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CLINICAL INVESTIGATION **Cervix**

THE AMERICAN BRACHYTHERAPY SOCIETY RECOMMENDATIONS FOR HIGH-DOSE-RATE BRACHYTHERAPY FOR CARCINOMA OF THE CERVIX

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Purpose: This report presents guidelines for using high-dose-rate (HDR) brachytherapy in the management of patients with cervical cancer, taking into consideration the current availability of resources in most institutions.
Methods: Members of the American Brachytherapy Society (ABS) with expertise in HDR brachytherapy for cervical cancer performed a literature review, supplemented their clinical experience to formulate guidelines for HDR brachytherapy of cervical cancer.
Results: The ABS strongly recommends that definitive irradiation for cervical carcinoma must include brachytherapy as a component. Each institution should follow a consistent treatment policy when performing HDR brachytherapy, including complete documentation of treatment parameters and correlation with clinical outcome, such as pelvic control, survival, and complications. The goals are to treat Point A to at least a total low-dose-rate (LDR) equivalent of 80–85 Gy for early stage disease and 85–90 Gy for advanced stage. The pelvic sidewall dose recommendations are 50–55 Gy for early lesions and 55–65 Gy for advanced ones. The relative doses given by external beam radiation therapy (EBRT) vs. brachytherapy depend upon the initial volume of disease, the ability to displace the bladder and rectum, the degree of tumor regression during pelvic irradiation, and institutional preference. As with LDR brachytherapy, every attempt should be made to keep the bladder and rectal doses below 80 Gy and 75 Gy LDR equivalent doses, respectively. Interstitial brachytherapy should be considered for patients with disease that cannot be optimally encompassed by intracavitary brachytherapy. While recognizing that many efficacious HDR fractionation schedules exist, some suggested dose and fractionation schemes for combining the EBRT with HDR brachytherapy for each stage of disease are presented. These recommendations are intended only as guidelines, and the suggested fractionation schemes have not been thoroughly tested. The responsibility for the medical decisions ultimately rests with the treating radiation oncologist.
Conclusion: Guidelines are established for HDR brachytherapy for cervical cancer. Practitioners and cooperative groups are encouraged to use these guidelines to formulate their treatment and dose-reporting policies. These guidelines will be modified, as image-based treatment becomes more widely available. **© 2000 Elsevier Science Inc.**

Cervix neoplasm, Therapy, High-dose-rate, Brachytherapy, Intracavitary, Interstitial.

INTRODUCTION

The curative potential of radiation therapy in the management of carcinoma of the cervix is greatly enhanced by the use of intracavitary brachytherapy (1–4). The success of brachytherapy requires the delivery of a high radiation dose directly to the tumor while sparing, to some degree, the surrounding normal tissues. Cervical carcinoma has traditionally been treated with low-dose-rate (LDR) brachytherapy. High-dose-rate (HDR) brachytherapy was developed to overcome potential disadvantages of LDR brachytherapy (radiation exposure to medical staff, prolonged treatment time, mandatory hospitalization, and applicator movement) (5–7). HDR brachytherapy, although used successfully for over 30 years in Japan and Europe, has encountered considerable resistance in the United States, because of concerns regarding its potential toxicity (8). Over the last decade, due to its advantages (Table 1), HDR has begun to gain acceptance in the United States.

The primary disadvantage of HDR brachytherapy is the potential late toxicity of large doses per fraction. As with external beam radiation therapy (EBRT), which also delivers radiation at high-dose rates, these radiobiologic disadvantages can be overcome through adequate fractionation. Additionally, in HDR, late tissue complications might be

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Table 1. Advantages of HDR vs. LDR in cancer of the cervix

1. Eliminates radiation exposure hazard for caregivers, visitors; eliminates source preparation and transportation.
2. Allows shorter treatment times:
   a) Less patient discomfort because prolonged bed rest is eliminated
   b) It is possible to treat patients who may not tolerate long periods of isolation and those who are at high risk for acute cardiopulmonary toxicity due to prolonged bed rest.
   c) There is less risk of applicator movement during therapy.
   d) Reduced hospitalization (due to outpatient therapy) results in cost shifting.
   e) Possibly allows greater displacement of nearby normal tissues (by packing or using rectal retractor), which could potentially reduce rectal and bladder morbidity.
   f) It is possible to treat larger number of patients in institutions that have a high volume of cervical cancer patients but insufficient inpatient facilities (for example, in some developing countries).
3. Allows use of smaller diameter sources than are used in LDR:
   a) This reduces the need for dilatation of the cervix and, therefore, reduces the need for heavy sedation or general anesthesia.
   b) High-risk patients who are unable to tolerate general anesthesia can now be more safely treated.
   c) Physically easier to insert applicator into the cervix.
4. Makes treatment-dose-distribution optimization possible. The variation of dwell time with the single stepping source allows an almost infinite variation of the effective source strength and source positions allowing for greater control of the dose distribution and potentially less morbidity.
5. Allows integration of EBRT and HDR, which can lead to a shorter overall duration of treatment and potentially to better tumor control.

Abbreviations: HDR = high-dose-rate; LDR = low-dose-rate; EBRT = external beam radiation therapy.

minimized more effectively than in LDR, because greater normal tissue displacement (e.g., bladder anteriorly and rectum posteriorly) is possible because of the short treatment times and available retraction devices (9, 10).

Several studies (including randomized and non-randomized prospective clinical trials, survey of published studies, and meta-analyses) have compared LDR brachytherapy to HDR brachytherapy in the management of cervical cancer. In summary, these have demonstrated comparable local control, survival, and morbidity (11–20, 21–23). Some even showed lowered rectal morbidity with the use of HDR (14, 17, 18).

Some of the national cooperative groups (GOG, RTOG) are now incorporating HDR as a component of the treatment of cancer of the cervix. However, there is wide variation in its clinical practice, few radiation oncologists in the United States have extensive experience, and there are few established guidelines for its clinical use (24–26). The American Brachytherapy Society (ABS) therefore formed a committee to issue guidelines specifically for the use of HDR brachytherapy for cervical carcinoma. Because the published literature gives insufficient details of the implant techniques, technical details have also been included in this report.

METHODS

The members of the American Brachytherapy Society with expertise in HDR cervical brachytherapy performed a literature review and, supplemented with their clinical experience and biomathematic modeling, formulated guidelines for HDR brachytherapy for cervical carcinoma. Specific recommendations were made for therapy in the community and in the research setting. These recommendations were by consensus and supported by evidence in the literature whenever possible. However, when there were areas of controversy and lack of consensus, these were so noted. Directions for future investigations were formulated. Because published literature does not elucidate how the linear–quadratic model is to be applied to obtain equivalent doses to be used in HDR brachytherapy of the cervix, examples are included as an appendix to this article. External experts who were not members of the panel reviewed this report. The Board of Directors of the ABS approved this final document.

RESULTS

General recommendations

The ABS recommends that brachytherapy must be included as a component of the definitive radiation therapy for cervical carcinoma, based on the Patterns of Care studies that show that recurrences and complications are decreased when brachytherapy is used in addition to EBRT (1, 27–30). Good applicator placement must be achieved to obtain improved local control, survival and lower morbidity (4, 31, 32). The relative doses given by EBRT vs. brachytherapy depend upon the initial volume of disease, the ability to displace the bladder and rectum, the degree of tumor regression during pelvic irradiation, and institutional preference. Interstitial brachytherapy should be considered for patients with disease that cannot be optimally encompassed by intracavitary brachytherapy.

The ABS recommends keeping the total treatment duration to less than 8 weeks, because prolongation of total-treatment duration can adversely affect local control and survival (33–36). The overall treatment duration would be unduly prolonged if the HDR was started only after completion of EBRT, because multiple insertions are required for HDR. The recommendation is therefore to interdigitate the implants during the EBRT (but EBRT is not given on the day of HDR). Typically, if the vaginal geometry is optimal, HDR brachytherapy is started after 2 weeks of EBRT. HDR is then continued once a week, with the EBRT being given the other 4 days of the week. If, due to large tumor volume, it is necessary to delay the start of HDR brachytherapy, it is advisable to perform two implants per week after the EBRT has been completed, to keep the total treatment duration to less than 8 weeks.

Each institution should follow a consistent treatment policy when performing HDR brachytherapy, including complete documentation of treatment parameters and correlation

Table 2. Suggested doses of EBRT and HDR brachytherapy to be used in treating early cervical cancer

EBRT (Gy) @ 1.8 Gy/fraction	No. of HDR fractions	HDR dose/ fraction
20	6	7.5
20	7	6.5
20	8	6.0
45	5	6.0
45	6	5.3

Abbreviations: EBRT = external beam radiation therapy; HDR = high-dose-rate; LDR = low-dose-rate.

with clinical outcome, such as pelvic control, survival, and complication (26).

External beam therapy

The ABS recognizes that the whole pelvic EBRT dose varies from institution to institution. The HDR fraction size and number depends on the EBRT dose (Table 2 and 3). Some institutions prefer to limit the whole pelvis dose for patients with early disease and to perform the first intracavitary insertion after 20 Gy, with further EBRT delivered with a central block in place. The ABS recommends careful attention to the complex matching between the intracavitary system and the edge of the midline block, which is critical to the success of this approach (37). If a lower EBRT dose is chosen for patients with early disease, the ABS recommends increasing the HDR fraction size and/or number of fractions (Table 2). However, the individual fraction size should be kept to less than 7.5 Gy due to reports of higher toxicity with larger fraction sizes (17, 22). Most institutions prefer to deliver 40–50 Gy of EBRT to the entire pelvis. In these cases, the brachytherapy dose is decreased (Table 2).

There is no consensus regarding the use of midline blocks. The ABS recommends that, if used, simple rectangular blocks should routinely be between 4- and 5-cm wide at midplane when intracavitary brachytherapy applicators are used. Optimally, customized midline blocks based on radiographs taken with similar isocenters and reflecting the isodose distribution of the implant should be considered, if possible. When a midline block is inserted before 40 Gy, it should not extend to the top of the pelvic field because it will shield the common iliac and presacral nodes. When there is suspicion of uterosacral ligament involvement, it is safer to avoid early placement of a midline block, which could potentially shield disease posterior to the implant (38). There are changes in implant position when multiple HDR fractions are performed over time. It is therefore necessary to reassess the midline block configuration after each implant. Every attempt should be made to replicate the position of the applicators at the first implant, if the geometry is optimal, so that the EBRT fields may be continued with a midline block in place. If EBRT doses greater than 45–50 Gy are to be given, the fields should be coned down after the initial 45–50 Gy in an effort to exclude small bowel.

Table 3. Suggested doses of EBRT and HDR brachytherapy to be used in treating advanced cervical cancer

EBRT (Gy) @ 1.8 Gy/fraction	No. of HDR fractions	HDR dose/ fraction
45	5	6.5
45	6	5.8
50.4	4	7.0
50.4	5	6.0
50.4	6	5.3

Abbreviations: EBRT = external beam radiation therapy; HDR = high-dose-rate; LDR = low-dose-rate.

Chemotherapy

The ABS recommends the addition of cis-platinum based chemotherapy during pelvic EBRT since five prospective randomized trials have recently demonstrated a 10–15% increase in local control and survival without increase in complications when concurrent chemotherapy was added to radiation therapy (external beam and LDR brachytherapy) (39–44). However, chemotherapy should not be administered concomitantly with brachytherapy, unless it is in the context of a controlled clinical trial, because increased complications have been reported with concomitant chemotherapy and brachytherapy (45–48).

Insertion techniques

The ABS recommends use of multiple HDR insertions to allow progressive tumor volume reduction, allowing more effective disease coverage with the subsequent application. The ABS recommends the applicator position and packing to be adjusted from fraction to fraction if there were any deficiencies in the initial insertions. Optimum applicator placement and attention to details are critical in maximizing local control and minimizing complications. The ABS recommends considering placement with ultrasound and fluoroscopic guidance, particularly in patients with altered cervical anatomy because the narrow HDR tandem potentially presents a higher risk for uterine perforation.

It is important to choose an applicator that can optimally treat the disease and can be placed in an anatomically distorted vagina (49). When tandem and ovoids are used, the largest ovoid diameter that can be accommodated in the fornices without displacement should be inserted. The ring applicator is particularly useful when the vaginal fornices are asymmetric or absent and it is popular because it has a reproducible geometry and is easy to insert (50, 51). It is important that the plastic caps of the ring applicator be in place with each insertion, because excessive vagina mucosal doses would be delivered without them. It is also important not to activate the entire ring circumference; usually the lateral 4–6 dwell positions are activated on each side of the ring, dependent upon the ring diameter. Another useful device, particularly for patients with a narrow vagina, is the Henschke-type applicator, which can frequently be inserted

when Fletcher-type ovoids cannot be accommodated. If a tandem and ovoid or tandem and ring applicator cannot be inserted because of vaginal narrowing, the absence of fornices, or vaginal extension of disease, interstitial implantation is preferred. Only if this is not available, a tandem and cylinder applicator may be used. It should be realized that use of the cylinder results in lower parametrial doses and higher bladder and rectal doses relative to tumor, with a possible increase in complications and pelvic failures (49, 52).

The ABS recommends that conscious sedation should be used for intracavitary HDR insertions whenever possible and be administered by individuals who are properly trained and are familiar with this approach. In high-risk patients, intensive monitoring is required, and appropriate medical personnel and monitoring equipment must be available. Other anesthetic options include paracervical blocks, epidural or spinal anesthesia, or general anesthesia, although some institutions do not use any sedation after the first insertion. Patient discomfort can, however, lead to suboptimal packing and the inability to place the optimal applicator size. If the applicator position is not optimal, it can be very difficult to make applicator adjustments when the patient is not sedated and cannot be positioned in stirrups. Caution should be exercised in accepting suboptimal applicator position in this situation.

The ABS recommends placing cervical markers for radiologic identification of cervical position and to determine the relationship of the vaginal applicators to the cervix. The use of Smit sleeve may facilitate applicator placement and decrease the risk of uterine perforation (53, 54). Others find the insertion to be easier without using a Smit sleeve. The ABS deems the use of Smit sleeve as an institutional preference.

The ABS recommends displacing the bladder and rectum away from the applicator by using an in-built rectal retractor, radiopaque gauze, a posterior vaginal speculum blade, or an inflatable catheter bulb to increase the therapeutic ratio. Insertion of the rectal retractors may actually displace the applicators toward the bladder, making anterior vaginal packing even more important.

The ABS recommends use of external fixation devices to help prevent applicator movement. Commercially available options for external fixation include the perineal bar and the base plate and clamp device. To avoid uterine perforation in instances in which it is necessary to move patients between rooms, the base plate and clamp device should be temporarily detached or the perineal bar should be used instead. However, the ABS does not advocate caudal retraction of the cervix with a tenaculum, which is practiced at some institutions (9).

The ABS recommends obtaining good-quality radiographs for treatment planning and dosimetry with each fraction, unless the applicator position is nearly identical to the first fraction. Ideally, the applicator insertion, radiograph generation, and treatment should be in a dedicated brachytherapy suite so that there is no need to move the patient. However, it is recognized that it is not possible for all institutions to have a dedicated brachytherapy suite equipped with imaging equipment. Options include transferring patients either from the operating room or a procedure room in the department, to the simulator for radiograph generation, and then transferring to the treatment room. Every effort should be made to minimize patient and applicator movement, so that the dosimetry performed on treatment-planning radiographs matches patient and applicator position during the subsequent treatment. The position of the applicators may change if patient position changes. Increased bladder doses have been reported with the extended supine position (55). Some institutions obtain radiographs and treat in the dorsal lithotomy position; others radiograph and treat in the supine extended position. To avoid any discrepancy in normal tissue doses between these two positions, the ABS recommends treating in the same position as that in the localization radiograph.

Dose specification

Ideally, the dose should be prescribed to the individual patient's target volume. Unfortunately, many facilities currently lack the capability to determine the volume at risk, nor is there sufficient information in the literature to establish a better delineated target volume than the customarily used Point A. The original definition of the Manchester System (56) found Point A by drawing a line connecting the superior aspects of the vaginal ovoids and measuring 2-cm superior along the tandem from the interception with this line and then 2-cm perpendicular to this in the lateral direction. The failure of localization radiographs to show the surfaces of the ovoids made implementation of this process difficult; so, in 1953, Tod and Meredith changed the procedure to begin at the most inferior point of the sources in the tandem (57). With the Manchester applicator, these two definitions essentially locate the same point. Use of this definition (or a common variant beginning at the flange abutting the cervical os) with other applicators results in Point A locations with a wider variation with respect to the ovoids (58). The variation of Point A often occurs in a high-gradient region of the isodose distribution. The result of this variation is that 2 patients with minor differences in the application can receive markedly different amounts of radiation. A consistent location for a dose-specification point should fall sufficiently superior to the ovoids where the dose distribution runs parallel to the tandem. The ABS recommends prescribing the dose to a new point (henceforth called Point H to differentiate from any of the other definitions of Point A).

In a tandem and ovoid insertion, finding Point H begins with drawing a line connecting the mid-dwell positions of the ovoids. From the intersection of this line with the tandem, move superiorly along the tandem 2 cm plus the radius of the ovoids, and then 2-cm perpendicular to the tandem in the lateral direction (see Fig. 1).

In a tandem and ring insertion, finding Point H begins with drawing a line connecting the mid-dwell positions of

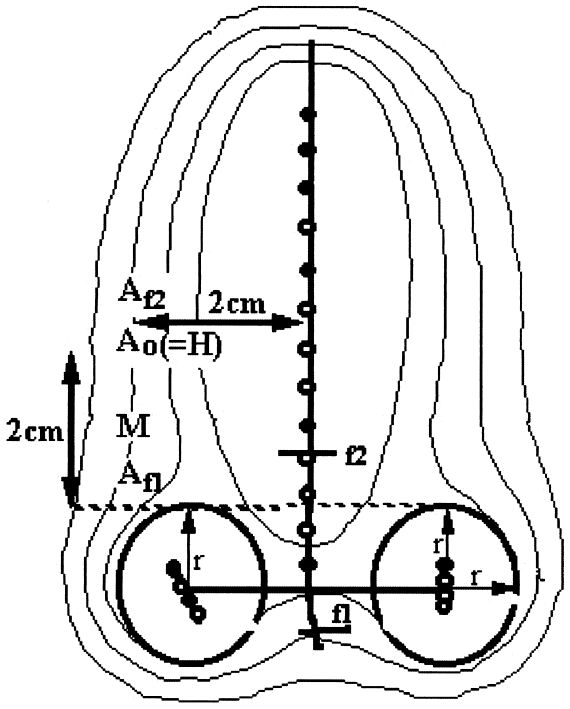

Fig. 1. An illustration of geometry relevant for intracavitary dosimetry, for a tandem and ovoid application. Finding Point H begins with drawing a line connecting the mid-dwell positions of the ovoids. From the intersection of this line with the tandem, move superiorly along the tandem 2 cm plus the radius of the ovoids, and then 2-cm perpendicular to the tandem in the lateral direction. The figure also shows variations in the position of the conventional Point A based on its definition. A_o locates Point A from 2 cm cephalad from the tops of the ovoids according to the original definition by the Manchester System. The position of A_{f1} and A_{f2} follow the revised definition, being 2 cm cephalad of the cervical stopper. In the figure, f1 and f2 show two possible positions for the stopper, each the basis for their respective Point A. Point M follows the definition in the Madison System. The two most cephalad points, A_o and A_{f2} fall away from the high gradient region near the ovoids, but only A_o does so reproducibly. Point H in the text identically duplicates A_o without requiring visualization of the ovoid caps.

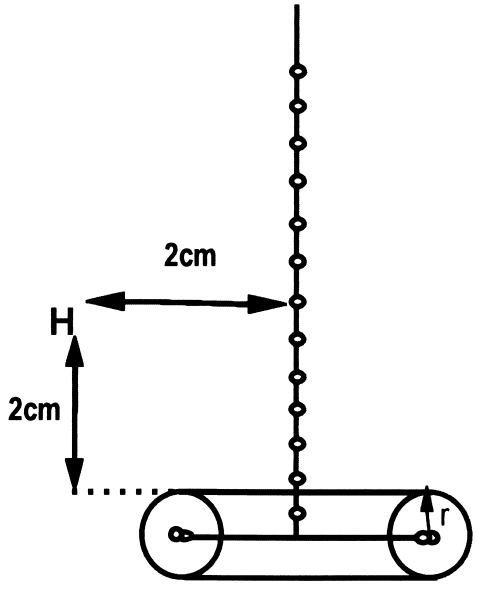

Fig. 2. In a tandem and ring insertion, finding Point H begins with drawing a line connecting the mid-dwell positions of the ring. From the intersection of this line with the tandem, move superiorly along the tandem 2 cm plus the thickness of the ring (including the cap), and then 2 cm perpendicular to the tandem in the lateral direction.

the ring. From the intersection of this line with the tandem, move superiorly along the tandem 2 cm plus the thickness of the ring (including the cap), and then 2-cm perpendicular to the tandem in the lateral direction (see Fig. 2).

For treatment using a tandem and cylinders, the isodose surfaces run nearly parallel to the applicator, and positioning of the dose-definition point becomes less of a problem. The conventional definition works well, placing the point 2-cm cephalad along the tandem from the cervical flange and 2-cm perpendicular to the tandem in the lateral direction.

Optimization

Achieving a good dose distribution with high-dose-rate brachytherapy requires both good insertion of the appliance *and* good optimization. Good optimization requires a sufficient number of dose-definition points to allow the optimization algorithm to determine the dwell weights to obtain the dose-distribution shape. Figure 3 shows an example of optimization.

Important aspects of the optimization include the following:

- Tandem optimization points should begin approximately 1-cm inferior to the first (superior-most) dwell position and should continue through a point approximately 1-cm superior to the surface of the vaginal appliance. Optimization of the superior-most dwell often proves too restrictive, and extending the points further inferiorly conflicts with the optimization to the vagina.
- Optimization points should fall no further than 1 cm apart along the tandem and should fall in both lateral directions. Greater separations provide insufficient specification for the optimization algorithm. Specification on a single side becomes susceptible to the influence of slight tandem rotations or asymmetries with respect to the vaginal applicator.
- The vaginal optimization points should fall either at the vaginal surface or at a specified depth (usually 0.5 cm). If the points fall at depth, the dose at the vaginal surface should also be calculated. Vaginal optimization points should fall in the lateral direction so as not to conflict with the tandem optimization.

It should be realized that incorrect optimization is worse than no optimization at all. Institutions that are not experienced in the use of optimization should follow standard treatment plans that are used in larger centers or supplied by the equipment manufacturer.

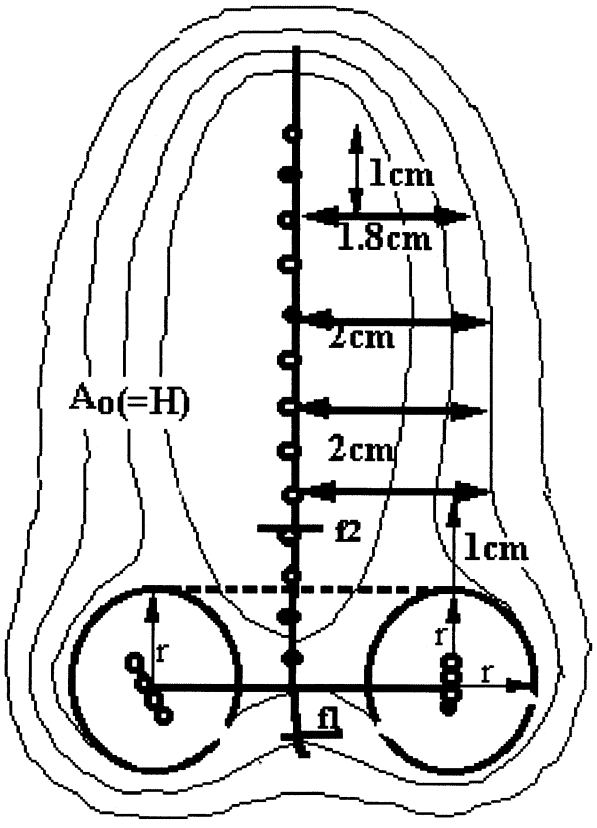

Fig. 3. Illustrates the placement of optimization points for brachytherapy treatment in cervical carcinoma.

Dose calculation to anatomic structures of interest

Adequate treatment requires delivery of the prescribed dose to the target, while avoiding complications requires maintaining doses to sensitive neighboring structures below their tolerance doses. The standard locations for specifying rectal and bladder doses established by the International Commission for Radiation Units (ICRU) in Report 38 (59) do not give the location of the maximum dose to the organs consistently (60–61). Complications probably relate to the degree to which the walls of these organs are exposed to doses exceeding their tolerance. Unfortunately, assessing the true dose delivered requires dosimetry based on better soft-tissue imaging than is possible with standard plane radiography and thus exceeds the capabilities of many centers performing HDR brachytherapy for cervical cancer. Until the capability to perform such dosimetry becomes common, the ABS recommends the following for assessment of the dose to normal tissues:

1. Attempts should be made to keep the dose to the nominal rectal and bladder points below 80% of the dose to Point H (9).

2. Nominal bladder point: Practitioners should use the standard ICRU definition for the bladder dose point with a minor change. The bladder point falls on the surface of a Foley balloon filled with 7 cc of iodinated radiographic contrast (diluted if necessary so as not to obscure the localization markers on the AP radiograph) snugged into the trigone of the bladder. The point selected should correspond to the maximum dose on the surface of this balloon. That point may not be the most posterior aspect of the balloon if it is situated either to one side or significantly superior or inferior to the vaginal applicator. Because bladder complications remain a minor problem with HDR cervical treatment, more detailed localization procedures appear unwarranted until better imaging becomes commonplace.

3. Nominal rectum point: The rectal dose point falls at the location of the maximum dose at the anterior rectal wall in the region of the vaginal applicator. The standard ICRU Report 38 definition of rectal point (0.5-cm posterior to the posterior vaginal wall) can be used for its ease of use and to maintain standardization. Alternatively, the anterior rectal wall may be visualized by injecting a diluted solution of barium contrast (50% contrast: 50% water) with some air contrast into the rectum. After coating the rectum, as much of the contrast material as possible should be withdrawn. It may be necessary to enter several points into the dose calculations in order to find the maximum dose. Alternate localization tools, such as lead markers in a catheter, or measurement devices are not recommended, because they often lie much posterior to the anterior wall and therefore result in erroneously low point doses. Attention should also be given to radiographic visualization and dose to the sigmoid colon as it may pass close to the tandem.

4. Regional lymph nodes: The brachytherapy component of the dose to the lymph nodes remains small compared with that from the external-beam treatments, but it should be included in any combined treatment. The ABS recommends calculating the dose to the points defined in ICRU Report 38 as the Pelvic Wall Points. Because of the minor contributions of the brachytherapy to other nodal locations, other lymph-node doses need not be calculated. The ABS recommends *not* using the Manchester Points B as representative of lymph-node locations, nor carrying these dose points in any national protocols.

Quality assurance

Because the localization, dose calculation, and the treatment delivery for HDR brachytherapy proceed rapidly, errors in the treatment can easily occur before they are detected. This makes an effective quality-assurance program for the HDR treatment plans even more important than for LDR treatments. A recent report (Task Group 59) from the American Association of Physicists in Medicine specifically addresses the issues of quality assurance (QA) for high dose-rate brachytherapy (62). The recommendations in this report should be reviewed before starting any HDR program. Much of the quality assurance remains the same for all HDR brachytherapy cases (e.g., morning tests of the treatment unit) and will not be discussed here. The aspects of QA directed at preventing errors due to mistakes in the treatment planning, however, become treatment-type specific. Some of the important recommendations of this report are summarized below as they relate to treatment for patients with cancer of the cervix.

- The treatment prescription should include the following:

1. a clear designation of the nominal target for the dose specification;
2. a description of the shape of the dose distribution through inclusion of the positioning of optimization points and their relative weights;
3. the fractionation scheme, including the absolute total dose in Gy to the target location, the dose per fraction, and the number of fractions (the redundancy serves as a consistency check).

- The treatment plan should be independently reviewed by a physicist or medical dosimetrist not involved with the generation of the treatment plan, and the physician, and should include checks on the following:

1. that the dosimetry input information is correct and consistent;
2. that the dose per fraction and dose specification location match the treatment prescription, and that the treatment prescription follows the facility's protocol for treatment of patients with cancer of the cervix;
3. that the dose distribution achieved matches with the desired distribution, given any physical constraints such as dose-limiting structures;
4. that the reconstructed implant geometry matches radiographic projections;
5. that the distance from machine reference point to the most distal dwell location is consistent with the treatment geometry;
6. that doses to normal structures remain within tolerances;
7. that the dwell times and locations and the step size programmed into the treatment unit match those on the plan, and that the source tracks have been programmed into the proper treatment unit channels;
8. that the treatment unit recalls the program and adjusts times for decay correctly for subsequent treatment fractions, if this feature is used.

- Part of the review screens the treatment plan for major errors through the use of some objective criteria. Both for the intracavitary and the interstitial approaches, the report presents some examples of consistency tests. These tests compare quantities specific to the patient (such as the product of the total dwell time and the source strength divided by the dose) with a table of the ranges for the quantity normally encountered with correct treatment plans.

The report also addresses training requirements. Radiation oncologists and medical physicists at a facility just beginning an HDR brachytherapy program for the treatment of patients with cancer of the cervix should spend time learning the procedure at a facility with extensive experience in the treatment modality.

Dose recommendations

When EBRT and HDR brachytherapy are combined, the goals are to treat Point A (or Point H) to an LDR equivalent of 80–85 Gy for early-stage disease and 85–90 Gy for advanced stage. Early disease is defined as nonbulky Stage I/II, less than 4-cm diameter; advanced diseased is defined as greater than 4-cm diameter or Stage IIIB. The pelvic-sidewall dose recommendations are 50–55 Gy for smaller lesions and 55–60 Gy for larger ones.

The HDR doses can be obtained by converting the LDR-equivalent doses using the linear–quadratic equation (see Appendix). Because of the dose-rate effect in HDR, the total physical doses will be lower for HDR than for LDR brachytherapy. The conversion of HDR doses to LDR-equivalent doses may not be practical on a day-to-day basis, hence, equivalent tables (63) and simplified computer programs (64) have been developed.

While recognizing that many efficacious HDR fractionation schedules exist, the ABS has developed suggested tables for combining the EBRT with HDR brachytherapy for patients with early and advanced stage of disease, respectively (Tables 2 and 3). These fractionation guidelines are based on published literature and the experience of the panel members, modified by the linear–quadratic formula. It must be emphasized that the dose recommendations in Tables 2 and 3 are intended to serve only as a guide; it should be noted that these schedules have not been thoroughly tested clinically. The responsibility for the medical decisions ultimately rests with the treating physician. Physicians performing HDR brachytherapy need to understand the radiobiologic implications of varying the external and implant dose contributions and the importance of technique. Poor implant techniques will yield poor results, regardless of fractionation schedules. Dose optimization does not compensate for poor applicator positioning or inadequate geometry.

The recommended HDR dose and dose per fraction depends on the whole-pelvic dose delivered (Tables 2 and 3). For example, if the EBRT contribution to Point A is increased from 20 to 45 Gy, the HDR dose per fraction will decrease from 7.5 Gy to 5.3 Gy for 6 fractions. Also, if only 20 Gy is given to the whole pelvis, the remaining dose to the pelvic lymph nodes must be given with a midline pelvic block without shielding the iliac lymph nodes. The recommended HDR dose per fraction may vary by ± 0.25 Gy. It is emphasized that extra care must be taken to ensure adequate bladder and rectal packing when using high dose (> 7 Gy) per fraction. The decision to emphasize the EBRT more than the brachytherapy is contingent upon the initial volume of disease, the ability to displace the bladder and rectum, degree of tumor regression during pelvic radiation, and institutional preference.

Maintaining the same HDR dose from one fraction to the next is contingent upon both the tumor response and dose to the normal tissues. As with LDR brachytherapy, every attempt is made to keep the bladder dose below the LDR equivalent of 80 Gy and the rectal dose below 75 Gy. As above, the linear–quadratic model is used to convert the HDR doses to LDR dose equivalents, using late tissue effect parameters (commonly α/β ratio of 3, see Appendix).

Clinical situations frequently arise where normal tissue tolerance is approached or exceeded. Therapeutic strategies to address this clinical dilemma include decreasing the HDR fraction size (which requires an increase in the fraction number), increasing the EBRT contribution to Point A while lowering the total HDR dose, or using an interstitial implant. Because there are uncertainties in the location of normal tissue points (as discussed earlier), some institutions maintain the tumor dose and accept the higher risks of exceeding the nominal normal tissue tolerance parameters so as not to compromise tumor control.

Interstitial HDR brachytherapy

In some clinical situations (bulky lesions, narrow vaginal apex, inability to enter the cervical os, extension to the lateral parametria or pelvic sidewall, and lower vaginal extension) intracavitary brachytherapy may achieve suboptimal dose distributions (65–71). The ABS recommends use of interstitial brachytherapy (either LDR or HDR) in these cases, because a better dose distribution can be achieved. Interstitial implants are more elaborate and invasive than intracavitary procedures. Consequently, greater attention to the catheter placement is necessary to fully encompass the tumor while avoiding the bladder, rectum, and small bowel. The clinical advantages of interstitial over intracavitary brachytherapy may be offset by serious complications if these critical normal structures are inadvertently included in the high-dose region of the implant. Further, the advantages of HDR interstitial brachytherapy over LDR interstitial brachytherapy must be counterbalanced against the need to use a larger number of HDR fractions and the inconvenience of having to treat the patient twice a day.

The ABS suggests interdigitating HDR interstitial brachytherapy with pelvic EBRT, starting the HDR after 2–4 weeks of pelvic EBRT to allow for some tumor regression. The recommended whole pelvic EBRT doses are similar to those used for intracavitary HDR (Tables 2 and 3). The ABS recommends that, if used, the midline block for interstitial brachytherapy should correspond to the isodose distribution. One method is to create a block matched to the anterior–posterior projection of the 100% isodose. The critical structures requiring protection from the high-dose region are the bladder trigone, ureterovesical junction, rectum, and small bowel. A block larger than the implant should be avoided because it might result in underdosage of the parametria.

The ABS recommends use of a perineal template and spinal anesthesia for the implant procedure. The use of intraspinal morphine often eliminates the need for additional pain medication, and the applicator is generally removed in less than 24 h. The ABS recommends combinations of digital rectal examination, laparoscopy, laparotomy, cystoscopy, proctosigmoidoscopy, transrectal ultrasound, transabdominal ultrasound, CT scan, and/or fluoroscopy to guide the needle/catheter placement (72–75). If needles are placed along the vaginal cylinder adjacent to the vaginal mucosa, the vaginal doses must be reduced by the placement of a sleeve over the cylinder (76), or by decreasing the weighting of the dwell positions adjacent to the vagina. The other aspects of the HDR insertion procedure are similar to LDR interstitial brachytherapy.

Table 4. California Endocuritherapy Cancer Center protocol for interstitial HDR brachytherapy of cervical cancer*

	IB/IIA (< 4 cm)	IB/IIA (> 4 cm)	IIB/IIIA/ IIIB
Whole pelvic EBRT dose	25 Gy	30 Gy	36 Gy
Sidewall total EBRT dose	50 Gy	50 Gy	50 Gy
HDR dose per fraction × number	6 Gy × 6	5.75 Gy × 6	5.5 Gy × 6

* The tumor doses presented can safely be administered only when brachytherapy doses to the rectum and bladder are limited to 65% and 75% of the tumor dose, respectively.

Abbreviations: EBRT = external beam radiation therapy; HDR = high-dose-rate.

The ABS recommends obtaining simulation radiographs for treatment planning. If available, computerized tomography (75) or magnetic resonance imaging (77) can be used to produce true three-dimensional (3D) isodose calculations and delineate the relationship of the implant to tumor and normal anatomical structures.

HDR interstitial brachytherapy may be delivered by a variety of alternative fractionation schemes. There is a paucity of published experience, and the number of implant procedures and the "fractions" per implant session have not been standardized. The treatment protocol used at one institution with extensive experience in HDR interstitial brachytherapy is presented in Table 4 (78). Due to the larger treatment volumes and the different prescription methods, the total LDR-equivalent doses appear to be somewhat lower than those used for HDR-intracavitary brachytherapy. The treatment protocol may be modified upon considerations, such as curative vs. palliative intent, location and extent of the lesion, proportion of radiation course given with EBRT, the level of anesthesia risk, and other factors. Concomitant chemotherapy during HDR-interstitial brachytherapy should be avoided to prevent undue toxicity until further studies become available.

FUTURE DIRECTIONS

Current HDR-planning methods uses standard radiographs. The limitations of defining the actual tumor and normal tissue volumes have been documented. By using MRI, Russel *et al.* reported how bulky cervical cancers can be missed with conventional EBRT fields (79). Through CT-based brachytherapy planning, Schoeppel *et al.* found that the ICRU normal tissue doses are not a true reflection of the actual doses that these tissues receive (61). The optimization achieved with HDR most likely can be further improved if 3D imaging (using CT or MRI) is used to

increase the dose delivery to the target volume while minimizing the dose to the surrounding normal tissues (80, 81). This will necessitate the use of CT and MR compatible HDR applicators (61, 82). The manufacturers need to develop the necessary software and hardware required to implement 3D dosimetry as has been accomplished for permanent prostate implant.

CONCLUSION

Guidelines for HDR brachytherapy for cancer of the cervix are presented. Practitioners and cooperative groups are encouraged to use these guidelines to formulate their treatment and dose-reporting policies. These guidelines will be modified as image-based treatment becomes more widely available.

DISCLAIMER

These guidelines are a statement of consensus of the authors regarding currently accepted approaches to treatment. The suggested dose and fractionation schemes have not been thoroughly tested. Any clinician following these guidelines is expected to use independent medical judgment in the context of individual clinical circumstance to determine any patient's care or treatment. The American Brachytherapy Society makes neither representation nor warranties of any kind regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

REFERENCES

1. Lanciano RM, Won M, Coia LR, *et al.* Pretreatment and treatment factors associated with improved outcome in squamous cell carcinoma of the uterine cervix: A final report of the 1973 and 1978 patterns of care studies. *Int J Radiat Oncol Biol Phys* 1991;20:667–676.
2. Montana GS, Fowler WC, Varra MA, *et al.* Carcinoma of the cervix, stage III: Results of radiation therapy. *Cancer* 1986; 57:148–154.
3. Perez CA, Breaux S, Madoc-Jones H, *et al.* Radiation therapy alone in the treatment of carcinoma of the uterine cervix: I. Analysis of tumor recurrence. *Cancer* 1983;51:1393–1402.
4. Eifel PJ, Morris M, Oswald MJ. The influence of tumor size and growth habit on outcome of patients with FIGO stage IB squamous cell carcinoma of the uterine cervix. *Int J Radiat Oncol Biol Phys* 1993;27(1):127–128.
5. Henschke UK, Hilaris BS, Mahan GD. Remote afterloading with intracavitary applicators. *Radiology* 1964;83:344–345.
6. O'Connell D, Howard N, Joslin CAF, *et al.* A new remotely controlled unit for the treatment of uterine carcinoma. *Lancet* 1965;2:570–571.
7. Wakabayashi M, Irie G, Sugawara T, *et al.* The trial production of remote after-loading system unit. Japan. *Jpn J Clin Radiol* 1966;11:678–648.
8. Eifel PJ. High-dose rate brachytherapy for carcinoma of the cervix: High tech or high risk. *Int J Radiat Oncol Biol Phys* 1992;24:383–386.
9. Stitt JA, Fowler JF, Thomadsen BR, *et al.* HDR intracavitary brachytherapy for carcinoma of the cervix—the Madison system, I: Clinical and radiobiological considerations. *Int J Radiat Oncol Biol Phys* 1992;24:335–348.
10. Thomadsen BR, Shahabi S, Stitt JA, *et al.* HDR intracavitary brachytherapy for carcinoma of the cervix—the Madison system, II: Procedural and physical considerations. *Int J Radiat Oncol Biol Phys* 1991;24:349–357.
11. Akine Y, Tokita N, Ogino T, *et al.* Dose equivalence for high-dose rate to low-dose rate intracavitary irradiation in the treatment of cancer of the uterine cervix. *Int J Radiat Oncol Biol Phys* 1990;19:1511–1514.
12. Arai T, Nakano T, Morita S, *et al.* High-dose-rate remote afterloading intracavitary radiation therapy for cancer of the uterine cervix. *Cancer* 1992;69:175–180.
13. Cikaric S. Radiation therapy of cervical carcinoma using either HDR or LDR afterloading: comparison of 5-year results and complications. *Strahlenther Onkol* 1988;82(Suppl.):119–122.
14. Fu KK, Phillips TL. High-dose rate vs, low-dose rate intracavitary brachytherapy for carcinoma of the cervix. *Int J Radiat Oncol Biol Phys* 1990;19:791–796.
15. Glaser FH. Comparison of HDR afterloading with ^{192}Ir versus conventional radium therapy in cervix cancer: 5-year results and complications. *Strahlenther Onkol* 1988;82(Suppl.):106–113.
16. Kuipers T. High dose-rate intracavitary irradiation: Results of treatment. In: Mould RF, editor. Brachytherapy. Leersum, The Netherlands: Nucleotron Trading BV; 1985. p. 169–175.
17. Orton CG, Seyedsadr M, Somnay A. Comparison of high and low dose rate remote afterloading for cervix cancer and the importance of fractionation. *Int J Radiat Oncol Biol Phys* 1991;21:1425–1434.
18. Patel FD, Sharma SC, Negi PS, *et al.* Low dose rate vs HDR brachytherapy in the treatment of carcinoma of the uterine cervix: A clinical trial. *Int J Radiat Oncol Biol Phys* 1994;28: 335–341.
19. Sarkaria JN, Petereit DG, Stitt JA, *et al.* A comparison of the efficacy and complication rates of low-dose rate vs high-dose rate brachytherapy in the treatment of uterine cervical carcinoma. *Int J Radiat Oncol Biol Phys* 1994;30:75–82.
20. Shigematsu Y, Nishiyama K, Masaki N, *et al.* Treatment of carcinoma of the uterine cervix by remotely controlled afterloading intracavitary radiotherapy with HDR: A comparative study with a low-dose rate system. *Int J Radiat Oncol Biol Phys* 1983;9:351–356.
21. Teshima T, Inoue T, Ikeda H, *et al.* High-dose rate and low-dose rate intracavitary therapy for carcinoma of the uterine cervix. *Cancer* 1993;72:2409–2414.
22. Orton CG. High and low dose rate brachytherapy for cervical cancer. *Acta Oncol* 1998;37:117–125.
23. Petereit DG, Pearcey R. Literature analysis of high dose rate brachytherapy fractionation schedules in the treatment of cervical cancer: Is there an optimal fractionation schedule? *Int J Radiat Oncol Biol Phys* 1999;43:359–366.
24. Nag S, Owen J, Farnan N, *et al.* Survey of brachytherapy practice in the United States: A report of the clinical research committee of the American Endocurietherapy Society. *Int J Radiat Oncol Biol Phys* 1995;31:103–107.
25. Nag S, Orton C, Young D, *et al.* American Brachytherapy Society Survey of brachytherapy practice for carcinoma of the cervix in the United States. *Gynecol Oncol* 1999;73:111–118.
26. Nag S. Abitbol AA, Anderson LL, *et al.* Consensus guidelines for HDR remote brachytherapy in cervical, endometrial, and endobronchial tumors. *Int J Radiat Oncol Biol Phys* 1993;27: 1241–1244.

27. Hanks GE, Kerring DF, Kramer S. Patterns of care outcome studies. Results of the national practice in cancer of the cervix. *Cancer* 1983;51:959–967.
28. Coia L, Won M, Lanciano R, *et al.* The patterns of care outcome study for cancer of the uterine cervix. Results of the second national practice survey. *Cancer* 1990;66:2451–2456.
29. Montana GS, Hanlon AL, Brickner TL, *et al.* Carcinoma of the cervix: Patterns of care studies: Review of 1978, 1983, and 1988–1989 surveys. *Int J Radiat Oncol Biol Phys* 1995;32(5): 1481–1486.
30. Montana GS, Martz KL, Hanks GE. Patterns and sites of failure in cervix cancer treated in the USA in 1978. *Int J Radiat Oncol Biol Phys* 1991;20:87–93.
31. Corn BW, Hanlon AL, Pajak TF, *et al.* Technically accurate intracavitary insertions improve pelvic control and survival among patients with locally advanced carcinoma of the uterine cervix. *Gynecol Oncol* 1994;53:294–300.
32. Perez CA, Breaux S. Bedwinek JM, *et al.* Radiation therapy alone in the treatment of carcinoma of the uterine cervix II. Analysis of complications. *Cancer* 1984;54:235–246.
33. Grinsky T, Rey A, Roche B, *et al.* Overall treatment time in advanced cervical carcinomas: A critical parameter in treatment outcome. *Int J Radiat Oncol Biol Phys* 1993;27:1051–1056.
34. Perez CA, Grigsby PW, Castro-Vita H, *et al.* Carcinoma of the uterine cervix. I. Impact of prolongation of overall treatment time and timing of brachytherapy on outcome of radiation therapy. *Int J Radiat Oncol Biol Phys* 1995;32(5):1275–1288.
35. Petereit DG, Sarkaria JN, Hartmann TJ, *et al.* Adverse effect of treatment prolongation in cervical carcinoma. *Int J Radiat Oncol Biol Phys* 1995;32:1301–1307.
36. Lanciano RM, Pajak TF, Martz K, *et al.* The influence of treatment time on outcome for squamous cell cancer of the uterine cervix treated with radiation: A patterns-of-care study. *Int J Radiat Oncol Biol Phys* 1993;25:391–397.
37. Eifel PJ, Levenback C, Wharton JT, *et al.* Time course and incidence of late complications in patients treated with radiation therapy for FIGO stage IB carcinoma of the uterine cervix. *Int J Radiat Oncol Biol Phys* 1995;32:1289–1300.
38. Erickson B. Intracavitary applications in the treatment of cancer of the cervix, part 1: Low dose rate techniques. *J Brachyther Int* 1997;13:179–205.
39. Morris M, Eifel P, Lu J, *et al.* Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. *N Engl J Med* 1999;340(15): 1137–1143.
40. Keys HM, Bundy BN, Stehman FB, *et al.* Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. *N Engl J Med* 1999;340:1154–1161.
41. Rose PG, Bundy BN, Watkins EB, *et al.* Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *N Engl J Med* 1999;340:1144–1153.
42. Whitney CW, Sause W, Bundy BN, *et al.* A randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stages IIB–IVA carcinoma of the cervix with negative para-aortic lymph nodes. *J Clin Oncol* 1999;17:1339–1348.
43. Peters WA III, Liu PY, Barrett R, *et al.* Cisplatin, 5-fluorouracil plus radiation therapy are superior to radiation therapy as adjunctive in high-risk, early-stage carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: Report of a phase III inter-group study. Presented at the 30th Annual Meeting of the Society of Gynecologic Oncologists; 1999 Mar 20–24; San Francisco.
44. Thomas GM. Improved treatment for cervical cancer, concurrent chemotherapy and radiotherapy. *N Engl J Med* 1999; 340(15):1198–1199.
45. Kavanagh BD, Bentel GC, Montana GS. Soft tissue complication rates after low dose rate brachytherapy using customized perineal templates. *Int J Radiat Oncol Biol Phys* 1994; 30:508.
46. Clark BG, Souhami L, Roman TN, *et al.* Rectal complications in patients with carcinoma of the cervix treated with concomitant cisplatin and external beam irradiation with high-dose-rate brachytherapy: A dosimetric analysis. *Int J Radiat Oncol Biol Phys* 1994;28(5)1243–1250.
47. Clark BG, Souhami L, Roman TN, *et al.* The prediction of late rectal complications in patients treated with high dose-rate brachytherapy for carcinoma of the cervix. *Int J Radiat Oncol Biol Phys* 1997;38:989–993.
48. Souhami L, Seymour R, Roman TN, *et al.* Weekly cisplatin plus external beam radiotherapy and HDR brachytherapy in patients with locally advanced carcinoma of the cervix. *Int J Radiat Oncol Biol Phys* 1993;27:871–878.
49. Erickson BA. Intracavitary applications in the treatment of cancer of the cervix, part II: High dose rate techniques. *J Brachyther Int* 1997;13:271–287.
50. Abitbol AA, Houdek P, Schwade JG, *et al.* Ring applicator with rectal retractor: Applicability to HDR brachytherapy of cervical cancer. *Selectron Brachyther J* 1990;4:68–69.
51. Wollin M, Kagan AR, Olch A, *et al.* Comparison of the ring applicator and the Fletcher applicator for HDR gynaecological brachytherapy. *Selectron Brachyther J* 1991;2(Suppl.):25–27.
52. Crook JM, Esche BA, Chaplain G, *et al.* Dose-volume analysis and the prevention of radiation sequelae in cervical cancer. *Radiother Oncol* 1987;8:321–332.
53. Smit BJ. HDR brachytherapy for cervical carcinoma using the indwelling intrauterine tube. *Selectron Brachyther J* 1991;5: 28–32.
54. Smit BJ, du Toit JP, Groenewald WA. An indwelling intrauterine tube to facilitate intracavitary radiotherapy of carcinoma of the cervix. *Br J Radiol* 1989;62:68–69.
55. Joelsson I, Backstrom A. Dose rate measurements in bladder and rectum intracavitary radiation of carcinoma of the uterine cervix. *Acta Radiol* 1969;8:343–359.
56. Tod M, Meredith W. A dosage system for use in the treatment of cancer of the uterine cervix. *Br J Radiol* 1938;11:809–824.
57. Tod M, Meredith W. Treatment of cancer of the cervix uteri—a revised "Manchester method." *Br J Radiol* 1953;26: 252–257.
58. Potish R, Gerbi B, Engler GP. Dose prescription, dose specification, and applicator geometry in intracavitary therapy. In: Williamson JF, editor. Brachytherapy physics. Madison, WI: Medical Physics Publishing; 1995. p. 379–410.
59. ICRU report 38. Dose and volume specification for reporting intracavitary therapy in gynecology. Bethesda, MD: International Commission on Radiation Units and Measurements; 1985. p. 1–20.
60. Schoeppel SL, LaVigne ML, Martel MK, *et al.* Three-dimensional treatment planning of intracavitary gynecologic implants: Analysis of ten cases and implications for dose specification. *Int J Radiat Oncol Biol Phys* 1994;28:277–283.
61. Schoeppel SL, Frass BA, Hopkins MP, *et al.* A CT-compatible version of the Fletcher system intracavitary applicator: Clinical application and 3-dimensional treatment planning. *Int J Radiat Oncol Biol Phys* 1989;17:1103–1109.
62. AAPM Radiation Therapy Committee Task Group No. 59, Kubo HD, Glasgow GP, Pethel TD, *et al.* High dose-rate brachytherapy treatment delivery *Med Phys* 1998;25(4):375–403.
63. Orton CG. Radiobiology. In: Nag S, editor. Principles and practice of brachytherapy. Armonk, NY: Futura Publishing; 1997. p. 27–45.
64. Nag S, Gupta N. A simple method of obtaining equivalent

doses for use in HDR brachytherapy. *Int J Radiat Oncol Biol Phys* 2000;46:507–513.
65. Ampuero F, Doss LL, Khan M, *et al.* The Syed-Neblett interstitial template in locally advanced gynecological malignancies. *Int J Radiat Oncol Biol Phys* 1983;9:1897–1903.
66. Aristizabal SA, Valencia A, Ocampo G, *et al.* Interstitial parametrial irradiation in cancer of the cervix stage IIB–IIIB: Analysis of pelvic control and complications. *Endocurie Hypertherm Oncol* 1985;1:41–48.
67. Erickson B, Gillin MT. Interstitial implantation of gynecological malignancies. In: Nag S, editor. Principles and practice of brachytherapy. Armonk, NY: Futura Publishing; 1997. p. 515–552.
68. Feder BH, Syed AMN, Neblett, D. Treatment of extensive carcinoma of the cervix with the "transperineal parametrial butterfly." *Int J Radiat Oncol Biol Phys* 1978;4:735–742.
69. Martinez A, Edmundson GK, Clarke D. The role of transperineal template implants in gynecological malignancies. *Brachyther J* 1991;5:107–113.
70. Syed AMN, Puthawala AA, Neblett D, *et al.* Transperineal interstitial-intracavitary "syed-neblett" applicator in the treatment of carcinoma of the uterine cervix. *Endocuriether Hypertherm Oncol* 1986;2:1–13.
71. Ezzell GA, Luthmann RW. Clinical implementation of dwell-time optimization techniques for single stepping-source remote afterloaders. In: Williamson JF, Thomadsen BR, Nath R, editors. Brachytherapy physics. Madison, WI: Medical Physics Publishing; 1995. p. 617–640.
72. Erickson B, Foley WD, Gillin M, *et al.* Ultrasound-guided transperineal interstitial implantation of pelvic malignancies: Description of the technique. *Endocuriether Hypertherm Oncol* 1995;11:107–113.
73. Nag S, Martínez-Monge, R., Ellis, R., *et al.* The use of fluoroscopy to guide needle placement in interstitial gynecological brachytherapy. *Int J Radiat Oncol Biol Phys* 1998;40: 415–420.
74. Demanes DJ, Rodriguez RR, Hsu I-CJ, *et al.* HDR remote afterloading gynaecological template interstitial brachytherapy: Rationale, indications and technique. Activity. *Intl Nucletron Radiother J* 1996;8:14–21.
75. Erickson B, Albano K, Gillin M. CT-guided interstitial implantation of gynecologic malignancies. *Int J Radiat Oncol Biol Phys* 1996;36:699–709.
76. Erickson B, Albano K, Withnell J, *et al.* Modification of the Syed-Neblett template system to enable loading of the vaginal obturator. *Endocuriether Hypertherm Oncol* 1996;12:7–16.
77. Erickson BA, Erickson SJ, Prost RW, *et al.* Magnetic resonance imaging following interstitial implantation of pelvic malignancies. *Radiat Oncol Invest* 1995;2:295–300.
78. Demanes JD, Rodrequez RR, Bendre DD, *et al.* High dose rate transperineal intestitial brachytherapy for cervical cancer: High pelvic control and low conplication rates. *Int J Radiat Oncol Biol Phys* 1999;45:105–115.
79. Russel AH, Walter JP, Anderson MW, *et al.* Sagittal magnetic resonance imaging in the design of lateral radiation treatment portals for patients with locally advanced squamous cancer of the cervix. *Int J Radiat Oncol Biol Phys* 1992;23:449–455.
80. Kapp KS, Stuecklschweiger GF, Kapp DS, *et al.* Dosimetry of intracavitary placements for uterine and cervical carcinoma: Results of orthogonal film, TLD, and CT assisted techniques. *Radiother Oncol* 1992;24:137–146.
81. Stuecklschweiger GF, Arian-Schad KS, Poier E, *et al.* Bladder and rectal dose of gynecologic high-dose rate implants: Comparison of orthogonal radiographic measurements with in vivo and CT-assisted measurements. *Radiology* 1991;181:889–894.
82. Schoeppel SL, Ellis JH, LaVigne ML, *et al.* Magnetic resonance imaging during intracavitary gynecologic brachytherapy. *Int J Radiat Oncol Biol Phys* 1992;23:169–174.

APPENDIX

The linear–quadratic model

The linear–quadratic (L–Q) model is widely used for the determination of isobiologically effective treatment schedules when conventional regimes are modified. Biologically effective doses (BEDs) calculated using the L–Q model are equated for both tumor and late-reacting normal tissues for the conventional and modified treatments. For details of the L–Q model and its application readers are referred to Orton (63) or Nag and Gupta (64). The following examples demonstrate the application of this model to the design of high-dose-rate (HDR) fractionation schedules.

Change from low-dose-rate (LDR) to HDR.

Problem: What dose/fraction of HDR delivered in six fractions will be equivalent in terms of tumor control to 60 Gy delivered to Point A at 0.55 Gy h^{-1}?

Solution: Assume α/β (tumor) = 10 Gy, μ (tumor) = 0.46 h^{-1}.

Then: BED (LDR) = $60[1 + (2 \times 0.55)/(0.46 \times 10)] = 74.3$

Equating this to the BED for 6 HDR fractions with dose/fraction d gives:

$$74.3 = 6d(1 + d/10)$$

Solving this quadratic equation for d gives: $d = 7.20$ Gy.

Conclusion: 6 fractions of 7.20 Gy with HDR is equivalent in terms of tumor control to 60 Gy delivered at 0.55 Gy h^{-1}.

Effect of change to HDR on late effects.

Problem: If it is assumed that the effective dose to rectal/bladder tissues in the above example is 75% of the Point A dose for the LDR treatments (i.e., the geometric sparing factor, f, is 0.75), what geometric sparing factor is required for the HDR treatments in order for the two regimes to be equivalent in terms of late reactions?

Solution: Assume α/β (late) = 3 Gy, μ (late) = 0.46 h^{-1}.

Then: BED (LDR) = $60 \times 0.75[1 + (2 \times 0.55 \times 0.75)/(0.46 \times 3)] = 71.9$.

Equating this to the BED for HDR with sparing factor f gives:

$$71.9 = 6 \times 7.20f(1 + 7.20f/3).$$

Solving this quadratic equation for f gives: $f = 0.65$.

Conclusion: To keep the risk of late normal tissue damage constant in the above conversion from LDR to HDR, it is necessary to reduce the effective dose to rectal/bladder tissues to about 65% of the Point A dose.