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Special Article

The role of postoperative radiation therapy for endometrial cancer: Executive Summary of an American Society for Radiation Oncology evidence-based guideline

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Abstract

Purpose: To present evidence-based guidelines for adjuvant radiation in the treatment of endometrial cancer.

Methods and materials: Key clinical questions to be addressed in this evidence-based guideline on endometrial cancer were identified. A comprehensive literature review was performed to identify studies that included no adjuvant therapy, or pelvic radiation or vaginal brachytherapy with or without systemic chemotherapy. Outcomes included local control, survival rates, and overall assessment of quality of life.

Results: Patients with grade 1 or 2 cancers with either no invasion or <50% myometrial invasion (MI), especially when no other high risk features are present, can be safely observed after hysterectomy. Vaginal cuff brachytherapy is as effective as pelvic radiation therapy at preventing vaginal recurrence for patients with grade 1 or 2 cancers with ≥50% MI or grade 3 tumors with <50% MI. Patients with grade 3 cancer with ≥50% MI or cervical stroma invasion may benefit from pelvic radiation to reduce the risk of pelvic recurrence. There is limited evidence for a benefit to vaginal cuff brachytherapy following pelvic radiation. Multimodality treatment is recommended for patients with positive nodes or involved uterine serosa, ovaries or fallopian tubes, vagina, bladder, or rectum.

Conclusions: External beam and vaginal brachytherapy remain integral aspects of adjuvant therapy for endometrial cancer.

Introduction

The optimal adjuvant treatment for endometrial cancer remains poorly defined despite the prevalence of the disease and a large number of completed prospective studies. This ambiguity can be attributed to inadequate power in many of these studies due to heterogeneity in patient selection criteria, low recurrence rates in early-stage endometrial cancer, and competing risk of death from other causes in women with endometrial cancer. The goal of this article is to provide evidence-based guidelines for adjuvant radiation in the treatment of endometrial cancer. This clinical practice guideline has been endorsed by the Society of Gynecologic Oncology.

Methods and materials

Process and literature review

Please see full-text version for details of the panel selection and review process (this information can be found online as supplemental material at www.practicalradonc.org). An analytic framework, based on the identified population, interventions, comparators, and outcomes was used to refine the search. The population was defined as women of all races, age ≥18 years with stage I-IV endometrial cancer of any histologic grade. Searches were conducted for studies that included patients treated with no adjuvant therapy, or pelvic and/or vaginal brachytherapy with or without systemic chemotherapy. Initially, 1077 abstracts were identified. A total of 330 articles were fully abstracted to provide supporting evidence for the clinical guideline recommendations. The 5 key questions (KQs) and guideline statements are shown in Table 1.

Grading of evidence, recommendations, and consensus methodology

When available, high-quality evidence formed the basis of the recommendation statements in accordance with the Institute of Medicine standards and was categorized by the *American College of Physicians (ACP) Strength of Evidence Rating*. A modified Delphi approach was used to grade the strength of the evidence (ie, strong or weak). Panelists rated the agreement with each recommendation pertaining to the KQs on a 5-point Likert scale, ranging from strongly disagree to strongly agree, as depicted in Table 1 of the full-text version (available as supplemental material online only at www.practicalradonc.org [higher score corresponds with stronger agreement]); a prespecified threshold of ≥75% of raters was determined to indicate when consensus was achieved.[1]

KQ1: Which patients with endometrioid endometrial cancer require no additional therapy after hysterectomy?

Outcomes for low-risk patients

Tumors that are stage I, grade 1 or grade 2, with <50% invasion and endometrioid histology, and which lack risk features such as lymphovascular space invasion or cervical involvement, are generally considered low risk, with an absolute risk of recurrence of <5%. A randomized trial of vaginal brachytherapy versus no further treatment in patients with low-risk endometrial cancer (grade 1 or 2

Table 1 Summary of key questions and guideline statements

Key Question #1: Which patients with endometrioid endometrial cancer require no additional therapy after hysterectomy?	Following total abdominal hysterectomy with or without node dissection, no radiation therapy is a reasonable option for patients with 1) no residual disease in the hysterectomy specimen despite positive biopsy (Grade: strong recommendation, low-quality evidence) or 2) grade 1 or 2 cancers with either no invasion or less than 50% myometrial invasion, especially when no other high-risk features are present (Grade: strong recommendation, high-quality evidence). Patients with the following pathologic features may be reasonably treated with or without vaginal brachytherapy 1) grade 3 cancers without myometrial invasion (Grade: strong recommendation, low-quality evidence) or 2) grade 1 or 2 cancers with less than 50% myometrial invasion and higher risk features such as age greater than 60 and/or lymphovascular space invasion (Grade: strong recommendation, moderate-quality evidence).
Key Question #2: Which patients with endometrioid endometrial cancer should receive vaginal cuff radiation?	Vaginal cuff brachytherapy is as effective as pelvic radiation therapy at preventing vaginal recurrence for patients with 1) grade 1 or 2 cancers with $\geq 50\%$ myometrial invasion or 2) grade 3 tumors with $<50\%$ myometrial invasion (Grade: strong recommendation, moderate-quality evidence). Vaginal cuff brachytherapy is preferred to pelvic radiation in patients with these risk factors particularly in patients who have had comprehensive nodal assessment (Grade: strong recommendation, low-quality evidence).
Key Question #3A: Which women with early stage endometrial cancer should receive postoperative external beam radiation?	Pelvic radiation is an effective means of decreasing pelvic recurrence for early stage patients but has not been proven to improve overall survival. Patients with grade 3 cancer with $\geq 50\%$ myometrial invasion or cervical stroma invasion may benefit from pelvic radiation to reduce the risk of pelvic recurrence (Grade: strong recommendation, high-quality evidence). Patients with grade 1 or 2 tumors with $\geq 50\%$ myometrial invasion may also benefit from pelvic radiation to reduce pelvic recurrence rates if other risk factors are present such as age > 60 years and/or lymphovascular space invasion (Grade: strong recommendation, high-quality evidence).
Key Question #3B: Which women with stage III-IVA endometrial cancer should receive postoperative external beam radiation?	The use of pelvic radiation has been shown to improve survival in some settings. The best available evidence at this time suggests that a reasonable option for adjuvant treatment of patients with positive nodes, or involved uterine serosa, ovaries/fallopian tubes, vagina, bladder, or rectum includes external beam radiation therapy as well as adjuvant chemotherapy (Grade: strong recommendation, moderate-quality evidence). Chemotherapy (Grade: weak recommendation, moderate-quality evidence) or radiation therapy alone (Grade: weak recommendation, low-quality evidence) may be considered for some patients based on pathologic risk factors for pelvic recurrence.
Key Question #4: When should brachytherapy be used in addition to external beam radiation?	Prospective data is lacking to validate the use of vaginal brachytherapy after pelvic radiation and retrospective studies show little conclusive evidence of a benefit, albeit with small patient numbers. Use of vaginal brachytherapy in patients also undergoing pelvic external beam radiation may not generally be warranted, unless risk factors for vaginal recurrence are present (Grade: weak recommendation, low-quality evidence).
Key Question #5: How should radiation therapy and chemotherapy be integrated in the management of endometrial cancer?	The best available evidence suggests that concurrent chemoradiation followed by adjuvant chemotherapy is indicated for patients with positive nodes or involved uterine serosa, ovaries/fallopian tubes, vagina, bladder, or rectum (Grade: strong recommendation, moderate-quality evidence). Alternative sequencing strategies with external beam radiation and chemotherapy are also acceptable (Grade: weak recommendation, low-quality evidence). Chemotherapy (moderate-quality evidence) or radiation therapy alone (low-quality evidence) may be considered for some patients based on pathologic risk factors for pelvic recurrence.

endometrioid cancer with <50% invasion) reported a nonsignificant reduction in vaginal recurrence in the group receiving brachytherapy (3.1% vs 1.2%, $P = .11$).[2] These findings support observing patients with low-risk findings following hysterectomy.

KQ2: Which patients with endometrioid endometrial cancer should receive vaginal cuff radiation?

Vaginal cuff brachytherapy

The most common site of relapse in women with early stage endometrial cancer who do not receive adjuvant radiation therapy is the vaginal cuff.[3] Vaginal cuff brachytherapy reduces the risk of recurrence in the vagina and causes significantly less toxicity than pelvic radiation therapy. The side effects of vaginal cuff irradiation are generally limited to vaginal complications and mild urinary side effects. In the randomized trial described above, 9% of patients receiving brachytherapy developed grade 1 and 2 vaginal toxicity as compared with 1.5% of patients in the observation arm.[2] Grade 1 and 2 urinary side effects were also slightly more common after vaginal irradiation (2.8% vs 0.6%, respectively, $P = .063$) but brachytherapy did not impact the rates of gastrointestinal toxicity.[2]

Brachytherapy dose has been shown to impact vaginal toxicity. A significant reduction in vaginal length was noted when 6 fractions of 5 Gy, rather than 2.5 Gy, were prescribed to 5 mm.[4] There was no difference in rates of vaginal recurrence between these 2 regimens. Seven Gy × 3 prescribed to 5 mm depth is a commonly used fractionation scheme that delivers a comparable dose for late effects to the vaginal surface when compared to the higher dose regimen in the Sorbe trial. As a result, this regimen may be expected to lead to increased vaginal fibrosis as compared with lower dose per fraction regimens. Effective lower dose regimens (6 Gy × 5 or 4 Gy × 6 prescribed to the vaginal surface) have been reported with excellent vaginal control rates and minimal vaginal toxicity.[5] Details on the best technical approach to deliver vaginal cuff brachytherapy have been recently reviewed.[6]

Vaginal cuff radiation therapy for patients with intermediate-risk or high-intermediate risk endometrial cancer

Variable definitions have been used to classify intermediate-risk endometrial cancer, but this group generally includes stage I or II disease with risk factors such as deep myometrial invasion (MI), higher grade, LVSI, and/or older age. The PORTEC [Postoperative Radiation Therapy in Endometrial Carcinoma], and the GOG-99 [Gynecologic Oncology Group] studies enrolled patients at "intermediate risk" and defined a subset of these patients who were at higher risk and thus referred to as "high-intermediate risk".[3,7]

Several studies have investigated whether adjuvant pelvic radiation, vaginal cuff brachytherapy, or observation is optimal for stage I and II patients with intermediate-risk endometrial cancer. The first study, conducted by the Norwegian Radium Hospital, enrolled all clinical stage I endometrial cancers.[8] All patients received brachytherapy followed by a randomization to pelvic radiation or no additional therapy. The addition of external beam radiation decreased local recurrence (7% vs 2%, $P < .01$). Among the subset with deeply invasive grade 3 tumors (19%, 100 of 540 patients enrolled), the overall survival appeared to be higher in the group that received pelvic radiation although no statistical analysis was reported and this was not a planned subset analysis.

More recently, the PORTEC-2 study compared vaginal cuff brachytherapy to pelvic radiation for patients with high-intermediate risk endometrial cancer.[9] Eligibility required that patients be older than 60 with deeply invasive grade 1 or 2 disease or minimally invasive grade 3 disease. The primary endpoint, vaginal recurrence, was equivalent in the external beam and the brachytherapy only arms (1.6% vs 1.8%, $P = .7$). Patients treated with external beam radiation therapy (EBRT) had a lower rate of pelvic recurrence (0.5% vs 3.8%, $P = .02$), but the absolute rate of pelvic recurrence was low in the nonpelvic radiation therapy (RT) arm. A central pathology review was performed after patients were randomized, demonstrating that 79% of patients enrolled in the study had grade 1 cancers. These results suggest that the use of vaginal cuff radiation may be equivalent to pelvic radiation in patients with intermediate risk findings such as deeply invasive grade 1 disease. However, PORTEC-2 included very few patients with deeply invasive grade 2 disease and none with deeply invasive grade 3 disease; therefore, this study does not provide evidence for using vaginal cuff brachytherapy in place of pelvic radiation in these patients.

The most recently reported study compared pelvic radiation followed by vaginal cuff brachytherapy to vaginal irradiation for "medium-risk" endometrial cancer. The results of this study were similar to PORTEC-2, demonstrating that pelvic radiation reduced locoregional relapse rates (1.5% vs 5%, $P = .013$) with no difference in overall survival.[10]

KQ3: Which women with endometrial cancer should receive postoperative external beam radiation?

Pelvic radiation

Pelvic radiation offers the advantage of treating the vagina in addition to the regional lymphatics at risk. As a result, the decision to deliver pelvic radiation is closely tied to the risk of involved pelvic nodes. Pelvic radiation can cause grade 2 or higher diarrhea in 50%-80% of

patients receiving pelvic radiation during and in the immediate posttreatment period.[11] The degree to which IMRT can reduce these symptoms is the focus of an ongoing randomized RTOG study, TIME-C, which is comparing IMRT to standard pelvic radiation. The primary endpoint of this study will be a patient-reported measure of GI toxicity in order to measure the clinical impact of IMRT in this setting.

Evidence for pelvic radiation in intermediate- and high-intermediate risk endometrial cancer

Several trials of slightly different patient populations have compared treatment with EBRT to no adjuvant therapy in patients with early stage endometrial cancer. PORTEC-1 randomized patients with deeply invasive grade 1 or 2 disease or minimally invasive grade 2 or 3 disease to receive pelvic RT (46 Gy) or no further treatment.[3] Pelvic radiation resulted in a reduction in the rate of local recurrence (4% in the RT group and 14% in the control group, $P < .001$). Five-year overall survival rates were similar in the 2 groups: 81% (radiation therapy) and 85% (controls), $P = .31$.

Gynecologic Oncology Group (GOG)-99 was a randomized study that compared pelvic radiation to no additional therapy for patients with stage I or II endometrial cancer with any myometrial invasion.[7] Similar to PORTEC-1, pelvic radiation decreased local recurrence but there was no significant difference in overall survival in the 2 groups. The authors identified a "high-intermediate risk" subset in which the 2-year cumulative incidence of recurrence was 26% without RT versus 6% in the radiation arm. Within this high-risk subset, the 4-year cumulative incidence of death was 26% in patients who did not receive radiation as compared to 12% in patients who did receive RT (no P value reported). It is important to note that neither PORTEC-1 nor GOG-99 was powered to detect a difference in survival.

Recently, the ASTEC [A Study in the Treatment of Endometrial Cancer] study group investigated the benefit of pelvic radiation in patients with early stage uterine confined endometrial cancer; the primary endpoint was overall survival.[12] Approximately 50% of patients on the control arm received vaginal brachytherapy. Isolated pelvic recurrence rate was 6.1% versus 2.9% in the patients that received pelvic radiation but there was no difference in overall survival. There was no evidence that the efficacy of pelvic radiation differed in patients who did or did not undergo lymph node dissection.

Three randomized studies have demonstrated that vaginal radiation provides a comparable reduction in vaginal recurrence as pelvic radiation and that pelvic recurrence rates are low among intermediate-risk patients treated with vaginal cuff brachytherapy. Due to the small number of higher risk patients in these studies, these studies do not provide support for replacing pelvic radiation with vaginal cuff brachytherapy in patients at high risk for pelvic recurrence. Further evidence to address this question may come from the ongoing GOG 0249 study, which is randomizing high-intermediate risk patients to pelvic radiation versus vaginal cuff brachytherapy followed by chemotherapy.

Studies conducted using the Surveillance, Epidemiology, and End Results (SEER) database have also addressed the benefit of pelvic radiation in endometrial cancer. Among 21,249 women, of whom 19.2% received pelvic radiation, patients with invasion of the outer half of the myometrium had significantly better overall survival when pelvic radiation was delivered.[13]

Evidence for external beam radiation in high-risk endometrial cancer

High-risk endometrial cancer has been variably defined in the literature, with deeply invasive grade 3 endometrial cancers through stage III being defined as high risk. Other studies define this group as stage III or IV with disease confined to the peritoneum. Postoperative radiation has tended to be considered standard in this group although a comparative study of adjuvant radiation versus no treatment for this group of patients has not been conducted.[14,15] Several prospective randomized trials have been performed comparing RT to chemotherapy in high-risk patients.

The GOG-122 study compared adjuvant whole-abdominal RT to chemotherapy (doxorubicin and cisplatin for 8 cycles) in patients with stage III or IV (including peritoneally confined with 2 cm or less residual disease) endometrial cancer.[16] The proportion of patients with stage IV disease was higher in the chemotherapy arm so the reported results were "stage-adjusted." The rate of progression-free survival (PFS) after adjusting for stage was significantly higher in the chemotherapy arm than in the whole-abdominal RT arm (5-year PFS rate, 50% vs 38%). The primary endpoint for this randomized trial, PFS, would have revealed no significant difference between the 2 arms without stage adjustment (PFS 42% vs 38%, P value not reported). As a result of this post hoc stage adjustment without reporting the primary randomized trial endpoint (ie, unadjusted), the evidence derived from this trial was classified as "moderate" rather than "high." A major limitation of the study was the inclusion of patients with unresected lesions up to 2 cm in whom the radiation doses delivered would be considered inadequate. Despite the limitations of this study, it established a role for chemotherapy in the treatment of endometrial cancer.

Maggi et al[17] conducted a randomized trial for patients with high-risk endometrioid endometrial cancer (stage IG3 with >50% MI, stage IIG3 with MI >50%, and stage III) comparing adjuvant chemotherapy to adjuvant RT for high-risk endometrial cancer. Chemotherapy consisted of 5 cycles of cisplatin, doxorubicin, and cyclophosphamide. Patients on the RT arm received 45-50 Gy to the pelvis. There was no significant difference in overall or PFS

between the pelvic RT and chemotherapy arms, but there was a nonsignificant trend toward delayed metastasis in the chemotherapy arm and delayed pelvic relapse in the RT arm.

The study by the Japanese Gynecologic Oncology Group (JGOG) randomized patients with deeply invasive stage I through stage IIIC endometrial cancer treated with cyclophosphamide, doxorubicin, and cisplatin or pelvic RT.[18] The majority (77.4%) of the registered patients had stage IC or II lesions, and only 11.9% had stage IIIC lesions. There was no significant difference between the chemotherapy and RT groups in overall or PFS or pattern of relapse. A small high-risk subset was identified that had improved PFS with chemotherapy. However, the study was not stratified for analysis of this subset, nor was this a planned subset analysis, which limits the utility of this observation.

Pelvic recurrence rates have been reported to range from 19%-50% of patients with node positive endometrial cancer who are treated with chemotherapy without external beam,[16,19-21] suggesting that adjuvant RT should be combined with systemic chemotherapy in patients with high-risk endometrial cancer.[17,20-22] Patients with stage III endometrial cancer with grade 1 or 2 endometrioid cancers have excellent outcomes following EBRT alone, which may be appropriate treatment especially for patients with comorbidities that increase the risk of complications from adjuvant chemotherapy.[20] The ongoing GOG 0258 study is comparing pelvic radiation with concurrent and adjuvant chemotherapy to chemotherapy without pelvic radiation in patients with high-risk endometrial cancer, which may shed light on the benefit of pelvic radiation in this setting.

Other pathologic findings can sway decisions regarding indications for pelvic radiation. Cervical stromal invasion is considered a high-risk feature for local recurrence and such patients are generally treated with pelvic radiation following total abdominal hysterectomy. On the other hand, ovarian involvement is generally considered a high-risk feature for peritoneal dissemination. Decisions about RT may be tailored in some cases based on pathologic risk factors for pelvic recurrence.

KQ4: When should brachytherapy be used in addition to external beam radiation?

Rationale for vaginal cuff brachytherapy after pelvic radiation

Supplemental vaginal cuff brachytherapy following pelvic EBRT is widely employed and often included in prospective trial design with the goal of decreasing vaginal recurrence. However, there have been no randomized trials to measure the benefit of brachytherapy after external beam. In this section, we will review available evidence regarding the role of vaginal brachytherapy after pelvic radiation.

Evidence for vaginal cuff brachytherapy after pelvic radiation

The low rate of vaginal recurrence in patients receiving pelvic radiation without brachytherapy leaves little margin for improvement with the addition of brachytherapy.

In the pelvic RT arms of PORTEC-1 and 2, the rates of vaginal recurrence were 2.3% and 1.6%, respectively.[3,9] Among patients with deeply invasive grade 3 tumors, which were included in a nonrandomized cohort of patients who received 46 Gy of pelvic radiation, 2% vaginal apex recurrences were reported.[22] In the JGOG study 1% of women treated with 45-50 Gy of pelvic radiation developed vaginal recurrence.[18]

Several retrospective studies have compared outcomes among patients with endometrial cancer treated with pelvic radiation with and without brachytherapy. Rossi et al[23] compared outcomes in patients with stage IIIC endometrial cancer treated with various approaches utilizing SEER data. Their data suggested that the addition of brachytherapy to external beam radiation was associated with superior outcomes in patients coded as having "direct extension." No data on rate of vaginal recurrence were available and imbalances in clinical or pathologic factors that influence treatment decisions may account for these findings.

Randall et al[24] and Greven et al[25] compared outcomes with stage I endometrial cancer treated with or without brachytherapy after pelvic radiation. Local failure rates in patients receiving external beam versus external beam followed by brachytherapy were not significantly different in either study. Among patients with cervical involvement, the delivery of brachytherapy also did not impact 5-year pelvic disease control.[25,26]

Some studies have reported higher rates of toxicity among patients receiving both brachytherapy and external beam. Randall et al[24] detected a significantly higher rate of complications among patients receiving cuff brachytherapy (18.6% EBRT + cuff vs 3.8% EBRT, $P = .01$) . The higher effective cuff doses (30-50 Gy vaginal cuff boost with low-dose-rate) used in this study may not reflect expected toxicity with the current fractionated high-dose-rate of 5-6 Gy prescribed to the vaginal surface for 2-3 fractions.

KQ5: How should radiation therapy and chemotherapy be integrated in the management of endometrial cancer?

Rationale for combining chemotherapy and external beam radiation in patients with high-risk endometrial cancer

Combined-modality treatment may be the optimal approach to minimize the risk of pelvic and distant recurrence. Feasibility of this approach was tested by the RTOG 9708 study that treated patients with grade 2 or 3 endometrial adenocarcinoma with either > 50% MI, cervical stromal invasion, or pelvic-confined extrauterine disease with concurrent chemoradiation (50 mg/m^2 on days 1 and

28) followed by adjuvant chemotherapy (4 cycles of cisplatin and paclitaxel given at 4-week intervals).[27] Toxicity was acceptable and 98% of patients were able to complete the planned treatment regimen. Overall survival and disease-free survival rates at 4 years were 85% and 81%, respectively. The pelvic recurrence rate was only 2% at 4 years. A similar regimen has been employed as 1 arm of GOG 0258, which is comparing combined-modality treatment to chemotherapy alone for patients with high-risk endometrial cancer.

Evidence for chemoradiation approaches

Hogberg et al[28] reported on the role of combined RT and chemotherapy delivered using a sequential approach for patients with high-risk endometrial cancer. These investigators reported merged data from 2 independent randomized studies: the Instituto Mario Negri (MANGO), and the Nordic Society for Gynaecologic Oncology (NSGO)/European Organization for Research and Treatment of Cancer (EORTC). The NSGO/EORTC included predominantly high-risk stage I and II patients (97%) while MANGO included stage II and III patients with endometrioid histology. Patients were randomized in each trial to RT alone or RT with adjuvant chemotherapy. Progression-free survival was significantly higher in the arm receiving chemotherapy in the NSGO study while the MANGO trial independently showed a trend toward a PFS benefit with chemotherapy (hazard ratio [HR], 0.61; 95% confidence interval [CI], 0.33-1.12; P = .10). In the combined dataset, patients who received combined-modality treatment had a 36% reduction in recurrence and improved cancer-specific survival (HR, 0.55; 95% CI, 0.35-0.88; P = .01). Surprisingly, the benefit was limited to the endometrioid histology subgroup as there was no benefit to chemotherapy seen in the NSGO/EORTC trial for patients with papillary serous or clear cell histology (HR, 0.83; 95% CI, 0.42-1.64; P = .59). Of note, this was an unplanned subset analysis, which was not powered to address this question.

The optimal sequencing of radiation and chemotherapy was investigated by Alverez Secord et al[29] by comparing the outcome of 356 women treated with different approaches. After controlling for stage, age, grade, race, histology, and cytoreduction status but not institution, a subgroup analysis of 83 patients found overall survival was best in patients treated with chemotherapy followed by radiation therapy followed by additional chemotherapy, referred to as a "sandwich" regimen. The retrospective nature, small patient number, imbalance in histologic subtypes between the arms as well as the complex modeling performed are significant limitations of this study. This strategy has the advantage of ensuring that RT does not compromise the ability to deliver adjuvant chemotherapy. A disadvantage is that radiation therapy is delayed beyond the immediate postoperative period which may negatively impact local control based on observations in other disease sites. Furthermore, chemotherapy delivery is interrupted which has unknown effects on the efficacy of treatment.

Conclusions

External beam and vaginal brachytherapy remain integral aspects of adjuvant therapy for endometrial cancer. The clinical and pathologic risk factors for recurrence are well characterized and high-quality evidence demonstrates that radiation therapy reduces pelvis recurrences. The decision to deliver external beam, brachytherapy, or no adjuvant radiation should be decided after careful consideration of an individual's risk factors for local recurrence. Ongoing trials should provide further insights into the optimal use of radiation therapy.

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new developments that are not reflected in this guideline, and that may, over time, be a basis for ASTRO to consider revisiting and updating the guideline.

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