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Scientific Article

Geographic and Physician-Level Variation in the Use of Hypofractionated Radiation Therapy for Breast Cancer in the U.S.: A Cross-Classified Multilevel Analysis

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Purpose: We aimed to assess geographic and physician-level variation for hypofractionated whole-breast irradiation (HF-WBI) use for early-stage breast cancer patients in the United States. We further evaluated the association between HF-WBI use and demographic factors after accounting for these variations.

Methods and Materials: We performed a retrospective study of early-stage breast cancer patients using private employer-sponsored insurance claims from 2008 to 2017. Patients were clustered according to geographic level and by radiation oncologist. Bayesian cross-classified multilevel logistic models were used to examine the geographic heterogeneity and variation of radiation oncologists simultaneously. Intracluster correlation coefficient (ICC) and median odds ratios (MOR) were calculated to quantify the variation at different levels. We also used the cross-classified model to identify patient demographic factors associated with receiving HF-WBI.

Results: The study included 79,747 women (74.0%) who received conventionally fractionated whole-breast irradiation (CF-WBI) and 27,999 women (26.0%) who underwent HF-WBI. HF-WBI adoption increased significantly across time (2008-2017). The variation in HF-WBI utilization was attributed mostly to physician-level variability (MOR = 2.59). The variability of HF-WBI utilization across core-based statistical areas (CBSAs) (MOR = 1.55) was found to be the strongest among all geographic classifications. After accounting for variability in both CBSAs and radiation oncologists, age, receiving chemotherapy, and several community-level factors, including distance from home to facility, community education level, and racial composition, were found to be associated with HF-WBI utilization.

Conclusion: This study demonstrated geographic and physician-level heterogeneity in the use of HF-WBI among early-stage breast cancer patients. HF-WBI utilization was also found to be associated with patient and community-level characteristics. Given observed physician-level variability, intervention through continuing medical education could help doctors to better understand the advantages of HF-WBI and promote the adoption of HF-WBI in the U.S. Influence of physician-level characteristics on HF-WBI utilization merits further study.

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Introduction

Hypofractionated whole-breast irradiation (HF-WBI) is a radiation therapy with larger dose per fraction and a shorter schedule,[1-3] compared with conventionally fractionated whole-breast irradiation (CF-WBI), after breast-conserving surgery for patients with early-stage breast cancer.[4,5] Multiple randomized clinical trials have confirmed that the safety and efficacy of HF-WBI are equivalent to CF-WBI regarding local recurrence and disease-free survival.[1-3,6] Compared with CF-WBI, HF-WBI has been found to reduce acute toxicity[7,8] and improve quality of life.[7] HF-WBI has also been observed to be associated with lower expenditure.[4,9] In the 2011 American Society for Radiation Oncology (ASTRO) guidelines, HF-WBI was recommended for women older than 50 with pT1−2N0 tumors that are not treated with chemotherapy.[10] HF-WBI has been set as the preferred standard of care for early-stage breast cancer patients in many countries.[11-13] The uptake of HF-WBI has been high in Canada and several European countries, but slower than anticipated in the United States (U.S.).[5,14,15] Several studies have found that the heterogeneity of physician-related factors accounted for the variability in the use of HF-WBI.[16,17] The lag in HF-WBI adoption has been attributed to physician preference, and patients have been more likely to receive HF-WBI if treated by female physicians.[16] The geographic region has been confirmed to have a moderate effect on the variability of HF-WBI use.[5,16,18,19]

However, previous studies predominantly concentrated on variation across large census regions[5,18] or in patients over 65 who are covered by Medicare.[16,19] Medicare is a federal health insurance program in the U.S. primarily for individuals age 65 years and older, certain young people with disabilities, and those with end-stage renal disease.[20] Approximately 160 million Americans currently benefit from health coverage through employer-sponsored insurance plans.[21] The majority of individuals under age 65 in the U.S. obtain their health insurance coverage either through their employer or the employer of a family member.[22] The heterogeneity of HF-WBI use among other age groups, separate from the Medicare population, that account for geographic and physician-level variation has not been comprehensively studied. Our study aims to measure and model both the geographic variation and physician-level variation in HF-WBI utilization in the U.S. We also evaluate the association between HF-WBI use in early-stage breast cancer patients and demographic characteristics when accounting for these variations.

Methods and Materials

Data

The Health Care Cost Institute (HCCI)[23] is a nonprofit, independent research entity with a comprehensive database covering around 55 million commercially insured individuals per year. The HCCI maintains health care claims data from Aetna, Humana, Kaiser Permanente, and UnitedHealth care, collectively accounting for one-third of the employer-sponsored insurance population in the U.S. The HCCI covers information on health services' cost and use, health care spending, and essential plan characteristics, allowing researchers and policymakers to investigate health care utilization and costs.

Study Population

Women with incident breast cancer were identified from the HCCI database (2008-2017) if they had a minimum of 2 insurance claims within a year, featuring breast cancer diagnosis codes based on the International Classification of Diseases, Nine [ICD-9] and Tenth [ICD-10] Revisions, and underwent whole-breast irradiation after breast conserving surgery, as indicated by Current Procedural Terminology (CPT) codes (Table E1). Patients who started radiation therapy after August 31, 2017 were excluded from the study to ensure the accuracy of determining the type of radiation therapy received, as their radiation therapy course may have extended beyond December 2017. Male patients and patients with missing age, missing/incomplete information on radiation therapy delivery, and missing information on geographic units and treating doctors were also excluded (Fig. E1).

Outcomes

The primary outcome of the study is the type of radiation therapy received. HF-WBI was defined as receipt of 15 to 24 radiation fractions, and CF-WBI was defined as receipt of 25 to 40 fractions. If the number of radiation fractions was either 11 to 14 or greater than 40, we used the duration of radiation therapy to define HF-WBI (21-31 days) versus CF-WBI (39-120 days). Radiation therapy type for 96.6% of patients was determined by radiation fractions, and that for 3.4% of patients was determined by radiation therapy duration.

Other Variables

Patients were clustered at different levels of geographic units:[1] census regions,[2] states and Washington DC,[3] metropolitan and micropolitan statistical areas of the U.S. Census (collectively known as core-based statistical area or CBSA),[4] hospital referral regions (HRR) of Dartmouth Atlas, and[5] zip codes. Zip codes are nested within HRRs,[24] and a few zip codes overlap the boundaries of states and CBSAs.[25,26] The boundaries of CBSAs and HRRs often cross state lines.[27,28] Patients were also clustered at the radiation oncologist level. Distinct radiation oncologists were identified using an encrypted National Provider Identifier (NPI) and provider specialty. They were clustered based on the most frequently reported radiation oncologists if treated by multiple radiation oncologists.

Table 1 presents patient characteristics that were examined in the study population. Breast cancer diagnosis was categorized as either invasive or ductal carcinoma in situ (DCIS). The receipt of chemotherapy was defined based on CPT codes (Table E1). An adapted version of the Charlson comorbidity index[29,30] was used to assess comorbid conditions. There were 5 types of employer-sponsored insurance plans in our study: point-of-service plan (POS), preferred provider organization (PPO), health maintenance organization (HMO), exclusive provider organization (EPO), or private fee-for-service (PFS).[31,32] PFS is a type of Medicare Advantage Plan, within which enrollees can choose among providers who are lawfully authorized to offer services and agree to the plan's terms and conditions of payment.[33,34] The other 4 are commercial health plans designed to meet different health care needs, each associated with different premium levels and out-of-pocket costs. HMO plans offer lower premiums and out-of-pocket costs than PPOs, but they usually have limited provider networks, do not cover services from out-of-network providers, and might require a referral from a primary care provider before seeing a specialist. PPO plans typically have higher premiums and out-of-pocket costs than HMOs but allow for greater flexibility through a larger network of providers. POS plans are a hybrid of HMOs and PPOs, with premiums between HMOs and PPOs, larger networks of providers, and referral requirements. EPO plans usually have lower costs than PPOs, but they only pay for in-network services.[31,32] We also included a variable indicating whether a health plan was a high-deductible health plan (HDHP), which has lower monthly payments but higher deductibles.[32]

Several demographic variables at the community level were assessed by examining the zip code of each patient's residence, including racial composition, the proportion of college graduates, and the proportion of individuals below the poverty line. 2018 U.S. Census-level data[35] were used to determine these variables. A zip code was classified as a mixed community if no racial group composed more than 50% of its residents. Distance from home to the facility was defined by calculating the "crowfly" distance between patients' zip codes and treatment facilities.

Statistical analysis

Patients in the study were nested separately within geographic units and radiation oncologists. These 2 levels were cross-nested. Patients from the same geographic area are likely to be treated by different oncologists, and an oncologist is expected to have patients from different geographic areas. We used Bayesian cross-classified multilevel logistic model to simultaneously assess the variation of geographic units and radiation oncologist heterogeneity.[36] The full cross-classified logistic model is written as

$$\log\left(\frac{p_i}{1-p_i}\right) = \beta_i X + \theta_{j(i)} + \delta_{k(i)}$$

where p_i denotes patient i's probability of receiving HF-WBI, and $1 - p_i$ is the probability of receiving CF-WBI. $\beta_i X$ indicates a set of fixed effects of patients i's characteristics, such as age and insurance type, as well as the intercept. Each patient i was nested within a geographic region (j) and a physician (k). $\theta_{j(i)}$ denotes the random effect of the jth geographic region that the ith patient comes from. $\delta_{k(i)}$ denotes the random effect of the kth radiation oncologist who gives WBI treatment to the ith patient. We ran 5000 burn-in iterations and 20,000 additional iterations to estimate model parameters. Noninformative priors were specified in the Bayesian modeling.

If there is only one random effect term and no fixed effects, the full cross-classified logistic model reduces to a classic 2-level random effect logistic model. We fitted 6 2-level random effect logistic models with patients nested within each of the 5 levels of geographic units described above or radiation oncologists. We then fitted 6 Bayesian cross-classified logistic models to evaluate the variation of physician level and geographic region, 4 of which were multilevel random effect logistic models, and 2 were additionally adjusted for patient fixed effects.

We report intracluster correlation coefficients (ICC) and median odds ratios (MOR) for the interpretation of variation at various levels.[37-39] The ICC compares the variance between clusters with the sum of all variances (ie, region, physician, and logistic variances). The ICC ranges from 0 to 1 and refers to the correlation between patients within the same geographic region or treated by the same physician. The MOR, ranging from 1 to infinity, refers to the median odds ratio of the outcome for all possible pairs of patients with equivalent covariates randomly selected from different levels.[38,39] The MOR translates multilevel variations to the scale of odds ratios and can be compared with odds ratios of fixed effects. A MOR with the value of

Table 1 Characteristics of breast cancer patients receiving whole breast radiation therapy

	CF-WBI	HF-WBI	% of HF-WBI
Year of diagnosis			
2008	5579	459	7.6
2009	8518	967	10.2
2010	8828	1244	12.4
2011	9038	1539	14.6
2012	9489	1929	16.9
2013	9276	2432	20.8
2014	8469	3434	28.8
2015	7765	4734	37.9
2016	7797	6314	44.7
2017	4988	4947	49.8
Age group			
<35	860	88	9.3
35-44	7384	1135	13.3
45-54	20935	5103	19.6
55-64	24283	8356	25.6
65-74	18573	8814	32.2
75-84	6949	3953	36.3
85+	763	550	41.9
Type of breast cancer diagnosis			
Invasive	71900	23980	25.0
DCIS	7847	4019	33.9
Chemotherapy			
No	49172	22858	31.7
Yes	30575	5141	14.4
Charlson comorbidity index			
0	41852	9991	19.3
1	13360	3790	22.1
2	11880	6874	36.7
3+	12655	7344	36.7
Insurance Type			
EPO	3588	900	20.1
HMO	13555	5053	27.2
PFS	1134	327	22.4
POS	39406	12052	23.4
PPO	16298	7297	30.9
High deductible plan			
No	69169	24132	25.9
Yes	10578	3867	26.8

(*continued on next page*)

Table 1 (*Continued*)

	CF-WBI	HF-WBI	% of HF-WBI
Distance from home to facility			
<10 miles	44323	14669	24.9
10-24.9 miles	20774	7582	26.7
25-49.9 miles	4190	1776	29.8
≥50 miles	3279	1826	35.8
% of college graduates in community*			
<23.4%	17291	5077	22.7
23.4-35.5%	20489	6587	24.3
35.6-51.0%	21115	7570	26.4
>51.0%	20851	8764	29.6
% of residents below poverty line*			
<5.9%	21031	8312	28.3
5.9-9.7%	20696	7409	26.4
9.7-15.5%	19563	6558	25.1
>15.5%	18456	5719	23.7
Racial composition in community*			
White >50%	69927	24941	26.3
Black >50%	5015	1469	22.7
Asian >50%	356	110	23.6
Mixed community	4449	1479	24.9

Abbreviations: CF-WBI = conventionally fractionated whole breast irradiation; HF-WBI = hypofractionated whole-breast irradiation; DCIS = ductal carcinoma in situ; EPO = exclusive provider organization; HMO = health maintenance organization; PFS = private fee-for-service; POS = point of service; PPO = preferred provider organization.

*Community demographic features are based on the zip code of the patient’s residence.

1 indicates identical outcomes across different geographic units or physicians (equivalent to an ICC of 0). We compared cross-classified multilevel logistic models considering the ICC and MOR in each level and model complexity to evaluate models for assessing variation. All analyses were conducted in Stata 15 (StataCorp LLC). *P* values <.05 were considered statistically significant.

Results

This study comprised 107,746 post-lumpectomy breast cancer patients treated from 2008 to 2017, including 95,880 invasive breast cancer patients and 11,866 DCIS patients. Of them, 26.0% received HF-WBI, and 74.0% received CF-WBI. As shown in Table 1, HF-WBI utilization increased over time, from 7.6% in 2008 to 49.8% in 2017. The HF-WBI utilization rate was observed to increase with age. A higher proportion of women with DCIS (33.9%) compared with women with invasive breast cancer (25.0%) received HF-WBI. The proportion of receipt of HF-WBI among women who had not been treated with chemotherapy (31.7%) was higher than that among women who had been treated with chemotherapy (14.4%). The proportion of HF-WBI utilization varied across different insurance types. Patients enrolled in PPO plans were found to have the highest proportion of receiving HF-WBI (30.9%) among all insurance plans. The proportion of patients receiving HF-WBI increased as the distance from home to facility increased. Patients residing in communities with a higher proportion of college graduates and those living in communities with a higher proportion of residents below the poverty line had lower HF-WBI utilization rates.

The patients lived in all 50 U.S. states and Washington, DC. They lived in 12,008 zip codes, 395 CBSA units, and 297 HRR units. They were treated by 6591 radiation oncologists. There was weak-to-moderate geographic variation in HF-WBI utilization across states and Washington, DC, with an ICC of 0.033 and MOR of 1.38 (Table 2). There was moderate geographic variation across HRRs (ICC = 0.080; MOR = 1.67). Figure 1 illustrates geographic heterogeneity in using HF-WBI across HRRs, with the highest utilization rates in Rochester,

Table 2 Variation and clustering by geographic areas and radiation oncologists: Bayesian multilevel models

Cluster factor	Number of units	ICC (95% CI)	MOR (95% CI)
2-level random effects logistic models			
Census regions	9	0.014 (0.005-0.039)	1.23 (1.13-1.42)
States and Washington, DC	51	0.033 (0.021-0.050)	1.38 (1.29-1.49)
Hospital referral region (HRR) of Dartmouth Atlas	297	0.080 (0.067-0.096)	1.67 (1.59-1.76)
Core based statistical area (CBSA) of the Census	395	0.097 (0.081-0.115)	1.76 (1.67-1.87)
Zip codes	12,008	0.095 (0.089-0.103)	1.75 (1.72-1.79)
Radiation oncologist	6591	0.272 (0.259-0.286)	2.88 (2.78-2.99)
Cross-classified multilevel logistic model 1			
Radiation oncologist	6591	0.270 (0.258-0.284)	2.88 (2.78-2.99)
Zip code	12,008	0.006 (0.004-0.009)	1.18 (1.14-1.21)
Cross-classified multilevel logistic model 2			
Radiation oncologist	6591	0.225 (0.213-0.236)	2.59 (2.50-2.69)
Hospital referral region (HRR) of Dartmouth Atlas	297	0.035 (0.027-0.045)	1.46 (1.38-1.54)
Cross-classified multilevel logistic model 3			
Radiation oncologist	6591	0.222 (0.212-0.233)	2.59 (2.50-2.69)
Core based statistical area (CBSA) of the Census	395	0.047 (0.035-0.059)	1.55 (1.46-1.65)
Cross-classified multilevel logistic model 4*			
Radiation oncologist	6,591	0.212 (0.202-0.221)	2.54 (2.45-2.64)
Core based statistical area (CBSA) of the Census	395	0.059 (0.045-0.075)	1.64 (1.53-1.76)
Cross-classified multilevel logistic model 5			
Radiation oncologist	6591	0.218 (0.208-0.226)	2.56 (2.47-2.66)
Core based statistical area (CBSA) of the Census	395	0.038 (0.027-0.050)	1.48 (1.38-1.58)
Hospital referral region (HRR) of Dartmouth Atlas	297	0.009 (0.004-0.017)	1.21 (1.13-1.30)
Cross-classified multilevel logistic model 6*			
Radiation oncologist	6591	0.202 (0.194-0.210)	2.47 (2.38-2.56)
Core based statistical area (CBSA) of the Census	395	0.040 (0.025-0.054)	1.49 (1.37-1.61)
Hospital referral region (HRR) of Dartmouth Atlas	297	0.018 (0.009-0.029)	1.31 (1.21-1.42)

Abbreviations: CI = credibility interval; ICC = intracluster correlation coefficient; MOR = median odds ratio.

*Multivariable mixed effects models adjusting for year of diagnosis, age, tumor stage, comorbidity index, distance from home to the clinic, community education, and race composition.

Minnesota; Charlottesville, Virginia; and Covington, Kentucky. Variability of HF-WBI utilization across CBSAs (ICC = 0.097; MOR = 1.76) was the strongest among all geographic area levels, followed by zip codes (ICC = 0.095; MOR = 1.75) though there were many more zip code units (Table 2). Figure 2 illustrates geographic heterogeneity across CBSAs, with the highest utilization rates in the metropolitan areas of Rochester, Minnesota; Ithaca, New York; and Durham-Chapel Hill, North Carolina. Variability across radiation oncologists (ICC = 0.272; MOR = 2.88) was substantially larger than variability across geographic areas (Table 2), (ie, 2 patients treated by the same radiation oncologist were more likely to have the same radiation therapy type than 2 patients living in the same geographic area). After adjusting for the variability of radiation oncologists using cross-classified multilevel models (models 1, 2, 3), MORs for geographic areas, especially zip codes, were reduced. As HRR and CBSA units overlapped, we fitted a cross-classified multilevel model with CBSA, HRR, and radiation oncologists as clustering units (model 5). We found that the variability of HRR was mostly captured by CBSA in the model, as the adjusted ICC for HRR was only 0.009. Therefore, the cross-classified model with radiation oncologist and CBSA (model 3) was the most parsimonious, and we added fixed effects to obtain a final model (model 4): the adjusted MOR was 2.54 (95% CI, 2.45-2.64) for radiation oncologist and 1.64 (95% CI, 1.53-1.76) for CBSA. Furthermore, we conducted multilevel analysis separately for patients aged 64 or younger

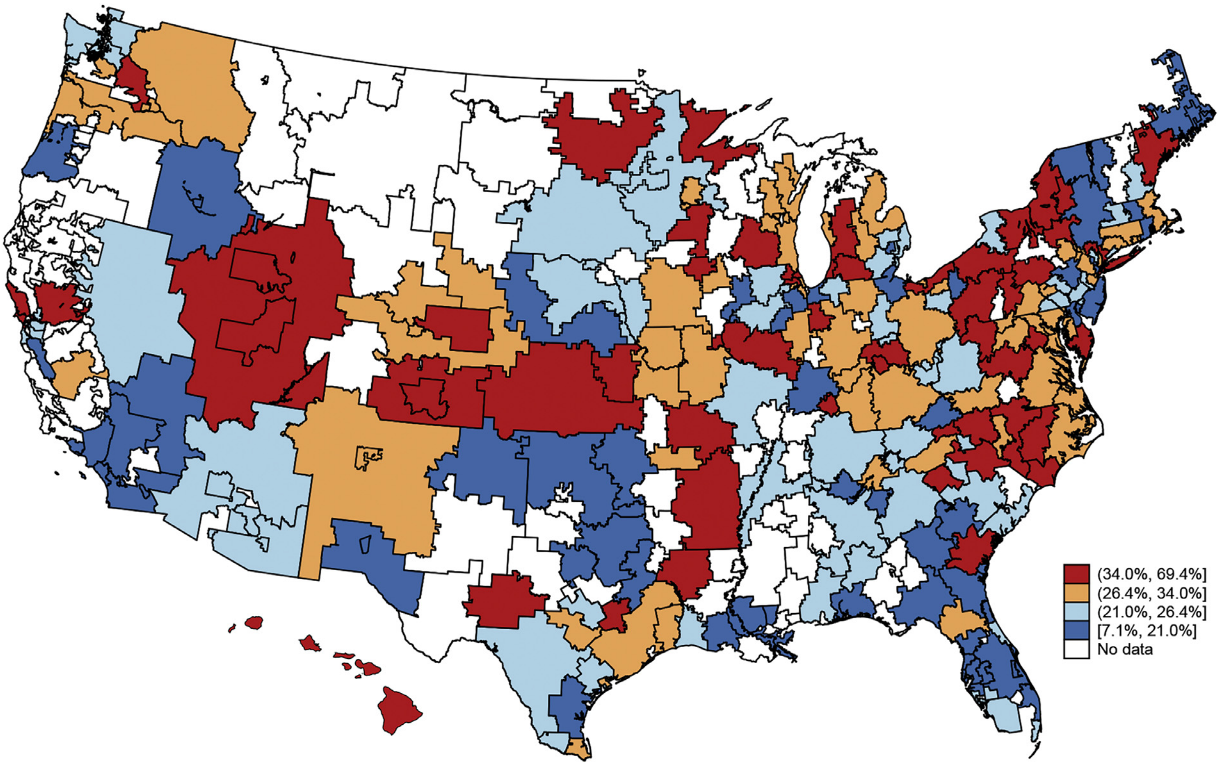

Figure 1 Percentage of patients receiving hypofractionated radiation therapy (HF-WBI) per hospital referral region (HRR). Only HRRs with at least 30 patients were plotted.

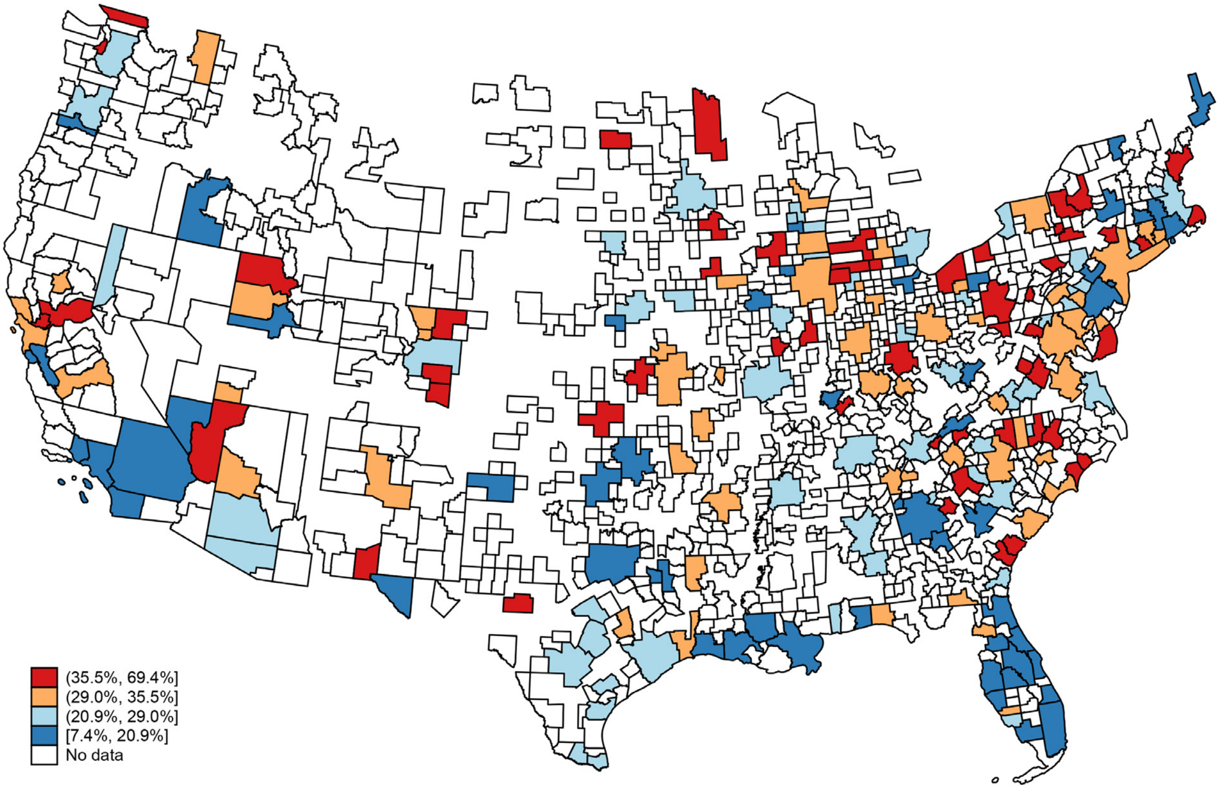

Figure 2 Percentage of patients receiving hypofractionated radiation therapy (HF-WBI) per census-designated core-based statistical area (CBSA). Only core-based statistical areas with at least 20 patients were plotted.

(commercial health plans) and patients aged 65 or older (Medicare Advantage plans), finding no substantial differences between young and elderly patients in terms of both geographic and physician-level variations (Table E2). However, the geographic variation (eg, CBSA) was somewhat higher in older patients (MOR = 1.94) than in younger patients (MOR = 1.71).

Table 3 reports the fixed effects of the final multivariable, multilevel logistic regression model after accounting for the variation of radiation oncologists and CBSA (model 4). The receipt of HF-WBI steadily increased over time. Women of older age groups were more likely to receive HF-WBI. Women treated with chemotherapy were notably less likely to receive HF-WBI. The receipt of HF-WBI was found to be associated with several community-level characteristics. There was a positive dose-response relationship between HF-WBI utilization and distance from patients' homes to the facility. Patients in communities with higher proportions of college graduates were more likely to receive HF-WBI.

Discussion

This study models the geographic and physician-level variation in HF-WBI use for women with early-stage breast cancer across the U.S. between 2008 and 2017. The relationship between HF-WBI utilization and patient characteristics is also evaluated in a multilevel cross-classified model controlling for those variations. Our results demonstrate that HF-WBI utilization is geographically heterogeneous across the U.S. and highlight that the variation in HF-WBI use is attributed mostly to physician-level variability. These findings are consistent with other U.S. studies.[16,19,40] U.S. uptake of HF-WBI rapidly increased from 2008 to 2017 but has lagged compared with other countries. Our finding—that patient characteristics (ie, older age, not being treated with chemotherapy, longer distance from the facility, and residing in a community with a higher educational level) were associated with a higher likelihood of receiving HF-WBI, after accounting for geographic and physician-level variation—is consistent with previous literature.[9,19,41,42]

The role of radiation oncologists in HF-WBI has been investigated in the U.S.[4,16,17] and in Europe[43] due to their serving as the primary gatekeepers determining radiation modality. Bekelman et al showed that the density of radiation oncologists was associated with a higher likelihood of HF-WBI.[4] Surveys of radiation oncologists have found large variation in preference for HF-WBI across doctors in the U.S. and Europe.[40,43] Using data from the Surveillance, Epidemiology, and End Results -Medicare linked database, Boero et al estimated the effect of radiation oncologists on HF-WBI use to be an MOR of 3.08 in breast cancer patients older than 65.[16] Quite consistently, we found the MOR for radiation oncologists was 2.95 for patients 65 or older and 2.98 for patients younger than 65. Despite key clinical findings of similar efficacy and toxicity profiles, physicians hesitate to use HF-WBI due to concerns about potential cardiac toxicities associated with higher doses per fraction, as discussed in previous studies.[43-45] Financial considerations can also play an important role in HF-WBI adoption. Studies have shown that HF-WBI reduced costs and personal financial adversity.[9,46,47] Physicians may not be motivated to recommend lower-number-fractionation schedules due to lower revenue per patient compared with CF-WBI, especially for U.S. physicians under a fee-for-service reimbursement structure. This may explain the relatively slow uptake of HF-WBI utilization in the U.S. The 2018 ASTRO guideline recommending HF-WBI to women with breast cancer regardless of age, tumor grade, or receptor status[48] may accelerate the adoption of HF-WBI. Hsieh et al found academic radiation oncologists responded to HF-WBI related questions with higher agreement with the 2018 ASTRO guideline, compared with community radiation oncologists.[49] This suggests a potential lag in HF-WBI adoption within community-based contexts, despite a stronger recommendation.

Although radiation oncologists play a very important role in using HF-WBI, patients may also play a role. One study has found that patient's refusal (27.3%) contributes to the decision of not receiving HF-WBI more than physician's preference for non-HF-WBI options (15.2%) in off-pathway decisions.[50] We cannot comment on the effect of patient preference on variability of HF-WBI utilization based on the current HCCI database. Future studies could explore the role of patient involvement in the decision-making process regarding using HF-WBI.

Several studies have found geographic heterogeneity in the use of HF-WBI among elderly patients across the U.S.[16,19] Our study expanded this literature to patients of all ages and evaluated HF-WBI utilization patterns across different geographic classifications. Boero et al found moderate variation in HF-WBI use across counties of doctor practice with an MOR of 2.10 in patients older than 65.[16] The county is a geographic level roughly between CBSA and zip code. We found significant geographic variation in HF-WBI receipt at the CBSA, HRR, and zip code levels. Consistent with Boero et al, we estimated that the MOR was 1.94 and 2.04 for CBSA and zip code, respectively, in patients 65 or older. We also found that geographic variation was somewhat lower in patients younger than 65, with MOR of 1.71 and 1.79, respectively, for CBSA and zip code. Our study is the first to model geographic and physician-level variation using cross-classified multilevel models with relatively comprehensive data extracted from the commercial insurance market in all 50 U.S. states and Washington, DC. Interestingly, we found geographic variation, especially at the zip code level, was reduced after adjusting for variation across radiation oncologists. This suggests that local geographic

Table 3 Bayesian cross-classified multilevel logistic regression on receiving hypofractionated radiation therapy in patients[*]

	Adjusted OR	95% CI
Year of diagnosis		
2008	1 (Ref.)	
2009	1.35	1.29-1.41
2010	1.66	1.61-1.72
2011	2.13	2.06-2.20
2012	2.40	2.30-2.51
2013	3.25	3.14-3.37
2014	5.48	5.31-5.66
2015	9.45	9.15-9.76
2016	13.47	12.87-14.11
2017	16.49	15.92-17.04
Age group		
<35	0.71	0.70-0.73
35-44	1 (Ref.)	
45-54	1.35	1.31-1.39
55-64	2.00	1.96-2.04
65-74	2.61	2.55-2.69
75-84	3.78	3.69-3.86
85+	5.16	5.03-5.30
Type of breast cancer diagnosis		
Invasive	1 (Ref.)	
DCIS	1.02	0.99-1.06
Chemotherapy		
No	1 (Ref.)	
Yes	0.30	0.29-0.31
Charlson comorbidity index		
0	1 (Ref.)	
1	1.03	1.00-1.06
2	1.11	1.07-1.15
3+	0.97	0.95-0.99
Distance from patients' home to facility		
<10 miles	1 (Ref.)	
10-24.9 miles	1.06	1.05-1.08
25-49.9 miles	1.18	1.13-1.23
≥50 miles	1.24	1.19-1.30
% of college graduates in community[†]		
<23.4%	1 (Ref.)	
23.4-35.5%	1.09	1.04-1.13
35.6-51.0%	1.14	1.10-1.19

(*continued on next page*)

Table 3 (*Continued*)

	Adjusted OR	95% CI
>51.0%	1.35	1.31-1.39
Racial composition in community[†]		
White >50%	1 (Ref.)	
Black >50%	0.99	0.94-1.04
Asian >50%	1.18	1.15-1.22
Mixed community	1.02	1.00-1.05

Abbreviations: CI = credibility interval; DCIS = ductal carcinoma in situ; OR = odds ratio.

*Two random effects were estimated in the cross-classified multilevel model: radiation oncologists and core based statistical area (CBSA) of the Census

variation at the zip code level in HF-WBI utilization is mainly due to radiation oncologist effects.

Ward et al found that cancer care utilization was associated with insurance type, and the cost of employer-sponsored health plan premiums has been rising faster than the rise of employees' earnings.[22] We observed a larger proportion of patients under PPO plans undergoing HF-WBI than all other insurance types, possibly because PPOs usually require higher out-of-pocket costs compared with other commercial health insurance plans.[31] However, insurance type was no longer significantly associated with HF-WBI utilization after adjusting for radiation oncologists and geographic heterogeneity in the multilevel analysis, suggesting that cost structure is not an important reason for HF-WBI use.

We found a strong dose-response relationship between distance from the patient's home to the treatment facility and HF-WBI utilization. Increased convenience and cost-effectiveness have may explain this association, as suggested by previous literature.[4,9,51,52] Previous studies have found that racial disparities existed in using HF-WBI,[16,18,41] and communities with diverse racial components were more likely to receive HF-WBI.[9] Communities with more diversity may yield increased openness to acceptance of new therapies. Nevertheless, after accounting for geographic and physician-level variation in our study, there is insufficient evidence in favor of higher HF-WBI utilization in mixed communities. Results suggested that communities with a majority of Asian individuals had a significantly higher likelihood of receiving HF-WBI, similar to results in several previous studies.[5,45] Our analysis revealed that patients residing in well-educated communities had higher HF-WBI utilization. Higher community education level is potentially associated with higher health literacy, which may help patients to accept new treatment modalities. Given that radiation oncologists play a leading role in determining radiation fractionation, these community factors may have limited contribution to the choice of HF-WBI. Continuing medical education through scientific conferences, seminars, and online venues, such as theMednet,[53] could help doctors to better understand the advantages of HF-WBI and promote the new clinical guidelines.

Our study has limitations. First, our study includes only employer-sponsored insurance claims for breast cancer patients receiving radiation therapy, which may not be generalizable to populations with other health insurance plans. Second, certain physician-level characteristics can influence their preference for HF-WBI use, including age, gender, years of practice, and school of medical training.[16,17] The HCCI database does not cover that granular information on the type of physician, so we acknowledge that we can only quantify the overall variation across radiation oncologists but cannot pinpoint exact reasons for this variation. Third, HCCI data were only available until 2017 in this study, which hindered additional analysis of the most recent publication of 2018 ASTRO guideline on HF-WBI and the impact of COVID-19 pandemic. These factors may affect future HF-WBI adoption, and we anticipate a rapid increase in HF-WBI utilization beyond our study period. But to our knowledge, few studies to date have studied uptake after the 2018 ASTRO guideline was released or post pandemic. Future studies should further investigate the trend and the current situation of HF-WBI use in the U.S.

In conclusion, HF-WBI utilization increased over time (from 2008 to 2017) in the U.S., but it may take a long time for its full adoption in the U.S. This study demonstrated physician-level and geographic heterogeneity in using HF-WBI among women with early-stage breast cancer. The impact of physicians' medical training and institutional practices on HF-WBI use needs to be further studied, as variation in HF-WBI use was found to be most attributable to physician-level factors. Community- and patient-level characteristics were also found to contribute to variation in HF-WBI utilization. In addition, ultrahypofractionated (UHF) radiation therapy for breast cancer was found to be comparable in efficacy and toxicity to moderate HF-WBI,[54,55] and the adoption of UHF radiation therapy is on the rise.[56] Future studies should further investigate the impact of reimbursement systems on the adoption of UHF in the U.S.

Disclosures

None.

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Supplementary materials

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