

XXXIII CONGRESSO NAZIONALE AIRO

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PALAZZO DEI CONGRESSI

Radioterapia Oncologica: l'evoluzione al servizio dei pazienti

## LA RECIDIVA IN CUPOLA VAGINALE: IL RUOLO DELLA RADIOTERAPIA INTERVENTISTICA

VAGINAL RECURRENCE IN PREVIOUSLY IRRADIATED GYNECOLOGICAL CANCER: ROLE OF INTERVENTIONAL RADIOTHERAPY  
(3D IMAGE GUIDED BRACHYTHERAPY)

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Associazione Italiana  
Radioterapia e Oncologia clinica

## DICHIARAZIONE

Relatore: Federica Piccolo

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario :**NIENTE DA DICHIARARE**
  - Consulenza ad aziende con interessi commerciali in campo sanitario: **NIENTE DA DICHIARARE**
  - Fondi per la ricerca da aziende con interessi commerciali in campo sanitario :**NIENTE DA DICHIARARE**
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- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario: **NIENTE DA DICHIARARE** Altro

Local recurrence in gynecologic remains a **highly challenging clinical issue**, especially when it developed in a previously irradiated field.

Most **local cancer recurrences** occur at the **vaginal cuff**, which is commonly within an area of prior radiation.

A **multidisciplinary approach** is necessary

The proposed curative-intent treatments are:

- SURGERY
- RE-IRRADIATION

**3D-IGBT for reirradiation in the context of local recurrences from gynecological malignancies.**





ELSEVIER



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**BRACHYTHERAPY**



Brachytherapy 19 (2020) 127–138

Gynecologic Oncology

## American Brachytherapy Society working group report on the patterns of care and a literature review of reirradiation for gynecologic cancers

Alina Sturdza<sup>1,\*</sup>, Akila N. Viswanathan<sup>2</sup>, Beth Erickson<sup>3</sup>, Catheryn Yashar<sup>4</sup>,  
Andrew Bruggeman<sup>4</sup>, Jonathan Feddock<sup>5</sup>, Ann Klopp<sup>6</sup>, Sushil Beriwal<sup>7</sup>, David Gaffney<sup>8</sup>,  
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Table 1  
Reirradiation studies that used brachytherapy

Series	Date	Study type	Patients (n)	Gyn ReRT (n)	Primary site	Treatment type	HDR/LDR	Median ReRT dose (dose range for each)	Median followup	Local control	Overall survival	Toxicity
Martinez-Monge, <i>et al.</i> (15)	2014	Prospective	50	25	Mixed	Interstitial	HDR	38 Gy in 8 BID (consecutive)	2.8 yrs	71.4% at 5 yrs	59.3% at 2 yr 39.5% at 5-yr	20% Grade 3+ 1 Grade 5
Badakh, <i>et al.</i> (16)	2009	Prospective	22	22	Cervix	Interstitial	HDR	25.8 Gy (12–45 Gy)	NR	NR	Median OS 9.2 mo	4 Grade 4
Ling, <i>et al.</i> (17)	2019	Retrospective	22	22	Uterine	IC/interstitial	HDR	Median HR-CTV $D_{90}$ 64.5 Gy (IQR: 49.6–75.8)	27.6 mo	66% @ 3 yrs	68% OS at 3 yrs	No Grade $\geq$ 3 acute or late
Umezawa, <i>et al.</i> (18)	2018	Retrospective	18	18	Cervix	Interstitial	HDR	62.6 Gy (48.6–82.5)	18 mo	51.3% at 2 yrs	60.8% at 2 yrs	2 Grade 3, 1 Grade 4
Ling <i>et al.</i> (17)	2019	Retrospective	22	22	Uterine	IC/interstitial	HDR	Median HR-CTV $D_{90}$ 64.5 Gy	27.6 mo	65.8% At 3 yrs	68.1% at 3 yrs	No Grade $\geq$ 3 acute or late
Kamran, <i>et al.</i> (19, 20)	2017	Retrospective	66	24	Uterine	Interstitial	HDR	45.2 Gy (27.2–67.9)	33 mo	71% at 3 yrs	54% at 3 yrs	33% Grade 3
Feddock, <i>et al.</i> (21)	2017	Retrospective	61	61	Mixed	Interstitial	LDR	45 (20–75)	16.3 mo	73% LC at death	52% OS at last f/u	Grade $\geq$ 3 16.7%
Huang, <i>et al.</i> (22)	2016	Retrospective	40	16	Uterine	Interstitial	HDR	74 Gy (cumulative)	18 mo	53% at 2 yrs	67% at 2 yrs	4 Grade 3
Liu, <i>et al.</i> (23)	2016	Cohort	16	16	Cervix	Interstitial	HDR	52.5 Gy	NR	NR	NR	NR
Murakami, <i>et al.</i> (24)	2016	Retrospective	26	10	Cervix	Interstitial	HDR	68.4 Gy (48.4–94.2)*	NR	45% at 3 yrs	51% at 3 yrs	1 Grade 4, 1 Grade 2
Amsbaugh, <i>et al.</i> (25)	2015	Retrospective	21	18	Mixed	Interstitial	both	LDR 41.5; HDR 22.5 Gy	16.5 mo	71.5% at 1 yr	82% at 1 yr	Grade 3: 28.5% vaginal, 9.5% urinary, 19% rectal
Zolciak-Siwinska, <i>et al.</i> (26)	2014	Retrospective	20	20	Mixed	Interstitial/ Intracavitary	HDR	48.8 Gy (19–91 Gy)	31 mo	45% at 3 yrs	68% at 3 yrs	3 Grade 3 (15%)
Mahantshetty, <i>et al.</i> (27)	2014	Retrospective	30	30	Cervix	Interstitial	HDR	42 Gy	25 mo	44% at 2 yrs	52% at 2 yrs	3 Grade 3 GU 3 Grade 3 GI (20%)
Mabuchi, <i>et al.</i> (28)	2013	Retrospective	52	52	Cervix	Interstitial	HDR	42 Gy/7 BID fractions	55.6 mo	77%	Median 32 mo	25% Grade 3 or 4
Wooten, <i>et al.</i> (29)	2013	Retrospective	14	7	Mixed	Interstitial	LDR	78.25 Gy (Cs131 median 27.5 Gy)*	12 mo*	88% at 1 yr*	Median 12 mo*	1 Grade 3*
Yoshida, <i>et al.</i> (30)	2013	Retrospective	114	14	Cervix	Interstitial	HDR	42–51 Gy in 7–8 BID fx	41 mo	NR	NR	1 fistula; vaginal Grade 0/1/2: 29%/57%/14%
Weitmann, <i>et al.</i> (14)	2006	Retrospective	23	23	Mixed	Interstitial	HDR	64 Gy	64 mo	47% at 5 yrs	43% DSS at 5 yrs	5 Grade 3 (22%)
Gupta, <i>et al.</i> (31)	1999	Retrospective	69	15	Mixed	Interstitial	HDR	35 Gy (25–55)	4.7 yrs	49% at 3 yrs	NR	14% Grade 4*

HR-CTV = high-risk clinical target volume; HDR = High-dose-rate; LDR = low-dose-rate; NR = not reported; DSS = disease specific survival; GU = genitourinary; GI = gastrointestinal; LC = local control; OS = overall survival.

Only included studies published within the past 20 years. Some studies did not report results separately for patients receiving reirradiation (indicated with \*).



Brachytherapy ■ (2017) ■

BRACHYTHERAPY

MR- versus CT-based high-dose-rate interstitial brachytherapy for vaginal recurrence of endometrial cancer

Sophia C. Kamran<sup>1,2</sup>, Matthias M. Manuel<sup>1,2</sup>, Paul Catalano<sup>2</sup>, Linda Cho<sup>2,5</sup>, Antonio L. Damato<sup>2</sup>, Larissa J. Lee<sup>2</sup>, Ehad J. Schmidt<sup>1,5</sup>, Akila N. Viswanathan<sup>1,2,6,7,8</sup><sup>1</sup>Harvard Radiation Oncology Program, Harvard Medical School, Boston, MA<sup>2</sup>Department of Radiation Oncology, Brigham and Women's Hospital/Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA<sup>3</sup>Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute and Department of Biostatistics, Harvard School of Public Health, Boston, MA<sup>4</sup>Johns Hopkins Bloomberg School of Public Health, Baltimore, MD<sup>5</sup>Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY<sup>6</sup>Department of Radiation Oncology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

66 patients with LOCAL RECURRENCE of endometrial cancer, 24 were reirradiated using IGABT.

**The authors delivered a dose of radiation which they felt was necessary to control the tumor even if this meant exceeding the standard organ at risk (OAR) tissue tolerances.**

The mean cumulative radiation dose to the high-risk clinical target volume (HRCTV) (including prior treatment) was **89.2 Gy** (range 52.5-106.6).

8 patients received previous treatment with **BRACHYTHERAPY only** (equivalent dose in 2 Gy [EQD2] ~30 Gy), had a mean time between first and second course of radiation of 34 months, and had a mean **reirradiation EQD2 dose of ~51 Gy**.

- 3-year local control was 80%
- 2 patients developed G3 toxicity.

4 patients received prior treatment with **EBRT** (EQD2 ~44 Gy), had a median time between first and second course of radiation of 42 months, and had a **mean reirradiation EQD2 dose of ~42 Gy**.

- 3-year local control was 100%.
- 1 patient developed G3 toxicity.

12 patients received prior **EBRT and BRACHYTHERAPY** (EQD2 ~60 Gy), had a mean time of 39 months between first and second course of radiation, and had a **mean reirradiation EQD2 dose of ~40 Gy**.

- 3-years local control was 60%
- 5 patients developed G3 toxicities.



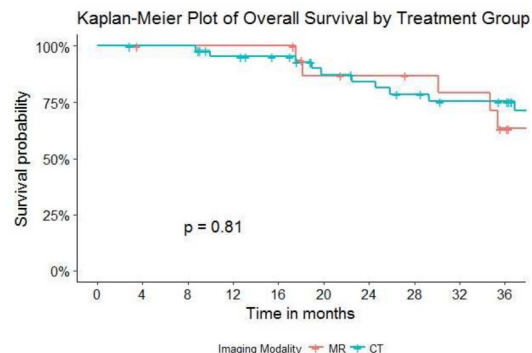
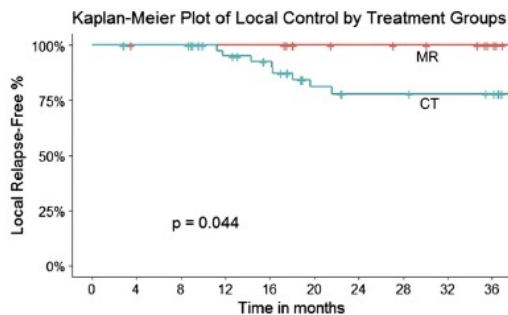
Brachytherapy • (2017) •

BRACHYTHERAPY

MR- versus CT-based high-dose-rate interstitial brachytherapy for vaginal recurrence of endometrial cancer

Sophia C. Kamran<sup>1,4</sup>, Matthias M. Manuel<sup>1,5</sup>, Paul Catalano<sup>2</sup>, Linda Cho<sup>3,5</sup>, Antonio L. Damato<sup>6</sup>, Larissa J. Lee<sup>7</sup>, Ehad J. Schmidt<sup>8</sup>, Akila N. Viswanathan<sup>1,2,9,10</sup><sup>1</sup>Harvard Radiation Oncology Program, Harvard Medical School, Boston, MA<sup>2</sup>Department of Radiation Oncology, Brigham and Women's Hospital/Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA<sup>3</sup>Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute and Department of Biostatistics, Harvard School of Public Health, Boston, MA<sup>4</sup>Johns Hopkins Bloomberg School of Public Health, Baltimore, MD<sup>5</sup>Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY<sup>6</sup>Department of Radiation Oncology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

- This study is the first to evaluate and compare clinical outcomes of MR- and CT-guided ISBT for vaginal recurrence of endometrial cancer.



b: Toxicities among reirradiation cases (assessed using the Common Toxicity Criteria Version 4.3)

Characteristics	Grade	CT-based ISBT re-RT (n = 15)	CT-based ISBT no re-RT (n = 33)	p-value	MR-based ISBT re-RT (n = 9)	MR-based ISBT no re-RT (n = 9)	p-value
Rectal	Grade 1	2 (13%)	8 (24%)	0.94	3 (33%)	1 (11%)	0.92
	Grade 2	0 (0%)	9 (27%)	0.84	1 (11%)	3 (33%)	0.92
	Grade 3	4 (27%)	6 (18%)	0.95	2 (22%)	0 (0%)	0.89
Urinary	Grade 1	1 (7%)	4 (12%)	0.96	3 (33%)	2 (22%)	0.92
	Grade 2	4 (27%)	3 (9%)	0.88	0 (0%)	1 (11%)	0.92
	Grade 3	3 (20%)	6 (18%)	0.99	1 (11%)	0 (0%)	0.92

Despite the worse prognostic features of MR patients, there was a **benefit in local control and less toxicity for patients treated with MR-based HDR ISBT.**



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Outcomes after definitive re-irradiation with 3D brachytherapy with or without external beam radiation therapy for vaginal recurrence of endometrial cancer

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22 patients with vaginal relapse of previously-irradiated endometrial cancer.

**The retreatment dose was determined based on treating until not exceeding a cumulative rectosigmoid and bladder D2cc (EQD2) dose of 75 Gy and 90 Gy, respectively.**

- 12 patients received prior vaginal **BRACHYTHERAPY** only with most receiving 21 Gy in three fractions,
- 5 patients received prior **EBRT** to a median dose of 45 Gy
- 5 received prior **EBRT +BRACHYTHERAPY**

The median time interval between the first and second course of radiation was **26.6 months**.

**The median D90 HR-CTV EQD2 (including prior dose) was 65 Gy.**

The 3-year local control was 66%, and one late G3 ureteral toxicity was noted. No > G3 toxicity.





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Brachytherapy ■ (2014) ■

BRACHYTHERAPY

Reirradiation using high-dose-rate brachytherapy in recurrent carcinoma of uterine cervix

Umesh Mahantshetty<sup>\*</sup>, Nikhil Kalyani, Reena Engineer, Supriya Chopra, Swamidas Jamema, Yogesh Ghadi, Deepak Deshpande, Shyamkishore Shrivastava  
*Department of Radiation Oncology and Medical Physics, Tata Memorial Centre, Mumbai, India*

30 patients with local cervical cancer recurrence were retreated with brachytherapy alone .

- 20 had a recurrence at the vaginal cuff after prior surgery and radiation
- 4 had a central recurrence after prior definitive treatment with radiation.

The median time between courses of radiation was **25 months**.

The **median brachytherapy dose delivered was EQD2 42 Gy**.

2-year local control was 44%.

**Local control seemed to be higher in patients receiving > EQD2 40 Gy (52% vs. 34%, p 5 0.05).**

2-year G3 toxicity (rectal, bladder, or vaginal) was seen in **23%**. Grade III radiation proctitis and cystitis was seen in 3 patients each, and Grade II small bowel toxicity was seen in 3 patients.



Brachytherapy ■ (2017) ■

BRACHYTHERAPY

## Image-guided interstitial high-dose-rate brachytherapy for locally recurrent uterine cervical cancer: A single-institution study

Rei Umezawa<sup>1,2,\*</sup>, Naoya Murakami<sup>1</sup>, Satoshi Nakamura<sup>1</sup>, Akihisa Wakita<sup>1</sup>, Hiroyuki Okamoto<sup>1</sup>, Keisuke Tsuchida<sup>1</sup>, Tairo Kashihara<sup>1</sup>, Kazuma Kobayashi<sup>1</sup>, Ken Harada<sup>1</sup>, Kana Takahashi<sup>1</sup>, Koji Inaba<sup>1</sup>, Yoshinori Ito<sup>1</sup>, Hiroshi Igaki<sup>1</sup>, Koji Masui<sup>1</sup>, Ken Yoshida<sup>1</sup>, Keiichi Jingu<sup>3</sup>, Nikolaos Tselis<sup>4</sup>, Jun Itami<sup>1</sup>

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## 18 patients with local gross recurrence of cervical cancer

- 14 had previously received **surgery followed by RT**
- 4 had received **definitive radiation**.

The median interval between treatments was 14.9 months.

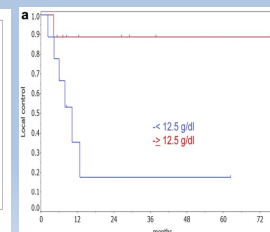
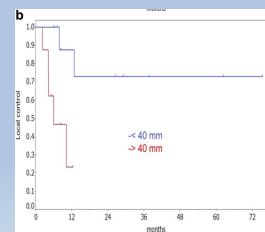
The **median CTV D90 was 62.6 Gy** (range 48.6-82.5 Gy).

2-year local control was 51.3%.

Late Grade 3 or higher toxicity was seen in three patients (16.6%).

On univariate analysis, maximum tumor diameter and Hb were significantly associated with local control but dose was not.

Factor	2-year LC rate (%) (95% CI)	p-value	2-year FFS rate (%) (95% CI)	p-value	2-year OS rate (%) (95% CI)	p-value
Age at reirradiation		0.804		0.363		0.977
<60 years	51.3 (25.7–76.3)		20.0 (5.0–54.1)		70.0 (37.6–90.0)	
≥60 years	43.8 (11.4–82.5)		18.3 (2.9–63.7)		42.9 (11.1–81.9)	
FIGO stage at initial diagnosis		0.862		0.911		0.399
I–II	48.5 (21.6–76.3)		21.4 (7.1–49.4)		52.6 (26.5–77.3)	
III–IV	75.0 (23.8–96.6)		0		100	
Pathology		0.56		0.521		0.527
SCC	53.3 (24.3–80.3)		16.7 (4.2–47.7)		60.2 (29.1–84.7)	
non-SCC	53.3 (13.9–89.0)		25.0 (3.8–73.8)		62.5 (21.9–90.9)	
Hemoglobin level at reirradiation		0.028*		0.421		0.153
<12.5 g/dL	17.8 (2.6–63.7)		11.1 (1.6–50.0)		38.9 (13.2–72.6)	
≥12.5 g/dL	88.9 (50.0–98.5)		29.6 (8.3–66.3)		88.9 (50.0–98.5)	
Maximum tumor diameter at reirradiation		0.009*		0.069		0.154
<40 mm	72.9 (34.4–93.3)		30.0 (10.0–62.4)		85.7 (41.9–99.8)	
≥40 mm	23.4 (3.7–71.0)		12.5 (1.7–53.7)		31.3 (8.2–69.8)	
Prior chemotherapy		0.095		0.226		0.176
Yes	31.1 (8.5–68.7)		0		59.7 (28.8–84.4)	
No	80.0 (30.9–97.2)		34.1 (12.3–65.6)		62.5 (21.9–90.9)	
Prior radiotherapy		0.397		0.73		0.539
Definitive	50.0 (12.3–87.7)		25.0 (3.4–76.2)		66.6 (15.4–95.7)	
Postoperative	52.5 (23.3–80.1)		19.0 (5.4–49.4)		58.4 (30.2–82.1)	
Interval to reirradiation		0.644		0.468		0.444
<12 months	53.6 (19.2–84.9)		14.3 (2.0–58.1)		35.7 (9.3–75.1)	
≥12 months	50.5 (18.9–81.8)		24.2 (6.8–58.3)		77.1 (40.5–94.3)	
CTV D <sub>90</sub>		0.152		0.268		0.795
<65 Gy	36.0 (12.5–68.9)		30.0 (10.0–62.4)		57.1 (26.4–83.2)	
≥65 Gy	87.5 (46.3–98.3)		25.0 (6.3–62.3)		72.9 (34.4–93.3)	



## *Literature review*

### BRACHYTHERAPY DOSE

- Dose is delivered most commonly using a **high-dose-rate (HDR)**
- Many centers use twice daily (**BID**) **HDR fractionation** with a median **dose prescription per fraction of 4 and 6 Gy** (range 2.3-8 Gy) and a median **number of fractions between 5 and 10** (range 3-15)
- Only a few centers reported on once a day or weekly fractionation schemes: 7 Gy 2-3 fractions weekly; 5-7 Gy 4-6 fractions weekly.

### BRACHYTHERAPY INSERTION TECHNIQUE

- Intracavitary-brachytherapy (ICBT) may be appropriate for reirradiation; however, in most cases, the extent of disease is  $>0.5$  cm in depth and so it is less commonly used.
- **Interstitial-brachytherapy (ISBT)** is well suited for the management of central and paracentral lesions because there is access through a transperineal approach and its surface/depth dose profile is better than that of intracavitary brachytherapy

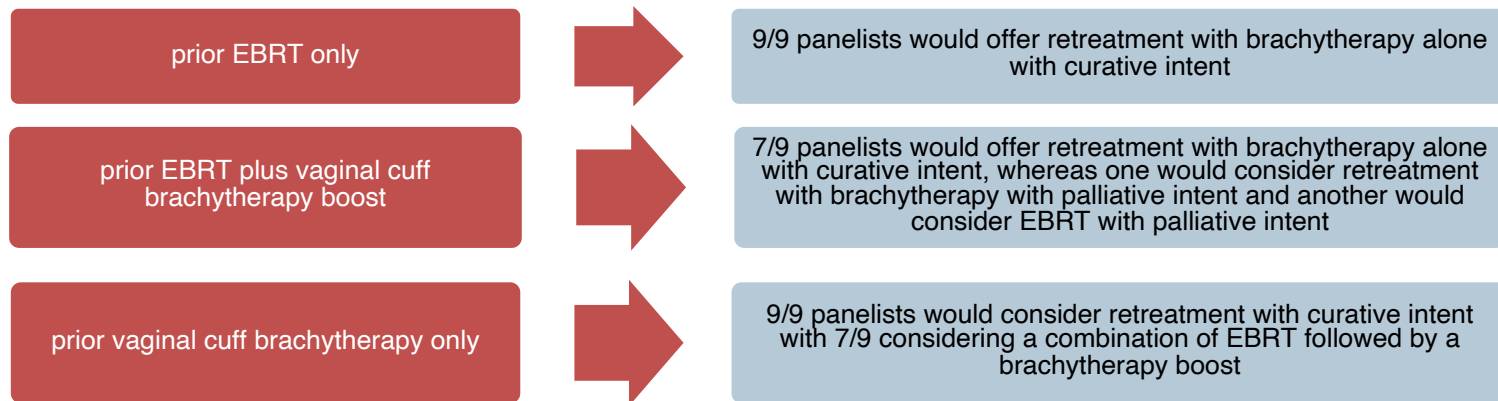
## Current practice

Online survey of 10 experts regarding their retreatment practices was also conducted.

Four different clinical scenarios:

- The first three clinical scenarios all had the same clinical presentation of a patient with an endometrial cancer recurrence in the vaginal vault.

The three different scenarios just changed the adjuvant treatment the patient received: EBRT only, EBRT +BT boost and BT only.



## ***Current practice***

Online survey of 10 experts regarding their retreatment practices was also conducted.

- The fourth clinical scenarios:

patient with cervical cancer treated with surgery followed by adjuvant who develops a side wall recurrence.



8/9 panelists would treat this patient with curative intent:

- Four would consider using brachytherapy alone
- Four would consider using non-SBRT EBRT
- one would consider using SBRT



## ***Current practice***

Online survey of 10 experts regarding their retreatment practices was also conducted.

### **Prescription Dose:**

When using brachytherapy alone with curative intent in the retreatment setting for a patient with prior EBRT, 6/9 would treat with a dose > 40 Gy.

If the patient had received prior EBRT and vaginal cuff brachytherapy, 5/9 would treat with a brachytherapy dose >40 Gy when treating with curative intent.

If the patient had received vaginal cuff brachytherapy, only then 8/9 would treat with a dose >40 Gy when treating with curative intent

### **Target delineation:**

HR-CTV in the reirradiation setting as gross disease on MRI/CT and clinical examination only with one of the panelists also considering gray zones seen on MRI.

The utilization and definition of an IR-CTV is more variable.

### **Time between a prior radiation and retreatment:**

There was no consensus, two panelists require at least 6-12 months, three > 1 year, and three do not consider time

## ***Current practice***

Online survey of 10 experts regarding their retreatment practices was also conducted.

### ❑ **Dose constraints for organs at risk :**

- Choose to intentionally exceed normal tissue tolerance to achieve an intended dose to the tumor (most studies report > G3 toxicities over 15%)
- Choose to keep them below standard OAR tolerances (where the cumulative recto-sigmoid and bladder D2cc (EQD2) was limited to <75 Gy and < 90 Gy)
- dose constraints for the vagina are an area needing further investigation:
- ✓ Murakami et al. found D2cc to be predictive of toxicity with a cut-point of 145 Gy EQD2. Patients over this cutoff had a 23.5% risk of vaginal ulcer. (Murakami N, Kato T, Miyamoto Y, Nakamura S, Wakita A, Okamoto H, Tsuchida K, Kashihara T, Kobayashi K, Harada K, Kitaguchi M, Sekii S, Takahashi K, Umezawa R, Inaba K, Ito Y, Igaki H, Itami J. Salvage High-dose-rate Interstitial Brachytherapy for Pelvic Recurrent Cervical Carcinoma After Hysterectomy. *Anticancer Res.* 2016 May;36(5):2413-21. PMID: 27127151.)
- ✓ Yoshida et al. reported G4 fistula at 127.6 Gy. (Yoshida K, Yamazaki H, Kotsuma T, Takenaka T, Masui K, Yoshioka Y, Uesugi Y, Shimbo T, Yoshikawa N, Yoshioka H, Narumi Y, Tatsumi K, Tanaka E. Treatment results of image-guided high-dose-rate interstitial brachytherapy for pelvic recurrence of uterine cancer. *Brachytherapy.* 2015 Jul-Aug;14(4):440-8. doi: 10.1016/j.brachy.2015.02.195. Epub 2015 Apr 7. PMID: 25858904.)

> [Brachytherapy](#). 2022 May-Jun;21(3):263-272. doi: 10.1016/j.brachy.2021.12.010. Epub 2022 Jan 22.

## Clinical outcomes and dosimetric predictors of toxicity for re-irradiation of vaginal recurrence of endometrial cancer

Larissa J Lee<sup>1</sup>, Gabriela M Alban<sup>1</sup>, Teresa Cheng<sup>1</sup>, Ivan Buzurovic<sup>1</sup>, Jennifer Pretz<sup>1</sup>, Lisa Singer<sup>1</sup>,  
Martin T King<sup>2</sup>

Dosimetric analysis was performed to **identify predictors of late toxicity in the re-irradiation setting**.

32 patients with vaginal recurrence of endometrial cancer received salvage brachytherapy with or without pelvic radiotherapy (RT).

Prior RT modalities:

- vaginal brachytherapy (19, 59%) → 21Gy
- pelvic RT (7, 22%) → 45Gy
- both (6, 19%) → cumulative dose 61 Gy

The median D90 for the HR-CTV in EQD2 was **47 Gy** for salvage brachytherapy alone and **72 Gy** for EBRT and brachytherapy

	Salvage BT alone (N=7)	Salvage EBRT and BT (N=25)
Median fractional HDR brachytherapy dose	6 Gy (range, 4.5–8)	5 Gy (range, 3–6)
Median number of HDR fractions	7 (range, 5–12)	5 (range, 3–7)
Median HDR brachytherapy dose	42 Gy (range, 36–54)	22.6 Gy (range, 16.3–30.8)
Median prescription dose in EQD2	59.5 Gy (range, 48–64.8)	71.5 Gy (range, 56.9–81.8)
Median D90 for HR-CTV in EQD2	46.6 Gy (range, 30.9–70.2)	71.6 Gy (range, 54.7–103.4)

	Salvage BT alone (N=7)	Salvage EBRT and BT (N=25)
Median D2cc for OAR in EQD2		
Bladder	29.0 Gy (range, 15–48)	61.4 Gy (range, 38.3–78)
Rectum	39.2 Gy (range, 17.3–80)	55.8 Gy (range, 39–71.5)
Sigmoid	9.4 Gy (range, 0–42.3)	48.4 Gy (range, 27.2–73.2)
Median cumulative D2cc for OAR in EQD2		
Bladder	83.6 Gy (range, 59.3–98.5)	99.0 Gy (range, 78.2–124.7)
Rectum	92.3 Gy (range, 73.2–110.6)	93.6 Gy (range, 76.6–119.6)
Sigmoid	63.4 Gy (range, 44.2–97.2)	89.1 Gy (range, 69.2–120.5)

Lee LJ, Alban GM, Cheng T, Buzurovic I, Pretz J, Singer L, King MT. Clinical outcomes and dosimetric predictors of toxicity for re-irradiation of vaginal recurrence of endometrial cancer. *Brachytherapy*. 2022 May-Jun;21(3):263-272. doi: 10.1016/j.brachy.2021.12.010. Epub 2022 Jan 22. PMID: 35078717.

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Clinical outcomes and dosimetric predictors of toxicity for re-irradiation of vaginal recurrence of endometrial cancer

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Martin T King<sup>2</sup>

## Toxicity

**Late grade 2 GI toxicity** was reported in 4 (**13%**) patients, most commonly rectal bleeding managed conservatively. Five (**16%**) patients had **late grade 3 GI toxicity**, including two with rectovaginal fistula requiring colostomy, one with diverting colostomy for severe proctitis, and two treated with argon plasma coagulation for rectal bleeding.

**Late grade 2 GU toxicity** was noted in 6 (**19%**) patients, including four with urinary incontinence, two with hematuria and one with moderate dysuria.

Four (**13%**) patients had **late grade 3 GU toxicity**, including two with hydronephrosis requiring intervention, one with vesicovaginal fistula and one with urethral obstruction requiring self-catheterization.

**Grade 2 and 3 vaginal toxicity** was reported in 3 (**9%**) and 5 (**16%**) patients, respectively, namely vaginal discharge and/or bleeding ( $n=3$ ), significant stenosis that interfered with exam ( $n=4$ ), and necrosis requiring debridement ( $n=1$ ).



## Toxicity

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**Clinical outcomes and dosimetric predictors of toxicity for re-irradiation of vaginal recurrence of endometrial cancer**

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D2cc rectum for the re-irradiation course was similar for patients with grade 0–1 and grade 2 GI toxicity: **median D2cc in EQD2: 53.5 Gy vs. 53.6 Gy**, respectively.

For patients with grade 3 rectal toxicity, the median **D2cc rectum was 59.3 Gy**

On dosimetric analysis, cumulative **D2cc rectum** (sum of prior and salvage RT courses) was an **independent predictor of grade 2+ and grade 3 GI toxicity**.

**The estimated dose for cumulative D2cc rectum that resulted in a 10% risk of grade 2 GI toxicity was 86 Gy and for grade 3 GI toxicity was 92 Gy.**

## Take home messages

The ideal reirradiation treatment course is not known. Part of this is related to the fact that the clinical context of a recurrence is very heterogeneous. There is insufficient evidence to developed guidelines to help standardize practice.

Brachytherapy (ISBT) seems to be the therapy modality of choice.

Clinical outcomes using HDR IGABT in recurrent endometrial cancer demonstrate local control rates between 53% and 66% and limited  $\geq$  G3 toxicities. Clinical outcomes for cervical cancer report local control rates between 44% and 51.3%, and  $\geq$  G3 toxicities between 16.6% and 25%

Determining the “right” dose in the reirradiation setting is much more of an “art” rather than a science and these are reflected in the wide range of doses reported in the literature. The HDR data are more varied with some studies suggesting improved local control outcomes at doses  $>40$  Gy

A longer time interval between the first and second course of radiation as well as recurrences  $<4$  cm tend to have improved outcomes

Multidisciplinary management is critical to develop individualized plans and to clearly communicate potential side effects and expected treatment outcome. The risk of late GI toxicity may be reduced by limiting cumulative D2cc rectum to  $<86$  Gy.

**Grazie per l'attenzione...**

