Published in final edited form as:

Int J Radiat Oncol Biol Phys. 2012 May 1; 83(1): . doi:10.1016/j.ijrobp.2011.05.052.

Trends in the Utilization of Adjuvant Vaginal Cuff Brachytherapy and/or External Beam Radiation Treatment in Stage I and II Endometrial Cancer: A Surveillance, Epidemiology, and End-Results Study

Mehul K. Patel, M.D.^{*}, Michele L. Cote, Ph.D.[†], Rouba Ali-Fehmi, M.D.[‡], Thomas Buekers, M.D.[§], Adnan R. Munkarah, M.D.[§], and Mohamed A. Elshaikh, M.D.^{*}

^{*}Department of Radiation Oncology, Henry Ford Health System, Detroit, Michigan

[†]Karmanos Cancer Institute and Wayne State University Detroit, Michigan

[‡]Department of Pathology, Wayne State University School of Medicine, Detroit, Michigan

[§]Department of Women's Health Services, Division of Gynecologic Oncology, Henry Ford Health System, Detroit, Michigan

Abstract

Purpose—The optimal adjuvant radiation treatment for endometrial carcinoma (EC) remains controversial. Adjuvant vaginal cuff brachytherapy (VB) has emerged as an increasingly common treatment modality. However, the time trends for using VB, external beam radiation therapy (EBRT), or combined therapy (VB+EBRT) have not been well characterized. We therefore examined the utilization trends of VB, EBRT, and VB+EBRT for adjuvant RT in International Federation of Gynecologic Oncology (FIGO) stage I and II EC over time.

Methods and Materials—We evaluated treatment patterns for 48,122 patients with EC diagnosed between January 1995 and December 2005, using the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) public use database. Chi-squared tests were used to assess differences by radiation type (VB, EBRT, and VB+EBRT) and various demographic and clinical variables.

Results—Analyses were limited to 9,815 patients (20.4%) with EC who met the inclusion criteria. Among women who received adjuvant RT, the proportion receiving VB increased yearly (12.9% in 1995 compared to 32.8% in 2005 ($p < 0.0001$)). The increasing use of VB was proportional to the decreasing use of EBRT (56.1% in 1995 to 45.8% in 2005; $p < 0.0001$) and VB+EBRT (31.0% in 1995 to 21.4% in 2005; $p < 0.001$).

Conclusions—This population-based report demonstrates an increasing trend in the use of VB in the adjuvant setting after hysterectomy for treatment of women with FIGO stage I–II EC. VB alone appears to be replacing pelvic EBRT and VB+EBRT therapy in the management of stage I–II EC.

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Reprint requests to: Mohamed A. Elshaikh, M.D., Department of Radiation Oncology, Henry Ford Hospital, 2799 West Grand Blvd., Detroit, MI 48202. Tel: (313) 916-1021; Fax: (313) 916-3235; melshai1@hfhs.org.

Presented at the 51st Annual Meeting of the American Society of Radiation Oncology, Chicago IL, November 1–5, 2009; and the 41st Annual Meeting of the Society of Gynecologic Oncology, San Francisco, CA, March 14–17, 2010.

Conflict of interest: none.

Keywords

Adjuvant; Brachytherapy; Radiation treatment; SEER; Trends; Uterine carcinoma

Introduction

In the United States, uterine cancer is the most common female genital tract malignancy, with an estimated 43,470 cases and 7,950 deaths in 2010 (1). In approximately 75% of cases, the disease is confined to the uterus and cervix at diagnosis (2). The standard treatment for stage I and II disease is total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH/BSO) followed by observation or adjuvant radiation therapy and, in some cases, chemotherapy. Options for adjuvant radiation treatment include pelvic external beam radiation therapy (EBRT) or vaginal brachytherapy (VB) or both (EBRT+VB). However, when radiation is used, the choice of adjuvant radiation modality to best treat patients is controversial.

National Comprehensive Cancer Network practice guidelines recommend observation for stage IA (Grade 1) endometrial adenocarcinoma when adverse factors such as advanced age, positive lymphovascular space invasion, large tumor size, and lower uterine segment (cervical/glandular) involvement are not present (3). In all other uterine cancer-confined cases, recommendations range from observation to VB and/or pelvic RT.

Two modern prospective adjuvant trials have evaluated the efficacy of pelvic EBRT. These postoperative trials randomized patients with early-stage intermediate-risk endometrial adenocarcinoma to undergo observation or EBRT only. The Postoperative Radiotherapy in Endometrial Carcinoma (PORTEC) study included patients with stage IB (Grade 2 or 3) or stage IC (Grade 1 or 2) disease, who underwent TAH/BSO with no routine lymphadenectomy and were randomized to receive either pelvic radiotherapy to a dose of 46 Gy or observation (4). In the Gynecologic Oncology Group (GOG) 99 study, patients with stage IB, IC, or occult stage II disease were eligible for the study (5). Patients underwent TAH/BSO with lymphadenectomy followed by either EBRT to a dose of 50.4 Gy to the pelvis or observation. Both trials demonstrated a decrease in local regional recurrence by 50% without an improvement in overall survival.

In 2003, the American Brachytherapy Society surveyed 551 radiation oncologists. Respondents were asked if they noted an increasing trend for gynecologists to refer patients for VB as opposed to EBRT. Responses showed 54% of respondents believed the trend for VB was increasing, 33% of respondents did not, and 13% of respondents had no opinion (6).

Likewise, in surveys by the Society of Gynecologic Oncologists in 1999 and in 2005, an increasing number of respondents believed that endometrial cancer (EC) surgery required lymphadenectomy (7). Compared to the 1999 survey, respondents in 2005 were more likely to describe surgery for EC as a complete lymphadenectomy (76% in 2005 vs. 44% in 1999) and believed in its therapeutic value (71% in 2005 vs. 66% in 1999), resulting in a decrease in the recommendation for pelvic EBRT.

The objective of this study was to examine the utilization trends of VB, EBRT, and VB +EBRT for adjuvant radiation treatment of 1988 International Federation of Gynecologic Oncology (FIGO) stages I and II EC, using National Cancer Institute's Surveillance Epidemiology and End Results (SEER) public use database.

Methods and Materials

This study used public use data from 17 registries of the SEER program (8), which was initiated by the National Cancer Institute (<http://seer.cancer.gov/data/access.html>). in 1973 to report population-based estimates of cancer incidence, mortality, and survival in the United States. The 17 SEER registries currently cover approximately 26% of the total U.S. population and include the states of Connecticut, Hawaii, Iowa, New Mexico, Kentucky, Louisiana, New Jersey, and Utah; the metropolitan areas of Atlanta, Detroit, and San Francisco-Oakland; Los Angeles County, the four-county area of San Jose-Monterey, and greater California; the 13-county area of Seattle-Puget Sound; rural Georgia; and the Alaska Native tumor registry (9). The populations in these areas are generally representative of the United States population as a whole, although they are somewhat more urban and racially diverse. After cancer is diagnosed by biopsy, medical records are abstracted for patient demographics, primary tumor site, morphology, stage at diagnosis, and first course of cancer-directed treatment (10).

Subjects include women diagnosed with a first primary, histologically confirmed uterine malignancy (according to International Classification of Diseases for Oncology, 3rd edition [ICD-O-3] histology codes for corpus uteri [primary sites C54–C55.9] 8050, 8070, 8140, 8255, 8260, 8310, 8380, 8382, 8383, 8441, 8460, 8461, 8480, 8481, 8560, and 8570) (11). Treatment patterns for 48,122 patients with EC diagnosed between January 1, 1995, and December 31, 2005, were evaluated. Patients with missing treatment data were excluded. Because the goal was to evaluate differences among specific adjuvant radiation modalities, those cases that did not receive adjuvant radiation therapy were excluded ($n = 38,307$). Patients younger than 18 years of age were also excluded ($n = 12$).

A total of 9,815 patients met the inclusion criteria of the study. Differences in distribution of variables by type of adjuvant radiation treatment (VB, EBRT, and VB+EBRT) were assessed for statistical significance by chi-square test, generating two-sided p values. Findings were considered statistically significant at an α value of <0.05 .

Covariates included age (<60 vs. 60 years old); race (black, white); U.S. region (South [consisting of Atlanta, rural Georgia, Kentucky, and Louisiana], Midwest [consisting of Detroit and Iowa], West [including San Francisco-Oakland, CA; New Mexico, Utah, San Jose/Monterey, Los Angeles, and greater California], and Northwest [consisting of Hawaii, Seattle, and Alaska]); marital status (married, unmarried); lymph node dissection (yes, no); number of lymph nodes examined (<10 vs. 10); tumor grade (1, 2, 3, or 4); surgical stage based on 1988 FIGO staging (IA, IB, IC, II, I-NOS, II-NOS); and histological type (endometrioid, serous/clear cell). All data were analyzed using SAS version 9.0 statistical software (Cary, NC).

Results

Patient characteristics

In the current study cohort of 9,815 patients with EC, 33.4% of women were less than 60 years of age, 66.6% were 60 years old or older; 13.2% were single; 51.6% were married; 10.2% were separated or divorced; 22.0% were widowed; and the marital status of 3.0% of women was unknown at the time of diagnosis. Ethnically, 80.2% of patients were white non-Hispanic, 6.6% were black non-Hispanic, 5.4% were Hispanic, and 7.8% were other. Geographically, 36.6 % were from Western United States, 26.1% were from the East, 17.2 % were from the Midwest, 9.4% were from the Northwest, and 10.7% were from the South. A higher proportion of patients from the Midwest were treated with VB+EBRT. Regardless of demographic category, most patients were treated with EBRT (Table 1).

Tumor characteristics

Based on histology, 6% of the study population were classified with either clear cell or serous type cancer, while 94% of tumors were endometrioid adenocarcinoma: 24.9% of tumors were Grade 1, 41.4% of tumors were Grade 2, and 33.7% of tumors were Grade 3 or 4.

Five percent of the patients treated with adjuvant radiotherapy had FIGO stage IA tumors, 31% of patients had IB, and 31.3% of patients had stage IC tumors. Seven percent of tumors were classified as stage I, not otherwise specified. With regard to stage II, 8.4% of tumors were stage IIA, and 9.5% of tumors were stage IIB. Additionally, 7.8% of stage II tumors were not otherwise specified. Furthermore, 40.4% of patients' surgeries did not include lymph node dissection, and in 5% of cases were unknown, whereas 54.5% of patients' surgeries included nodal dissection, of which 57.7% had 10 or more nodes removed. Regardless of tumor characteristic, pelvic EBRT was the most frequently utilized treatment overall (Table 2).

Utilization trends

The proportion of patients who received any form of adjuvant radiation treatment remained stable during the study period. In 1995, 21.5% of study patients received adjuvant RT compared to 20.3% of patients in 2005 ($p = 0.09$).

Figure 1 shows treatment patterns stratified by year of diagnosis (1995–2005). The use of EBRT fell from 56.1% in 1995 to 45.8% in 2005 ($p < 0.0001$). Use of VB+EBRT combined also decreased over the same time period, from 31.0% in 1995 to 21.4% in 2005 ($p < 0.0001$). During the same time period, an increase in the use of VB was observed from 12.9% in 1995 to 32.8% in 2005 ($p < 0.0001$).

Figure 2 shows the trend regarding treatment modality by age. From 1995 to 2005, among those women who received adjuvant radiation treatment, women who were 60 years old or older were more likely to receive EBRT than women younger than 60 ($p = 0.02$). However, the utilization of EBRT has been decreasing in both age groups. In the older age group, use of EBRT decreased from 59.2% in 1995 to 47.3% in 2005. In women younger than 60, the use of EBRT was 49.2% in 1995 compared to 43.6% in 2005.

Likewise, the combination of EBRT+VB has been decreasing in both groups. In the older group, utilization has gone from 28.8% in 1995 to 21.7% in 2005, and in the younger group, the change has been more dramatic, from 36.1% in 1995 to 20.9% in 2005. Meanwhile, the use of VB has increased approximately 20% for both groups.

With regard to histologic type, there is no difference in the utilization of EBRT ($p = 0.10$) or VB+EBRT ($p = 0.62$) for patients with clear cell/serous tumors versus those with endometrioid adenocarcinoma. However, significantly fewer patients received VB for clear cell/serous tumors than for endometrioid adenocarcinoma over the study period ($p = 0.0008$). Differences seen with regard to increasing utilization of VB overall are due to increasing utilization of VB in endometrioid adenocarcinoma, from 11.9% in 1995 to 34% in 2005 ($p < 0.0001$). There was a decrease, albeit not statistically significant, in the utilization of VB for clear cell/serous histology from 28.2% in 1995 to 17.7% in 2005 ($p = 0.59$).

Figure 3 shows the impact of lymph node dissection on the choice of treatment modality over time. Over the study time period, women who did not undergo lymph node dissection were more likely to receive EBRT or EBRT+VB than women whose treatment included lymph node dissection ($p < 0.0001$). There was not a statistically significant difference in the

type of adjuvant radiation treatment over time for women with no lymph nodes dissected ($p = 0.89$). There appeared to be a trend for decreasing utilization of EBRT from 58.5% in 1995 to 43.9% in 2005 ($p = 0.06$) in cases where lymph nodes were dissected. Also, there was increased utilization of VB in women with lymph nodal dissection, from 10.8% in 1995 to 36% in 2005. When lymph node dissection was performed, the median number of lymph nodes examined in our study increased from 9 in 1995 to 13 in 2005 ($p < 0.0001$). For patients with more than 10 lymph nodes examined, the utilization of EBRT decreased from 58.3% in 1995 to 41.2% in 2005 ($p < 0.0001$). For those patients with fewer than 10 lymph nodes examined, use of EBRT decreased, albeit not as dramatically, from 61.5% in 1995 to 49.6% in 2005 ($p = 0.01$).

Figure 4 shows variations by race when examining treatment for white versus black patients ($p < 0.0001$). The proportion of black women who received EBRT was greater than that of white women ($p = 0.03$). Indeed the proportion of black patients who received EBRT has remained steady from 54% in 1995 to 57% in 2005 (ranging from utilization low of 42% in 2002 to a high of 72% in 1999). The percentage of white women who received EBRT in 1995 was 56.2%, and this number decreased to 44% in 2005. There are no differences by race in the proportion of women who receive VB ($p = 0.88$) or VB+EBRT ($p = 0.14$) in the study. However, there is a relatively small number of black patients who underwent adjuvant radiation therapy in this study.

In Figure 5, there are no differences shown between the proportions of patients receiving EBRT, VB, or VB+EBRT with regard to marital status. Similar rates of decline in the utilization of EBRT and EBRT+VB and an increase in the utilization of VB were observed for both groups.

Figure 6 shows the proportion of patients receiving EBRT, VB, or VB+EBRT by geographic region. EBRT is the most common adjuvant treatment modality used across all regions. This is evident in the West as EBRT accounts for greater than 60% of the adjuvant treatment delivered. Use of VB alone is most common in the East and Northwest, accounting for greater than 30% of the cases treated with adjuvant therapy. In the Midwest, use of the combination of EBRT+VB was relatively common, accounting for 35% of the cases treated.

Discussion

Results of the current study demonstrate that the use of pelvic EBRT declined from 1995 to 2005, whereas the use of VB increased during the same time period. These results suggest a significant shift in the treatment approach to early-stage EC over the study period.

Two large prospective randomized studies have demonstrated the benefit of pelvic EBRT with regard to a decrease in both pelvic and vaginal recurrence. However, rates of genitourinary and gastrointestinal acute and chronic side effects were increased with the therapy. In the radiation arm of GOG-99, six cases of Grade 3 bowel obstruction were seen, including two deaths related to small bowel injury (5). Given the toxicity associated with pelvic radiation treatment, it was recommended that it be limited to patients with high intermediate-risk features based on age, grade, depth of myometrial invasion, and lymphovascular space invasion. In the PORTEC study, Grade 2 genitourinary and gastrointestinal toxicity were observed in 2.7% and 5.9% of patients, respectively (4).

To our knowledge, there are no published cooperative group trials randomizing patients with intermediate risk early-stage endometrial adenocarcinoma to receive postoperative adjuvant VB or observation. Nevertheless, in the PORTEC study, 72% of the recurrences in intermediate-risk patients who did not receive adjuvant radiation therapy were located in the

vagina (4, 12). Also, of the patients who did not receive postoperative radiation therapy in the GOG-99 study, 77.8% of locoregional failures included the vagina as a component of failure (5).

In a retrospective study by Jolly *et al.* (13), the outcomes of 243 patients with stage I and II (occult) endometrioid adenocarcinoma (no clear cell or serous papillary) treated with VB alone were compared to those who received EBRT and observation in the GOG-99 study. With a median follow-up of 3.2 years, there were two locoregional recurrences (4% failure rate), which compared favorably to the GOG-99 EBRT arm. Lin *et al.* (14) reviewed the Washington University experience with 78 patients with FIGO stage IA to II (occult) endometrioid adenocarcinoma receiving postoperative VB or VB+EBRT and found no differences in disease-free or overall survival with the addition of EBRT (14). However, two patients treated with VB+EBRT had Grade 3 to 4 gastrointestinal complications. The authors concluded that VB alone results in minimal morbidity and is adequate local therapy for intermediate-risk patients with endometrioid adenocarcinoma after complete surgical staging. Based on these studies, vaginal brachytherapy alone was suggested based on the efficacy of reducing vaginal recurrences while maintaining a better quality of life compared to adjuvant pelvic external beam treatment.

Most recently, the PORTEC-2 study, a Dutch multicenter randomized trial, included patients greater than age 60 with stage IC (Grade 1 or 2) disease or stage IB (Grade 3) disease or patients of any age with stage 2A disease (apart from Grade 3, with greater than 50% myometrial invasion) (15). All patients underwent TAH/BSO without lymphadenectomy and were randomized to receive VB or pelvic EBRT. The study, at 45 months of follow-up, has demonstrated that VB is as effective as pelvic EBRT in ensuring vaginal control, with fewer gastrointestinal toxic effects. The authors concluded that VB should be the adjuvant treatment of choice for patients with EC of high intermediate risk (15). However, the estimated 5-year rate of pelvic recurrence was significantly higher in the VB arm, at 3.8%, than in the EBRT arm, at 0.5% ($p = 0.02$).

In the current study, when lymph node examination was performed, the median number of lymph nodes examined increased from 9 in 1995 to 13 in 2005 ($p < 0.0001$). With extended surgical staging, histologic risk factors may more effectively direct postoperative treatment. In a large single-institution retrospective study by Lutman *et al.* (16), pelvic lymph node count was found to be an important prognostic variable for FIGO stage I and II endometrial carcinoma with high-risk histology. Patients with no recurrence or those with only vaginal recurrences had significantly more pelvic lymph nodes identified than patients with distant recurrences ($p = 0.012$ and $p = 0.022$, respectively).

Smith *et al.* (17), in a study utilizing the SEER database, demonstrated that the presence of a lymph node dissection and an increased number of nodes dissected predicted for improved overall and uterine-specific survival in women with adenocarcinoma of the endometrium. With a trend toward a greater number of pelvic lymph nodes dissected and a large proportion of failures limited to the vagina, the approach limited to vaginal brachytherapy appears to be increasing in the United States.

Other studies, however, have been unable to demonstrate a therapeutic effect of lymphadenectomy. In the Adjuvant Study for Treatment of Endometrial cancer (ASTEC) study, over 1,400 patients were randomized to receive TAH/BSO with or without pelvic lymphadenectomy. There was no benefit in recurrence-free survival or overall survival for pelvic lymphadenectomy in women with early-stage EC (18, 19).

With regard to age, women less than age 60 were less likely to receive EBRT than women who were 60 years of age and older. The increased use of EBRT in older women may be related to the large cooperative trials which have recommended pelvic radiotherapy for women who are in the high intermediate-risk category. In those studies, older age was one of the criteria for high intermediate risk. Nevertheless, there is a decreasing trend for EBRT across both age groups.

Racial variations in the use of specific treatment modalities for adjuvant EC treatment have been reported. In a study by Madison *et al.* (20), African-American patients with EC who were included in the Detroit area SEER cancer registry were more likely to receive radiation therapy compared to Whites (36.1% vs. 30.7%, respectively). After adjusting for stage at diagnosis, the difference was not statistically significant. Details regarding the type of radiation were not available. In the current study, black women received EBRT more often than white women, although, the number of black patients in the current study is relatively small.

There were no significant differences regarding the type of adjuvant treatment as it related to marital status. For other cancers, marital status has been found to influence the choice of therapy. In a SEER study by Copeland *et al.* (21), there were differences in impact on prostate brachytherapy by marital status (21). Married men more commonly received radical prostatectomy, whereas nonmarried men received EBRT and radical prostatectomy equally. However, this study does not demonstrate a difference with regard to marital status. Perhaps there is a difference with regard to the primary therapy for the management of prostate cancer in men compared to adjuvant treatment for EC in women.

Regional variations in the United States between the use of adjuvant radiation therapy for early-stage uterine cancer have been found in the current study. They have also been reported in a previous study. Lee *et al.* (22) observed that the largest variability in radiation therapy use was between different regions within the SEER program. Geographic location had a large effect on overall radiation use and therapy choice. The reason for these discrepancies is unclear. There was a difference in adjuvant EBRT use in a recent population-based study by Kwon and colleagues (23). The purpose of that study was to determine whether there were regional differences in uterine cancer treatment and outcomes in the context of a single-payer, publicly funded health care system. The use of adjuvant VB, however, was not reported in that study. The regional effect in North America is unlikely to be due to case mixture or patient characteristics and more a function of regional practice style. Further research in this area is needed to determine the factors related to this observation.

In determining the significance of this study, limitations should be considered. Within the SEER study, information regarding radiation techniques such as treatment fields, dose, and fractionation are not included. Also, chemotherapy utilization is not captured in the SEER database. Patient information including compliance with treatment and comorbidities are not captured either. Furthermore, the specific lymph node stations which have been dissected are not recorded in the SEER database. Chuang *et al.* (24) proposed nine different lymph node sites to be dissected in order to accurately stage a patient with EC, including left and right para-aortic, common iliac, external iliac, hypogastric, and obturator lymph nodes. A selective approach to sampling that includes biopsy results from both para-aortic and bilateral pelvic lymphatic zones appeared to provide an accurate estimate of true node negativity.

Conclusions

Given its limitations, the present study does not seek to define treatment recommendations. However, based on these data, there appears to be a greater role of lymphadenectomy in the United States. Overall, the proportion of cases treated with vaginal brachytherapy is increasing, and pelvic EBRT is decreasing in frequency, but these frequencies vary by region. If the trend toward greater utilization of VB continues, it may lead to a fundamental shift toward more conservative approaches in the management of endometrial adenocarcinoma.

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Summary

The SEER database was used to evaluate trends in utilization of adjuvant vaginal cuff brachytherapy (VB) and/or external beam radiation (EBRT) in Stage I and II endometrial cancer from 1995 to 2005.

Among women who received adjuvant radiation, the proportion treated with VB increased yearly and EBRT and the combination of VB and EBRT decreased. This suggests a fundamental shift toward more conservative approaches in the management of endometrial cancer.

Fig. 1.
Percentage of EC patients who received different adjuvant radiation treatment modalities between 1995 and 2005 is shown.

Fig. 2.
Percentage of EC patients who received adjuvant radiation treatment modalities between 1995 and 2005, stratified by age is shown.

Fig. 3.

Percentage of EC patients who received adjuvant radiation treatment modalities between 1995 and 2005, stratified by number of lymph nodes examined, is shown.

Fig. 4.

Percentage of EC patients who received adjuvant radiation treatment modalities between 1995 and 2005, stratified by race, is shown.

Fig. 5. Percentage of EC patients who received adjuvant radiation treatment modalities between 1995 and 2005, stratified by marital status, is shown.

Fig. 6. Percentage of EC patients who received adjuvant radiation treatment modalities between 1995 and 2005, stratified by geographic region, is shown.

Characteristics of patients with localized endometrial carcinoma in the SEER-17 (1995–2005) study who received adjuvant radiation treatment

Table 1

Characteristic	EBRT (n = 4,985)		Brachytherapy (n = 2,212)		Combination (n = 2,618)		p value	
	n	%	n	%	n	%	All 3	BR vs. other
Age at diagnosis (years)								
<60	1,563	31.4	805	36.4	909	34.7	<0.0001	0.0007
60+	3,422	68.6	1,407	63.6	1,709	65.3		
Marital Status							<0.0001	<0.0001
Single	704	14.1	274	12.4	318	12.2		
Married	2,479	49.7	1,204	54.4	1,383	52.8		
Separated/divorced	508	10.2	210	9.5	280	10.7		
Widowed	1,163	23.3	437	19.8	563	21.5		
Unknown	131	2.6	87	3.9	74	2.8		
Race/Ethnicity							<0.0001	<0.0001
White non-Hispanic	3,894	78.1	1,895	85.7	2,079	79.4		
Black non-Hispanic	379	7.6	104	4.7	168	6.4		
Hispanic	270	5.4	97	4.4	162	6.2		
Other	442	8.9	116	5.2	209	8		
Region							<0.0001	<0.0001
West	2,175	43.6	611	27.6	807	30.8		
East	1,024	20.5	827	37.4	711	27.2		
Midwest	810	16.3	274	12.4	605	23.1		
Northwest	418	8.4	288	13	215	8.2		
South	558	11.2	212	9.6	280	10.7		

Abbreviation: BR = Brachytherapy.

Table 2

Treatment modality based on tumor characteristics of those with localized endometrial carcinoma in the SEER-17 study (1995–2005)

Characteristic	EBRT (n = 4,985)		Brachytherapy (n = 2,212)		Combination (n = 2,618)		p value	
	n	%	n	%	n	%	All 3	BR vs. other
Histology								
Endometrial	4,576	91.8	2,099	94.9	2,448	93.5	<0.0001	<0.0001
Clear cell + serous	409	8.2	113	5.1	170	6.5		
Tumor grade								
1	1,201	24.1	639	28.9	608	23.2	<0.0001	<0.0001
2	1,952	39.2	993	44.9	1,118	42.7		
3 and 4	1,832	38.7	580	26.2	892	34.1		
Tumor stage								
IA	226	4.5	143	6.5	121	4.6	<0.0001	<0.0001
IB	1,436	28.8	1,040	47	568	21.7		
IC	1,829	36.7	498	22.5	747	28.5		
I, nos	367	7.4	111	5	209	8		
IIA	350	7	218	9.9	253	9.7		
IIB	402	8.1	118	5.3	417	15.9		
II, nos	375	7.5	84	3.8	303	11.6		
Nodes examined								
Yes	2,169	43.5	650	29.4	1,150	43.9	<0.0001	<0.0001
No	2,534	50.8	1,462	66.1	1,356	51.8		
Unknown	282	5.7	100	4.5	112	4.3		
Number of nodes								
<10	1,229	48.5	428	29.3	610	45	<0.0001	<0.0001
10+	1,305	51.5	1,034	70.7	746	55		

Abbreviations: BR = Brachytherapy; nos = Not Otherwise Specified.