have equal access to RT after BCS to eliminate this racial disparity.

The use of hypofractionated (HF) whole breast RT after BCS is supported by multiple randomized controlled trials in patients with early stage breast cancer.[10-13] It has been shown to be as efficacious as conventionally fractionated RT,[10-14] result in lower rates of acute toxicity,[15,16] and potentially have less late toxicity.[10] HF breast RT is a more convenient and less costly form of treatment. If offered to women of color at similar rates as white women, HF breast RT would afford a survival benefit from RT compared with surgery alone.

In 2011, the American Society for Radiation Oncology (ASTRO) published an evidence-based guideline on whole breast fractionation, which included a systematic literature review of randomized trials examining the use of HF breast RT. HF breast RT was recommended for patients ≥50 years old with pathologic T1-2N0 disease treated with BCS, no use of systemic chemotherapy, and dose heterogeneity ±7% at central axis.[17] ASTRO further encouraged HF radiation use in its Choosing Wisely campaign several years later.[18]

Adoption of HF RT in US practices has been slow, and although rates increased over time for patients with breast cancer overall,[19-22] prior research has suggested substantial variability in uptake at the practice level.[20] However, limited data are available regarding whether utilization rates of HF breast RT differ by race and ethnicity.

Previous HF breast RT practice patterns in the state of Michigan found that practice and provider level variation accounted for most of the variability in HF use.[20] However, the statewide variation in HF breast RT has not been comprehensively evaluated by race. The goal of our study was to determine whether HF whole breast RT after BCS was being similarly used across racial groups in the state of Michigan.

Methods and Materials

The Michigan Radiation Oncology Quality Consortium (MROQC) is a collaborative state-wide effort of radiation oncologists, physicists, data abstractors, and administrators across Michigan to improve patients' experiences with RT. MROQC is financially supported by Blue Cross Blue Shield (BCBS) of Michigan and the Blue Care Network of Michigan as part of the BCBSM Value Partnerships Program. The goal of MROQC is to identify and implement RT best practices to help reduce treatment side effects and treatment-related costs.[23] Deidentified patient-level clinical and radiation dosimetric data are collected within the centralized MROQC database.

The MROQC breast cancer database was queried for all patients with breast cancer completing radiation from January 1, 2012 to December 31, 2018 accrued from 25 institutions throughout Michigan. Suitable physics data were required to determine whether the patient received conventionally fractionated (CF) or HF whole breast irradiation. We defined HF as radiation to the whole breast with daily fraction size of 2.5 Gy or greater. Daily fraction sizes of 1.8 or 2 Gy for the primary plan were considered CF. Patients treated in the supine position only were included to ensure consistency for the breast separation measurements. Clinical data to determine the patient's race was also required for analysis, with self-reported race categories of white, black, and Asian. Races other than white, black, and Asian were much less frequently reported and thus were excluded from the analysis owing to small numbers.

To understand the association of race with HF use, we used multilevel logistic regression, adjusting for important confounding variables believed *a priori* to be related to HF use. Particularly important was the determination of whether the patient met the 2011 ASTRO consensus guidelines for HF use: age ≥50 years, node negative, T1-T2 tumor size, and breast separation distance <25 cm (as a measure of central axis dose homogeneity).[17] Along with eligibility, the logistic regression model was adjusted for laterality of disease, body mass index, breast volume, number of medical comorbidities (0, 1, 2, 3+), disease stage, triple negative breast cancer, use of intensity modulated RT versus 3-dimensional conformal RT, the year of treatment, and whether the treating facility teaches resident physicians.

To account for practice-pattern similarities at the treating institution level, single-level patient models were expanded to include a second level (multilevel model), clustering patients by treating facility. Whether the facility treating the patient was a teaching or nonteaching institution was the sole facility-level covariate. The intraclass correlational coefficient and variance partitioning coefficient (VPC) were calculated for the multilevel models to specify the amount of variability in HF use attributable to facility differences in usual practice. Additionally, as a sensitivity analysis, we implemented the models for only 2011 ASTRO whole breast hypofractionation guideline-eligible cases, keeping all other modeling aspects identical.

Results

Table 1 presents the characteristics of the 9634 patients from January 2012 to December 2018 who were enrolled in MROQC and treated with BCS and whole breast RT and who self-reported their race as white (81%), black (17%), or Asian (2%). A lower percentage of whites (31.7%) were treated at teaching centers, compared with 66.7% of blacks and 64.8% of Asians. In the entire cohort, 83.6% underwent a radiation boost to the surgical bed. Data were analyzed from 25 institutions, 5 of which were teaching centers.

Figure 1 shows the rate of HF radiation utilization over time overall and by race. Utilization of HF radiation increased over time for all races from 2012 to 2018. In particular, there was a notable increase in HF radiation use for black patients relative to other races from 2014 to 2015, 21.6% to 40.8%, respectively. However, as of 2018, proportionally fewer Asian and black patients received HF radiation than white patients. The highest rate of HF adoption is seen in white patients in 2018, with 72.7% receiving HF radiation in that year compared with 56.7% of blacks and 67.6% of Asians. The *P* value for the comparison of HF use by race for the year of 2018, adjusted for patient-level covariates, is .0411.

Figure 2 shows the rate of HF radiation use over time overall, by race, and by teaching and nonteaching centers. Similarly high rates of HF use are seen for white patients treated in either setting. HF use for Asian patients is higher at teaching versus nonteaching centers. Lower rates of HF use for black patients are seen at both teaching and nonteaching facilities, although in the earlier years (2013-2016) there are lower rates of HF use among black patients at nonteaching centers than at teaching centers. In 2018, the racial disparities in HF use are most pronounced between white and black patients treated at teaching facilities (77.4% and 61.9%, respectively) and between white versus black and Asian patients treated at nonteaching facilities (71.0% versus 47.4% and 46.2%, respectively).

In the patient-level model (Table 2), black and Asian patients were significantly less likely to receive HF breast radiation than white patients after adjustment for important clinical covariates and whether the patient was treated at a teaching or nonteaching institution (black race odds ratio [OR] 0.70; 95% confidence interval [CI], 0.61-0.81), Asian race OR 0.69 (95% CI, 0.48-0.99; $P < .0001$ for both). Additional factors that were significantly associated with a lower likelihood of HF use include left-sided cancer (OR 0.85; 95% CI, 0.77-0.93; $P = .001$), triple negative cancer (OR 0.65; 95% CI, 0.55-0.78; $P < .0001$), stage 2 to 3 disease (stage 2: OR 0.37 [95% CI, 0.33-0.42]; stage 3: OR 0.02 [95% CI, 0.01-0.05]; $P < .0001$ for both), and larger breast volume (1050-1550 mL: OR 0.80 [95% CI, 0.69-0.93]; ≥1550 mL: OR 0.78 [95% CI, 0.65-0.93]; $P = .0011$ for both). Factors significantly associated with a greater likelihood of HF use include later year of treatment (OR 1.68; 95% CI, 1.62-1.73) per year; $P < .0001$), smaller breast volume (<750 mL: OR 1.03; 95% CI, 0.89-1.20; $P = .0011$), older age (OR 1.05; 95% CI, 1.04-1.05 per year; $P < .0001$), stage 0 disease (OR 1.73; 95% CI, 1.50-1.99; $P < .0001$), ASTRO 2011 Guideline eligibility (OR 3.95; 95% CI, 3.46-4.52; $P < .0001$), and teaching center treatment (OR 1.60; 95% CI, 1.43-1.78; $P < .0001$). The VPC was calculated for the empty patient-level model, yielding the intraclass correlation coefficient, 18.2%. This suggests that clustering of patients within hospitals accounts for 18.2% of the variance in HF use across MROQC.

Table 3 reports the adjusted multivariable, 2-level logistic regression model explaining HF radiation use. This model confirms that the rate of HF radiation has been significantly increasing with each year of MROQC measurement (OR 1.86; 95% CI, 1.57-2.20 per year;

Table 1 Patient characteristics

Variable	Level	All patients (N = 9634)	Whites (N = 7785)	Blacks (N = 1650)	Asians (N = 199)	*P* value
Year, n (%)	2012	599 (6.2)	469 (6.0)	117 (7.1)	13 (6.5)	.0115
	2013	1118 (11.6)	893 (11.5)	200 (12.1)	25 (12.6)	
	2014	1472 (15.3)	1163 (14.9)	281 (17.0)	28 (14.1)	
	2015	1813 (18.8)	1466 (18.8)	318 (19.3)	29 (14.6)	
	2016	1854 (19.2)	1528 (19.6)	292 (17.7)	34 (17.1)	
	2017	1629 (16.9)	1318 (16.9)	278 (16.9)	33 (16.6)	
	2018	1149 (11.9)	948 (12.2)	164 (9.9)	37 (18.6)	
Teaching center, n (%)	No	5938 (61.6)	5318 (68.3)	550 (33.3)	70 (35.2)	<.0001
	Yes	3696 (38.4)	2467 (31.7)	1100 (66.7)	129 (64.8)	
Age, mean (SD) [range]	Continuous	61.7 (10.9) [21.9-94.1]	62.0 (10.7) [26.4-94.1]	61.1 (11.5) [21.9-93.9]	55.5 (10.9) [29.8-79.6]	<.0001
BMI categories, n (%)	Underweight <18.5	196 (2.0)	170 (2.2)	17 (1.0)	9 (4.5)	<.0001
	Normal 18.5-<25	2309 (24.0)	1988 (25.5)	216 (13.1)	105 (52.8)	
	Overweight 25-<30	2892 (30.0)	2397 (30.8)	436 (26.4)	59 (29.7)	
	Obesity I 30-<35	2176 (22.6)	1684 (21.6)	466 (28.2)	26 (13.1)	
	Obesity II 35-<40	1173 (12.2)	885 (11.4)	288 (17.5)	0 (0.0)	
	Obesity III >40	888 (9.2)	661 (8.5)	227 (13.8)	0 (0.0)	
Breast volume (mL), n (%)	Not reported	363 (3.8)	313 (4.0)	39 (2.4)	11 (5.5)	<.0001
	<750	2838 (29.5)	2357 (30.3)	364 (22.1)	117 (58.8)	
	750-<1050	2040 (21.2)	1718 (22.1)	284 (17.2)	38 (19.1)	
	1050-<1550	2418 (25.1)	1938 (24.9)	452 (27.4)	28 (14.1)	
	≥1550	1975 (20.5)	1459 (18.7)	511 (31.0)	5 (2.5)	
Laterality, n (%)	Left	4758 (49.4)	3892 (50.0)	784 (47.5)	82 (41.2)	.0124
	Right	4876 (50.6)	3893 (50.0)	866 (52.5)	117 (58.8)	
Separation >25 cm, n (%)	No	7106 (73.8)	5878 (75.5)	1049 (63.6)	179 (90.0)	<.0001
	Yes	2528 (26.2)	1907 (24.5)	601 (36.4)	20 (10.1)	
Comorbidity count, n (%)	Not reported	6 (0.06)	5 (0.06)	1 (0.06)	0 (0.0)	<.0001
	0	4080 (42.4)	3572 (45.9)	387 (23.5)	121 (60.8)	
	1	3285 (34.1)	2641 (33.9)	597 (36.2)	47 (23.6)	
	2	1596 (16.6)	1126 (14.5)	441 (26.7)	29 (14.6)	
	3+	667 (6.9)	441 (5.7)	224 (13.6)	2 (1.0)	
Group stage, n (%)	Not reported	54 (0.6)	44 (0.6)	9 (0.6)	1 (0.5)	<.0001
	0	1888 (19.6)	1469 (18.9)	377 (22.9)	42 (21.1)	
	1	4796 (49.8)	4023 (51.7)	682 (41.3)	91 (45.7)	
	2	2606 (27.1)	2033 (26.1)	513 (31.1)	60 (30.2)	
	3	290 (3.0)	216 (2.8)	69 (4.2)	5 (2.5)	
ER, n (%)	Not reported	65 (0.7)	51 (0.7)	13 (0.8)	1 (0.5)	<.0001
	Negative	1527 (15.9)	1074 (13.8)	415 (25.2)	38 (19.1)	
	Positive	8042 (83.5)	6660 (85.6)	1222 (74.1)	160 (80.4)	
PR, n (%)	Not reported	202 (2.1)	169 (2.2)	30 (1.8)	3 (1.5)	<.0001
	Negative	2259 (23.5)	1662 (21.4)	555 (33.6)	42 (21.1)	
	Positive	7173 (74.5)	5954 (76.5)	1065 (64.6)	154 (77.4)	
HER2, n (%)	Not reported	514 (5.3)	412 (5.3)	91 (5.5)	11 (5.5)	<.0001
	Negative	6672 (69.3)	5484 (70.4)	1059 (64.2)	129 (64.8)	
	Positive	1038 (10.8)	808 (10.4)	202 (12.2)	28 (14.1)	
	Not Done	1410 (14.6)	1081 (13.9)	298 (18.1)	31 (15.6)	
TNBC, n (%)	Not reported	40 (0.4)	33 (0.4)	6 (0.4)	1 (0.5)	<.0001
	No	8639 (89.7)	7108 (91.3)	1355 (82.1)	176 (88.4)	
	Yes	955 (9.9)	644 (8.3)	289 (17.5)	22 (11.1)	
Chemotherapy, n (%)	Not reported	118 (1.2)	105 (1.4)	8 (0.5)	5 (2.5)	<.0001
	No	6551 (68.0)	5445 (69.9)	987 (59.8)	119 (59.8)	
	Yes	2965 (30.8)	2235 (28.7)	655 (39.7)	75 (37.7)	
Hormone therapy, n (%)	Not reported	2242 (23.3)	1841 (23.7)	345 (20.9)	56 (28.1)	.0918
	No	2503 (26.0)	1978 (25.4)	471 (28.6)	54 (27.1)	
	Yes	4889 (50.8)	3966 (50.9)	834 (50.6)	89 (44.7)	

(*continued on next page*)

Table 1 (*continued*)

Variable	Level	All patients (N = 9634)	Whites (N = 7785)	Blacks (N = 1650)	Asians (N = 199)	*P* value
Technique/ fractionation, n (%)	Not reported	468 (4.9)	404 (5.2)	50 (3.0)	14 (7.0)	<.0001
	3DRT/CF	2981 (30.9)	2497 (32.1)	408 (24.7)	76 (38.2)	
	3DRT/HF	2437 (25.3)	2193 (28.2)	194 (11.8)	50 (25.1)	
	IMRT/CF	1973 (20.5)	1347 (17.3)	592 (35.9)	34 (17.1)	
	IMRT/HF	1775 (18.4)	1344 (17.3)	406 (24.6)	25 (12.6)	
Mean breast dose (Gy), mean (SD) [range]	Continuous	49.3 (4.4) [32.9-71.2]	49.1 (4.4) [32.9-71.2]	50.5 (4.6) [39.2-66.7]	49.5 (4.2) [41.3-64.4]	<.0001
Mean dose to lumpectomy bed (Gy), mean (SD) [range]	Continuous	56.3 (7.1) [32.9-72.7]	56.3 (7.2) [32.9-72.7]	58.4 (6.4) [41.4-72.3]	57.6 (6.5) [43.3-71.0]	<.0001
2011 HF guideline eligible, n (%)	No	6921 (71.8)	5440 (69.9)	1334 (80.9)	147 (73.9)	<.0001
	Yes	2713 (28.2)	2345 (30.1)	316 (19.2)	52 (26.1)	

Abbreviations: 3DCRT = 3-dimensional radiation therapy; BMI = body mass index; CF = conventionally fractionated whole breast irradiation; ER = estrogen receptor; HER2 = human epidermal growth factor receptor 2; HF = hypofractionated whole breast irradiation; IMRT = Intensity Modulated Radiation Therapy; PR = progesterone receptor; SD = standard deviation; TNBC = triple negative breast cancer.

$P < .0001$). Additional features found to be significant for receipt of HF radiation include older age (OR 1.05; 95% CI, 1.04-1.07 per year; $P < .0001$), stage 0 disease (OR 1.86; 95% CI, 1.35-2.58; $P = .0002$), and ASTRO 2011 Guideline eligibility (OR 5.38; 95% CI, 4.62-6.27; $P < .0001$). Features found to be significant for a lower likelihood of HF radiation include left-sided cancer (OR 0.80; 95% CI, 0.72-0.90; $P = .0002$), larger breast volume (1050-1550 mL: OR 0.77 [95% CI, 0.64-0.92], $P = .0045$; ≥1550 mL: OR 0.72 [95% CI, 0.54-0.95], $P = .0228$), stage 2 to 3 disease (stage 2: OR 0.30 [95% CI, 0.25-0.37]; stage 3: OR 0.01 [95% CI; 0.00-0.03]; $P < .0001$ for both), and triple negative cancer (OR 0.57; 95% CI, 0.41-0.80; $P = .0011$). Notably, after adjusting for these covariates and for clustering of patients with hospitals, black and Asian races were no longer significantly associated with lack of HF use (black race: OR 0.96 [95% CI, 0.83-1.11], $P = .5636$; Asian race: OR 0.80 [95% CI, 0.51-1.24], $P = .3080$).

The percentage of the total variance explained by the covariates in this model is 41.4%. The percentage of total variance unexplained by the covariates at level 1

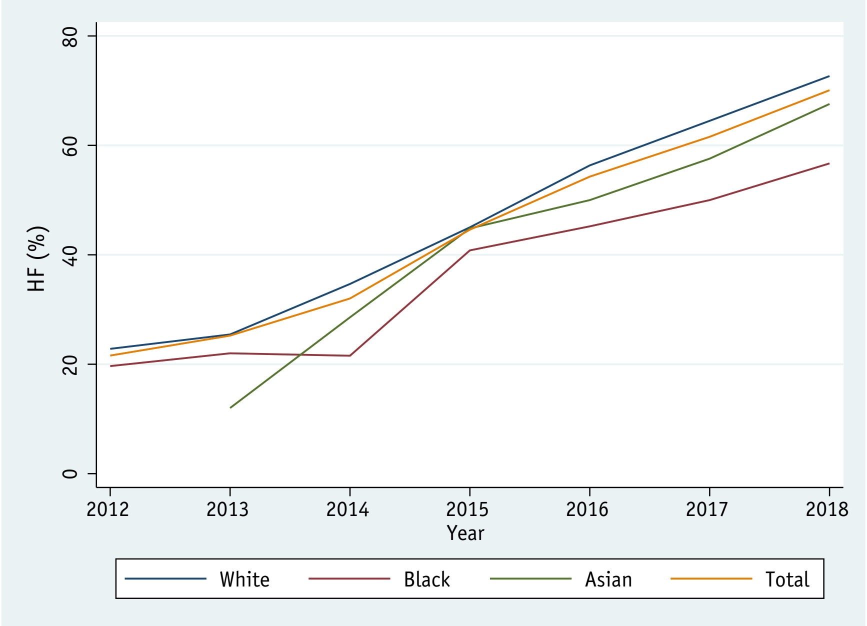

Fig. 1. Hypofractionated (HF) breast radiation rates over time in the state of Michigan by race, with white race in blue, black race in red, Asian race in green, and total cases represented in orange.

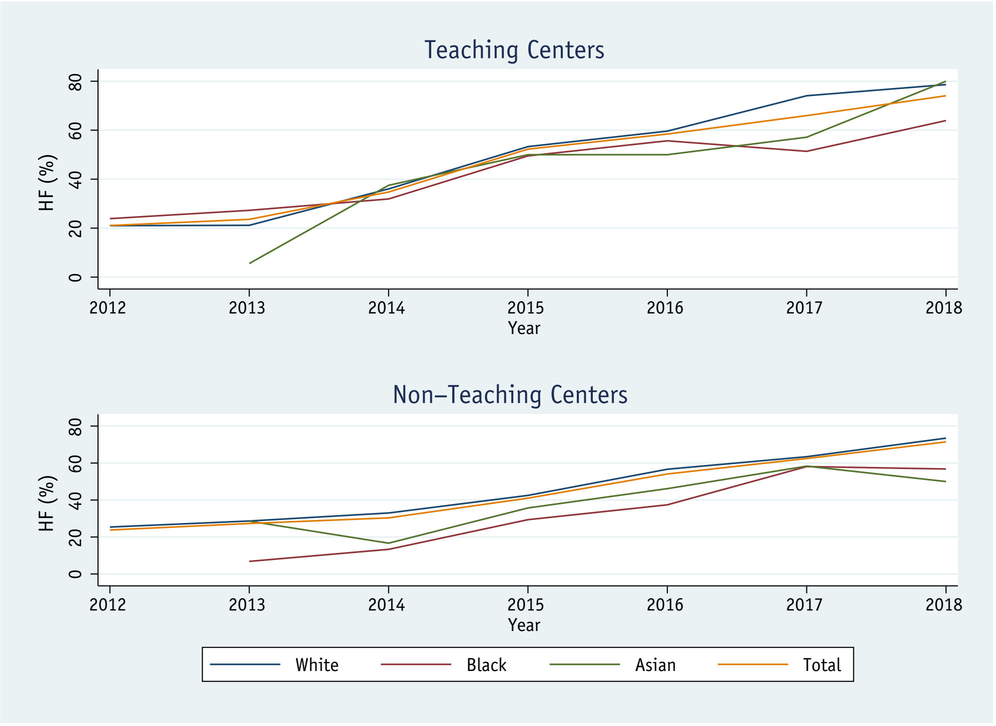

Fig. 2. Hypofractionated (HF) breast radiation rates over time in the state of Michigan by race and type of treatment facility, with white race in blue, black race in red, Asian race in green, and total cases represented in orange.

(patient-level model) is 42.0%. The VPC, or the percentage of the total variance unexplained at level 2 (multilevel model) by covariates but attributable to hospital clustering, is 18.0%, basically unchanged from the patient-level model (18.2%).

The sensitivity analysis results from examining only the 2011 ASTRO HF guideline eligible cases showed that there remains a statistically significant (P = .0018) association with race overall, with black and Asian patients estimated to be less likely to receive HF than white patients (OR 0.64 [95% CI, 0.46-0.87] and OR 0.90 [95% CI, 0.42-1.91], respectively) but only the black versus white race comparison is significant. Also consistent with the overall analysis, when the 2011 ASTRO HF guideline eligible patients are clustered within treatment sites, using a multilevel model, the race association is no longer significant.

Discussion

In this study of breast cancer radiation practice patterns across Michigan, we found that white patients were substantially more likely to receive HF RT than black or Asian patients. The rate of HF whole breast RT has been increasing over time, but disparities persist by race. The greatest disparity between white and black patients existed in the most recent year studied (2018), with a P value of .0411 for the comparison of HF use by race after adjusting for patient-level covariates. Use of HF increased significantly for black patients between the years of 2014 and 2015 (21.6% to 40.8%) and gradually increased each successive year but was not at the level of HF utilization among white patients. The disparity persisted whether black patients were treated at teaching or nonteaching centers, but the difference between white and black patients treated with HF was more pronounced at nonteaching centers compared with teaching centers in 2018 (73.5% vs 56.8% at nonteaching centers compared with 78.6 vs 63.9% at teaching centers for white vs black, respectively).

Facility variation appears to account for the observed racial disparities in HF radiation use. After adjusting for the effects of clustering of patients with hospitals in our multilevel model, black and Asian patients were not significantly less likely to receive HF RT than white patients. This suggests that practice patterns at different institutions appear to contribute to the variability of HF utilization by race.

Previous studies have indicated that non-white women are less likely to enroll on HF breast RT trials; disease stage was found to account for the racial disparity in one of the trials.[24] In a SEER-Medicare analysis of patients treated from 2004 to 2010, race (non-white vs white) was not found to be significant for HF receipt.[21] However, rates of HF use among both groups were quite low (∼7%), and the analysis was subject to several limitations, including restriction to elderly patients (>65 years old) and lack of ability to strictly define a fractionation approach using claims data.[19] In comparison, our study sample includes an era when uptake of hypofractionation was more common and relies on prospectively collected detailed radiation

Table 2 Multiple variable, patient-level models explaining HF receipt

Variable/level	OR	CI	*P* value
Year (continuous + 1 y)	1.68	1.62-1.73	<.0001
Left vs right laterality	0.85	0.77-0.93	.0010
BMI			
Obesity I (30-<35) vs normal (18.5-<25)	0.95	0.80-1.13	.1467
Obesity II (35-<40) vs normal (18.5-<25)	0.96	0.78-1.18	-
Obesity III (>40) vs normal (18.5-<25)	0.81	0.63-1.02	-
Overweight (25-<30) vs normal (18.5-<25)	1.06	0.92-1.23	-
Underweight (<18.5) vs normal (18.5-<25)	0.80	0.55-1.15	-
Breast volume			
<750 mL vs 750-<1050 mL	1.03	0.89-1.20	.0011
1050-<1550 mL vs 750-<1050 mL	0.80	0.69-0.93	-
>1550 mL vs 750-<1050 mL	0.78	0.65-0.93	-
Comorbidity count			
1 vs 0	0.94	0.83-1.06	.3757
2 vs 0	0.88	0.75-1.03	-
3 + vs 0	0.88	0.71-1.09	-
Age (continuous + 1 y)	1.05	1.04-1.05	<.0001
Race			
Asian vs white	0.69	0.48-0.99	<.0001
Black vs white	0.70	0.61-0.81	-
Group stage			
0 vs 1	1.73	1.50-1.99	<.0001
2 vs 1	0.37	0.33-0.42	-
3 vs 1	0.02	0.01-0.05	-
TNBC (yes vs no)	0.65	0.55-0.78	<.0001
IMRT (yes vs no)	1.02	0.92-1.13	.7758
2011 guideline eligible (yes vs no)	3.95	3.46-4.52	<.0001
Teaching facility (yes vs no)	1.60	1.43-1.78	<.0001

Abbreviations: BMI = body mass index; CI = confidence interval; HF = hypofractionated breast irradiation; IMRT = intensity modulated radiation therapy; OR = odds ratio; TNBC = triple negative breast cancer.

Table 3 Multiple variable, multilevel logistic regression models explaining HF receipt

Characteristics	OR	95% CI Lower	95% CI Upper	*P* value
Patient level				
Year (continuous + 1 y)	1.86	1.57	2.20	<.0001
Laterality				
Left	0.80	0.72	0.90	.0002
Right	1.00	-	-	-
BMI				
Obesity I (30-<35)	1.06	0.87	1.28	.5672
Obesity II (35-<40)	1.10	0.82	1.46	.5288
Obesity III (>40)	0.88	0.62	1.26	.4968
Overweight (25-<30)	1.13	0.99	1.30	.0754
Underweight (<18.5)	1.02	0.70	1.50	.9090
Normal (18.5-<25)	1.00	-	-	-
Breast volume				
<750 mL	1.09	0.92	1.29	.3418
1050-<1550 mL	0.77	0.64	0.92	.0045
>1550 mL	0.72	0.54	0.95	.0228
750-<1050 mL	1.00	-	-	-
Comorbidity count				
1	0.98	0.89	1.07	.6087
2	0.90	0.77	1.06	.2169
3+	0.93	0.77	1.12	.4606
None (0)	1.00	-	-	-
Age (continuous + 1 y)	1.05	1.04	1.07	<.0001
Race				
Asian	0.80	0.51	1.24	.3080
Black	0.96	0.83	1.11	.5636
White	1.00	-	-	-
Group stage				
0	1.86	1.35	2.58	.0002
2	0.30	0.25	0.37	<.0001
3	0.01	0.00	0.03	<.0001
1	1.00	-	-	-
TNBC (yes)	0.57	0.41	0.80	.0011
TNBC (no)	1.00	-	-	-
IMRT (yes)	1.32	0.81	2.16	.2650
IMRT (no)	1.00	-	-	-
2011 guideline eligible	5.38	4.62	6.27	<.0001
2011 guideline ineligible	1.00	-	-	-
Hospital level				
Teaching	1.94	0.80	4.67	.1418
Nonteaching	1.00	-	-	-

Abbreviations: BMI = body mass index; CI = confidence interval; HF = hypofractionated breast irradiation; IMRT = intensity modulated radiation therapy; OR = odds ratio; TNBC = triple negative breast cancer.

information for each patient, which allows for a high level of confidence in the fractionation method and RT doses used.[25] Although more limited geographically than these analyses, our study is not age restricted, and the racial characterizations are also more detailed than those in the SEER-Medicare study.

The racial distribution in our study was similar to statewide and national distributions. According to the US Census Bureau's Quick Facts guide for the state of Michigan,[26] the white, black, and Asian percentages in 2017 were 79.4%, 14.1%, and 3.2%, respectively. The national US Census racial percentages for the entire United States in 2018 for white, black, and Asian race were 76.5%, 13.4%, and 5.9%, respectively.[27] In comparison, patients self-reported their race as 81% white, 17% black, and 2% Asian in our study, which is therefore slightly enriched for black race. The similarity in racial distributions between patients in our study and statewide and national percentages provides confidence that we analyzed a representative sample of racially diverse patients and supports potential generalizability of our findings.

An important part of our analysis was accounting for 2011 ASTRO Hypofractionation Guideline eligibility, which recommended consideration of HF breast RT use in women $\geq$50 years old with pathologic T1-2N0 disease treated with BCS, not treated with systemic chemotherapy, and with dose heterogeneity $\pm$7% at the central axis.[17] The most recent 2018 ASTRO Guideline for whole breast fractionation now encourages hypofractionation for even more patients.[14] Women of any age with early-stage breast cancer are considered appropriate for HF use, and patients with any node-negative breast cancer can be considered for HF if the intent is to treat the whole breast with RT. The most recent guideline includes dose homogeneity considerations limiting hot spots >105% and suggests that patients with any tumor grade, hormone receptor status, HER2 receptor status, margin status, and breast size should be considered for HF breast RT.[14] The new guideline has the potential to further reduce the racial disparity in HF use. For example, in our cohort we observed that black and Asian patients had proportionally higher rates of TNBC (18% and 11%, respectively) compared with white patients (8%) and that black patients had a greater mean breast volume than white patients. The difference in TNBC rates is an important finding and may account in part for the racial disparity we observed in HF use, assuming some clinicians may have more comfort with using CF in patients with TNBC; the outcomes of TNBC patients in the randomized clinical trials investigating HF are not well-known because detailed hormone receptor status was not routinely collected at the time of these trials.

In the context of other studies, our study has some similarities and differences. Gillespie et al examined geographic disparities in HF radiation in elderly (>65 years old) women across the United States from 2000 to 2012. The authors reported increased utilization of HF breast RT in older patients, later year of treatment, and at teaching hospitals, which were all concordant with our study. However, on multivariable analysis, they found that non-white race was associated with significantly higher use of HF.[28] The patients included in their study were treated in an earlier era with only 10% to 14% of patients receiving HF compared with CF. The study sample consisted of Medicare beneficiaries across the United States. Radiation treatment type (HF or CF) was determined solely by the number of fractions rather than by using detailed patient-level dosimetric data. Because there was wide geographic variation in the use of HF RT (0%-61%) in their study, it is possible that centers with proportionally higher HF rates included a higher percentage of non-white patients. Another study of patients treated from 2008 to 2015 examining predictors of radiation-induced skin toxicity reported a lower percentage of black patients receiving HF breast RT after lumpectomy (10/68) compared with non-black patients (46/162). Although it was not the focus of their study, the noted lower proportion of black patients receiving HF breast RT aligns with our study results.[29]

Whether the differences observed in the present series in breast radiation treatment technique by race have any impact on race-specific toxicity or side effects remains to be investigated. A previous report indicated that patients in Michigan receiving HF breast RT compared with CF breast RT were significantly less likely to experience acute side effects, including moist desquamation, breast pain, and dermatitis bother.[15] However, this previous work did not compare toxicities by race. We anticipate that HF radiation in all races would be well tolerated after accounting for medical comorbidities, but we plan to analyze our data using rigorous statistical methods.

A retrospective series observed minimal skin toxicities in black patients treated with HF radiation using either supine or prone technique.[30] Moreover, another retrospective study that included a racially diverse population reported lower rates of moist desquamation and grade 2+ dermatitis in patients receiving HF versus CF breast RT, and toxicities did not vary by race.[29] A further study that included Hispanic, black, and non-Hispanic white patients explored predictors of radiation skin toxicity and similarly found that HF breast RT was associated with significantly lower skin toxicity of all grades compared with CF, and there were no significant differences by race.[31] We plan to analyze the outcomes in our MROQC patients to evaluate this question.

A major potential advantage of HF RT for patients is its ability to reduce health care costs. Financial toxicity has been convincingly shown to be higher in certain racial and ethnic minority patient populations such as black patients with breast cancer.[32,33] Even after adjusting for income amount, education level, and employment status, it has been shown that women of racial and ethnic minorities are most vulnerable to the financial burden attributable to breast cancer.[32] Given that black women may be more likely to have financial toxicity from treatment, racial disparities in the use of HF breast RT are particularly concerning. It is troubling to observe disparities in treatment that may serve to further increase the burden and cost of cancer therapy in black Americans and other racial and ethnic minorities. It is therefore imperative that both teaching and nonteaching institutions ensure that all patients eligible for HF breast RT after BCS, particularly racial and ethnic minorities, receive fair consideration for this more affordable and convenient treatment option.

This study has several strengths and limitations. The strengths of this study include the large sample size with prospectively collected individual patient-level radiation dosimetric data, representative racial distribution similar to statewide and national racial distributions, and multilevel analyses that account for potential confounding variables identified *a priori*. The limitations of this study include its observational nature, the inability to determine causality, and a lack of provider-level modeling to further assess practice variation. We did not include provider-level analysis because our intent was to examine the collective effect of practice patterns rather than to ascertain individual provider differences. Although our study is observational, it provides a real-world perspective on practice patterns in a large patient cohort over a 7-year period across multiple institutions. Causality cannot be determined from our study, but there are a number of possible contributing factors to the differences observed in HF use, including patient preferences, provider preferences, access to a center performing a proportionally higher rate of HF treatment, and insurance coverage, among others. There are likely multifactorial contributions to the practice patterns observed. Our study results lend confidence to the notion that facility-level variation contributes at least in part to the differences observed in HF use.

Conclusions

This study reveals concerning racial disparities in the receipt of HF whole breast irradiation in Michigan and suggests that differences in facility-specific HF breast radiation use appear to have contributed to these results. Additional inquiry is necessary to determine whether further reduction in facility-level variation may reduce and ultimately eliminate disparities in accessing HF treatment. Especially given evidence that black patients with breast cancer are most vulnerable to experiencing financial toxicity and continue to have worse mortality outcomes, further research is necessary to build on these findings and ensure equal access by race to equally efficacious treatment that is less burdensome and less costly.

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