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Post Operative Vaginal Cuff Brachytherapy

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Cervix Cancer Education Symposium, January 2016, Bangkok, Thailand

Postoperative Vaginal Cuff Brachytherapy

- Can be used as a boost to external beam radiation in either cervical or endometrial cancer.
  - Done with positive margins, stage II disease and those considered hi risk.
- Rarely used alone postoperatively in cervical cancer.
- Most common application is the postoperative treatment of endometrial cancer.

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Indications

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PORTEC Trial

Post Operative Radiation Therapy in Endometrial Carcinoma

- **Selected Clinical Stage I**
  - **Grade 1 ≥ ½ MI**
  - **Grade 2 any MI**
  - **Grade 3 < ½ MI**
- **715 Patients**
- **TAH + BSO without LN Sampling**
- **All histologies**

- **Regimen 1**
  - **Pelvic radiotheraoy**
  - **46 Gy / 23 Fractions**
  - **No Vaginal Brachytherapy**
- **Regimen 2**
  - **No further Treatment**

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PORTEC – 10-year outcome with PA review

Locoregional recurrence (actuarial rates)

All pts	5-yr	10-yr	*p*
RT	3%	5%	
No RT	13%	14%	<0.001
Exclusion of IB grade 1 (n=134):			
RT	4%	5%	
No RT	15%	17%	<0.001

Creutzberg, Lancet 2000; Scholten, IJROBP 2005

PORTEC – 15-year outcome (Median f/u: 13.3 Years)

- *Locoregional recurrence (actuarial rates)*
  - 5.8 % in the Radiotherapy Arm
  - 15.5 % in the NAT Arm

Nout et al; JCO, 2011

Site of Loco-regional Recurrences

- 74% of the locoregional recurrences were isolated vaginal recurrences.

Nout, et al; JCO 2011

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GOG 99 Trial

- **Stage IB - II (Occult)**
- **Pap/Serous-Clear Cell Excluded**
- **392 Patients**
- TAH + BSO **with selective Bilateral Pelvic & Para- aortic lymphadenectomy**
- **Assessment of peritoneal cytology**

- **Regimen 1**

Pelvic radiotheraoy

50.4 Gy / 1.8 Gy/ Fraction

No Vaginal Brachytherapy

- **Regimen 2**

No further Treatment

Keys et al. Gynecol Oncol 2004; 92;744

Overall Results

- Median follow-up of surviving patients – 68 months.
- The 24-month cumulative incidence of recurrence (CIR) rate was 3% in the RT group and 12 % in the no additional therapy group.
- 13 of the 18 loco-regional recurrences in the NAT arm were in the vaginal vault (72%)

The "Myth" that Isolated Vaginal Recurrences are Easily Salvageable

- Accompanying editorial to GOG 99 by Michael Berman noted: "Yet vaginal recurrences usually are treated successfully with radiotherapy in patient not previously treated with adjunctive radiation"
- The data from GOG 99 noted that 12 of 13 patients in the NAT arm were treated with salvage radiotherapy – crude observations noted 5 of these thirteen died of endometrial cancer.

Salvage RT Series
Locally Recurrent Endometrial Cancer

Author	Number	Local Control	5 Years Survival
Kuten (1989)	51	35%	18%
Jereczek(2000)	73	48%	25%
Curran (1988)	47	48%	31%
Jhingran (2003)	91	75%	43%
Hoekstra (1993)	26	84%	44%
Sears (1994)	45	54%	44%
Hart (1998)	26	65%	53%
Wylie (2000)	58	65%	53%
Lin (2005)	50	74%	53%
Creutzberg (2003)	35	77%	66%

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PORTEC - 2 trial (2002-2006)

Stage I-IIA endometrial carcinoma

- ***age ≥ 60 and IC grade 1-2, or IB grade 3***
- ***stage 2A (except grade 3 > 1/2)***
- ***surgery: TAH-BSO***

R
- pelvic radiotherapy
- vaginal brachytherapy

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PORTEC-2

Randomized Between:

Pelvic Radiotherapy – 46 Gy in 23 fractions

VS

Vaginal Brachytherapy – 21 Gy HDR or 30 Gy LDR

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	Events/ total	Estimated 5-year (%; 95% CI)	Hazard ratio (95% CI)*	Log-rank p value*
Vaginal recurrence				
EBRT	4/214	1·6% (0·5–4·9)	1·00	0·74
VBT	3/213	1·8% (0·6–5·9)	0·78 (0·17–3·49)	
Pelvic recurrence				
EBRT	1/214	0·5% (0·1–3·4)	1·00	0·02
VBT	8/213	3·8% (1·9–7·5)	8·29 (1·04–66·4)	
Locoregional recurrence				
EBRT	5/214	2·1% (0·8–5·8)	1·00	0·17
VBT	10/213	5·1% (2·8–9·6)	2·08 (0·71–6·09)	
Distant metastases				
EBRT	13/214	5·7% (3·3–9·9)	1·00	0·46
VBT	16/213	8·3% (5·1–13·4)	1·32 (0·63–2·74)	
First failure type				
Vaginal recurrence				
EBRT	2/214	1·1% (0·3–4·4)	1·00	0·57
VBT	1/213	0·9% (0·1–6·2)	0·51 (0·05–5·58)	
Pelvic recurrence				
EBRT	1/214	0·5% (0·1–3·4)	1·00	0·30
VBT	3/213	1·5% (0·5–4·5)	3·10 (0·32–29·9)	
Survival				
Disease-free survival				
EBRT	31/214	78·1% (69·7–86·5)	1·00	0·74
VBT	32/213	82·7% (76·9–88·6)	1·09 (0·66–1·78)	
Overall survival				
EBRT	26/214	79·6% (71·2–88·0)	1·00	0·57
VBT	29/213	84·8% (79·3–90·3)	1·17 (0·69–1·98)	

EBRT=external beam radiotherapy. VBT=vaginal brachytherapy. *Both log-rank tests and Cox proportional hazards models are stratified for FIGO (International Federation of Gynecology and Obstetrics) stage.

Table 3: **Recurrence and survival (all patients), after a median follow-up of 45 months**

Selected Pathological Stage I&II Postoperative RT studies

Author	Stage	RT	Vaginal Recurrence	Pelvic Recurrence	5 Years Survival
Alektiar	IB G1-2	VB	-	4%	94%
Alektiar	IB – IIB	VB	2%	4%	93%
Anderson	IB – IC	VB	0.9%	1.9%	84%
Boz	IA G3 - IC	P	-	4%	88%
Calvin	IIA – B	P+/-VB, VB	2%	4%	85.2%
Carey	IB G3 – II	P+/-VB	-	3.9%	81%
Chadha	IB G3 – IC	VB	-	0%	81%
Feltmate	II	P+/-VB, VB	3.7%	3.7%	93%
Greven	IA - IIB	P+/-VB, VB	3.7%	0.7%	86%
Nori	I – II	VB +/- P	-	2%	96.6%
Rush	IB – IC	P	0%	0%	92%
Weiss	IC	P	0%	1.6%	86%

Burke T., Muggie F, Mundt AJ., Uterine Cancer
In Devita, Hellman, Rosenberg, (eds.),
Principles and Practice or Radiation Oncology(2005)

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Vaginal Brachytherapy Techniques

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American Brachytherapy Society consensus guidelines for adjuvant vaginal cuff brachytherapy after hysterectomy.

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Brachytherapy 11(2012) 58-47.

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Target and Technique

- Most commonly the upper vagina
- HDR in most institutions
- Single Channel Cylinder

Dose Fractionation

- 7 Gy X 3 to 0.5 cm is the most commonly prescribed fractionation scheme.
- Many sites use different fractionation schemes.
- I use 5.5 Gy X 4 to 0.5 cm.

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Table 5
Author estimates of vaginal recurrence with and without vaginal brachytherapy based on risk group.

Primary Risk Factors	Age >60, LVSI, and/or large tumor size	Risk Group	Observation	VBT	Authors' recommendation
Non-invasive, Gr 1–2	−	Low	0–2% [5,67]	0–1%	Observation
Non-invasive Gr 1–2	+	Low	0–2% [5,67]	0–1%	Observation
<1/2 MMI Gr 1–2	−	Low-int	3–4% [3,4,7,22]	0–2% [22,30]	Observation OR Referral to radiation oncology
<1/2 MMI, Gr 1–2 OR non-invasive Gr 3	+ +/−	Low-int	5–6% [3,4,7]	0–2% [22,30]	Referral to radiation oncology
>1/2 MMI, Gr 1–2 OR <1/2 MMI, Gr 3	− −	Int	8–10% [3,4,7]	0–3% [18,29]	VBT
>1/2 MMI, Gr 1–2 OR <1/2 MMI, Gr 3	+ +	High-int	13–19% [3,4,7]	2–3% [28,29]	VBT, but consider EBRT based on risk factors & nodal dissection

Harkenrider, M.M., Block, A.M., Siddiqui, Z.A., Small, W Jr. The Role of Vaginal Cuff Brachytherapy in Endometrial Cancer. Gyn Onc, 2015 Feb; 136(2): 365-372.

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Non-invasive Gr 1-2	+	Low	0-2% [5,67]	0-1%	Observation
<1/2 MMI Gr 1-2	-	Low-Int	3-4% [3,4,7,22]	0-2% [22,30]	Observation OR Referral to radiation oncology
<1/2 MMI, Gr 1-2 OR non-invasive Gr 3	+ +/-	Low-Int	5-6% [3,4,7]	0-2% [22,30]	Referral to radiation oncology
>1/2 MMI, Gr 1-2 OR <1/2 MMI, Gr 3	- -	Int	8-10% [3,4,7]	0-3% [18,29]	VBT
>1/2 MMI, Gr 1-2 OR <1/2 MMI, Gr 3	+ +	High-Int	13-19% [3,4,7]	2-3% [28,29]	VBT, but consider EBRT based on risk factors & nodal dissection

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Questions?

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