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14. ABSTRACT Scope and Purpose. Prior research evidence that has suggested that regional variation and socioeconomic barriers in breast cancer treatment remain substantial problems for patients across the nation. The purpose of our project was to characterize national patterns in the treatment of early invasive breast cancer in older women with incident disease. We specifically sought to characterize disparities in care and regional variation in treatment patterns. Methods. We sought to apply a novel resource, comprehensive national Medicare claims data, to study disparities in care and outcomes in women with breast cancer. We calculated national and state-by-state absolute and standardized utilization rates of radiotherapy (RT) and chemotherapy in patients with early invasive breast cancer treated with conservative surgery (CS); analyzed the modifying effect of race on RT utilization; and evaluated the utility of claims-based covariates in predicting breast cancer stage. Multivariate logistic regression was used to model these outcomes. Findings. Significant regional variation in utilization of breast cancer treatment existed in our cohort of older women diagnosed with invasive disease, even after standardization for patient and disease characteristics. In addition, significant racial disparities in care existed, with non-white women significantly less likely than white women to receive RT after CS, despite this treatment modality generally considered standard treatment. Conclusions. Our research adds to the existing literature by providing the first comprehensive national sample to address these study questions. Our future research will extend on our current findings by determining whether these variations in breast cancer treatment also affect outcomes, such as cancer recurrence, mortality, and costs of cancer care.					
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INTRODUCTION

The purpose of our project was to characterize national patterns in the treatment of early invasive breast cancer in older women with incident disease. We specifically sought to characterize disparities in care and regional variation in treatment patterns. Our study subject was in response to prior research evidence that has suggested that regional variation and socioeconomic barriers in breast cancer treatment remain substantial problems for patients across the nation. In fact, though in 1999, the Institute of Medicine National Cancer Policy Board issued a call to improve the quality of cancer care nationally⁽¹⁾, a recent study indicated that progress in overcoming disparities in cancer care has been insufficient⁽²⁾. For our project, we sought to apply a novel resource, comprehensive national Medicare claims data, to study disparities in care and outcomes in women with breast cancer. Our proposed project is intended to span a total of three years. To date, at the culmination of Year 1 of this project, our main objective was to characterize the scope of treatment disparities and the magnitude of regional variation in care, using cross-sectional data. As we anticipate Years 2-3, we intend to assess the impact of these disparities on breast cancer outcomes and costs. The following narrative will detail results obtained from our project over the course of Year 1.

BODY

Task Summary from Statement of Work (SOW)

(From original SOW, submitted February 2007)

Task 1. *To assess standardized utilization rates of radiation therapy and chemotherapy.*

Deliverable A: Preparation of abstract for national scientific meeting

Deliverable B: Preparation of manuscript for submission at peer-reviewed journal.

Objectives

Analysis 1: To present overall national and state-by-state absolute and standardized utilization rates of treatment

Analysis 2: To present utilization rates of radiotherapy (RT) after conservative surgery (CS) by race, a significant modifying factor, in order to quantify disparities in breast cancer treatment, given that RT after CS is generally considered standard therapy

Analysis 3: To present utilization rates of brachytherapy, in order to help quantify the uptake in an emerging area of treatment across the United States

Analysis 4: To present a validation sample of breast cancer patients and evaluate and validate the utility of claims-based covariates in predicting breast cancer stage

Methods

Study sample

To accomplish SOW Task 1, we derived a study sample using the national Medicare dataset. The national Medicare dataset includes comprehensive claims information with beneficiary-specific data on all Medicare beneficiaries in the United States. Files contain data collected by Medicare for reimbursement of health care services for each beneficiary and include institutional (inpatient and outpatient) as well as non-institutional (physician or other providers) final action claims⁽³⁾. To define a cohort of patients with incident disease in 2003 required claims data spanning 2002 to 2004 to have complete information on the claims history the year prior to diagnosis and information on claims up a year after diagnosis, as detailed below.

In summary, our initial study population consisted of **853,273** women who had any diagnosis of invasive breast cancer in 2003, based on an International Classification of Diseases, Ninth Revision (ICD-9) diagnosis code of 174. As this denominator would have included incident and prevalent cases in 2003, we applied the following algorithm to refine our study sample: From our initial study population, we included **83,611** patients age ≥ 65 years who underwent breast conserving surgery (BCS) in between 01/01/2003 and 12/31/2003. From this sample, we excluded **10,457** patients without at least 2 diagnosis claims (on different dates) of invasive breast cancer between 01/01/2003 and 12/31/2004 (earliest date of diagnosis claim must have occurred during the year 2003), with no more than 6 months between the date of BCS and the earliest breast cancer diagnosis claim date. To exclude prevalent cases, we then excluded **15,377** patients with breast cancer-related diagnosis or procedure claims between 01/01/2002 and 12/31/2002. To ensure that BCS was intended to be the primary cancer-directed surgery, we then excluded **15,870** patients who underwent mastectomy within three months of BCS. To limit our sample to patients with early stage invasive breast cancer, we then excluded **1,082** patients who had two or more diagnosis claims of metastatic disease from three months before to three month after the diagnosis date. To improve sample homogeneity, we also excluded **2,964** patients who were receiving Medicare coverage due to end stage renal disease (ESRD) or disability. Finally, to ensure complete claims information to determine patients' cancer treatment course and comorbidities, we excluded **3,781** patients who lacked Part A or B coverage or had intermittent HMO coverage in the 9 months after their breast cancer diagnosis date or in the 1 year before their diagnosis date (of these patients, 2,143 had incomplete information in the year prior to diagnosis due to being younger than 66 years of age). For our study, breast cancer diagnosis date was considered the earliest diagnosis claim date. This left a final sample size of **34,080** patients. Our algorithm was based on a prior validated algorithm for identifying breast cancer patients using claims data⁽⁴⁾.

In addition, as a secondary task to complement Task 1 goals, we derived a validation sample using the SEER-Medicare database in order to derive an algorithm based on multivariate modeling and to characterize the sensitivity and specificity for identifying (predicting) stage in breast cancer patients. Using available claims in SEER-Medicare, we developed a prediction

equation to identify patients with distant disease at diagnosis and, among patients without distant disease, a prediction equation to classify the extent of locoregional disease. The purpose of this algorithm was to establish the value and use of covariates for predicting breast cancer stage, which is not directly available through Medicare claims data.

Data management and statistical analysis

All covariates were derived from Medicare files, including the denominator file (DN) and claims files (CL). Demographic data included age at diagnosis (DN), race (DN), and state (DN). Geographic regions grouped states together based on geographic proximity (DN). Disease- and treatment-related variables included axillary lymph node involvement (CL), axillary lymph node dissection (CL), receipt of any radiotherapy up to 9 months after diagnosis (CL), receipt of brachytherapy (CL), receipt of any chemotherapy up to 9 months after diagnosis (CL), receipt of adriamycin (CL) or taxol (CL), any staging imaging (CL), number of hospitalizations in the year after diagnosis (CL), and number of medical oncology, radiation oncology, and surgery visits in the year after diagnosis (CL). Variables indicating preventive healthcare and interactions with the healthcare system included mammography in the year prior to diagnosis (CL) and number of physician visits in the year prior to diagnosis (CL). In addition, severity of comorbid disease for each patient was calculated based on a modified Charlson comorbidity score validated in prior claims-based studies: 0 (no comorbidity), 1 (mild to moderate), or 2 (severe)⁽⁵⁾. This score combined comorbidities recorded in Medicare claims from 12 months prior to cancer diagnosis. To enhance specificity of comorbid disease diagnoses, patients must have had at least 1 inpatient (Part A) claim or at least 2 outpatient (Part B) claims more than 30 days apart⁽⁵⁾.
(Table 1)

For characterization of treatment utilization, bivariate associations between treatment and other covariates were tested using the Pearson chi-square test for categorical variables and the Wilcoxon rank sum test for continuous variables. A multivariate logistic model tested the adjusted association between predictors and treatment. Covariates were selected *a priori* based on significance in bivariate analyses ($P < 0.25$) and significance in prior studies of cancer patients⁽⁶⁻¹²⁾. Logistic models also derived standardized treatment rates, based on unadjusted percent use of radiotherapy and chemotherapy, standardized for covariates.

Stage prediction algorithm

For creating a stage prediction algorithm, our initial study population consisted of 150,764 women (age ≥ 65 years) diagnosed with breast cancer between 1992 and 2002 identified through SEER-Medicare. From this population, we excluded 5,217 patients with unknown stage and 19,816 with *in situ* disease. We further excluded 8,716 patients who did not have Medicare Fee-for-Service coverage from 12 months prior to 9 months after diagnosis date, and the 308 patients age < 66 , since these patients potentially would not have had comprehensive claims information to define the independent predictor covariates. This left a final sample size of **77,306** patients in our study.

Table 1. Claims codes searched to define variables of interest

Predictor Variable	Time period searched	ICD-9 Diagnosis Codes	ICD-9 Procedure Codes	CPT Codes	Revenue Center	Other File
Demographic						
Age	At diagnosis	-	-	-	-	Available through SEER or denominator file
Race	At diagnosis	-	-	-	-	Available through SEER or denominator file
Extent of disease						
Axillary LN involvement	3 mos before to 3 mos after	1963	-	-	-	-
Metastatic disease	3 mos before to 3 mos after	1962, 1965-6, 197, 1970, 1971, 1972, 1973, 1974, 1975, 1976, 1977, 1978, 198, 1980, 1981, 1982, 1983, 1984, 1985, 1986, 1987, 1988, 19881, 19882, 19889	-	-	-	-
Cancer treatment						
No. visits to surgeon	In the year after diagnosis	-	-	-	-	Physician specialty available through carrier claims
No. visits to medical oncologist	In the year after diagnosis	-	-	-	-	Physician specialty available through carrier claims
No. visits to radiation oncologist	In the year after diagnosis	-	-	-	-	Physician specialty available through carrier claims
Imaging (CT, MRI, PET, or bone scan)	In the 3 months after diagnosis	-	8801, 8703, 8741, 8891, 8896, 8874, 9218, 9214	70450, 70460, 70470, 70551-3, 71250, 71260, 71270, 72192-4, 74150, 74160, 74170, 76700, 78315, 78320, 78812-6, G0213-5	0351, 0352	-
Radiation therapy	In the 9 months after diagnosis	V580, V661, V671	9221-7, 9229	77401-77525, 77761-77799	0330, 0333	-
Brachytherapy	In the 9 months after diagnosis	-	-	19296-19298, 77750, 77761-77763, 77776-77778, 77781-77784, 77789-77790, 77799, 01827, Q3001, C9714, C9715	-	-
Breast conserving surgery	In the 9 months after diagnosis	-	8520-3, 8525	19110, 19120, 19125, 19160, 19162	-	-
Mastectomy	In the 9 months after diagnosis	-	8541-8	19180, 19182, 19200, 19220, 19240	-	-
Axillary LN dissection	3 mos before to 1 year after	-	4023, 4051, 8543, 8547	38740, 38745, 19162, 19200, 19220, 19240	-	-
Chemotherapy (any agent)	In the 9 months after diagnosis	V581, V662, V672	9925	96400-96549, J9000-9, Q0083-5	0331, 0332, 0335	-
Adriamycin	-	-	-	J9000-1, J9180	-	-
Taxol	-	-	-	J9170, J9265	-	-
Preventive care and interaction with healthcare system						
No. physician visits	In the year prior to diagnosis	-	-	-	-	From all Medicare files
Screening mammography	In the year prior to diagnosis	V7611, V7612	8737, 8736	77055-6, 77058-9, 76090-2, G0202, G0204, G0206	0401, 0403	-
Influenza vaccine	In the year prior to diagnosis	V0481	-	90658, G0008	-	-
General health status						
Any hospital admission	In the year after diagnosis	-	-	-	-	From inpatient files
Charlson comorbidity score	In the year prior to diagnosis up to 1 month after diagnosis	-	-	-	-	As per prior studies

Dependent variable: Cancer stage

The “gold standard” for cancer stage at diagnosis was determined using a combination of tumor variables available through SEER. Distant disease was determined using American Joint Committee on Cancer (AJCC) historic stage as reported to SEER, which indicates tumor present in any distant site at cancer diagnosis (compared with tumor limited only to local or regional sites at diagnosis). For our analysis, patients with any distant disease were considered Stage IV.

Patients without distant (Stage IV) disease had local or regional AJCC historic stage. These patients were further categorized into T and N stage using SEER variables for tumor size and extent of disease. Tumor size and extent was categorized as ≤2 cm (T1); >2 to 5 cm (T2); >5 cm (T3); or invading into the chest wall, ribs, intercostals or serratus anterior muscles, extensive invasion into the skin, inflammatory carcinoma, or further contiguous extension into the skin (T4). Nodal disease was categorized as 0 positive lymph nodes (N0); 1 to 3 positive lymph nodes (N1); 4 to 9 positive lymph nodes (N2); or 10 or more positive lymph nodes (N3)⁽¹³⁾. Due to the extent of missing data in the SEER database, location of positive lymph nodes was not included in N stage categories. Stage I included T1N0 disease, Stage II included

T0N1, T1N1, T2N0, T2N1, and T3N0 disease, Stage III included T0-2N2, T3N1-2, T4N0-2, and T0-4N3 disease. These classifications are based on AJCC 2003 staging criteria⁽¹⁴⁾.

Independent Predictors

Predictor covariates were obtained by searching through inpatient, outpatient, and carrier Medicare claims or the denominator file for SEER-Medicare linked data for demographic variables. A comprehensive list of International Classification of Diseases, Ninth Revision (ICD-9), Common Procedural Terminology (CPT), and Revenue Center codes for each predictor are listed in **Table 1**.

Statistical analysis

We derived two separate logistic models. The first model tested the associations between predictor covariates and the dichotomous outcome Stage IV versus non-Stage IV disease. Among the subset of patients who were not categorized as having Stage IV disease, the second model tested the associations between predictor covariates and the dichotomous outcome Stage I/II versus Stage III disease.

Each model was derived from a “derivation set,” selected using simple random sampling without replacement (**38,653 of 77,306** patients selected for the first model and **33,562 of 67,123** patients selected for the second model). Parsimonious models were selected based on statistical significance in the multivariate model and model fit. The remaining patients constituted “validation sets”. In the validation sets, parameter estimates from the derivation sets were used to calculate each patient’s probability of Stage I/II, III, or IV disease (calculated probability = $1/(1+\exp^{-(\text{intercept} + \beta_1x_1 + \beta_2x_2\dots)})$). To determine an optimal probability value for categorizing tumor stage in each patient, test characteristics (sensitivity, specificity, positive predictive value [PPV], and negative predictive value [NPV]) were derived for probability cutpoints between 0.05 and 0.90.

Statistical analyses were conducted using SAS version 9.1.3 (SAS Institute Inc, Cary, NC), and all statistical tests assumed a 2-tailed α of 0.05.

Results

Medicare study sample characteristics

Of the **34,080** women with invasive breast cancer treated with CS, 91% (N=31,127) were white, 6% (N=2,077) were black, and 3% (N=876) were other race. Mean age of the sample was 76 (standard deviation 7), with 79% of patients age 70 years and older. Sixty-eight percent of women were free of other comorbidities at diagnosis. Ninety-five percent of women had received a mammogram within the year prior to breast cancer diagnosis. A total of 39% underwent axillary lymph node dissection or had a claim indicating axillary lymph node involvement.

Utilization of RT and chemotherapy across the United States

Absolute percent use and standardized rates

Seventy-three percent of women received RT after CS and 13% received chemotherapy as part of their initial treatment course. However, there was significant variation in the utilization of these treatments across the United States, with as little as 50% to as much as 85% utilization of RT after CS by state ($P<0.001$); while utilization of chemotherapy ranged from 8% to 22% by state ($P<0.001$) (**Figure 1a, 2a**). After standardization of utilization rates by covariates, significant geographic variation still existed (**Figure 1b, 2b**).

Figure 1a. RT in the United States (all women). Darker shading represents higher percent utilization. Categories: 50% to 60%, 61% to 65%, 66% to 70%, 71% to 73%, 74% to 75%, 76% to 85%, 86% to 100%

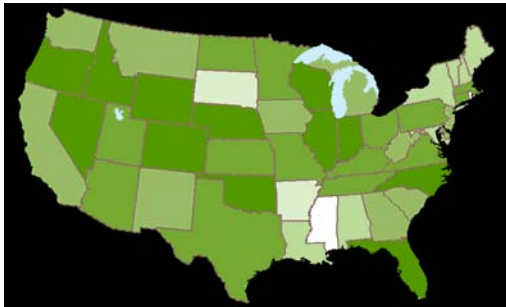


Figure 1b. RT in the United States (standardized risk adjusted rates)



Figure 2a. Chemotherapy in the United States (all women). Categories: 8% to 11%, 12% to 15%, 16% to 18%, 19% to 22%

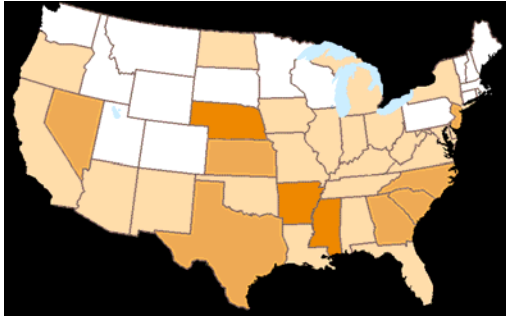


Figure 2b. Chemotherapy in the United States (standardized risk adjusted rates)

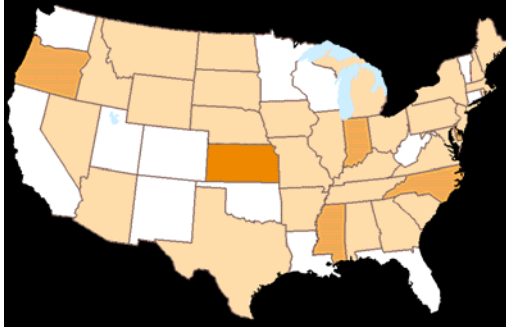


Figure 3. RT use in white women. Categories: 12% to 16%, 17% to 33%, 34% to 50%, 51% to 66%, 67% to 72%, 73% to 75%, 76% to 77%. Gray= data insufficient.

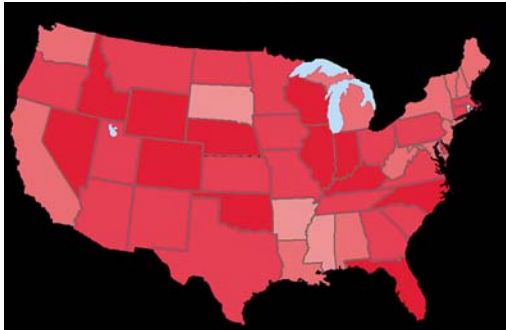
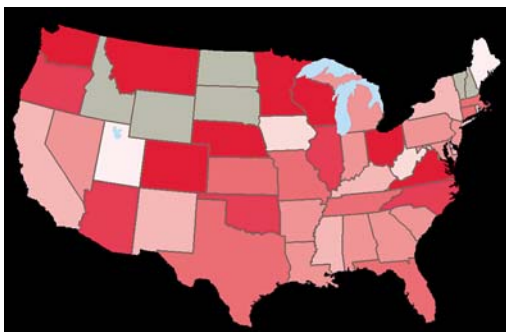


Figure 4. RT use in black women.



Utilization of RT and by race

Significant disparities existed in RT treatment by race, with 74% of white women, 65% of black women, and 66% of other women who received RT after CS ($P<0.001$). After adjusting for covariates, white women were still significantly more likely than black women to have received RT after CS (Odds Ratio [OR] 1.48, 95% Confidence Interval [CI] 1.34-1.63, $P<0.001$). There was a trend toward white women also being more likely than other (non-white, non-black) women to have received RT after CS, but this difference was marginally significant (OR= 1.22, 95% CI 1.04-1.42, $P=0.01$) (**Table 2**).

Table 2. Unadjusted and adjusted utilization of radiotherapy (RT) by race

Model: RT use	OR	95% CI		P
Unadjusted				
White vs. black patients	1.52	1.38	1.67	<0.001
White vs. other [†] patients	1.46	1.27	1.68	<0.001
Adjusted*				
White vs. black patients	1.48	1.34	1.63	<0.001
White vs. other [†] patients	1.22	1.04	1.42	0.01

* Adjusted for age, comorbidity, chemotherapy (adriamycin or taxol), axillary lymph node involvement, staging imaging, surgeon visits, mammography, physician visits, and region.

Race and utilization in younger patients

In the subset of patients age 70 and younger, in whom RT utilization after CS would be expected to be most common, racial disparities persisted, particularly between white women versus black women. A total of 83% of white women, 72% of black women, and 78% of other women in this younger group received RT after CS ($P<0.001$). The disparity between white and black women persisted even after adjusting for covariates (OR= 1.81, 95% CI 1.46-2.25, $P<0.001$).

Race and geographic variation in utilization

There was, however, substantial geographic variation in racial disparities. Regions with the most marked racial disparities included the Pacific West, the East South Central region, and the Northeast (**Table 3**). Black women fared particularly poorly in these regions, with less than 60% RT utilization after CS. (Note that regional and state data were not presented for “other” race due to insufficient numbers of patients in this category).

Table 3. Racial disparities in RT utilization after CS by region

Region	States	% in Whites	% in Blacks	P
Pacific West	CA, OR, WA	72	55	<0.001
Mountain West	AZ, CO, ID, MT, NV, NM, UT, WY	76	74	0.81
Midwest, West North Central	IA, KS, MN, MO, NE, ND, SD	74	72	0.77
Midwest, East North Central	IL, IN, MI, OH, WI	76	71	0.04
Northeast, New England	CT, ME, MA, NH, NJ, NY, VT	70	58	<0.001
Northeast, Mid-Atlantic	DE, DC, MD, PA, RI	72	59	<0.001
Southwest, West South Central	AR, LA, OK, TX	73	64	0.003
Southeast, East South Central	AL, KY, MS, TN	72	57	<0.001
Southeast, South Atlantic	FL, GA, NC, SC, VA, WV	77	69	<0.001

Brachytherapy

Of all patients treated with RT after CS, 97% were treated with external beam radiotherapy (EBRT) alone, 3% with brachytherapy alone, and <1% with EBRT plus brachytherapy boost. For patients treated with brachytherapy, 98% received interstitial therapy and 2% intracavitary therapy. Though percent utilization of brachytherapy modalities ranged from 1% to 4% across different locations in the US, no statistically significant variation was detected by state (P=0.62) or by region (P=0.32). In addition, brachytherapy use did not differ by race (P=0.63) or age (P=0.59).

Stage prediction

SEER-Medicare sample characteristics

In **77,306** patients, mean age was 76 (standard deviation 7), and 94% were white. Fifty-one percent were Stage I (**39,312**), 26% Stage II (**20,261**), 10% Stage III (**7,550**), 4% Stage IV (**3,220**) and 9% were non-distant disease but T or N stage unknown (**6,963**). Forty-five percent were treated with breast conserving surgery, 49% with mastectomy, 44% with radiotherapy, and 18% with chemotherapy (**Table 3**).

Predictors of cancer stage

For each predictor, parameter estimates and significance in final models are listed in **Tables 4-5**. The predictor variables including overall survival, mastectomy more than 9 months after diagnosis, geographic region, and year of treatment were not included in the final parsimonious model as these predictors did not substantially change parameter estimates.

Test characteristics for probability cutpoints

Stage IV

Fourteen percent of all patients and 72% of patients with Stage IV disease had a claims code indicating possible metastatic disease. After including other covariates in a multivariate model, the sensitivity was 83% for identifying Stage IV disease at a probability cutpoint of 0.05. At this cutpoint, specificity was 88%, PPV 24%, and NPV 99% (**Table 6**). The distribution of

calculated predicted probabilities in the validation set for patients with Stage IV versus Stage I-III disease is presented in **Figure 5**.

Stages I-III

In patients with any Stage I-III disease, 19% had a claims code indicating axillary lymph node involvement. Specifically, 2% of patients with Stage I disease, 36% with Stage II disease, and 64% of patients with Stage III disease had this claims code. After including other covariates in a multivariate model, the sensitivity was 89% for identifying Stage I/II disease at a probability cutpoint of 0.80. At this cutpoint, specificity was 72%, PPV 96%, and NPV 44%. For identifying Stage III disease, the sensitivity was 84% at a cutpoint of 0.10. At this cutpoint, specificity was 81%, PPV 35%, and NPV 98% (**Table 7**). The distribution of calculated predicted probabilities in the validation set for patients with Stage I/II versus Stage III disease is presented in **Figure 6**.

Table 3. SEER-Medicare validation sample characteristics

Predictor Variable	% of All Patients
Demographic	
Age (mean $\pm$ SD)	76 $\pm$ 7
White race	94
Stage	
Stage I	51
Stage II	26
Stage III	10
Stage IV	4
Stage I-III but T or N unknown	9
Extent of disease*	
Axillary LN involvement	19
Metastatic disease	14
Cancer treatment*	
No. visits to surgeon (mean $\pm$ SD)	4 $\pm$ 3
No. visits to medical oncologist (mean $\pm$ SD)	4 $\pm$ 9
No. visits to radiation oncologist (mean $\pm$ SD)	3 $\pm$ 5
Imaging (CT, MRI, PET, or bone scan)	25
Radiation therapy	44
Breast conserving surgery	45
Mastectomy	49
Axillary LN dissection	72
Chemotherapy (any agent)	18
Adriamycin	7
Taxol	3
Preventive care and interaction with healthcare system*	
No. physician visits	14 $\pm$ 12
Screening mammography	78
Influenza vaccine	34
General health status*	
No. hospital admission for any cause (mean $\pm$ SD)	1 $\pm$ 1
Charlson comorbidity score	
0 comorbid conditions	69
1 comorbid condition	18
2 or more comorbid conditions	8
Unknown	5

* As indicated by Medicare claims codes; thus percentage of patients with code for metastatic disease not equal to patients with Stage IV disease.

Table 4. Parameter estimates for logistic model : Stage IV versus Stage I-III

Predictor Variable	Parameter Estimate
Intercept	-4.6305
Age	0.0188
Black race	0.0506
Axillary LN involvement	-1.7376
Metastatic disease	2.3298
No. visits to surgeon	-0.0384
No. visits to medical oncologist	0.0221
No. visits to radiation oncologist	-0.0174
Imaging (CT, MRI, PET, or bone scan)	0.8913
Radiation therapy	0.3396
Breast conserving surgery vs Mastectomy	-0.7388
No surgery vs Mastectomy	0.8775
Axillary LN dissection	-1.7376
Chemotherapy (any agent)	0.4759
Adriamycin	0.1800
Taxol	0.5567
No. physician visits	-0.0167
Screening mammography	-0.6651
Influenza vaccine	-0.0871
Any hospital admission	0.057
Charlson comorbidity score	0.0452

Table 5. Parameter estimates for logistic model : Stage I-II versus Stage III

Predictor Variable	Parameter Estimate
Intercept	7.0392
Age	-0.0584
Black race	-0.3979
Axillary LN involvement	-2.2627
No. visits to surgeon	-0.0136
No. visits to medical oncologist	-0.00840
No. visits to radiation oncologist	-0.0190
Imaging (CT, MRI, PET, or bone scan)	-0.6091
Radiation therapy	-0.9907
Breast conserving surgery vs Mastectomy	1.9058
No surgery vs Mastectomy	-1.2998
Axillary LN dissection	0.4850
Chemotherapy (any agent)	-0.9181
Adriamycin	-0.2081
Taxol	-0.8360
No. physician visits	0.0103
Screening mammography	0.6884
Influenza vaccine	0.2960
Any hospital admission	-0.0968
Charlson comorbidity score	-0.0615

Table 6.

Predicting Stage IV versus Stages I-III*				
Probability Cutpoint	Sensitivity	Specificity	PPV	NPV
0.05	83	88	23	99
0.10	72	93	31	99
0.15	63	96	38	98
0.20	58	97	45	98
0.25	53	98	50	98
0.30	49	98	54	98
0.35	46	99	58	98
0.40	43	99	61	98
0.45	39	99	63	97
0.50	35	99	65	97
0.55	31	99	66	97
0.60	27	100	68	97
0.65	23	100	69	97
0.70	20	100	72	97
0.75	16	100	77	97
0.80	12	100	79	96
0.85	8	100	82	96
0.90	5	100	80	96

Abbreviations: PPV= positive predictive value, NPV= negative predictive value

* Sensitivity/specificity and PPV/NPV reversed for predicting Stage I-III versus Stage IV
with probability cutpoint= 1-probability cutpoint for Stage IV versus Stage I-III.

Table 7.

Predicting Stage I/II versus Stage III*				
Probability Cutpoint	Sensitivity	Specificity	PPV	NPV
0.05	100	1	89	84
0.10	100	3	89	84
0.15	100	7	90	83
0.20	100	10	90	79
0.25	99	14	90	77
0.30	99	19	91	75
0.35	99	23	91	72
0.40	99	28	92	70
0.45	98	32	92	67
0.50	98	38	93	65
0.55	97	43	93	62
0.60	96	48	94	59
0.65	95	53	94	55
0.70	93	59	95	52
0.75	91	65	95	48
0.80	89	72	96	44
0.85	85	78	97	40
0.90	81	84	98	35

Abbreviations: PPV= positive predictive value, NPV= negative predictive value

* Sensitivity/specificity and PPV/NPV reversed for predicting Stage III versus Stage I/II
with probability cutpoint= 1-probability cutpoint for Stage I/II versus Stage III.

Figure 5.

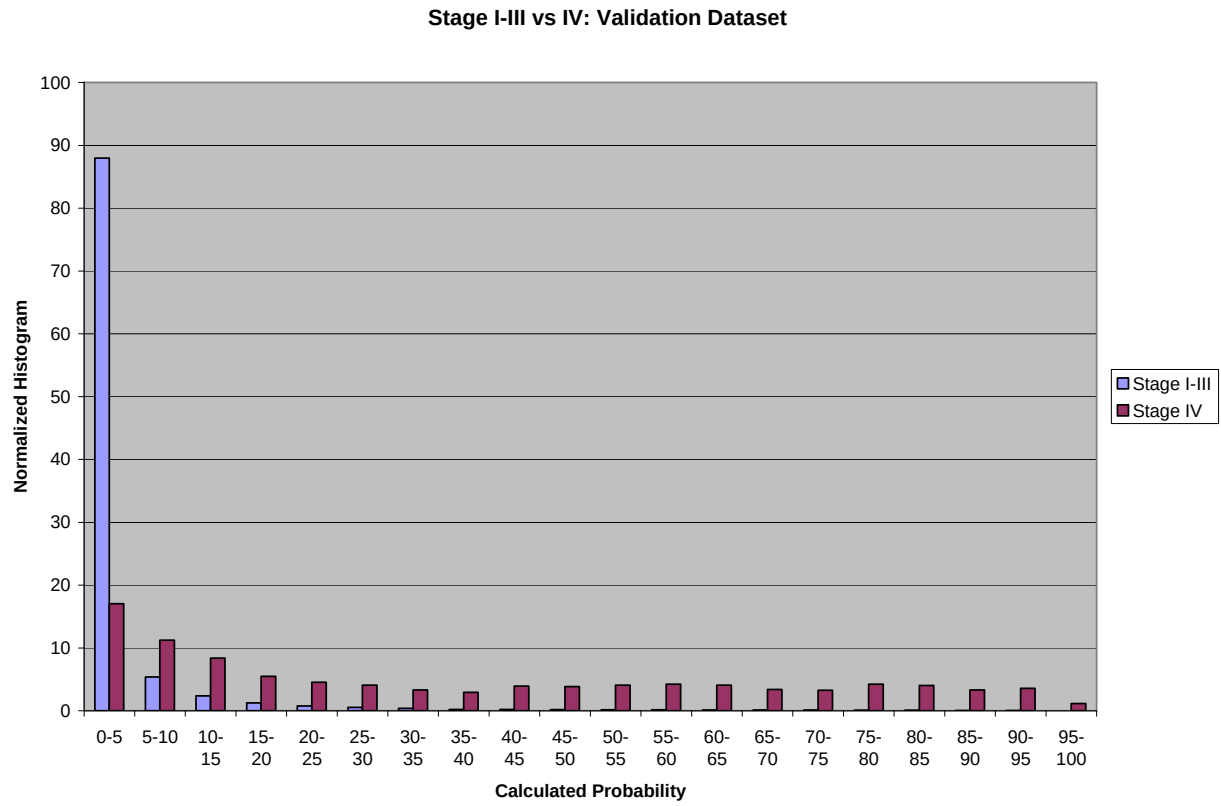
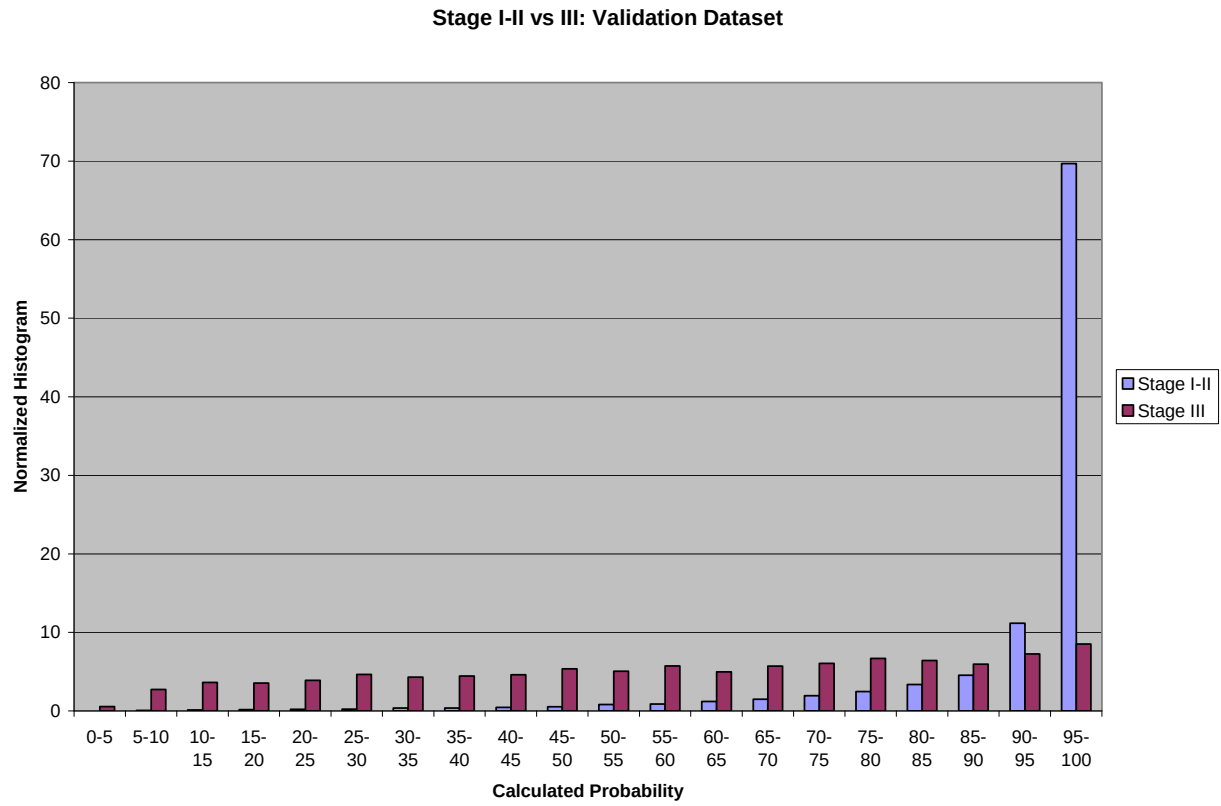


Figure 6.



Discussion

Summary

Analysis 1: To present overall national and state-by-state absolute and standardized utilization rates of treatment

Significant regional variation in utilization of breast cancer treatment existed in our cohort of older women diagnosed with invasive disease. Underlying causes of this variation remain to be elucidated. However, it is likely that this variation was, in part, due to differences in patient “case mix” (e.g. breast cancer stage, other comorbidities that would affect patients’ ability to receive treatment); as well as possible differences in treatment patterns and potential undertreatment of some patients. Standardized utilization (risk adjusted rates), however, were intended to account for case mix, though residual confounding may have existed, particularly as no direct cancer stage variable was available. Although standardization decreased differences amongst geographic regions, particularly in the use of chemotherapy, significant variation existed. This finding was particularly concerning given that RT after CS is generally considered standard therapy.

Analysis 2: To present utilization rates of radiotherapy (RT) after conservative surgery (CS) by race

Additionally, the finding of significant disparity by race was concerning. Even after adjustment for all major covariates, black women were significantly less likely than white women to receive RT after CS. Other non-white, non-black women were marginally less likely to receive the treatment. Though the underlying cause of the disparities is still not known, there are likely complex and multifactorial contributing issues. Potentially, providers may be undertreating certain patient populations. Alternatively, patients may decline treatment due to misconceptions about treatment or obstacles to care, such as access to care, distance from facility, or lack of social support. Interestingly, disparities were not uniform across the nation, with some areas of the United States actually delivering comparable care regardless of patient race. Other areas, however, showed marked racial disparities. Future efforts to improve breast cancer care will require overcoming these considerable disparities.

Analysis 3: To present utilization rates of brachytherapy, in order to help quantify the uptake in an emerging area of treatment across the United States

Several studies have demonstrated the potential value of brachytherapy in the treatment of breast cancer, either as local boost irradiation, or alone as accelerated partial breast irradiation, after breast conserving surgery (BCS). In 2002, the Food and Drug Administration approved the first balloon-based brachytherapy delivery system, signaling the beginning of broader incorporation of partial breast irradiation into breast cancer treatment. While subsequent studies have been seeking to define the patient population that will derive

optimal clinical benefit from breast brachytherapy, this treatment option has remained widely available for use in a variety of settings. However, no prior study has described the frequency of breast brachytherapy use in the US. Thus our analysis was important for characterizing utilization of breast brachytherapy across the nation at the inception of this era.

Analysis 4: To present a validation sample of breast cancer patients and evaluate/validate the value of claims-based covariates in predicting breast cancer stage

Results of our validation study demonstrated that Medicare claims data were important in assisting the prediction of cancer stage. Predictor equations were able to achieve over 80% sensitivity and over 80% specificity for identifying Stage IV disease as well as distinguishing Stage I/II from Stage III disease. Prediction models maximized the NPV when distinguishing Stage IV from Stage I-III disease. Prediction models maximized the PPV when distinguishing Stage I/II from III disease.

Our prediction models represent a substantial improvement compared with the models presented by Cooper et al. in a prior study⁽¹⁵⁾. To identify patients with distant disease, authors tested a single variable based on claims codes for metastatic disease. This single-predictor model demonstrated 60% sensitivity and 58% PPV. To distinguish patients with local versus regional disease, authors tested a single variable based on the claim code for axillary lymph node involvement. This single-predictor model demonstrated 62% sensitivity and 85% PPV. The relatively poor test characteristics demonstrated that these single-predictor models would be insufficient for predicting stage in breast cancer patients.

Our results suggest that, using a combination of multiple predictors along with claims codes for metastatic disease and axillary lymph node dissection, parameter estimates and calculated probabilities can be applied to the prediction of patient breast cancer stage. Specifically, for the Stage IV prediction model, a probability cutpoint between ≥ 0.05 and ≥ 0.10 would be highly specific and sensitive for identifying patients with Stage IV disease. For the Stage I/II prediction model, a cutpoint between ≥ 0.80 and ≥ 0.90 would be highly specific and sensitive for distinguishing patients with Stage I/II disease from patients with Stage III disease.

For the identification of patients with Stage IV disease, a selected probability cutpoint criterion could be translated into a dichotomous variable, and used either to select a sample of patients with Stage IV disease or used in a “rule out” context, as an exclusion criterion. The high NPV in our proposed model suggests that when using these cutpoints to identify a sample limited to patients with Stage I-III disease, the likelihood of misclassification bias (bias due to the inappropriate inclusion of patients with Stage IV disease in the sample) would be low. For distinguishing patients with Stage I/II versus III disease, the probability cutpoint criterion, translated into a dichotomous variable, could be useful in various contexts, such as excluding patients with Stage III disease, or creating a dichotomous covariate to adjust for potential confounding associated with stage I-III disease.

Prior studies and future work

Other previous studies have found significant differences in breast cancer treatment by geographic region, including the use of surgery, chemotherapy, and RT⁽¹⁶⁻²²⁾. Other studies have also suggested that disparities in treatment exist by race⁽²³⁻²⁵⁾, but these prior studies have been limited in study samples, for example to single-institution, single-state, or clinical trial samples. Therefore, our research adds to the existing literature by providing the first comprehensive national sample to address these study questions. Our future research will extend on our current findings by determining whether these variations in breast cancer treatment also affect outcomes, such as cancer recurrence, mortality, and costs of cancer care. Though our claims database provides a comprehensive national sample, the main limitation of claims data is the lack of clinical detail. Therefore, other future work may focus upon collecting more detailed, prospective data in order to understand the mechanisms underlying both provider and patient decision-making in breast cancer treatment.

KEY RESEARCH ACCOMPLISHMENTS

- Obtained comprehensive national Medicare data to define a study cohort of patients with incident breast cancer as well as validation subset cohort in the SEER-Medicare data.
- Accomplished data cleaning and management, in order to establish study sample, refine exclusion criteria, and define covariates and treatment variables
- Conducted univariate and multivariate data analysis, with main findings of crude and standardized rates of radiotherapy and chemotherapy treatment nationally.
- Further conducted stratified and subsidiary analyses, including an analysis of the disparities in radiotherapy treatment by race, rates of brachytherapy use across the nation, and a validation algorithm to predict breast cancer stage using claims data.
- Abstracts and poster presentations accepted to national scientific meetings (San Antonio Breast Cancer Symposium and ASCO 2008 Breast Cancer Symposium), details below.
- Preparation of manuscripts in progress, for submission at peer-reviewed journals

REPORTABLE OUTCOMES

Manuscripts

1. Smith GL, Shih YT, Giordano SH, Smith BD, Buchholz TA. Predicting breast cancer stage using Medicare administrative claims data. In progress.
2. Smith GL, Shih YT, Xu Y, Giordano SH, Smith BD, Perkins GH, Tereffe W, Woodward WA, Buchholz TA. Racial disparities in the treatment of early invasive breast cancer: A national Medicare study of radiotherapy after conservative surgery. In progress.
3. Smith GL, Smith BD, Giordano SH, Shih YC, Woodward WA, Strom EA, Perkins GH, Tereffe W, Yu T, Buchholz TA. Risk of hypothyroidism in older breast cancer patients treated with radiation. Cancer 2008 Mar 15;112(6):1371-9.

Abstracts and presentations

1. Smith GL, Shih YT, Xu Y, Giordano SH, Smith BD, Buchholz TA. Breast brachytherapy in the United States: How is this emerging modality being incorporated into the care of older breast cancer patients? Abstract submitted for presentation at the 2008 San Antonio Breast Cancer Symposium. Accepted for poster presentation (December 10-14, 2008). **SEE APPENDIX A**
2. Smith GL, Shih YT, Xu Y, Giordano SH, Smith BD, Perkins G, Tereffe W, Woodward WA, Buchholz TA. Racial disparities in treatment for early invasive breast cancer: a national Medicare study of radiotherapy after conservative surgery. Abstracted submitted for presentation at the ASCO 2008 Breast Cancer Symposium. Poster presentation (September 5-7, 2008). **SEE APPENDIX B**
3. Smith GL, Smith BD, Giordano SH, Shih YC, Woodward WA, Strom EA, Perkins GH, Oh JL, Tereffe W, Buchholz TA. Risk of hypothyroidism in older breast cancer patients treated with radiotherapy. FD-Era of Hope 2008. Poster presentation. **SEE APPENDIX C**

Participation

1. The University of Texas M. D. Anderson Cancer Center, Center for Research on Minority Health, 5th Annual Summer Workshop, Disparities in Health in America: Working Toward Social Justice (Summer 2007).

Databases

1. As derived from the national Medicare claims data, retrospective cohort of women age>65, diagnosed with incident invasive breast cancer in 2003, treated with conservative surgery.

Awards and Funding (based on experience/training supported by this award)

- July 2008 American Society of Clinical Oncology (ASCO) Breast Cancer Symposium Merit Award
- June 2008 M. D. Anderson Cancer Center Odyssey Fellow Award, to support the best postdoctoral trainees among the newest generation of cancer researchers at the institution
- January 2008 Susan G. Komen Houston Affiliate Travel Scholarship, to support participation at the American Society of Clinical Oncology 2008 Breast Cancer Symposium

Media and recognition

“Racial disparities in treatment for early invasive breast cancer: a national Medicare study of radiotherapy after conservative surgery” was highlighted by the ASCO 2008 Breast Cancer Symposium press program. In addition, our research was highlighted by Medscape oncology, Reuters, Healthday News, The Houston Chronicle, and Houston public radio. **SEE APPENDIX D.**

Updated CV, SEE APPENDIX E.

CONCLUSION

At the conclusion of Year 1 of our research, we have made significant progress toward accomplishing our project goals. Specifically, we have worked to accomplish the objectives stated for Year 1 in the Statement of Work. Using our novel, comprehensive national Medicare dataset, we conducted several retrospective analyses on a cohort of older women diagnosed with early invasive breast cancer. Results from our analyses provided novel insights that contribute to the existing scientific literature. The most striking results from our analyses suggest that variation in breast cancer care is significant, but even more concerning, that a substantial number of women fail to receive standard treatment. Our study found, in particular, that racial disparities exist in breast cancer care across the United States. Results from our studies have been highlighted in the scientific and lay communities.

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Breast brachytherapy in the United States: How is this emerging modality being incorporated into the care of older breast cancer patients?

Smith GL, Shih YT, Xu Y, Giordano SH, Smith BD, Buchholz TA

Introduction: Several studies have demonstrated the potential value of brachytherapy in the treatment of breast cancer, either as local boost irradiation, or alone as accelerated partial breast irradiation, after breast conserving surgery (BCS). In 2002, the Food and Drug Administration approved the first balloon-based brachytherapy delivery system, signaling the beginning of broader incorporation of partial breast irradiation into breast cancer treatment. While subsequent studies have been seeking to define the patient population that will derive optimal clinical benefit from breast brachytherapy, this treatment option has remained widely available for use in a variety of settings. However, no prior study has described the frequency of breast brachytherapy use in the US. In a population-based cohort of older breast cancer patients, we characterized utilization of breast brachytherapy across the nation at the inception of this era.

Methods: A cross-sectional sample from a national Medicare database identified 37,323 beneficiaries (age $\geq$ 65) with newly diagnosed invasive breast cancer treated with BCS in 2003. ICD-9 and CPT codes indicated receipt of external beam radiotherapy (EBRT) and brachytherapy. Percent use by state, region, age, and race was compared using Pearson χ^2 .

Results: Across the nation, 73% of older patients were treated with any radiotherapy after BCS. Of these patients, 97% were treated with EBRT alone, 3% with brachytherapy alone, and <1% with EBRT plus brachytherapy boost. For patients treated with brachytherapy, 98% received interstitial therapy and 2% intracavitary therapy. Though percent utilization of brachytherapy modalities ranged from 1% to 4% across different locations in the US, no statistically significant variation was detected by state ($P=0.62$) or by region ($P=0.32$). In addition, brachytherapy use did not differ by race ($P=0.63$) or age ($P=0.59$).

Conclusions: At the inception of the era in which partial breast irradiation was becoming incorporated into the care of breast cancer patients, only a small percentage of all patients received breast brachytherapy across the US. As contemporary data become available, future studies may seek to trace how this new treatment strategy is becoming more widely integrated into routine breast cancer treatment.

APPENDIX B. Abstract accepted and presented as a poster at ASCO 2008 Breast Cancer Symposium.

***Note:** Numbers differ slightly from Results above as above updated analysis use additional exclusion criteria.

Racial disparities in treatment for early invasive breast cancer: a national Medicare study of radiotherapy after conservative surgery

Smith GL, Shih YT, Xu Y, Giordano SH, Smith BD, Perkins G, Tereffe W, Woodward WA, Buchholz TA

Background:In breast cancer patients, evidence suggests that receipt of standard treatments varies by race. However, prior studies of racial disparities were conducted in limited samples, failing to include the majority of patients across the US. In a national sample of Medicare patients, we quantified racial disparities in radiotherapy (RT) use after conservative surgery (CS) for treatment of early invasive breast cancer.

Methods:A national Medicare database identified all beneficiaries (age $\geq$ 65) with newly diagnosed invasive breast cancer treated with CS in 2003. ICD-9 and CPT codes indicated receipt of RT. Medicare demographic data indicated race. Percent RT use in white vs. black patients was compared using Pearson χ^2 . Logistic regression modeled racial disparities in RT use adjusted for age and geographic region.

Results:In 34,759 breast cancer patients treated with CS, 32,562 (94%) were white and 2,197 (6%) were black. Mean age was 75 $\pm$ 7. 76% of whites received RT vs. 69% of blacks (P<0.001). After covariate adjustment, blacks were still less likely to receive RT (OR=0.62, 95% CI 0.56–0.69, P<0.001). Racial disparities varied significantly by region. Across regions, RT use ranged from 73% to 80% in whites, vs. 61% to 83% in blacks. Disparities existed in all regions except the Mountain West and portions of the Midwest. Blacks in the Pacific West, New England, and in the East South Central region fared particularly poorly, with only 61% RT use. In the subset of patients age<70, in whom RT use would be expected to be most common, racial disparities persisted. Specifically, 84% of whites vs. 78% of blacks in this younger group received RT (P<0.001).

Conclusion:In this unique, comprehensive national sample of older breast cancer patients, substantial racial disparities and regional variation existed for RT after CS. Future efforts to improve breast cancer care will require overcoming these considerable disparities.

Risk of hypothyroidism in older breast cancer patients treated with radiotherapy

Smith GL, Smith BD, Giordano SH, Shih YC, Woodward WA, Strom EA, Perkins GH, Oh JL, Tereffe W, Buchholz TA

Background: Hypothyroidism is a known complication after radiotherapy (XRT) when treatment fields include the thyroid gland. In breast cancer, though a portion of the thyroid gland may be included in treatment fields, no study has identified whether breast cancer patients have an increased risk of subsequent hypothyroidism. Therefore, in a cohort of older breast cancer patients, we sought to determine the incidence of hypothyroidism, quantify the magnitude of risk associated with XRT, and identify whether any higher-risk patient subgroup exists.

Methods: Using the Surveillance Epidemiology and End Results (SEER)-Medicare cohort, we identified 38,255 women (age $\geq$ 66) with stage 0 through III breast cancer diagnosed from 1992-2002 with no prior history of hypothyroidism (International Classification of Diseases codes 244; 244.0-3, 8-9). The association between XRT and subsequent hypothyroidism was tested using proportional hazards models adjusted for age, race, tumor characteristics (size, number of positive nodes, grade, histology, receptor status), treatment course, comorbidities, income, urban/rural setting, physician visits, SEER region, and year of treatment.

Results: Median follow-up was 4.6 years. Mean age was 75 $\pm$ 6 years, 86% of patients were white, and 95% had stage I to III disease. The 5-year incidence of hypothyroidism was 14% in patients treated with XRT and 14% in patients not treated with XRT ($P=0.25$). After adjusting for covariates, XRT conferred a marginal but not significant excess risk of subsequent hypothyroidism (Hazard Ratio= 1.09, 95% Confidence Interval 0.99 to 1.19, $P=0.07$). No higher-risk patient subgroup could be identified. Specifically, patients with 4 or more positive lymph nodes (more likely to receive XRT to a supraclavicular field), older age (age $\geq$ 75), treatment with chemotherapy, or treatment with breast conserving surgery were no more likely to develop hypothyroidism ($P>0.05$ for interactions). The incidence of hypothyroidism in the subgroup of patients with 4 or more positive nodes was 12%.

Conclusion: Development of hypothyroidism is common in older breast cancer survivors. We could not detect a significantly increased risk conferred by treatment with XRT, even in presumably high-risk patients receiving treatment to a supraclavicular field. With a follow-up of up to 5 years, risks are comparable to the nationwide prevalence of hypothyroidism in this age group, approximately 20%. However, given the potential for a marginally increased risk, future studies with longer follow-up may be warranted, as guidelines for long-term, routine thyroid function monitoring after treatment for breast cancer remain undefined.

APPENDIX D. News Release

News Release - M. D. Anderson Study Finds Racial Disparities Exist in Rates For Early Stage Breast Cancer - M. D. Anderson Cancer Center



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M. D. Anderson Study Finds Racial Disparities Exist in Radiation Therapy Rates For Early Stage Breast Cancer Largest study of its kind reveals blacks less likely than whites to receive standard of care

M. D. Anderson News Release 09/04/08

Black women are less likely than white women to receive radiation therapy after a lumpectomy, the standard of care for early stage breast cancer, according to a new study by researchers at The University of Texas M. D. Anderson Cancer Center.

The study, the largest of its kind, was presented today in advance of the American Society of Clinical Oncology (ASCO) Breast Cancer Symposium, and is the first national study to examine such racial disparities in radiation therapy. Led by Grace Li Smith, M.D., Ph.D., a postdoctoral fellow in M. D. Anderson's Department of Radiation Oncology, the researchers reviewed the Medicare records of more than 37,000 patients diagnosed with early stage breast cancer in 2003.

"Although there have been smaller studies of racial disparities in breast cancer care, no prior research has examined the differences across the nation in the rates of radiation therapy after lumpectomy between whites and blacks," said Smith, the study's first author. "The national Medicare database, because it's so comprehensive, allowed us to determine the extent to which racial disparities in radiation therapy affected patients across the country."

For the retrospective cohort study, Smith and her M. D. Anderson colleagues used Medicare claims to examine the treatment history of women aged 66 and older diagnosed in 2003 with early stage, newly diagnosed breast cancer. Of the 37,305 women who underwent a lumpectomy for their breast cancer, 34,024 were white and 2,305 were black. Overall, 74 percent of the white women received radiation therapy after their lumpectomy; in contrast, 65 percent of the black breast cancer patients received the same treatment.

"The use of radiation after lumpectomy is considered to be the standard of care for women with invasive breast cancer, as clinical trials have demonstrated that it both reduces the chance of recurrence and improves the chance of survival," said Thomas Buchholz, M.D., professor in the Department of Radiation Oncology and the study's senior author. "While there are some breast cancer patients, such as those over age 70, with significant co-morbidities for whom radiation would not be appropriate, this discrepancy remained consistent when specifically looking at patients under the age of 70."

Perhaps the most unexpected aspect of the study, said Smith, was the magnitude of the disparity in specific areas of the country: the Pacific West, 72 (whites) vs. 55 percent (blacks); East South Central, 72 (whites) vs. 57 percent (blacks), and the Northeast, 70 (whites) vs. 58 percent (blacks).

However, in some parts of the country - the Mountain West (76 percent vs. 74 percent) and the North Central Midwest (74 percent vs. 72 percent) - there was virtually no discrepancy in radiation rates between whites and blacks. That level of geographic non-disparity was also surprising and of great benefit for further research, said Smith.

"Until further research is conducted, we may only speculate about the underlying reasons why black and white women are not receiving radiation at the same rate. We don't know if fewer black women are receiving radiation simply because it is not offered to them, because they decline the treatment, or perhaps because they are unable to complete a whole course of treatment due to

<http://www.mdanderson.org/departments/newsroom...layFull&pn=00c8a30f-c468-11d4-80fb00508b603a14> (1 of 2) [9/17/2008 2:38:13 PM]

other health problems. These questions will be important subjects of future study. As a medical community, we need to identify and eliminate any obstacle prohibiting all women from receiving necessary care for their breast cancer."

Smith's plans for follow up research include evaluating the difference in radiation rates results in a difference in mortality. She also plans to investigate whether radiation patterns correlate with other illnesses secondary to breast cancer care, and if there are disparities in other types of cancer treatment.

Smith hopes that results from the study may prompt physicians and patients to work together to overcome some of the barriers to treatment.

"Physicians may be able to help patients identify specific barriers to their care and may be able to be influential in helping patients overcome such obstacles," said Smith. "Or, if there are concerns or misconceptions about radiation treatment, patients themselves may play a role by becoming educated about the value of radiation after lumpectomy and helping to disseminate this information into their communities."

In addition to Smith and Buchholz, other authors of the all-M. D. Anderson study include: Tina Shih, Ph.D., associate professor in the Department of Biostatistics; Ying Xu, M.D., senior statistical analyst, Division of Quantitative Sciences; Sharon Giordano, M.D., associate professor in the Department of Breast Medical Oncology; Benjamin Smith, M.D., adjunct assistant professor in the Department of Radiation Oncology; George Perkins, M.D., associate professor in the Department of Radiation Oncology; Welela Tereffe, M.D., assistant professor in the Department of Radiation Oncology; Wendy Woodward, M.D., Ph.D., assistant professor in the Department of Radiation Oncology.

The research was supported by a grant from the Department of Defense Breast Cancer Research Program, BC062438.

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APPENDIX E. CURRICULUM VITAE

Grace Li Smith, M.D., Ph.D., M.P.H.

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Email: glsmith@mdanderson.org

Background

Born March 1977 in Silver Spring, Maryland
Married May 1998 to Benjamin D. Smith, MD

Career Goals

To integrate my training in epidemiologic research and clinical medicine as a physician-scientist in the field of radiation oncology

Education and Training

2007-present	University of Texas M.D. Anderson Cancer Center , Houston, TX Postdoctoral Fellow, Department of Radiation Oncology Odyssey Fellow, 2008-present
2001-2007	Yale University School of Medicine, Medical Scientist Training Program (MSTP) , New Haven, CT Doctorate of Medicine, 2005, <i>cum laude</i> Yale University Graduate School of Arts and Sciences, Division of Epidemiology Doctorate of Philosophy, 2007 Masters of Philosophy, 2005, <i>distinguished</i>
2005-2006	Yale-New Haven Hospital , New Haven, CT Intern, Department of Internal Medicine
1998-2000	Yale University School of Public Health, Division of Chronic Disease Epidemiology Masters in Public Health, 2000
1994-1998	Rice University , Houston, TX Bachelor of Arts in Biology and in Sociology, 1998, <i>summa cum laude</i> , <i>Phi Beta Kappa</i>

Honors and Awards

2008	American Society of Clinical Oncology (ASCO) Breast Cancer Symposium Merit Award
2008	M. D. Anderson Cancer Center Odyssey Fellow Award, to support the best postdoctoral trainees among the newest generation of cancer researchers at the institution
2008	Susan G. Komen Houston Affiliate Travel Scholarship, to support participation at the American Society of Clinical Oncology 2008 Breast Cancer Symposium
2006	Original 1 st -author paper featured in <i>Nature Clinical Practice Nephrology</i> : Smith GL , et al. Arch Intern Med. 2006 May 22;166(10):1134-42.
2005	Comprehensive exams for Ph.D. passed with <i>distinguished</i> honors, for achieving the highest possible score in epidemiology, biostatistics, and specialty area exams
2005	American Cancer Society Prize, awarded for the outstanding M.D. thesis in cancer
2005	Farr Scholar, awarded for excellence in research, leadership and creativity in pursuit of medical knowledge as a Yale medical student
2005	Campbell Prize, awarded for the highest score on Step Two of the USMLE for graduating students of Yale University School of Medicine
2005	American Medical Women's Association Glasgow Memorial Achievement Citation, awarded for outstanding women graduates of Yale University School of Medicine
2004-2005	American Heart Association, Kidney in Cardiovascular Disease Council writing committee
2003	Co-Chair for educational session, American College of Cardiology national scientific meeting
1998-2000	Scholarship for academic excellence for Yale School of Epidemiology and Public Health

1998	Phi Beta Kappa
1994	Max Roy scholarship for academic excellence, Rice University
1994	National Merit Scholar
1994	Valedictorian, Quince Orchard High School

Publications & Presentations

Commentaries and Review Article

1. **Smith GL**. Commentary on “Disparities in breast cancer treatment and survival for women with disabilities” McCarthy EP et al. *Ann Intern Med* 145:637-645, 2006. *Breast Diseases Quarterly* 2007; 18:211.1
2. **Smith GL**, Buchholz TA. Commentary on “Radiotherapy following breast-conserving surgery for screen-detected ductal carcinoma in situ: indications and utilisation in the UK. Interim findings from the Sloane Project” Dodwell et al. *Br J Cancer* 97:725-9, 2007. *Breast Diseases Quarterly* 2008; 19:168.
3. Smith BD, **Smith GL**, Buchholz TA. Controversies over the role of radiation therapy for ductal carcinoma in situ. *Expert Rev Anticancer Ther.* 2008 Mar;8(3):433-41.
4. **Smith GL**, Buchholz TA. Commentary on “The use of radiation therapy after breast-conserving surgery in hormonally treated breast cancer patients is dependent on patient age, geographic region, and surgeon specialty” Chagpar et al. *Am J Surg* 2008 195:793-8. To be published in *Breast Diseases Quarterly* 2009.

Original Manuscripts:

1. **Smith GL**, Smith BD, Buchholz TA, Liao Z, Jeter M, Swisher SG, Hofstetter WL, Ajani JA, Komaki R, Cox JD. Patterns of care and local-regional treatment outcomes in older esophageal cancer patients. Accepted for publication. *Int J Radiat Oncol Biol Phys* 2008.
2. **Smith GL**, Smith BD, Buchholz TA, Giordano S, Frank S, Schwartz D, Garden A, Morrison W, Chao C, Woodward WA, Yom S, Weber R, Ang KK, Rosenthal D. Cerebrovascular disease risk in older head and neck cancer patients treated with radiation therapy. Accepted for publication. *J Clin Oncol* 2008. Aug 25 2008: Epub ahead of print.
3. **Smith GL**, Smith BD, Giordano SH, Shih YC, Woodward WA, Strom EA, Perkins GH, Tereffe W, Yu T, Buchholz TA. Risk of hypothyroidism in older breast cancer patients treated with radiation. *Cancer* 2008 Mar 15;112(6):1371-9.
4. Smith BD, Haffty BG, **Smith GL**, Hurria A, Buchholz TA, Gross CP. Utilization of Post-Mastectomy Radiation in Older Women. *Int J Radiat Oncol Biol Phys* 2008 May 1;71(1):98-106.
5. **Smith GL**, Masoudi FA, Shlipak MG, Krumholz HM, Parikh CR. Renal function predicts up to 10-year mortality risks after acute myocardial infarction (AMI) in elderly patients. *J Am Soc Nephrol* 2008 Jan 19;141-50. Featured in editorial, Feast and famine: Epidemiology and clinical trials in chronic kidney disease. *J Am Soc Nephrol* 2008 Jan 19; 2-4.
6. Austin B, Wang YF, **Smith GL**, Vaccarino V, Krumholz HM, McNamara R. Systolic function as a predictor of mortality and quality of life in long-term survivors with heart failure. Accepted for publication. *Clin Cardiol* 2007.
7. Parikh CR, Coca SG, **Smith GL**, Vaccarino V, Krumholz HM. Impact of chronic kidney disease on health-related quality-of-life improvement after coronary artery bypass surgery. *Arch Intern Med.* 2006 Oct 9;166(18):2014-9.
8. Brosius FC 3rd, Hostetter TH, Kelepouris E, Mitsnefes MM, Moe SM, Moore MA, Pennathur S, **Smith GL**, Wilson PW. Detection of chronic kidney disease in patients with or at increased risk of cardiovascular disease: a science advisory from the American Heart Association Kidney and Cardiovascular Disease Council; the Councils on High Blood Pressure Research, Cardiovascular Disease in the Young, and Epidemiology and

Prevention; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: Developed in Collaboration With the National Kidney Foundation. *Hypertension*. 2006 Oct;48(4):751-5.

9. Brosius FC 3rd, Hostetter TH, Kelepouris E, Mitsnefes MM, Moe SM, Moore MA, Pennathur S, **Smith GL**, Wilson PW. Detection of chronic kidney disease in patients with or at increased risk of cardiovascular disease: a science advisory from the American Heart Association Kidney And Cardiovascular Disease Council; the Councils on High Blood Pressure Research, Cardiovascular Disease in the Young, and Epidemiology and Prevention; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: developed in collaboration with the National Kidney Foundation. *Circulation*. 2006 Sep 5;114(10):1083-7.
10. Smith BD, Haffty BG, Buchholz TA, **Smith GL**, Galusha DH, Bekelman JE, Gross CP. Effectiveness of radiation therapy in older women with ductal carcinoma in situ. *J Natl Cancer Inst*. 2006 Sep 20;98(18):1302-10.
11. **Smith GL**, Smith BD, Haffty BG. Rationalization and regionalization of treatment for ductal carcinoma in situ of the breast. *Int J Radiat Oncol Biol Phys*. 2006 Aug 1;65(5):1397-403.
12. **Smith GL**, Shlipak MG, Havranek EP, Foody JM, Masoudi FA, Rathore SS, Krumholz HM. Serum urea nitrogen, creatinine, and estimators of renal function: mortality in older patients with cardiovascular disease. *Arch Intern Med*. 2006 May 22;166(10):1134-42.
13. Smith BD, Gross CP, **Smith GL**, Galusha DH, Bekelman JE, Haffty BG. Effectiveness of radiation therapy for older women with early breast cancer. *J Natl Cancer Inst*. 2006 May 17;98(10):681-90.
14. **Smith GL**, Lichtman JH, Bracken MB, Shlipak MG, Phillips CO, DiCapua P, Krumholz HM. Renal impairment and outcomes in heart failure: systematic review and meta-analysis. *J Am Coll Cardiol*. 2006 May 16;47(10):1987-96.
15. Kosiborod M, Curtis JP, Wang Y, **Smith GL**, Masoudi FA, Foody JM, Havranek EP, Krumholz HM. Anemia and outcomes in patients with heart failure: a study from the National Heart Care Project. *Arch Intern Med*. 2005 Oct 24;165(19):2237-44.
16. Cheng S, Lichtman JH, Amatruda JM, **Smith GL**, Mattera JA, Roumanis SA, Krumholz HM. Knowledge of blood pressure levels and targets in patients with coronary artery disease in the USA. *J Hum Hypertens*. 2005 Oct;19(10):769-74.
17. Smith BD, **Smith GL**, Cooper DL, Wilson LD. The cutaneous B-cell lymphoma prognostic index: a novel prognostic index derived from a population-based registry. *J Clin Oncol*. 2005 May 20;23(15):3390-5.
18. **Smith GL**, Shlipak MG, Havranek EP, Masoudi FA, McClellan WM, Foody JM, Rathore SS, Krumholz HM. Race and renal impairment in heart failure: mortality in blacks versus whites. *Circulation*. 2005 Mar 15;111(10):1270-7.
19. Smith BD, **Smith GL**, Haffty BG. Postmastectomy radiation and mortality in women with T1-2 node-positive breast cancer. *J Clin Oncol*. 2005 Mar 1;23(7):1409-19.
20. Cheng S, Lichtman JH, Amatruda JM, **Smith GL**, Mattera JA, Roumanis SA, Krumholz HM. Knowledge of cholesterol levels and targets in patients with coronary artery disease. *Prev Cardiol*. 2005 Winter;8(1):11-7.
21. Shlipak MG, **Smith GL**, Rathore SS, Massie BM, Krumholz HM. Renal function, digoxin therapy, and heart failure outcomes: evidence from the digoxin intervention group trial. *J Am Soc Nephrol*. 2004 Aug;15(8):2195-203.

22. Lichtman JH, Amatruda J, Yaari S, Cheng S, **Smith GL**, Mattera JA, Roumanis SA, Wang Y, Radford MJ, Krumholz HM. Clinical trial of an educational intervention to achieve recommended cholesterol levels in patients with coronary artery disease. *Am Heart J*. 2004 Mar;147(3):522-8.
23. Smith BD, Glusac EJ, McNiff JM, **Smith GL**, Heald PW, Cooper DL, Wilson LD. Primary cutaneous B-cell lymphoma treated with radiotherapy: a comparison of the European Organization for Research and Treatment of Cancer and the WHO classification systems. *J Clin Oncol*. 2004 Feb 15;22(4):634-9.
24. Rathore SS, Foody JM, Wang Y, **Smith GL**, Herrin J, Masoudi FA, Wolfe P, Havranek EP, Ordin DL, Krumholz HM. Race, quality of care, and outcomes of elderly patients hospitalized with heart failure. *JAMA*. 2003 May 21;289(19):2517-24.
25. **Smith GL**, Masoudi FA, Vaccarino V, Radford MJ, Krumholz HM. Outcomes in heart failure patients with preserved ejection fraction: mortality, readmission, and functional decline. *J Am Coll Cardiol*. 2003 May 7;41(9):1510-8.
26. **Smith GL**, Vaccarino V, Kosiborod M, Lichtman JH, Cheng S, Watnick SG, Krumholz HM. Worsening renal function: what is a clinically meaningful change in creatinine during hospitalization with heart failure? *J Card Fail*. 2003 Feb;9(1):13-25.
27. Kosiborod M, **Smith GL**, Radford MJ, Foody JM, Krumholz HM. The prognostic importance of anemia in patients with heart failure. *Am J Med*. 2003 Feb 1;114(2):112-9.
28. Krumholz HM, Amatruda J, **Smith GL**, Mattera JA, Roumanis SA, Radford MJ, Crombie P, Vaccarino V. Randomized trial of an education and support intervention to prevent readmission of patients with heart failure. *J Am Coll Cardiol*. 2002 Jan 2;39(1):83-9.
29. Havranek EP, Masoudi FA, **Smith GL**, Wolfe P, Ralston DL, Krumholz HM, Ordin DL. Lessons learned from the national heart failure project: a Center for Medicare and Medicaid services initiative to improve the care of Medicare beneficiaries with heart failure. *Congest Heart Fail*. 2001 Nov;7(6):334-336.
30. Wexler DJ, Chen J, **Smith GL**, Radford MJ, Yaari S, Bradford WD, Krumholz HM. Predictors of costs of caring for elderly patients discharged with heart failure. *Am Heart J*. 2001 Aug;142(2):350-7.
31. Smith BD, **Smith GL**, Carter D, DiGiovanna MP, Kasowitz KM, Sasaki CT, Haffty BG. Molecular marker expression in oral and oropharyngeal squamous cell carcinoma. *Arch Otolaryngol Head Neck Surg*. 2001 Jul;127(7):780-5.
32. Smith BD, **Smith GL**, Carter D, Sasaki CT, Haffty BG. Prognostic significance of vascular endothelial growth factor protein levels in oral and oropharyngeal squamous cell carcinoma. *J Clin Oncol*. 2000 May;18(10):2046-52.

In Progress

1. **Smith GL**, Smith BD, Garden AS, Rosenthal DI, Sherman SI, Morrison WH, Schwartz DL, Weber RS, Buchholz TA. Hypothyroidism in older head and neck cancer patients after treatment with radiation: A population-based study. Submitted for review.
2. **Smith GL**, Shih YT, Xu Y, Giordano SH, Smith BD, Perkins G, Tereffe W, Woodward WA, Buchholz TA. Racial disparities in treatment for early invasive breast cancer: a national Medicare study of radiotherapy after conservative surgery.
3. **Smith GL**, Shih YT, Xu Y, Giordano SH, Smith BD, Buchholz TA. Breast brachytherapy in the United States: How is this emerging modality being incorporated into the care of older breast cancer patients?

4. **Smith GL**, Shih YT, Giordano SH, Smith BD, Buchholz TA. Predicting breast cancer tumor stage using Medicare claims data.
5. Smith BD, **Smith GL**, Roberts KB, Buchholz TA. Baseline Utilization of Breast Radiotherapy Prior to Institution of the Medicare Practice Quality Reporting Initiative. Submitted for review.
6. Smith BD, **Smith GL**, Hurria A, Buchholz TA. The future of cancer incidence in the United States: Expected burdens upon an aging, changing nation.

Abstracts and Presentations at National Scientific Meetings:

1. **Smith GL**, Shih YT, Xu Y, Giordano SH, Smith BD, Buchholz TA. Breast brachytherapy in the United States: How is this emerging modality being incorporated into the care of older breast cancer patients? Abstract 2008. (Accepted for poster presentation: San Antonio Breast Cancer Symposium)
2. **Smith GL**, Shih YT, Xu Y, Giordano SH, Smith BD, Perkins GH, Tereffe W, Woodward WA, Buchholz TA. Racial disparities in treatment for early invasive breast cancer: A national Medicare study of radiotherapy after conservative surgery. Abstract 2008. (Poster presentation: American Society of Clinical Oncology 2008 Breast Cancer Symposium)
* Highlighted by Medscape Oncology, Cancer News, Reuters, Healthday news, Houston Chronicle, and Houston public radio.
3. **Smith GL**, Smith BD, Giordano SH, Shih YC, Woodward WA, Strom EA, Perkins GH, Oh JL, Tereffe W, Buchholz TA. Risk of hypothyroidism in older breast cancer patients treated with radiotherapy. Abstract 2007 (Poster presentation: American Society for Therapeutic Radiology and Oncology 2007, FD-Era of Hope 2008)
4. Roberts KB, Van Hoff J, **Smith GL**, Gurney JG, Kadan-Lottick NS. Radiotherapy for childhood gliomas: possible detriment in long term survival. Abstract 2007 (Poster presentation: American Radium Society).
5. **Smith GL**, Smith BD, Haffty BG. Trends and variation in radiotherapy use for ductal carcinoma in situ (DCIS): achieving a minimal standard. International Journal of Radiation Oncology, Biology, and Physics 60(1) Suppl: S209-10, 2004. (Oral presentation: American Society for Therapeutic Radiology and Oncology)
6. **Smith GL**, Lichtman JH, Krumholz HM. Functional status and quality of life in heart failure patients with renal impairment. Circulation 106(16):e76, 2002 (Abstract).
7. **Smith GL**, Vaccarino V, Kosiborod M, Lichtman JH, Cheng S, Krumholz HM. Worsening renal function: What is a clinically meaningful change in creatinine during hospitalization with heart failure? Journal of the American College of Cardiology 39 (5) Suppl A: Abstract 890-2, 2002. (Abstract) (Oral presentation: Annual meeting for the American College of Cardiology)
8. **Smith GL**, Radford MJ, Rathore SS, Lichtman JH, Watnick SG, Krumholz HM. Elevated serum creatinine and increased mortality in women and elderly heart failure patients. Journal of the American College of Cardiology 39 (5) Suppl A: Abstract 1098-170, 2002 Mar. (Abstract)
9. **Smith GL**, Havranek EP, Masoudi FA, Wolfe P, Ordin DL, Krumholz HM. Sex and heart failure with preserved systolic function. Journal of Cardiac Failure 7(3) Suppl 1:68, 2001. (Abstract)
10. **Smith GL**, Havranek EP, Masoudi FA, Wolfe P, Ordin DL, Krumholz HM. Sex differences in quality of care for patients with heart failure. Journal of Cardiac Failure 7(3) Suppl 1:76, 2001. (Abstract)

Theses

1. Ph.D.: **Smith GL**. Renal Impairment in Heart Failure: Prevalence, Prognosis, and Detection. 2007.

2. M.D.: **Smith GL**. Patterns of Treatment for Ductal Carcinoma in Situ of the Breast: Rationale for a Minimal Standard. 2005.
3. M.P.H.: **Smith GL**. Social Contact and Hospital Costs in Heart Failure Patients. 2000.
4. B.A. Honors: **Li G**. Race and Resource Utilization by Victims of Domestic Violence: the Houston Area Women's Center. 1998.

Grant Funding

1. Multidisciplinary Postdoctoral Award, Department of Defense Congressionally Directed Medical Research Programs, 2006 Breast Cancer Research Program. Term: July 2007-June 2010. Amount: \$692,344. Project title: Patterns of care and disparities in the treatment of early breast cancer.
2. Odyssey Fellow Award, M. D. Anderson Cancer Center. Term: September 2008-September 2010. Project title: Patterns of care for older breast cancer patients.

Certification

11/2006	United States Medical Licensing Examination, Step III, 99 of 99
1/2005	United States Medical Licensing Examination, Step II-Clinical Skills, <i>pass</i>
7/2004	United States Medical Licensing Examination, Step II-Clinical Knowledge, 99 of 99
6/2003	United States Medical Licensing Examination, Step I, 99 of 99

Peer Reviewer

International Journal of Radiation Oncology, Biology, and Physics

Teaching

2002-2003	Teaching Fellow, Cell Biology and Histology, Yale University School of Medicine
2000	Teaching Fellow, Data Management and Analysis, Yale University School of Public Health

Mentorship

June 2008- August 2008 Anna Zamarripa, The University of Texas M. D. Anderson Cancer Center Summer Intern Program