

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

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### ABSTRACT

**PURPOSE:** To develop recommendations for the use of adjuvant vaginal cuff brachytherapy after hysterectomy and update previous American Brachytherapy Society (ABS) guidelines.

**METHODS AND MATERIALS:** A panel of members of the ABS performed a literature review, supplemented their clinical experience, and formulated recommendations for adjuvant vaginal cuff brachytherapy.

**RESULTS:** The ABS endorses the National Comprehensive Cancer Network guidelines for indications for radiation therapy for patients with endometrial cancer and cervical cancer and the guidelines on quality assurance of the American Association on Physicists in Medicine. The ABS made specific recommendations for applicator selection, insertion techniques, target volume definition, dose fractionation, and specifications for postoperative adjuvant vaginal cuff therapy. The ABS recommends that applicator selection should be based on patient anatomy, target volume geometry, and physician judgment. The dose prescription point should be clearly specified. Suggested doses were tabulated for treatment with brachytherapy alone, and in combination with external beam radiation therapy, when applicable. A properly fitted brachytherapy applicator should be selected that conforms to the vaginal apex and achieves mucosal contact with optimal tumor and normal tissue dosimetry. Dose prescription points may be individually selected but doses should be reported at the vaginal surface and at 0.5-cm depth.

**CONCLUSIONS:** Recommendations are made for adjuvant vaginal cuff brachytherapy. Practitioners and cooperative groups are encouraged to use these recommendations to formulate their treatment and dose reporting policies. These recommendations will permit meaningful comparisons of reports from different institutions and lead to better and more appropriate use of vaginal brachytherapy. © 2012 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

### Keywords:

Endometrial neoplasm; Cervical neoplasm; High-dose rate; Low-dose rate; Brachytherapy; Radiotherapy

### Introduction

Endometrial carcinoma is the most common gynecologic malignancy in the United States, with 43,470 new cases in 2010 and an estimated 7,950 deaths. It constitutes 6% of female cancer, and accounts for 3% of all cancer deaths in women (1). The standard treatment for endometrial cancer is a total abdominal hysterectomy with bilateral

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salpingo-oophorectomy (TAH-BSO) with or without lymph node dissection. Adjuvant external beam radiation therapy (EBRT) and/or brachytherapy (typically postoperative) are integral components in the adjuvant therapy of select patients and radiation is a major component in the management of inoperable or recurrent endometrial cancers. The use of postoperative vaginal brachytherapy alone, without EBRT, for endometrial cancer has significantly increased in recent years (2). The recent Postoperative Radiation Therapy in Endometrial Cancer trial compared vaginal brachytherapy with EBRT in early-stage postoperative endometrial cancer patients. The study suggested that vaginal brachytherapy is equivalent to EBRT in preventing local vaginal recurrences and distant metastases (3). Although it is not the focus of the report, postoperative vaginal brachytherapy (usually with EBRT) is also indicated in some cases of cervical cancer. The technical principles for these indications are similar except that dose to the parametria may be a more important consideration in cervical cancer. This report was written as an update to the American Brachytherapy Society (ABS) recommendations for endometrial brachytherapy to provide current updated recommendations for adjuvant treatment of the vaginal cuff after hysterectomy (4).

## Methods and materials

In 2010, the ABS Board of Directors appointed a group of practitioners having extensive clinical experience and research to provide guidelines for the current practice of vaginal cuff brachytherapy. Sources of making recommendations include current guidelines published by medical societies, clinical trials, the published medical literature, and the clinical experience of the committee. Specific recommendations for therapy and recommendations for further investigations were made when there was a consensus. Where controversy exists or evidence was insufficient, the ABS declines to make specific recommendations. This report was reviewed and approved by the Board of Directors of the ABS.

## Results

The recommendations resulting from literature review and expert opinion of the panel members on patient selection, applicators, quality assurance (QA), dosimetry, and brachytherapy techniques are presented in the following sections.

### *Patient selection*

### *Treatment of the vaginal cuff as postoperative adjuvant therapy*

**Endometrial cancer.** The relative benefit and indications for adjuvant EBRT, brachytherapy, and chemotherapy, in

addition to surgery are being studied. There is a debate over when surgery alone is the sufficient treatment. Recent results of postoperative therapy of the vaginal cuff alone or in combination with EBRT are summarized in Tables 1 and 2 (3, 8–31). Vaginal brachytherapy alone vs. pelvic radiation therapy was compared by the recent Postoperative Radiation Therapy in Endometrial Cancer randomized trial for patients with a high–intermediate risk of local and regional recurrence. High–intermediate risk was defined as age 60 years or older and Stage 1C (The International Federation of Gynecology and Obstetrics 1988 staging: >50% myometrial invasion) Grade 1 and 2, Stage IB Grade 3, and Stage IIA (except Grade 3: >50% myometrial invasion). The trial noted the rates of recurrences between brachytherapy and EBRT were equivalent, both in terms of vaginal recurrences (1.6% vs. 1.8%) and locoregional recurrences—defined as pelvic, vaginal, or both (2.1% vs. 5.1%). Central pathology re-review showed a higher proportion in each arm of low grade (Grade 1) patients than was originally intended, with an increase from 48.5% of the patients to 78.6%, suggesting the results are generally applicable only to patients with the most favorable features (3).

Patient selection for adjuvant treatment should be determined by risk factor assessment, such as grade, myometrial invasion, lymphatic vascular space invasion, tumor size, lymph node status, tumor extension to the cervix or vagina, patient age, the presence and completeness of surgical staging, as well as consideration of comorbidities that may predispose patients to treatment-induced morbidity. Detailed discussions regarding patient selection, however, are beyond the scope of this report. The ABS generally endorses the guidelines put forth for patient selection by the National Comprehensive Cancer Network for adjuvant radiation therapy for endometrial cancer status post hysterectomy but advises that individual consideration be given to each patient's clinical situation (32).

Local recurrences in endometrial cancer are usually treated with EBRT and brachytherapy. The selection of brachytherapy technique (intracavitary vs. interstitial) is based on the depth of vaginal wall invasion and the distribution of the disease. In selected patients with more superficial (<5 mm) recurrences, intracavitary vaginal brachytherapy may be selected. For lesions invading a depth of 5 mm or more, intracavitary vaginal brachytherapy provides less complete tumor dose at depth compared with interstitial technique. Combination therapy with EBRT and vaginal brachytherapy is generally preferred because, according to some reports, it is associated with better control and studies have shown that more than 50% of a selected group of patients are curable (33, 34).

**Cervical cancer.** The use of adjuvant vaginal brachytherapy for cervical cancer is typically used in the setting of a boost after EBRT. There is no clear agreement as to the indications for vaginal brachytherapy after radical hysterectomy. In some cases, such as unsuspected cervical cancer,

Table 1  
Results of postoperative adjuvant cuff radiation therapy with brachytherapy alone

Author/reference	N	Treatment	Control/survival	Total pelvic recurrences (%) <sup>a</sup>	Vaginal recurrences (%)	Complications
Sorbe and Smeds (5)	404		5-y OS, 92%	3.0	0.7	6.9%, clinically significant
Noyes et al. (6)	63	16.2 Gy × 2 ovoids at surface	OS, 98.5%	1.6	0	No, Grade 3/4
Fanning et al. (7)	60	7 Gy × 3 at 0.5 cm	3-y NED, 100%	0	0	No, Grade 3/4
Kloetzer et al. (8)	108	10 Gy × 4 to 0.5 or 1.0 cm	3-y OS, 96%	0	0–3	0–12.6%, Grade 3/4
Hong et al. (9)	44	7 Gy × 3 at 0.5 cm	5-y DFS, 92%	0	2.9	No, Grade 3/4
MacLeod et al. (10)	141	8.5 Gy × 4 at surface		2	1.4	No, Grade 3/4
Weiss et al. (11)	122	7 Gy × 3 at surface	5-y NED, 94%	4.1	1.6	No, Grade 3/4
Petereit et al. (12)	191	16.2 Gy × 2 ovoids at surface	4-y OS, 95%	0.5	0	0.5%, Grade 4
Chadha et al. (13)	38	7 Gy × 3 at 0.5 cm	5-y OS, 93%	0	0	No, Grade 3/4
Eltabbakh et al. (14)	332	30 Gy at 0.5 cm (LDR)	5-y DFS, 98.9%	0.6	0	2.1%, Grade 3/4
Anderson et al. (15)	102	5 Gy × 3 at 0.5 cm	5-y OS, 84%	1.9	1	No, Grade 3/4
Horowitz et al. (16)	164	7 Gy × 3 at 0.5 cm	5-y OS, 87%	0.6	1.2	No, Grade 3/4
Rittenberg et al. (17)	53	5.6 Gy × 3 at 0.5 cm	5-y OS, 91%	0	0	No, Grade 3/4
Jolly et al. (18)	50	5 Gy × 5 at 0.5 cm	4-y OS, 97%	2	2	No, Grade 3/4
Alektiar et al. (19)	382	7 Gy × 3 at 0.5 cm	5-y OS, 93%	0	0.8	0.5%, Grade 3; 0.25%, Grade 4
Solhjem et al. (20)	100	7 Gy × 3 at 0.5 cm	3-y OS, 97.9%	0	0	No, Grade 3/4
Cengiz et al. (21)	31	7 Gy × 3 at 0.5 cm (HDR) or 70 Gy at surface (LDR)	5-y OS, 93%	3.2	0	No, Grade 3/4
Atahan et al. (22)	128	5.5 Gy × 5 at 0.5 cm	5-y OS, 96%	1.6	0	No, Grade 3/4
Lin et al. (23)	42	7 Gy × 3 at 0.5 cm (HDR) 65 Gy at surface, 30 Gy at 0.5 cm (LDR)		0	2	No, Grade 3/4
McCloskey et al. (24)	75	7 Gy × 3 at 0.5 cm		2.6	1.3	
Aalders et al. (25)	277	60 Gy at surface (LDR)	5-y OS, 89%	6.9 <sup>b</sup>		1%, Grade 4
Knocke et al. <sup>c</sup> (26)	325	8.5 Gy × 4–5 with intrauterine and 7 Gy × 1–2 with intravaginal at 2 cm from the center of the source	5-y OS, 52.7%	13.8 <sup>b</sup>		3.1%, Grade 3/4
PORTEC-2 <sup>d</sup> (3)	213	7 Gy × 3 at 0.5 cm (HDR) 30 Gy at 0.5 cm (LDR)	5-y, 84.8%	3.8	1.8	2.3%, Grade 3; no, Grade 4

DFS = disease-free survival; HDR = high-dose rate; LDR = low-dose rate; NED = no evidence of disease; OS = overall survival.

<sup>a</sup> Defined as pelvic alone and simultaneous pelvic plus vaginal.

<sup>b</sup> Vaginal and pelvis combined.

<sup>c</sup> Included some patients with external beam radiation therapy.

<sup>d</sup> Estimated 5-year recurrence results for vagina and pelvis alone.

patients who have had less than a radical hysterectomy need to be evaluated for pelvic radiation therapy, which usually is combined with a vaginal brachytherapy boost. The current National Comprehensive Cancer Network cervical cancer guidelines do not address the routine use of vaginal brachytherapy following hysterectomy for cervical cancer. Vaginal cuff boost should be considered in patients with a less than radical hysterectomy, close or positive margins, large or deeply invasive tumors, parametrial or vaginal involvement, or extensive lymphovascular invasion. The upper third of the vagina is typically removed during a radical hysterectomy limiting transvaginal access to the parametria and deeper pelvic tissues. The use of vaginal brachytherapy without EBRT to a positive parametrial margin has the same limitations as described for using postoperative intracavitary brachytherapy for bulky or deeply invasive vaginal tumors, that is, vaginal brachytherapy alone does not optimally treat deeply situated positive margins located in the lateral parametria or within the pelvis near the bladder or rectal dissection planes (35). Dose escalation with the combination of vaginal cuff

brachytherapy and EBRT used together should be considered in terms of the potential for improved tumor control and reducing the rate of side effects. EBRT and brachytherapy should be considered in patients who have had a TAH-BSO rather than a radical hysterectomy given that only a small rim of vagina is removed with the TAH-BSO and the lesser operation, as a single modality, is generally inadequate therapy for local tumor control.

#### Pretherapy evaluation

Before radiation therapy, the physician should discuss with the patient the risks, benefits, objectives, and alternatives of vaginal brachytherapy. The goal of adjuvant vaginal cuff brachytherapy as a single modality for patients with a low or intermediate risk of recurrence is to achieve high tumor control rates and to minimize the risks of toxicity. To take advantage of the favorable therapeutic ratio, care must be taken to select an optimal applicator and dosimetry profile that will adequately treat the vaginal mucosa and underlying tissues at risk for harboring residual

Table 2  
Results of postoperative adjuvant cuff radiation therapy with EBRT and vaginal brachytherapy

Author/reference	N	Treatment <sup>a</sup>	Control/survival	Pelvic recurrences (%)	Vaginal recurrences (%)	Complications
Lybeert et al. (27)	291 Postop	40 Gy EBRT + 5 Gy × 4 at 0.5 cm (HDR)	5-y NED I: 88% II: 68% III/IV: 50%	2.7	2.7	No, Grade 3/4
Nori et al. (28)	300	40 Gy EBRT + 7 Gy × 3 at 0.5 cm (HDR)	20-y DFS, 96%	0.3	2	No, Grade 3/4
Algan et al. <sup>b</sup> (29)	81	45 Gy EBRT + 4 Gy × 3 at 0.5 cm (HDR) or 30 Gy surface (LDR)	5-y OS, 83%	3	4	
Cannon et al. (30)	50	45–51 Gy EBRT + 5 Gy × 3/7.8 × 2 at surface (HDR)	5-y OS, 82%	4	0	2%, Grade 3; 2%, Grade 4
Fayed et al. (31)	1179	50.4 Gy EBRT + 2 Gy × 6 at 0.5 cm (HDR)/60–70 Gy total at surface (LDR) <sup>c</sup>	5-y OS, 70% (LDR) and 68% (HDR)	9 (LDR); 14 (HDR) <sup>d,e</sup>		1.9%, Grade 3/4
Aalders et al. (25)	263	40 Gy EBRT 60 Gy at surface (LDR)	5-y OS, 91%	2 <sup>e</sup>		0.7%, Grade 5; 0.4%, Grade 4

EBRT = external beam radiation therapy; HDR = high-dose rate; LDR = low-dose rate; NED = no evidence of disease; OS = overall survival.

<sup>a</sup> Most common treatment.

<sup>b</sup> Includes some patients treated with brachytherapy alone.

<sup>c</sup> Midline block after 20–30 Gy EBRT.

<sup>d</sup> Stage I patients.

<sup>e</sup> Total recurrences in pelvis and vagina, results not separated.

microscopic cancer and to be aware of any factors that could increase the risk of side effects. A complete pelvic examination should be performed and it must be determined that the vaginal cuff has healed before the therapy and that small bowel has not herniated through the vaginal apex. Adjuvant brachytherapy is usually not performed until at least 4 weeks have elapsed since surgery. The increasing use of robotic or laparoscopically assisted vaginal hysterectomies may increase the amount of time necessary for sufficient healing of the vaginal cuff. If there is a question about healing, the panel recommends the surgeon be consulted before proceeding with treatment. On occasion, particularly aggressive disease may have recurred in the interval between surgery and the initiation of radiation therapy. If recurrence is suspected, a biopsy should be performed to rule out gross residual disease and an alternative therapy plan adopted.

### Applicators

Applicator selection is an important consideration for achievement of optimal results with brachytherapy. A single applicator cannot treat all anatomical variants and disease presentations. Different applicator alternatives are required to accommodate these varied presentations and anatomic considerations. Some of the options and circumstances are described in this article, but individual physician judgment and experience are important in the proper selection of the applicator method. Custom applicators may be preferred or required.

A vaginal cylinder or ovoids are commonly used for post-hysterectomy adjuvant brachytherapy of the vaginal cuff. The choice of applicator for treatment of the vagina

is both institutional and patient dependent. Ovoids treat only the upper part of the vaginal (termed the vaginal cuff), whereas vaginal cylinder allows treatment of the entire length of the vagina. The shape of the vagina may determine the applicator selection in certain patients. In many patients, the postoperative vagina is roughly cylindrical and it can be treated adequately with a properly sized vaginal cylinder. Vaginal cylinders are preferable for patients with a narrow vagina. If a cylinder is chosen that is too small, there may be air gaps or folds leading to underdosage of the vaginal target tissue in these locations. Single channel cylinders have been shown to deliver a higher dose to the bladder and rectum for a given vaginal dose compared with ovoids but this problem may be ameliorated by the use of a multichannel cylinder. In some patients, the vagina may have an expansion in the lateral apices because of surgical remnants of the vaginal fornices. Such a postoperative anatomical configuration has been termed a “dog-ear” configuration and it may be better treated with ovoids, although there is no clinical information that ovoids reduces vaginal recurrences better than a vaginal cylinder. A vaginal cylinder may still be effective even if there is some underdosage to the “dog-ear” area of the vagina because sufficiently high doses are still delivered to these tissues. Vaginal ovoids can lead to underdosage at the central apex of the vagina if there is significant separation and a heterogeneous dose may occur depending on the specific packing used. Also, ovoids do not adequately treat the lower vaginal area. Thus, there are advantages and limitations to each type of applicator system. Combinations of ovoids and cylinders can be used to address these concerns but such an applicator system is not widely used, can have

significant dosimetric complexities, and is not commercially available. There is no literature to substantiate that one set of applicators reduces recurrence more than another because there is such range of applied doses and outcome comparisons are difficult.

**Cylinders.** The ABS recommends that institutions should have available vaginal cylinders in various lengths and diameters (ranging from 2.0 to 4 cm). Individual cylinders of predetermined lengths, or segmented cylinders that can be assembled to the required length, are available. The ABS suggests that when only the upper length of the vagina needs treatment, the cylinder should not extend to the vaginal introitus in an attempt to minimize patient discomfort. If the target is near the introitus, the cylinder should extend beyond the introitus to allow appropriate target coverage and normal tissue protection. Condoms can be placed over the cylinders when they are inserted into the vagina to extend applicator longevity and to facilitate cleaning and preparation.

Most vaginal cylinders have a single, central channel. The multichannel vaginal applicator is a variation of the vaginal cylinder (36, 37). This applicator contains a central channel and six peripheral channels along the surface of the cylinder. The central and peripheral channels increase dosimetry control and permit the user to compensate for single line source anisotropy at the vaginal apex. The multichannel applicator is available with a 3.0 cm diameter cylinder; however, additional sleeves are available to increase the diameter to 3.5 and 4.0 cm to reduce the mucosal dose by having the sources deeper in the applicator and further away from the vaginal surface thus increasing the depth dose. Differential loading of the channels allows shaping of the isodose distributions to various clinical presentations. Such multichannel applicators have been shown to reduce the dose to the bladder and rectum without a reduction in the target dose, although there needs to be careful attention to the technique to assure that the mucosal dose is not increased as compared with single channel applicators (38).

**Ovoids.** Fletcher-like shielded and unshielded vaginal ovoids are available in diameters of 2.0, 2.5, and 3.0 cm. Henschke-like hemispherical colpostats of 2.5- and 3.0-cm diameter with or without tungsten shielding are also available. In addition to the use of ovoids in the postoperative setting, dosimetric studies exist for ring applicators (39). The ABS deems the choice of applicators to be a physician or institutional preference, providing that the desired segment of vagina is adequately irradiated.

### *Brachytherapy techniques*

#### *Treatment of vaginal cuff as postoperative adjuvant therapy*

**Applicator insertion.** A visual inspection and manual examination of the vagina by the physician should precede

applicator insertion, most importantly, to assure a healed vaginal cuff, evaluate tissue reactions or, in rare instances, recurrent disease. In a subset of patients, the placement of a cylinder may be difficult secondary to surgical effects on the vagina, parity, hormonal status, or normal anatomic variants (e.g., larger vaginal apex in relation to introitus). Techniques that improve the ability of patients to better tolerate the procedure include a thorough discussion in advance to explain the process; lubrication of the applicator (consider the use of xylocaine jelly), performance of the insertion slowly to allow the perineal muscles to adjust, listening to patient feedback during the procedure; education in relaxation techniques; as well as considering premedication with anxiolytics, or pain medication, or the use of moderate sedation as indicated. Placement of a radio-opaque seed or clip(s) at the vaginal apex to verify that the applicator is in contact with the vaginal mucosa should be considered. These clips or seeds sometimes fall off or migrate deep to the mucosa and therefore may not always indicate the position of the apex. The pelvic exam is useful in determining which size cylinder will best and most comfortably fit the patient. Recommendations based on experience suggest that the physician place one finger into the vagina, applying gentle pressure to the perineal muscles while asking the patient to relax and breathe. Placement of a second finger into the vagina after the patient is relaxed and rotation of both fingers helps expand the introitus. If such a maneuver is easily performed, a 3.5 cm cylinder can probably be accommodated. In some multiparous patients, a 4.0 cm in diameter cylinder can be accommodated. However, if only one finger can be inserted, a 2.5 cm cylinder may be more suitable. For all other patients, a 3 cm cylinder is recommended. After applicator placement by the physician, an external immobilizing device is recommended to minimize movement between planning and treatment delivery. In the absence of marker placement, there needs to be some assurance of applicator contact with the upper vagina. If the applicator is inserted with the knees bent, when the legs are brought horizontal, it is helpful to loosen the applicator from the immobilization device and apply light cephalad pressure to ensure contact with the apex. This should also be done again just before the treatment. Pretreatment imaging should be used to confirm that the location of the applicator in the pelvis is consistent with a location in the upper vagina. Preinsertion measurement of the vaginal length subsequently compared with the length of the applicator noted on plain radiography could also be considered. Measuring the length of the vagina would also help in reporting the percentage of the vagina treated. CT simulation can help to confirm that there is no significant air gap and the applicator is in contact with the upper vagina.

**Vaginal cylinders.** It is imperative for the vaginal mucosa to be in contact with the applicator surface to achieve the optimal dose distribution. The ABS recommends use of the largest diameter cylinder or ovoids that can comfortably

fit snugly into the apex of the vagina. It is usually possible to confirm that the applicator is in direct contact with the vaginal apex mucosa by exerting gentle cephalad pressure on the applicator handle while assessing for patient discomfort. The applicator should subsequently be secured only after it returns to a more neutral position. The applicator should be positioned in the midline of the patient based on patient anatomy and comfort. Placing the applicator in the horizontal position, rather than pitching anterior toward the bladder or posterior toward the rectum, may reduce the dose of radiation to the normal structures. The position of the applicator should be rechecked just before treatment, and the position should be adjusted as needed.

*Vaginal ovoids.* When ovoids are inserted, their medial surfaces should touch, or nearly touch, to avoid a cold spot in the central vagina apex between the two ovoids. A rectal retractor or radio-opaque packing can be used to displace the rectum and bladder. It is important to verify that the packing and/or the rectal retractor has not displaced the applicators away from the vaginal apex.

#### *Dose fractionation regimens*

##### *Dose fractionation with brachytherapy alone*

The brachytherapy dose depends on the dose specification point, length of vagina treated, and whether EBRT is given. The larger the volume of vagina treated the larger the amount of normal tissue irradiated, which may be a factor in the choice of the fractionation pattern. The ABS recommends that the dose specification point be clearly documented in the patient's treatment record and be stated in any published reports. The usual EBRT dose (when given) is 45–50.4 Gy to the whole pelvis. Slightly lower central tumor dose 39.6 or 40 Gy with midline block added before completing the course is a strategy to reduce normal tissue doses and injury used by some institutions. The suggested doses for brachytherapy alone are generally not the product of prospective studies but have generally been formulated to deliver approximately 60 Gy low-dose rate (LDR) equivalent to the vaginal surface. Several institutions have implemented unique dose fractionation regimens, which achieve acceptable outcomes. As noted in Table 1, and used in the PORTEC 2 trial (3), 7 Gy  $\times$  3 prescribed to 0.5 cm is a common fractionation scheme. Lower LDR equivalent doses—namely 6 Gy  $\times$  5 (MD Anderson regimen) or 4 Gy  $\times$  6 (Dana-Farber/Brigham and Women's regimen) to the surface—have been used by member(s) of the panel with reported good results. Sorbe et al. (40) randomized 290 patients to 2.5 Gy/fraction vs. 5.0 Gy/fraction  $\times$  6 prescribed to 0.5 cm. There was only one vaginal recurrence noted in each arm of the study with increased vaginal shortening with higher fractions per treatment. The 2.5 Gy per fraction at 0.5 cm is similar to 4.0 Gy/fraction to the surface, which has also been reported to have excellent tumor control (41). If lower fractionation patterns (i.e., reduced LDR equivalent dose) are used,

extreme care must be taken to assure target coverage as higher doses may compensate for dosimetric underdosing, such as air gaps and “dog-ear” vaginal cuff configuration.

##### *Dose fractionation regimens as a boost*

When vaginal brachytherapy is used as a boost, vaginal surface LDR equivalent doses (EBRT and brachytherapy) are generally around 70 Gy. Common high-dose rate prescriptions include 45 Gy EBRT + 6 Gy  $\times$  3 (Radiation Therapy Oncology Group 0921 endometrial cancer regimen) to the vaginal mucosa or 50.4 Gy EBRT + 6 Gy  $\times$  2 (RTOG 0418 endometrial cancer regimen) to the vaginal mucosa. Higher brachytherapy doses should be considered for patients who have a positive margin or recurrent disease. Recommended dose for patients with recurrent disease is an LDR equivalent of at least 70–80 Gy to the vaginal lesion target with monitoring the normal tissue dose constraints (34). To facilitate comparisons, HDR doses can be converted, using the linear quadratic model, to give the LDR equivalent doses for tumor effects (42). It is suggested that for smaller cylinders prescribed to 0.5 cm, a higher number of fractions should be used because the dose to the vaginal surface may be relatively high.

##### *Dose specification and timing (HDR and LDR)*

It is recommended that, as a routine, the proximal 3–5 cm of the vagina be treated. Rarely, treatment of the entire vaginal canal may be considered in patients with papillary serous and/or clear cell histologies, Grade 3 disease, or patients with extensive lymphovascular invasion because of the increased risk of distal vaginal recurrence. However, most practicing physicians usually limit the length of vaginal treated (2). When using HDR, the dose distribution should be optimized to deliver the prescribed dose either at the vaginal surface or at some measured depth—usually 0.5-cm depth—depending on the institutional policy. For LDR, sources should be chosen to deliver approximately 100 cGy/h to the vaginal surface. Pathologic studies evaluating the depth of lymphatic channels from the vaginal surfaces demonstrated that approximately 95% are located within the first 3 mm (43). This finding suggests that dose prescribed to a depth of 0.5 cm would adequately cover the region. Regardless of the prescription point, the ABS recommends reporting doses at both the vaginal surface and at 0.5-cm mucosal depth. The panel recommends that, when using HDR, the treatment be delivered in multiple fractions per week if tolerance allows. Daily fractions, however, are not encouraged unless a lower daily dose is used. The practice of delivering one fraction/wk, especially as a boost after EBRT, is not recommended. For LDR, a single implant is commonly used.

##### *Prescription*

The ABS recommends a clear, dated, and signed written directive specifying the treatment site, the radionuclide, the

prescribed dose per fraction and total dose, and fractionation. The prescription point for the absorbed dose must be stated clearly and unambiguously. The type of applicator, optimization points (HDR), the method of optimization (HDR), the number of dwell positions (HDR), relative dwell weights (HDR), and the isodose distribution should be documented. In addition, there should also be a consideration for documentation of the adjacent normal tissue doses—specifically the bladder and rectum.

### *Localization*

Methods of localization include the use of portable X-ray units, conventional radiotherapy simulators, CT, or MRI imaging. Plain radiographic simulation only shows the applicator in relation to the pelvic bony structures and not in relation to the vaginal vault, unless radio-opaque marker seeds or clips have been placed at the vaginal vault. In comparison, the use of CT or MRI simulation can be used to visualize this relationship better. The utilization of CT has been undertaken more recently in an attempt to better delineate the dose to the vaginal mucosa and normal structures (44). CT simulation enables better identification of individualized normal structures, vaginal cuff at risk, and the vaginal applicator (45, 46). It may also reveal the occasional patient who has a very generous volume of tissue superior to vaginal cuff (above the vaginal suture line and mucosa of the vagina) who might be better served by EBRT. This information provides a means to optimize the dose based on proximity to the rectum and bladder based on the thickness of the vaginal wall. CT imaging can also help to identify large air gaps between the applicator and vaginal mucosa that, although often not significant, can cause underdosing of the mucosa in certain situations (45, 47). The best method of localization is the one that produces the least movement of the patient and the applicator during the planning period and before treatment delivery. That is to say, the goal is to achieve a stable implant so that the planning and treatment delivery position within the patient are as similar as possible. When using HDR, a dedicated HDR suite with in-room radiographic localization allows immediate imaging after applicator placement and more stability with less patient motion. Such an arrangement is ideal but not widely available.

The ABS recognizes that with the use of fixed geometry applicators, such as vaginal cylinders, localization radiographs are not mandatory for dosimetry purposes but are always useful for documentation and to provide information on the actual relationship of the applicator to target and to normal tissues. In addition, the need for routine calculation of the bladder and rectal doses when delivering vaginal brachytherapy alone has been questioned because of the relatively low dose to normal tissue and the overall low morbidity of therapy and the possible risks of a Foley catheter if cross-sectional planning is not accomplished (48). A definitive recommendation regarding the need for such calculations remains an open question.

### *Dosimetry—precalculated vs. patient specific (HDR)*

The ABS recognizes that although customized treatment plans for every fraction most accurately documents the actual total dose delivered to the patient, this practice is time consuming, involves technical costs, and probably does not improve patient outcomes. Hence, it may not be necessary to calculate customized treatment plans for every fraction for fixed geometry applicators. A customized treatment plan can be calculated once for each patient, and the same plan used for all fractions (48). The assumption in these patients is that the geometry of the implant remains the same for every insertion. Given the potential variable applicator position between fractions, it is recommended that the radiographs or other measures be taken to ensure that the applicator is in the same position in the vagina and relative to the bladder and rectum for each application. An alternative is to store an array of precalculated treatment plans for various applicators. Imaging may be obtained and the preplan that best matches the target geometry can be selected and modified for the current treatment.

### *Optimization (HDR)*

Optimization is defined as the manipulation of the HDR dwell positions or the dwell times, or both, so that the resultant dose distribution best conforms to the target volume. It is important to recognize that optimization is a tool to provide additional dose shaping capabilities for a good implant and should not be used to compensate for an improperly placed applicator or an inappropriate applicator. The choice of optimization algorithm and optimization points affects the dose distribution profoundly. The treating physician should therefore be able to critically evaluate an “optimized” plan to ensure that it meets the desired requirements of treating the target volume while minimizing dose to normal structures and minimizing hot or cold spots in the target volume. Given the common prescription points of the vaginal surface or 0.5 cm from the vaginal surface, optimization in vaginal cylinder therapy generally consist of shaping the dose distribution to the curve of the cylinder. Placing HDR optimization points only on the lateral surface of the vagina without having optimization points at the apex would produce unacceptably high doses at the vaginal apex and any overlying small bowel (49, 50). The ABS recommends placing optimization points both at the apex and along the curved portion of the cylinder dome in addition to the lateral vaginal mucosa. Source anisotropy can produce a lower dose at the vaginal apex and isotropic dose calculation model can result in as much as 30% underdosage at the vaginal apex (49, 51). However, the clinical significance of this is not known. The ABS recommends the use of proper anisotropic dose calculation model (49). Multichannel cylinders may be used to minimize the effect of anisotropy and to improve dosimetry (36–38). For ovoids, optimization points are placed at the surface of the ovoids or at 0.5-cm depth into vaginal mucosa according to the institutional prescription policy. If

the ovoids are separated, additional optimization points must be placed at the apex, midway between the ovoids, to avoid cold spots between them.

### Quality assurance

There are several documents that provide excellent general QA guidelines for brachytherapy. These reports may be categorized as follows: American Association on Physicists in Medicine (AAPM) Report 59: Code of practice for brachytherapy—report of the AAPM Radiation Therapy Committee Task Group No. 56, AAPM Report 41: Remote afterloading technology—a report of AAPM Task Group No. 41, AAPM Report 62: Quality assurance for clinical radiotherapy and treatment planning, AAPM Task Group No. 53, and AAPM Report 61: High dose-rate brachytherapy treatment delivery—a report of the AAPM Radiation Therapy Committee Task Group No. 59 (52–55). Annual in-service refresher training for all staff involved in brachytherapy procedures is required.

### Applicators

The ABS recommends periodic QA of applicators, including specific checks of the integrity of the applicators, their source guide tubes, and the position of the shields, if present.

### Treatment

The ABS recommends an independent review of the proposed plan of therapy by a second individual (physicist or medical dosimetrist), in addition to the primary planning physicist/dosimetrist. It should include checks, if applicable, that:

1. Dosimetry data are correct and consistent with institutional treatment guidelines.
2. The absorbed dose prescription point, absorbed dose per fraction, and number of fractions satisfy the facility's protocol.
3. The absorbed dose distribution from the plan matches the prescription.
4. Reconstructed applicator geometry matches that on the radiograph.
5. The distance from machine reference point to the most distal dwell position is consistent with treatment plan.
6. Absorbed doses to normal tissues, when calculated, are within tolerances.
7. The dwell times (HDR) for the generated plan fall within a range consistent with those for similar patients.
8. Treatment data (dwell times, locations, step sizes) programmed match those on the plan.
9. Subsequent HDR fractions using the same plan stored in the HDR unit are performed with the

correct data and with the current source activity, and the treatment time adjusted accordingly.

10. The HDR source activity for the treatment day is corrected for source decay in the treatment planning system/treatment console computer and verified by a separate independently calculated source decay chart or method.

Several other checks must be in place for multiple fraction treatments using the initial treatment plan or for the use of precalculated dosimetry. Among them are checks to ensure that the correct applicator is used for each fraction and applicator position is reproduced. The applicator size should be measured before each application to ensure the correct applicator is being used. A time out to ensure patient identity and review the above treatment checks should be performed before every procedure and fraction.

### Conclusion

Recommendations are made for vaginal cuff brachytherapy. Practitioners and cooperative groups are encouraged to use these recommendations as a guide to formulate their treatment and dose reporting policies. The best brachytherapy applications for the patient are ultimately achieved by the individual physician and medical physics judgment and implementation.

### Disclaimer

These guidelines represent consensus of the authors regarding currently accepted treatment. The suggested doses have been derived from a combination of literature review, the individual clinical experiences of the authors, and modified by biomathematical modeling. Although these doses seem reasonable to the authors, some of the dose fractionation schemes given may not have been extensively tested in clinical practice. These guidelines will be updated as significant new outcome data becomes available. Any clinician following these guidelines is expected to use their clinical judgment to determine an individual patient's treatment. The ABS makes no warranties of any kind regarding their use and disclaims any responsibility for their application in any way.

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