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Review Article

Compendium of fractionation choices for gynecologic HDR brachytherapy—An American Brachytherapy Society Task Group Report

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ABSTRACT

PURPOSE: The purpose of this study was to report a list of accepted fractionation schemes for high-dose-rate (HDR) brachytherapy for gynecological cancers in a definitive, neoadjuvant, or adjuvant setting.

METHODS AND MATERIALS: Members of the American Brachytherapy Society (ABS) Task Force with expertise in gynecological brachytherapy reviewed the literature and existing ABS guidelines regarding various dose-fractionation schedules for HDR brachytherapy to create this compendium. Other resources include current guidelines published by medical societies, clinical trials, the published medical literature, and the clinical experience of the ABS Task Force members. The ABS consensus statements for HDR brachytherapy practice were reviewed for these fractionation schemes and form the major source for this report. Specific recommendations for therapy and recommendations for further investigations were made when there was agreement.

RESULTS: A variety of dose-fractionation schedules for HDR brachytherapy alone or integrating brachytherapy with external-beam radiation exist. The choice of a given fractionation schedule may be appropriate depending on the practice situation for the patient and the resources available. While there is no single optimal dose-fractionation scheme for any disease site or clinical situation, higher doses per fraction with fewer fractions per regimen have been known to increase toxicity. The corresponding 2-Gray (Gy) per fraction radiobiologic equivalent doses have been provided (normalized therapy dose) to compare the various regimens where indicated and can be used to estimate isoeffective schedules.

CONCLUSIONS: This compendium of HDR brachytherapy fractionation schedules provides various options to the gynecologic brachytherapist and a ready reference for clinical use in the management of gynecological cancer treatments.

Keywords: Brachytherapy; Fractionation; Gynecological cancer; Consensus

Introduction

Gynecologic cancers cover a wide spectrum of female organs with tumor types occurring over the lifetime of a woman. Radiation therapy is a critical component of the multidisciplinary management of most of these tumors. Brachytherapy (which involves the application of a radioactive source in close proximity to the tumor/tumor bed) is an integral component of radiation treatment for these cancers as well. In tumors of certain organ sites such as advanced cervical and vaginal cancers, tumor control and overall

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survival are dramatically improved with a brachytherapy boost (1). Brachytherapy takes advantage of the inverse-square law, whereby radiation dose is inversely proportional to the square of the distance from the source. In practical terms, this allows for a very high dose to the tumor with relative sparing of the surrounding normal structures if technically well-performed (2).

High-dose-rate (HDR) intracavitary and interstitial brachytherapy have the advantages of limiting exposure to health care staff and increasing the ability to optimize the dose distribution to the target relative to organs at risk (OARs) (3). After determining what volume or point to prescribe to, one must select a dose-fractionation scheme (how many treatments, the dose per treatment, and method of dose specification). Brachytherapy dose fractions are larger than standard external-beam dose fractions. Given the potential for short- and long-term injury to normal tissues from large HDR doses per treatment, the radiation oncologist must carefully assess and minimize doses to OARs. A variety of dose-fractionation schedules are used in clinical practice for HDR brachytherapy depending on the gynecological tumor site. There is often a lack of consensus on dose-fractionation schedules and limited published data showing the benefit of one schedule over another.

This report will focus on the various accepted HDR dose-fractionation schemes for gynecologic HDR brachytherapy. This compendium document will review and make recommendations based on available literature of the most optimal fractionation choices for HDR brachytherapy for gynecological tumors.

Methods and materials

A variety of dose-fractionation schedules exist for gynecologic brachytherapy when given alone or combined with external-beam radiotherapy (EBRT). Gynecologic radiation oncology experts from the American Brachytherapy Society (ABS) evaluated the relevant literature on different HDR fractionation schemes, identified the most accepted and established regimens for various disease sites, and in discussion via conference calls, and supplemented this information with their clinical experience to formulate the current compendium. This report was reviewed and approved as a Gynecologic Cancer Task Force of the ABS.

Compendium

Determining biological equivalence in dose

It is well known that biological response is inadequately described by total absorbed dose alone. Temporal variations in how the total absorbed dose is delivered, such as dose per fraction, dose rate, and the overall treatment duration, can significantly impact treatment outcome, and accounting for such differences is necessary for exchange of clinical information. Although relating treatment to biological effect should include all factors influencing clinical outcome, the most commonly used mathematical model relating total absorbed dose and dose per fraction to outcome is the linear-quadratic cell survival formalism.

By protracting radiation delivery, the probability of repairing the quadratic component increases. This can be modeled by multiplying the quadratic component by the Lea-Catcheside protraction factor (G) that depends on the temporal distribution of dose and the rate of damage repair (4). HDR brachytherapy fractions are considered as short exposure times ($G = 1$) and the biological effects are considered the same as that for EBRT of the same dose per fraction.

It is often necessary to alter a fractionation regimen for various reasons. The linear-quadratic formalism offers a convenient isoeffect conversion from one fractionation pattern to another.

Because most experience is based on conventional 2 Gy per fraction data, it is recommended to convert each HDR brachytherapy schedule into a course which would give an equivalent biological effect when delivered in 2 Gy fractions (EQD2). As different α/β ratios change isoeffect conversions, ICRU 89 (5) recommends the equieffective dose delivered in 2 Gy fractions be given as $EQD2_{\alpha/\beta}$

Modern gynecological HDR brachytherapy target volume and normal OAR tolerance limits are based on a long history and experience with low-dose-rate (LDR) brachytherapy (6–8). HDR brachytherapy fractionation patterns are commonly determined to deliver LDR brachytherapy equivalence in terms of survival outcomes based on existing retrospective and prospective studies. To determine brachytherapy equivalence, it is often assumed that the total absorbed dose from LDR brachytherapy is equivalent to the total absorbed dose from EBRT when delivered in 2 Gy fractions. Radiobiological models agree with this convenient equivalency when assuming an α/β ratio of 3 Gy and 10 Gy for OAR and tumors, respectively, a repair half-time of 1.5–2 h, and LDR brachytherapy dose rates ranging from 40 to 60 cGy/h (9). For example, suggested HDR brachytherapy dose per fraction for adjuvant vaginal cuff brachytherapy alone have generally been formulated to deliver an approximate 60 Gy total LDR equivalent absorbed dose to the vaginal surface. The required HDR brachytherapy dose per fraction and total absorbed dose can then be determined by calculating the $EQD2_{10}$ for approximately 60 Gy, although lower equivalent doses have also been delivered with acceptable results (7). For courses that combine EBRT and HDR brachytherapy, as in the management of cervical cancer, the EQD2 should be determined for each form of radiation, respectively, followed by a simple summation.

For courses that combine EBRT and HDR brachytherapy, as in the management of cervical cancer, the EQD2 should be determined for each form of radiation, respectively, followed by mathematical summation for purposes of simplifying dose estimation to the high risk clinical target volume (HR-CTV). It is noted, however, that

EQD2 summation of dose or dose-volume parameters does not necessarily equate treatment plans. Unlike in EBRT, where dose variation within a target volume is kept to a minimum, brachytherapy dose distributions are inherently highly heterogeneous, making it challenging to compare plans. The actual absorbed dose to the CTV is very inhomogenous with the Cervix gross tumor volume (GTV) receiving much higher doses than the HR-CTV. In addition, the doses to the paracervical and parametrial tissues are better represented by the intermediate-risk CTV as defined by GEC-ESTRO. When using image-guided approaches, different target volumes can be used to describe the heterogenous, risk-adapted dose distribution (dose painting with brachytherapy). These have not been detailed in this compendium. In addition, it should be noted that the dose to 98% of the HR-CTV (D_{98}) is more accurately representative of doses to the peripheral extensions of the cervix tumor and should also be documented as recommended in ICRU 89.

Choosing the dose per fraction and total absorbed dose for the desired $EQD2_{10}$ will often depend on tumor size, site of disease, type of implant, proximity to OAR, treatment center logistics, and patient convenience. A variety of dose-fractionation schedules are used in clinical practice for HDR brachytherapy. While higher doses per fraction are more potent and may provide some convenience, studies suggest a potential for higher rates of complications with doses >7 Gy per fraction and they should be used carefully and with the optimal implant geometry after assessing doses to OARs (10). The various gynecological tumor sites and corresponding HDR dose-fractionation schemes form the next part of this report.

Intact cervical cancer (intracavitary ± needles for definitive tandem-based brachytherapy)

Point A–based prescription. Treatment with EBRT (with or without concomitant chemotherapy) and brachytherapy should be completed in less than 7–8 weeks as better local tumor control and survival can be expected (11,12). Some institutions interdigitate HDR brachytherapy with EBRT to shorten the total treatment duration, but this can only be carried out if adequate dose can be given to the residual disease. The most recent ABS consensus guidelines for HDR definitive brachytherapy for cervix cancer are from 2012 (8). Table 1 in the following (from the 2012 ABS guidelines for HDR cervix) brachytherapy (8) gives the commonly accepted fractionation schemes with median Point A prescriptions for tandem-based brachytherapy. These prescriptions as listed are before the use of optimization and may not accurately represent the doses for volume-based prescription, which is described in next section. Although in the United States, the most common HDR intracavitary regimen prescribes a total of five fractions, internationally, other fractionation schemes include four fractions of HDR (13).

Additional fractionation schemes for the HDR brachytherapy component are 3 × 8 Gy/fx (13,14) with equivalent $EQD2_{10}$ of 36–40 Gy (13,14) and while not commonly utilized but attractive for resource poor countries 2 × 9 Gy/fx can be considered (15,16). The previous ABS guidelines had recommended a maximum of 7.5 Gy/fx and a minimum of four fractions (17) to avoid toxicity. A recent clinical trial highlights the benefits of using a three fx regimen of 8 Gy/fx compared with a 4 fx regimen of 6 Gy/fx (18). This trial showed equivalent tumor and OAR toxicity for both regimens, giving an option of completing treatments in three fractions, which may be necessary in some situations for patients with logistic or compliance issues. An ABS consensus (19) for low- and middle-income countries recommended total $EQD2_{10}$ absorbed doses to the tumor of at least 80 Gy with the corresponding lower number of HDR fractions and use of larger doses per fraction such as 3 × 8 Gy/fx if necessary. The even larger fractionation of 2 × 9 Gy/fx was tested in a small clinical trial and lower toxicity than expected was attributed to general anesthetic and aggressive packing, which was thought to be able to displace OARs (15). Note that, however, a recent international trial showed greater local control benefit for a 4 × 7 Gy/fx compared with the 2 × 9 Gy/fx schedule (20) (Table 1).

Table 1
Suggested fractionation schemes for Point A–based brachytherapy for intact cervical cancer (modified from ABS guidelines) (8)

EBRT fractionation	Point A dose	$EQD2_{10}$ (Gy) to Point A
25 × 1.8 Gy	4 × 7 Gy	83.9
25 × 1.8 Gy	5 × 6 Gy	84.3
25 × 1.8 Gy	6 × 5 Gy	81.8
25 × 1.8 Gy	5 × 5.5 Gy	79.8

ABS = American Brachytherapy Society; EBRT = external-beam radiotherapy; EQD2 = normalized therapy dose.

For image-guided volume-based brachytherapy, these initial dose prescriptions can be used as a starting point for optimization to deliver the goal dose to the HR-CTV within normal tissue constraints.

3 × 8 Gy and 2 × 9 Gy are additional internationally used regimens.

Image-guided volume-based prescription. For institutions that use cross-sectional imaging to visualize the cervix and involved regions, the ABS guidelines are brief but state that the goal should be good coverage (i.e., $D_{90} \geq 100\%$ of intended prescription dose) to the HR-CTV (21). With a volume-based prescription, the initial dose prescription from Table 1 can be used as a starting point for HR-CTV prescription with typical loading pattern that should then be optimized to increase (or decrease) the achieved dose to the target with a D_{90} goal of 85–95 Gy $EQD2_{10}$ as recommended from the EMBRACE data (12,22–24). The higher doses (90–95 Gy) are generally recommended for larger tumor sizes at time of brachytherapy. This dose range should be targeted while balancing the doses to the OAR within recommended tolerance levels. In the Vienna series, this required hybrid intracavitary/interstitial techniques in approximately 45% of patients (23). When using a hybrid technique with T&O or T&R applicators, the loading of

Table 2
Vaginal cuff brachytherapy fractionation schedules after hysterectomy

Prescription point	Dose per fraction (Gy)	# Of fractions
0.5 cm depth from vaginal surface	7[a]	3
	5.5[b]	4
	5[c]	5
	2.5[d]	6
Vaginal surface	6[e]	5
	8.5[f]	4
	4[g]	6

[a] Portec-2 (30).
[b] ABS survey, also equivalent to f (3,31).
[c] Michigan series (32).
[d] Sorbe *et al*. (29).
[e] MDAC series.
[f] Australian series (33).
[g] DFCI series (34).

the interstitial needles has been recommended to not contain more than 10−20% of the total dwell time to avoid high-dose regions to the vagina and ureters (8). However, this loading recommendation may not be completely applicable with recent advanced applicators having more freedom in needle locations and needle trajectories. Experience with these newer applicators is limited and the loading patterns are yet undefined.

Dose limits for the normal tissues are as follows: The $EQD2_3$ limit to the D_{2cc} (the minimum dose in the most irradiated 2 cc normal tissue volume) that was suggested for the rectum and sigmoid is 70−75 Gy and for the D_{2cc} to the bladder is approximately 80−90 Gy (21). However, lower doses to the OAR have been recommended for practice based on European data. Recent publications from the EMBRACE cohort suggest a lower D_{2cc} rectal (≤65 Gy) and bladder dose (≤80 Gy) will result in less toxicity (24,25). From the same study, vaginal stenosis was correlated with an ICRU rectal point (now also called rectovaginal reference point) $EQD2_3$ dose of ≥65 Gy (26).

Postoperative uterine cancer

Brachytherapy alone. The indications for adjuvant radiation after surgery for early-stage uterine cancer are clearly defined in the ASTRO guidelines (27). The technical details for performance of vaginal cuff brachytherapy are described in the ABS 2012 consensus guidelines (7). There are various fractionation schemes used clinically with no general consensus about the superiority of one regimen over others. The ABS task force thus does not recommend one fractionation scheme over the other in their report (28).

Traditionally doses for brachytherapy have generally been formulated to deliver approximately 60−65 Gy LDR equivalent to the vaginal surface. Several institutions have implemented unique dose-fractionation regimens, which achieve acceptable outcomes based on their own published experience. There have not been any randomized trials comparing all these regimens. The study by Sorbe *et al*. (29) randomized 290 patients to 2.5 Gy/fx × 6 vs. 5.0 Gy/fx × 6 fractions prescribed to 0.5 cm depth. The outcomes were equal in both arms with increased vaginal shortening in the arm with higher doses per fraction. The most recent survey of vaginal brachytherapy practice (28) found that the most commonly used fractionation scheme is 7 Gy × 3 prescribed to 0.5 cm depth, followed by 6 Gy in 5 fx prescribed to the vaginal surface. The next most common were 5.5 Gy × 4 and 5 Gy × 5 to 0.5 cm depth and finally 7.5 Gy × 5 prescribed to the vaginal surface. Acceptable and commonly used fractionation schemes are shown in Table 2.

It should be noted that there is a wide variation in dose-fractionation schemes for vaginal cuff brachytherapy in practice (31). All these regimens appear effective based on institutional reports. The randomized Sorbe study (29) included low-risk population only (current Stage IA Grade 1 and 2), and while it did show increased vaginal toxicity with the higher dose regimen, the doses used for this regimen appear higher than the currently accepted doses prescribed to 5 mm depth from the cuff surface. Table 3 highlights the different dose regimens (with prescriptions to the surface and 0.5 cm depth) and corresponding $EQD2_{10}$ doses to vaginal surface for a 3 cm diameter cylinder. It should be noted that with a smaller diameter cylinder (2.5 cm), these prescriptions to 0.5 cm depth will need to be modified to achieve similar surface doses while reducing vaginal toxicity from the higher dose per fraction regimens (Table 3).

EBRT followed by vaginal brachytherapy boost. From the ABS consensus guidelines (7), the addition of a vaginal cuff

Table 3
Vaginal cuff brachytherapy schedules with corresponding surface doses for a 3 cm diameter cylinder

3 cm Cylinder dose	Prescription depth	Surface $EQD2_{10}$ per fx (Gy)	Total surface $EQD2_{10}$ (Gy)	5 mm depth $EQD2_{10}$ per fx (Gy)	Total 5 mm depth $EQD2_{10}$ (Gy)
7Gy × 3	5 mm	19.25	57.75	9.92	29.75
5.5 Gy × 4	5 mm	13.56	54.23	7.1	28.42
7.5 Gy × 5	Surface	10.94	54.69	5.92	29.6
5Gy × 5	5 mm	11.78	58.92	6.25	31.25
6Gy × 5	Surface	8	40	4.52	22.59
2.5 Gy × 6	5 mm	4.67	28	2.6	15.62

EQD2 = normalized therapy dose.

brachytherapy boost to external-beam pelvic radiation generally should result in a vaginal surface LDR equivalent (EBRT and brachytherapy) of 65−70 Gy. The recommended dose/fractionation schemes are shown in Table 4. These guidelines also suggest that higher brachytherapy doses should be considered for patients who have a superficial positive margins, bringing the total vaginal surface absorbed dose to 70−75 Gy (Table 4).

Recurrent uterine carcinoma in the vagina

In the exceptional situation of small, unifocal, thin (<0.5 cm thick) vaginal recurrences from uterine cancer, vaginal brachytherapy alone has been utilized. There are a few reports of brachytherapy used as a single modality, and as per a recent consensus statement (35), the current recommendation is to combine vaginal brachytherapy boost with pelvic EBRT. The recommended dose for patients with recurrent disease is an LDR equivalent of at least 75 Gy EQD2 to the vaginal lesion target with maintenance of the normal tissue dose constraints (35). As per the consensus after EBRT of 45 Gy, brachytherapy in doses of 5−5.5 Gy in 4−5 fx was the most common fractionation used, prescribed to the CTV (discussed in more detail in the interstitial section) (Table 5).

Primary uterine carcinoma

Primary uterine, clinical Fédération Internationale de Gynécologie et d'Obstétrique Stage 2. Patients with clinical stage II disease may be treated with preoperative (neoadjuvant) radiation therapy followed by simple hysterectomy. In patients with multiple co-morbidities that limit the ability for safe radical surgery, neoadjuvant radiotherapy can decrease the size and extent of bulky cervical disease, making surgery more likely to attain clear surgical margins (36). The LDR data generally recommend a total (EBRT + intracavitary brachytherapy) absorbed dose of 65−70 Gy (36,37). For an HDR uterine brachytherapy boost, the reported fractionation scheme after pelvic EBRT is 5−5.5 Gy for three to four fractions to the entire uterine cervix and upper vagina (38).

Definitive radiation for Fédération Internationale de Gynécologie et d'Obstétrique Stage 1 uterine cancer (medically inoperable). Medically inoperable patients are defined as patients whose medical comorbidities preclude primary surgery. This determination is generally made after multidisciplinary assessment of the treating team. The ABS consensus guidelines for these patients have been recently outlined (39). HDR intracavitary brachytherapy for this indication is often the sole modality or treated in concert with external radiation. The ABS recommended fractionation schemes are as follows:

Table 4
Vaginal cuff brachytherapy fractionation schedules after EBRT

EBRT fractionation	HDR fractionation
45 Gy/25 fx	5−6 Gy × 3 (to surface)
50.4 Gy/28 fx	6 Gy × 2 (to surface)

EBRT = external-beam radiotherapy; HDR = high-dose-rate.

Table 5
Suggested schedules for patients with very superficial (<5 mm) vaginal cuff recurrences (modified from previous ABS consensus) (3)

EBRT fractionation	HDR fractionation	Dose specification	$EQD2_{10}$ (Gy)
45 Gy/25 fx	7 Gy × 3	0.5 cm depth	74
45 Gy/25 fx	6 Gy × 4	0.5 cm depth	76.3
45 Gy/25 fx	6 Gy × 5	surface	84.3
45 Gy/25 fx	7 Gy × 4	surface	83.9

ABS = American Brachytherapy Society; EBRT = external-beam radiotherapy; EQD2 = normalized therapy dose; HDR = high-dose-rate.

Brachytherapy alone (none or minimal myometrial involvement on MRI without cervix involvement). The uterine CTV (entire uterus to the serosa), using HDR brachytherapy should get a dose between 48 and 62.5 Gy $EQD2_{10}$. The goal will be to deliver an $EQD2_{10}$ of 80−90 Gy to the GTV (Table 6).

EBRT and brachytherapy (with deep myometrial invasion or other risk factors for nodal metastases). The uterine CTV (entire uterus, cervix, and upper 1−2 cm of the vagina) using external beam + HDR (combination) should get a dose between 65 and 75 Gy $EQD2_{10}$. The goal will be to deliver an $EQD2_{10}$ of 80−90 Gy to the GTV (Table 7).

Interstitial brachytherapy for vaginal cancers (primary vaginal or uterine cancer recurrence)

Cancers involving the vagina (by their proximity to the lower gastrointestinal and genitourinary tracts) are often not amenable to curative organ-sparing surgery. Radiation therapy with brachytherapy is currently the most widely used and effective primary treatment for patients with invasive vaginal cancers. The ABS consensus guidelines on vaginal interstitial brachytherapy (40) recommend the dose and fractionation schedules shown in Table 8. Lesions that are thick (>0.5 cm) at the time of brachytherapy should be treated with interstitial brachytherapy. The number of implant procedures can be limited to one or two to minimize the morbidity of repeated procedures with multiple fractions delivered with each implantation procedure (Table 8).

Table 6
HDR brachytherapy (alone) schedules for medically inoperable Stage I uterine cancer

HDR fractionation	$EQD2_{10}$ (Gy)
6 Gy × 6	48
6.4 Gy × 6	52.5
7.3 Gy × 5	52.6
8.5 Gy × 4	52.4

EQD2 = normalized therapy dose; HDR = high-dose-rate.

Table 7
EBRT + HDR brachytherapy (boost) schedules for medically inoperable Stage I uterine cancer

EBRT total absorbed dose (Gy)	HDR fractionation	$EQD2_{10}$ (Gy)
45	6.5 Gy × 3	71.1
45	6.3 Gy × 3	69.9
45	5.2 Gy × 4	70.6
45	5 Gy × 5	75
45	8.5 Gy × 2	70.5
50.4	6.0 Gy × 2	65.6
50.4	3.75 Gy × 6	75.3

EBRT = external-beam radiotherapy; HDR = high-dose-rate; EQD2 = normalized therapy dose.

The same guidelines (40) recommend a lower total absorbed dose of 70–75 Gy and/or a lower dose per fraction for disease involving the distal vagina or in close proximity to the vulva or rectovaginal septum. Patients who have had poor response to EBRT or have large residual disease may benefit from higher total absorbed doses of 80–85 Gy.

Combined intracavitary/interstitial brachytherapy for intact cervical carcinoma

In large primary cervix cancers, where (*1*) tumor bulk exceeds intracavitary coverage, (*2*) tumor extensively involves vagina or extends to side wall, and/or (*3*) geometry prevents intracavitary applicator, HDR interstitial brachytherapy may be required for delivering adequate and safe tumor doses. The consensus cervical cancer brachytherapy guidelines by the ABS suggest the following fractionation schemes in this situation. Placement of the central tandem is recommended when a uterus is present, even when needles are used (8).

Table 8
Recommended schedules for HDR vaginal interstitial brachytherapy (template based) in combination with EBRT (modified from ABS guidelines) (40)

EBRT fractionation	HDR fractionation	CTV $EQD2_{10}$	Rectum D_{2cc} per fx to limit $EQD2_3 \leq 65$ Gy
36 Gy/18 fx	5 Gy × 6	72.9	≤4.1
	5.5 Gy × 6	78	≤4.1
39.6 Gy/22 fx	5 Gy × 6	76.4	≤3.8
	5.5 Gy × 6	81.5	≤3.8
45 Gy/25 fx	3 Gy × 9	73.6	≤2.55
	3 Gy × 10	76.8	≤2.38
	4.5 Gy × 5	71.5	≤3.75
	5 Gy × 5	75.5	≤3.75
	5.5 Gy × 5	79.8	≤3.75
	7 Gy × 3	74.1	≤5.2
50.4 Gy/28 fx	4.0 Gy × 5	72.9	≤3.25
	4.5 Gy × 5	76.8	≤3.25
	5 Gy × 5	80.9	≤3.25
	7 Gy × 3	79.4	≤4.55

ABS = American Brachytherapy Society; EBRT = external-beam radiotherapy; EQD2 = normalized therapy dose; HDR = high-dose-rate.

Table 9
Dose-fractionation regimens for template-based HDR interstitial brachytherapy after 45–50.4 Gy of EBRT for cervix cancer (with a single application)

EBRT fractionation	HDR fractionation	CTV $EQD2_{10}$ (Gy)
45 Gy/25 fractions	3.5 Gy × 9	79.7
	4.25 Gy × 7	79.6
	5 Gy × 5	75.5
50.4 Gy/28 fractions	3 Gy × 9	78.8
	4.5 Gy × 5	76.7

EBRT = external-beam radiotherapy; EQD2 = normalized therapy dose; HDR = high-dose-rate.

Twice-a-day treatments with approximately 6 h between fractions (based on general radiobiologic principles of normal tissue repair) over 1 week are generally preferred. The nine-fraction regimen is given over 4.5 days in 1 week with one insertion (Table 9). Another schedule favored by the Vienna group involves dose of 7 Gy × 4 fx to the HR-CTV in two procedures. This may be an option for patients who cannot tolerate five or more fractions in one admission (26). There is also a published regimen of 6 Gy × 6 fx (in two separated insertions) with acceptable results (41). Other regimens using other doses of external beam and brachytherapy fractionation (such as 5.5 Gy × 5 fx) are in use and are also acceptable with consideration of the normal-tissue $EQD2_3$ dose limits and recommended D_{90} goal between 85 and 95 Gy $EQD2_{10}$ for the HR-CTV. Close evaluation of the dose distribution to assure coverage of at risk areas is a crucial part of image-guided brachytherapy, and guidelines do not replace experience and good clinical judgment.

Conclusions

The preceding compendium is a result of a consensus from the ABS gynecologic task force of the most common recommended and accepted fractionation schemes for HDR treatment of various gynecological cancer sites. This is an attempt to provide the practitioner with a ready reference and EQD2 equivalents of these fractionation schemes, thus hopefully aiding the choice of the optimal regimen for patient care. It is understood that patient and treatment circumstances may necessitate a modification of these regimens and that may be acceptable based on the treating physician's clinical judgment.

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