



**Postoperative Radiation Therapy for Endometrial Cancer:
American Society of Clinical Oncology Clinical Practice Guideline
Endorsement of the American Society for Radiation Oncology
(ASTRO) Evidence-Based Guideline**

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Reprinted from Practical Radiation Oncology, vol. 4 (issue 3), Klopp, A, Smith, B., Alektiar, K., et al. The role of postoperative radiation therapy for endometrial cancer: Executive Summary of an American Society for Radiation Oncology evidence-based guideline, 137-144, (2014), with permission from Elsevier on behalf of the American Society for Radiation Oncology

Introduction

- Endometrial cancer is the most common gynecologic cancer among U.S. women, and second most common worldwide.
- Surgery is the primary treatment for endometrial cancer with many women (early stages, low risk of recurrence) requiring no additional treatment.
- Additional treatment for women with intermediate/high risk include radiation therapy, chemotherapy, or a combination of these modalities.
- To provide guidance on the use of postoperative radiation therapy for endometrial cancer, the American Society for Radiation Oncology (ASTRO) published evidence-based recommendations in *Practical Radiation Oncology* in 2014.

ASCO Endorsement Methodology

The ASCO Clinical Practice Guidelines Committee endorsement review process includes:

- a methodological review by ASCO guidelines staff
- a content review by an ad hoc expert panel
- final endorsement approval by ASCO CPGC.

The full ASCO Endorsement methodology supplement can be found at:

www.asco.org/endorsements/endometrial

The full original ASTRO Guideline Methodology can be found at:

[http://www.practicalradonc.org/article/S1879-8500\(14\)00005-8/fulltext](http://www.practicalradonc.org/article/S1879-8500(14)00005-8/fulltext)

Clinical Questions

- 1) Which patients with endometrioid endometrial cancer require no additional therapy after hysterectomy?
- 2) Which patients with endometrioid endometrial cancer should receive vaginal cuff radiation?
- 3) A) Which women with early-stage endometrial cancer should receive postoperative external beam radiation?
B) Which women with stage III-IVA endometrial cancer should receive postoperative external beam radiation?
- 4) When should brachytherapy be used in addition to external beam radiation?
- 5) How should radiation therapy and chemotherapy be integrated in the management of endometrial cancer?

Target Population and Audience

- Target population for the ASTRO guideline: women with stage I-IV endometrial cancer of any histologic grade.
- Target Audience: Medical oncologists, gynecologic oncologists, radiation oncologists, and surgical oncologists.

Summary of Recommendations

Q1: 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 without residual disease in the hysterectomy specimen despite positive biopsy (*despite a positive pre-hysterectomy biopsy of any grade*)
- Following total abdominal hysterectomy with or without node dissection, no radiation therapy is a reasonable option for patients with grade 1 or 2 cancers with either no invasion or <50% myometrial invasion.
- Vaginal cuff brachytherapy may be considered in patients with negative node dissection with grade 3 tumor without myometrial invasion.
- Vaginal cuff brachytherapy may be considered in patients with negative node dissection with grade 1 or 2 tumors with <50% myometrial invasion and higher-risk features, such as age >60 and/or LVSI.

Summary of Recommendations

Q2: 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 tumors with $\geq 50\%$ myometrial invasion or (2) grade 3 tumors with $< 50\%$ myometrial invasion.
- Vaginal cuff brachytherapy is preferred to pelvic radiation in patients with the above risk factors particularly in patients who have had comprehensive nodal assessment.

Summary of Recommendations

Q3: Which women should receive postoperative external beam radiation?

- *To date, there is no documented improvement in overall survival for women with endometrial cancer treated with EBRT, and long-term complications including bowel and bladder dysfunction or secondary cancers have been reported.*
- 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.
- Patients with grade 1 or 2 tumors with $\geq 50\%$ myometrial invasion may also benefit from pelvic radiation to reduce pelvic recurrence if other risk factors are present, such as age >60 years and/or LVSI. ***Vaginal brachytherapy may be a better option for patients with these features, especially if surgical staging was adequate and nodes were negative.***

Summary of Recommendations

Q3: Which women should receive postoperative external beam radiation?

- The best available evidence at this time suggests that reasonable options 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. ***The best evidence for this population supports the use of chemotherapy, but consideration of external beam radiation is reasonable.***
- Chemotherapy without external beam radiation may be considered for some patients with positive nodes, or involved uterine serosa, ovaries/fallopian tubes, vagina, bladder, or rectum based on pathologic risk factors for pelvic recurrence.
- Radiation therapy without chemotherapy may be considered for some patients with positive nodes, or involved uterine serosa, ovaries/fallopian tubes, vagina, bladder, or rectum based on pathologic risk factors for pelvic recurrence. ***Patients receiving chemotherapy appear to have improved survival compared with radiation alone, unless the patient is not a candidate for chemotherapy.***

Summary of Recommendations

Q4: 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 most retrospective studies show no evidence of a benefit, albeit with small patient numbers. Use of vaginal brachytherapy in patients also undergoing pelvic external beam radiation is not generally warranted, unless risk factors for vaginal recurrence are present.

Summary of Recommendations

Q5: How should radiation therapy and chemotherapy be integrated in the management of stage I-III endometrioid 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. ***Evidence regarding concurrent chemoradiation is limited at this time, and this recommendation is based on expert opinion; we anticipate level 1 evidence from upcoming prospective randomized clinical trials (GOG 0258 and PORTEC-3). Chemotherapy may also be considered in certain high-risk early stage endometrial cancer patients, and clinical trials of this question are underway.***
- Alternative sequencing strategies with external beam radiation and chemotherapy are also acceptable. ***Small, prospective trials have examined sequential radiation followed by chemotherapy. “Sandwich”-type therapy currently has only limited, non-randomized evidence.***

Discussion

The following topics are discussed at greater length within the endorsement:

- Lack of a survival benefit with external beam radiotherapy (EBRT) in early-stage disease
- Choosing vaginal brachytherapy over external beam radiotherapy in high-intermediate risk disease for locoregional control
- Long-term adverse effects of external beam radiation therapy
- Chemotherapy in women with high-risk, early-stage and advanced disease
- The importance of clinical trials
- Consideration of fertility and quality of life

Endorsement Recommendation

- ASCO endorses The Role of Postoperative Radiation Therapy for Endometrial Cancer: An ASTRO Evidence-Based Guideline, published in 2014 by Klopp et al in *Practical Radiation Oncology*, with qualifying statements.

Additional Resources

More information, including a Data Supplement with a reprint of all ASTRO recommendations, a Methodology Supplement, slide sets, and clinical tools and resources, is available at

www.asco.org/endorsements/endometrial

Original ASTRO Guideline:

[http://www.practicalradonc.org/article/S1879-8500\(14\)00005-8/fulltext](http://www.practicalradonc.org/article/S1879-8500(14)00005-8/fulltext)

Patient information is available at www.cancer.net

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