



# 子宫内膜癌分期（FIGO）

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## I 肿瘤限于子宫体

IA 肿瘤浸润深度 $<1/2$ 肌层

IB 肿瘤浸润深度 $\geq 1/2$ 肌层

## II 肿瘤浸润宫颈间质，但无宫体外蔓延

## III 肿瘤局部和（或）区域扩散

IIIA 肿瘤累及浆膜层和（或附件）

IIIB 肿瘤累及阴道和（或）宫旁

IIIC 盆腔淋巴结和（或）主动脉旁淋巴结转移

IIIC1 盆腔淋巴结转移

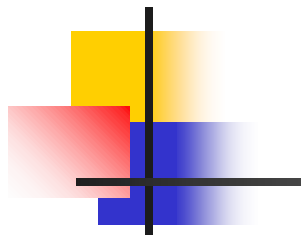
IIIC2 主动脉旁淋巴结转移伴有（或无）盆腔淋巴结转移

## IV 肿瘤浸及膀胱和（或）直肠粘膜，和（或）盆腔淋巴结转移

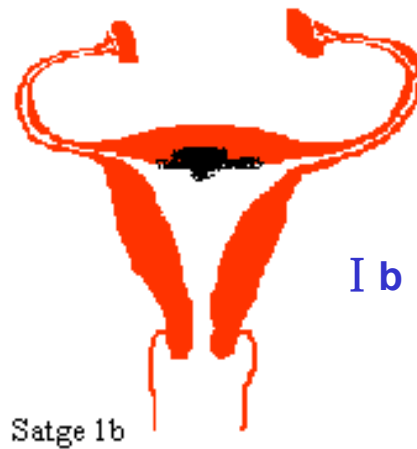
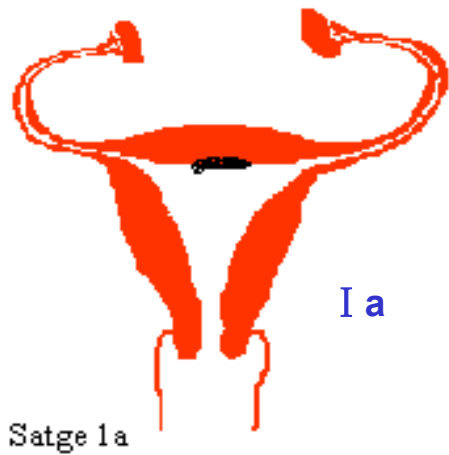
IV1 肿瘤浸及膀胱或直肠粘膜

IV2 远处转移，包括腹腔内和（或）腹股沟淋巴结转移

# 手术病理分期 (FIGO, 1988, ) Surgical Stage



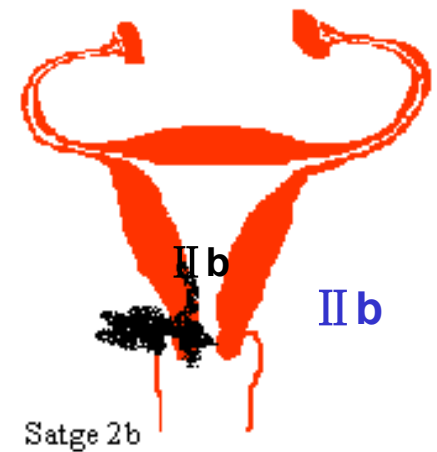
I a



I b

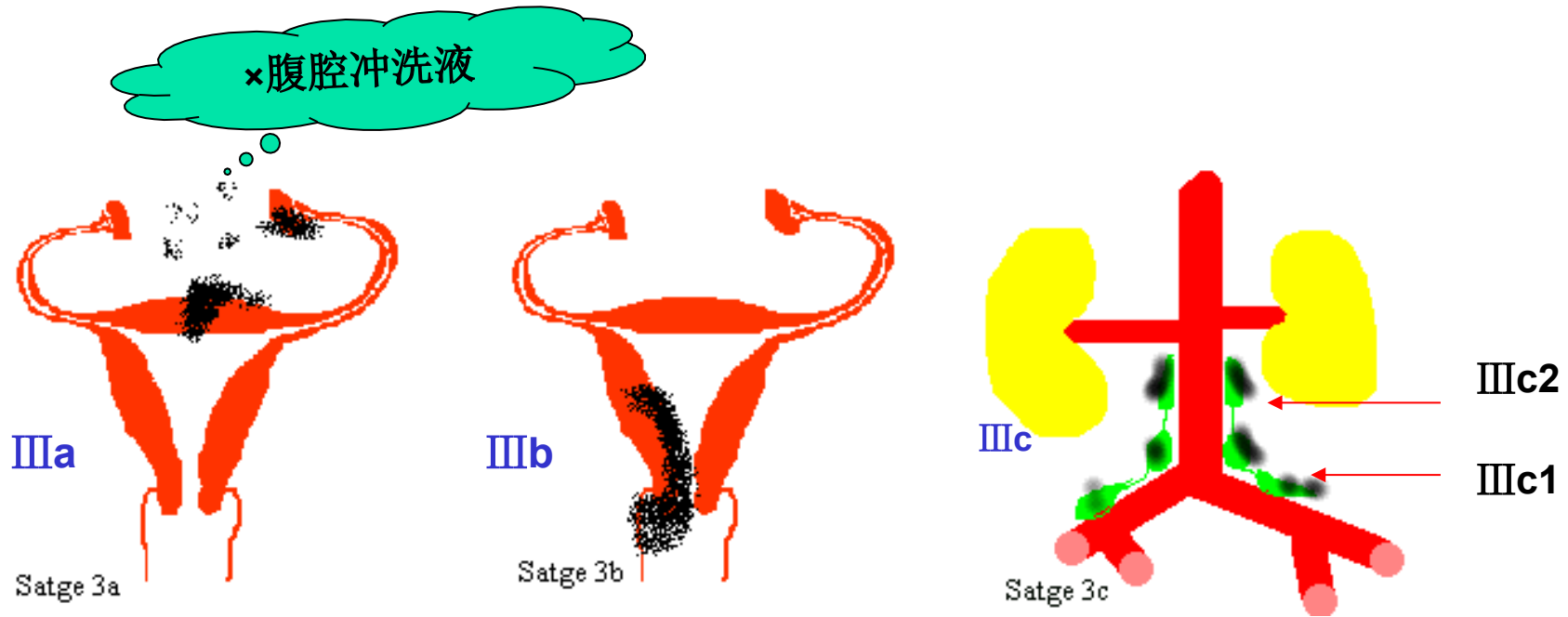


II



# 手术病理分期 (FIGO, 1988, )

## Surgical Stage



IVa期: 癌瘤浸润膀胱或直肠粘膜

IVb期: 远处转移

## 早期子宫内膜癌

**GOG: 仅考虑细胞分化程度和肌层浸润, 5  
年生存率92.7%**

Relationship between surgical-pathologic risk factors and outcome in stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study. *Gynecol Oncol*, 1991, 40:55-65.

# I期术后的辅助治疗



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Cancer  
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## NCCN Guidelines Version 3.2012 Endometrial Carcinoma

[NCCN Guidelines Index](#)  
[Uterine Neoplasms TOC](#)  
[Discussion](#)

All staging in guideline is based on updated 2010 FIGO staging. (See ST-1)

### CLINICAL FINDINGS

### ADVERSE RISK FACTORS<sup>m</sup> HISTOLOGIC GRADE/ADJUVANT TREATMENT<sup>b,n</sup>

		G1	G2	G3	
Completely surgically staged: Stage I	Stage IA (< 50%) myometrial invasion	Adverse risk factors not present	Observe	Observe or Vaginal brachytherapy	Observe or Vaginal brachytherapy
		Adverse risk factors present	Observe or Vaginal brachytherapy	Observe or Vaginal brachytherapy and/or pelvic RT (category 2B for pelvic RT)	Observe or Vaginal brachytherapy and/or Pelvic RT
	Stage IB (≥ 50%) myometrial invasion	Adverse risk factors not present	Observe or Vaginal brachytherapy	Observe or Vaginal brachytherapy	Observe or Vaginal brachytherapy and/or Pelvic RT
		Adverse risk factors present	Observe or Vaginal brachytherapy and/or Pelvic RT	Observe or Vaginal brachytherapy and/or Pelvic RT	Pelvic RT and/or Vaginal brachytherapy ± chemotherapy <sup>o,p</sup> (category 2B for chemotherapy) or Observe (category 2B)

# II期术后辅助治疗



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## NCCN Guidelines Version 3.2012 Endometrial Carcinoma

[NCCN Guidelines Index](#)  
[Uterine Neoplasms TOC](#)  
[Discussion](#)

All staging in guideline is based on updated 2010 FIGO staging. ([See ST-1](#))

### CLINICAL FINDINGS

### HISTOLOGIC GRADE/ADJUVANT TREATMENT<sup>b,n,p</sup>

G1

G2

G3

Completely  
surgically staged:  
Stage II<sup>q,r</sup>

Vaginal brachytherapy  
and/or pelvic RT

Pelvic RT  
+ vaginal brachytherapy

Pelvic RT  
+ vaginal brachytherapy  
± chemotherapy<sup>o,p</sup>  
(category 2B for chemotherapy)

Completely  
surgically staged:  
Stage IIIA

Chemotherapy ± RT  
or  
Tumor-directed RT  
± chemotherapy  
or  
Pelvic RT  
± vaginal brachytherapy

Chemotherapy ± RT  
or  
Tumor-directed RT  
± chemotherapy  
or  
Pelvic RT  
± vaginal brachytherapy

Chemotherapy ± RT  
or  
Tumor-directed RT  
± chemotherapy  
or  
Pelvic RT  
± vaginal brachytherapy



## 问题

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- 哪些需要术后辅助治疗
- 哪些腔内放疗足够
- 哪些的确需要盆腔放疗



# 术后复发及转移的高危因素

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- **高危因素：**

- 细胞学分化程度

- 肌层浸润

- 病理类型

- **相对高危因素：**

- 年龄

- 脉管瘤栓

- 肿瘤大小

- 子宫下段（宫颈腺体）受累





# Prognostic Factors

## Effect of individual prognostic factors on relative risk to survival

Prognostic factor	Relative risk
■ Endometrioid histology	
Grade 1	1.0
Grade 2	1.6
Grade 3	2.6
■ Serous histology	
Grade 1	2.9
Grade 2	4.4
Grade 3	6.6
■ Myometrial penetration	
endometrium only	1.0
inner 1/3	1.2
inner 2/3	1.6
outer 1/3	3.0
■ Positive washings	3.0
■ Age	
45 years	1.0
65 years	3.4
Lymphovascular space involvement	1.5

Keys et Al. A phase III trial of Surgery vs with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: A Gynecologic Oncology Group study. *Gynec. Oncology*. 92(3). 744-751. 2004



# Prognostic Factors

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危险因素	5年生存率
多于2个	17%
2个	66%
无或1个	95%

Creutzberg et Al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma; multicentric randomised trial. Lancet. 355: 1404-1411. 2000



# 危险度分组I (Risk Classification)

- **低危组 (LR)** : 肿瘤限于子宫, 侵犯肌层 $<50\%$ , 高、中分化
- **中危组 (IR)** : 侵犯子宫肌层 $\geq 50\%$ , 或G3, 或宫颈受侵。再根据3个高危因素: 脉管瘤栓, 外1/3肌层受累, 分化程度 (G2, G3)
  - 中高危 (HIR)** : 3个高危因素, 任何年龄;  
2个高危因素及50至69岁;  
1个高危因素及70岁以上.
  - 中低危 (LIR)** : 除上述中高危组以外的中危组
- **高危组 (HR)** : 子宫外或淋巴结转移。

Relationship between surgical-pathologic risk factors and outcome in stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study. *Gynecol Oncol*, 1991, 40:55-65.

A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol*. 2004 Mar; 92(3):744-51.



## 危险度分组II (Risk Classification )

- 低危组 (LR) : 局限于子宫内膜的G1和G2期的子宫内膜样腺癌
  
- 中危组 (IR) : 病变局限于子宫, 但肌层受侵或宫颈间质受侵, 包括 部分IA期, 全部IB期, 部分II期。再根据3个高危因素: 脉管瘤栓, 外1/3肌层受累, 分化程度 (G2, G3)
  - 中高危 (HIR) : 3个高危因素, 任何年龄;
  - 2个高危因素及50至69岁;
  - 1个高危因素, 70岁以上.
  - 中低危 (LIR) : 除上述中高危组以外的中危组
  
- 高危组 (HR) : 包括任何分化程度的宫颈大肿瘤受累, III期, IVA期, 及特殊病理类型如papillary serous or clear cell uterine tumors
  
  
- Contemporary management of endometrial cancer. Lancet. Apr 7;379(9823):1352-60.



# 危险度分组III (Risk Classification)

- 低危组 (LR) : I期子宫内膜样腺癌, G1和G2期, 肌层受侵 <50%
  
- 中危组 (IR) : 其它的I期子宫内膜样腺癌。
  - 中低危 (LIR) : 年龄<60岁;
    - G1或G2且肌层受累>50%;
    - G3肌层受侵<50%;
    - 无脉管瘤栓。
  - 中高危 (HIR) : 年龄>60岁;
    - G1或G2且肌层受累>50%;
    - G3肌层受侵<50%.
  
- 高危组 (HR) : I期的G3且肌层受累>50%, II期, III期的子宫内膜样腺癌, 及特殊病理类型如papillary serous or clear cell uterine tumors.
  - 
  - Surgery and postoperative radiotherapy versus surgery alone for patients with stage-I endometrial carcinoma: multicentre randomised trial. PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. Lancet. 2000 Apr 22;355(9213):1404-11.
  - The Role of Radiotherapy in Endometrial Cancer: Current Evidence and Trends. Curr Oncol Rep ( ) 13:472 - 478



## 低危组

### 子宫内膜样腺癌IA期，肌层受侵 <50%，G1和G2期

- 5年生存率达95%以上；
- 放疗不能改善局控率（包括阴道残端），总复发率及总生存率；
- 增加治疗相关并发症
- 局部复发后治疗仍取得高生存率。

■结论：不需要辅助治疗

■Elliott P, Green D, Coates A, et al. The efficacy of postoperative vaginal irradiation in preventing vaginal recurrence in endometrial cancer.

■ Int J Gynecol Cancer 1994; 4: 84 - 93.

■ Karolewski K, Kojs Z, Urbanski K, et al. The efficiency of treatment in patients with uterine-confined endometrial cancer. Eur J Gynaecol Oncol 2006; 27: 579 - 84.

■Touboul E, Belkacemi Y, Buffat L, et al. Adenocarcinoma of the endometrium treated with combined irradiation and surgery: study of 437 patients. Int J Radiat Oncol Biol Phys 2001; 50: 81 - 97.

■Mariani A, Webb MJ, Keeney GL, Haddock MG, Calori G, Podratz KC. Low-risk corpus cancer: is lymphadenectomy or radiotherapy necessary? Am J Obstet Gynecol 2000; 182: 1506 - 19.

■Sorbe B, Nordstrom B, Maenpaa J, et al. Intravaginal brachytherapy in FIGO stage I low-risk endometrial cancer: a controlled randomized study. Int J Gynecol Cancer ;19: 873 - 78.



## 中危组及高危组（早期子宫内膜癌）

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目前无令人信服的研究证实辅助治疗提高生存率。

- 中低危组
- 中高危组

# 术后辅助放疗

	Sample size	Inclusion criteria	Surgery	Treatment	Locoregional recurrence	Overall survival
Norwegian Radium Hospital <sup>57</sup>	540	Stage I (all)	TAH or BSO	Brachytherapy vs brachytherapy and pelvic radiotherapy	7% vs 2% (5 year) p<0.01	89% vs 91% (5 year) p=NS
PORTEC-1 <sup>55</sup>	715	Stage IB (grade 2, 3), stage IC (grade 1, 2)	TAH or BSO (LNS allowed)	Observation vs pelvic radiation	14% vs 4% (5 year), p<0.0001	85% vs 81% (5 year), p=0.0001
GOG 99 <sup>56</sup>	392	Stage IB, stage IC, stage II occult	TAH or BSO or LNS	Observation vs pelvic radiation	12% vs 3% (2 year), p=0.007	86% vs 92% (4 year), p=0.0001
ASTEC <sup>58</sup>	905	Stage IA or IB (grade 3), IC, IIA	TAH or BSO with or without LNS	Observation vs pelvic radiation	6.1% vs 3.2% (5 year), p=0.02	84% vs 84% (5 year), p=0.0001
PORTEC-2 <sup>59</sup>	427	Stage IC (grade 2, 3, age >60 years), IB (grade 3, age >60 years), IIA	TAH or BSO with or without LNS	Brachytherapy vs pelvic radiation	5.1% vs 2.1% (5 year), p=0.42	86% vs 82% (5 year), p=0.0001

TAH=total abdominal hysterectomy. BSO=bilateral salpingo-oophorectomy. LNS=lymph node surgery. NS=not significant.

**Table 3: Randomised controlled trials of adjuvant therapy for intermediate-risk endometrial cancer**

Contemporary management of endometrial cancer. Apr 7;379(9823):1352-60





# The Norwegian trial

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**方法：** 540 患者，手术+镭腔内放疗后，随机分为不加盆腔放疗组及加盆腔淋巴结放疗。随访3-10年。

**结果：**

1. 盆腔放疗组阴道残端及盆腔的复发率明显下降 (1.9 vs 6.9%,  $P < .01$ )
2. 盆腔放疗组远处转移率则增加 (9.9 vs 5.4%) .
3. 5年生存率无差异 (91% vs 89%)
4. G3, 肌层浸润大于50%的患者在局控率和总生存率上可能受益 (18% vs 27%) , 但样本量小, 无统计意义。

Aalders J, Abeler V, Kolstad P, Onsrud M. Postoperative external irradiation and prognostic parameters in stage I endometrial carcinoma: clinical and histopathologic study of 540 patients. *Obstet Gynecol.* 1980 Oct;56(4):419-27.



# PORTEC-1

## (Postoperative Radiation Therapy in Endometrial Carcinoma)

**方法:** 715I期子宫内膜样腺癌, G1肌层浸润大于50%, G2, G3肌层浸润小于50%. TAH-BSO, 随机分为术后体外放疗 (46Gy/2Gy) 和不加治疗组。

### 结果:

1. 局部复发率: 5年 4% vs 14% ( $p < 0.001$ ), 10年 5% vs 14% ( $p < 0.001$ )
2. OS: 5年 81% vs 85% ( $p = 0.31$ ). 10年: 68% vs 73% ( $p = 0.14$ ).
3. 肿瘤相关死亡率: 5年 9% vs 6% ( $p = 0.37$ ). 10年 10% vs 8% ( $p = 0.47$ ).
4. 治疗相关并发症: 25% vs 6% ( $p < 0.0001$ ).
5. 阴道复发后5年生存率64%, 盆腔复发及远处转移11%。
6. 未加放疗组局部复发75%位于阴道残端, 治疗后5年生存率70%。
7. 局部复发相关高危因素: G3, 大于60岁, 肌层浸润大于50%。

Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. Lancet. 2000 Apr 22;355(9213):1404-11.

Postoperative radiotherapy for Stage 1 endometrial carcinoma: long-term outcome of the randomized PORTEC trial with central pathology review. Int J Radiat Oncol Biol Phys. 2005;63:834-8.



# PORTEC-1

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## 结论:

- I期子宫内膜癌，术后放疗可降低局部复发率，但不提高总生存率.
- 放疗增加治疗相关并发症.
- 60 岁以下和G2肌层浸润小于50%的I期患者不建议术后放疗.

Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. *Lancet*. 2000 Apr 22;355(9213):1404-11.

Postoperative radiotherapy for Stage 1 endometrial carcinoma: long-term outcome of the randomized PORTEC trial with central pathology review. *Int J Radiat Oncol Biol Phys*. 2005;63:834-8.



# GOG99

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**方法:** 448 IR (IB, IC, and II ) , 其中HIR 33%, TAH-BSO+淋巴结切除术, 随机分成盆腔放疗 (50.4Gy/1.8Gy) 和不加治疗组。

**结果:**

1. OS无差异: 4年 92% (放疗组) vs 86% (对照组) (RH: 0.86; P=0.557).
2. 放疗减少局部 (阴道及盆腔) 复发: 18 (对照组) and 3 (放疗组);
3. HIR组CIR (累积复发率): 2-year 26% (对照组) versus 6% (放疗组); 4年27% vs 13%;
4. HIR组复发率增加;
5. LVSI与淋巴结转移, 远处转移强相关。
6. 治疗相关严重并发症: 4年13%;

A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol.* 2004 Mar;92(3):744-51.

# GOG99

## 结论:

1. 早期子宫内膜癌中危组，术后辅助放疗降低复发风险，不提高总生存率
2. 术后辅助放疗限于HIR。
3. 术后放疗增加治疗相关并发症。

A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol.* 2004 Mar;92(3):744-51.



# ASTEC and EN5 trials

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方法: 905, FIGO stage IA and IB G3; IC 和IIA all grades; 特殊病理类型, 手术(淋巴结是否切除不限), 随机体外放疗(40-46Gy)或观察. 腔内治疗不限, 包括观察组。

结果:

OS: 5年两组均为84%, hazard ratio 1.05 (95% CI 0.75-1.48; p=0.77).

观察组53%进行腔内治疗, 5 years 局部复发率 6.1%. 体外放疗组为3.2%

结论: 早期子宫内膜癌体外放疗既不能减少局部复发, 也不能提高生存率。

Blake P, Swart AM, Orton J, et al. Adjuvant external beam radiotherapy in the treatment of endometrial cancer (MRC ASTEC and NCIC CTG EN.5 randomised trials): pooled trial results, systematic review, and meta-analysis. *Lancet.* ;373:137–46. Largest randomized trial comparing pelvic EBRT to no adjuvant treatment after surgery for stage I EC.



## 术后辅助放疗

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**样本人群:** 21,249 patients , stage IA-IC, node-negative endometrial adenocarcinoma。

19.2%接受放疗，包括EBRT (62.5%)， VBT (17.9%) ， both (26.4%)

**结论:** IC期患者，术后辅助放疗提高了总生存率和相对生存率  
( $p < 0.001$ )

Lee CM, Szabo A, Shrieve DC, Macdonald OK, Gaffney DK. Frequency and effect of adjuvant radiation therapy among women with stage I endometrial adenocarcinoma. JAMA 2006; 295: 389–97.



# Meta分析1

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**分析对象：** 5个临床实验比较EBRT对I期子宫内膜癌的作用。 .

## **结果：**

低危组 (IA, IBG1, G2) : OR for overall survival 0.71; 95% CI 0.52-0.96).

中危组 (IC G1/2 and IBG3): OR 0.97; 95% CI 0.69-1.35.

高危组 (IC G3 ) : DFS OR 1.76; 95% CI 1.07-2.89

## **结论：**

中低危组 (IA, IBG1, G2) 不能从术后EBRT获益。

高危组 (IC G3 ) : DFS可获益10%。

Survival and recurrent disease after postoperative radiotherapy for early endometrial cancer: systematic review and meta-analysis. BJOG. 2007 Nov;114(11):1313-20. Epub 2007 Sep 5.





## Meta分析2

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分析对象：8个随机临床研究比较I期子宫内膜癌术后辅助放疗（EBRT或/和VBT），单纯VBT和观察组。其中6个研究为高质量研究。

结论：

低危患者不建议术后辅助放疗。

EBRT（with or without VBT）减少局部复发风险，但总生存率，肿瘤相关死亡率及远处转移率未获益。

HIR亚组，EBRT不能提高OS，VBT可有效控制阴道残端复发。

由于HR亚组入组有限，不排除EBRT生存率获益可能。

EBRT增加治疗相关并发症，降低生活质量。

未来增加对高危因素的定义及研究

Adjuvant radiotherapy for stage I endometrial cancer. Cochrane Database Syst Rev. Apr 18;4:CD003916.



## 术后辅助放疗

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- 辅助放疗减少局部复发，但不影响总生存率。
- 放疗后相关并发症尤其是严重并发症增加。
- 局部复发率与高危因素相关。
- LIR辅助放疗局控率无明显改善(<5%)。
- 辅助放疗建议限于有局部复发高位因素如HIR和HR亚组。



# 放疗方式选择

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- EBRT
- VBT
- Both



# PORTEC-2(EBRT VS VBT)

- 方法: 427, HIR (stage I or IIA endometrial carcinoma), 手术, pelvic EBRT (46 Gy in 23 fractions; n=214) or VBT (21 Gy high-dose rate in three fractions, or 30 Gy low-dose rate; n=213).
- 结果:
- 预计5年阴道复发率: 1.8% for VBT and 1.6 for EBRT (HR 0.78, 95% CI 0.17-3.49; p=0.74).
- 5年局部复发率: 5.1% for VBT and 2.1% for EBRT (HR 2.08, 0.71-6.09; p=0.17).
- 5年盆腔复发率: 1.5% (0.5-4.5) versus 0.5% (0.1-3.4) (HR 3.10, 0.32-29.9; p=0.30),
- 远处转移率: 8.3% [5.1-13.4] vs 5.7% [3.3-9.9]; (HR 1.32, 0.63-2.74; p=0.46).
- OS: 84.8% [95% CI 79.3-90.3] vs 79.6% [71.2-88.0]; (HR 1.17, 0.69-1.98; p=0.57)
- DFS: 82.7% [76.9-88.6] vs 78.1% [69.7-86.5]; (HR 1.09, 0.66-1.78; p=0.74).
- 急性胃肠道毒性: 12.6% [27/215] vs 53.8% [112/208]).
- Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial. Lancet. Mar 6;375(9717):816-23.



## PORTEC-2(EBRT VS VBT)

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**结论:**

**VBRT与EBRT在局部复发，远处转移及生存率无差异。**

**VBRT相对EBRT可减少治疗相关并发症，提高生活质量。**

**VBRT建议作为HIR的术后辅助治疗。**



# The Norwegian trial(VBT VS EBRT+VBT)

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**方法：** 540 患者，手术+镭腔内放疗后，随机分为不加盆腔放疗组及加盆腔淋巴结放疗. 随访3-10年。

**结果：**

1. 盆腔放疗组阴道残端及盆腔的复发率明显下降(1.9 vs 6.9%,  $P < .01$ )
2. 盆腔放疗组远处转移率则增加 (9.9 vs 5.4%).
3. 5年生存率无差异 (91% vs 89%)
4. G3, 肌层浸润大于50%的患者在局控率和总生存率上可能受益 (18% vs 27%)，但样本量小，无统计意义。

Aalders J, Abeler V, Kolstad P, Onsrud M. Postoperative external irradiation and prognostic parameters in stage I endometrial carcinoma: clinical and histopathologic study of 540 patients. *Obstet Gynecol.* 1980 Oct;56(4):419-27.

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