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## Evidence-based Series #4-10: Section 1

# Adjuvant Radiotherapy in Women with Stage I Endometrial Cancer: A Clinical Practice Guideline

*H. Lukka, A. Chambers, A. Fyles, K. Thephamongkhol, L. Elit, M. Fung-Kee-Fung, J. Kwon, T. Oliver,  
and members of the Gynecology Cancer Disease Site Group*

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### Questions

What is the role of adjuvant radiotherapy in women with stage I endometrial cancer? Specifically, are there subgroups of patients with stage I endometrial cancer who benefit from adjuvant radiotherapy? If so, which radiotherapy treatment is recommended? Outcomes of interest are survival, pelvic control, ultimate pelvic control, and toxicity.

### Target Population

Women with newly diagnosed stage I endometrial cancer who have undergone surgery, either complete surgical staging or total abdominal hysterectomy and bilateral salpingo-oophorectomy. Of interest are outcomes reported by risk of recurrence: low risk (stage IA, IB, grades 1 & 2), intermediate risk (stage IC, grades 1 & 2, or stage IA, IB, grade 3), or high risk (stage IC, grade 3).

### Recommendations

There is a lack of consistent well-conducted randomized controlled trial evidence related to the clinical questions. Based on the interpretation of evidence from the available randomized data and expert consensus opinion, the Gynecology Cancer Disease Site Group recommends the following:

- Regardless of surgical staging, adjuvant external beam radiotherapy:
  - is recommended for patients at **high risk** of recurrence.
  - is not recommended in patients at **low risk** of recurrence,
  - is a reasonable treatment option for patients at **intermediate risk** of recurrence,
    - Two randomized trials detected that adjuvant external beam radiotherapy improved pelvic control, but not survival, when compared to no further treatment.
    - In patients with no adjuvant therapy, salvage radiotherapy may be effective upon vaginal recurrence.
    - When considering adjuvant radiotherapy, the potential improvement in pelvic control needs to be weighed against the toxicity of radiotherapy.
    - Radiotherapy was associated with a low incidence of severe acute and late adverse effects; however, many patients experienced mild (grade 1 or 2) side effects. The long-term effects of radiotherapy are unknown at this time.

- There is insufficient evidence to reliably inform the use of intracavitary radiotherapy either alone or in combination with external beam radiotherapy.
  - One randomized trial detected improvements in pelvic control with combined radiotherapy; however, that trial was published in 1980, toxicity was not well reported, and subsequent trials with similar comparisons have not been identified.
  - There were no randomized trials directly comparing external beam radiotherapy alone versus intracavitary treatment alone.
- Complete surgical staging provides additional pathological information and may help guide treatment decisions involving adjuvant therapies.
- With the potential for substantial grade changes upon pathology review, which may influence decisions regarding adjuvant radiotherapy, it may be important for each jurisdiction to establish a level of quality assurance with specific indications for pathology review. However, the extent to which quality assurance can be determined is outside of the scope of this report.

### **Key Evidence**

- No significant differences in disease-free or overall survival were detected between treatment arms in any of the five randomized controlled trials identified in the search of the literature.
- Three trials detected significant improvements in pelvic control with the use of external beam radiotherapy (delivered either alone or in combination with intracavitary radiotherapy).
- No significant differences in distant recurrence were detected between treatment arms in any of the randomized trials.
- One trial reported that upon recurrence, salvage radiotherapy was effective for establishing pelvic control (70% survival rate at 5 years).
- As part of post hoc subgroup analyses, which should be interpreted with caution, three trials reported results according to risk of recurrence. The determination of risk of recurrence was not consistently defined across the trials; however, the magnitude of the reduction of pelvic recurrence with radiotherapy was:
  - for low-risk subgroups, an approximate 2%-5% reduction,
  - for intermediate-risk subgroups, an approximate 5%-10% reduction,
  - for high-risk subgroups, an approximate 15% reduction.

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#### *Contact Information*

For further information about this series, please contact **Dr. Michael Fung-Kee-Fung**, Chair, Gynecology Cancer Disease Site Group; Ottawa General Hospital, 501 Smyth Road, Ottawa, Ontario; Telephone: 613-737-8560, FAX: 613-737-8828

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