

## American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part III: Low-dose-rate and pulsed-dose-rate brachytherapy

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### ABSTRACT

**PURPOSE:** To develop a guideline for quality practice of low-dose-rate (LDR) and pulsed-dose-rate (PDR) brachytherapy for locally advanced cervical cancer.

**METHODS:** Members of the American Brachytherapy Society (ABS) with expertise in cervical cancer brachytherapy formulated updated guidelines for LDR and PDR brachytherapy for locally advanced (International Federation of Gynecology and Obstetrics [FIGO] Stages IB2–IVA) cervical cancer based on literature review and clinical experience.

**RESULTS:** The ABS strongly recommends the use of brachytherapy as a component of the definitive treatment of locally advanced cervical carcinoma. Precise applicator placement is necessary to maximize the probability of achieving local control without major side effects. The ABS recommends a cumulative delivered dose of approximately 80–90 Gy for definitive treatment. Dosimetry must be performed after each insertion before treatment delivery. The dose delivered to point A should be reported for all intracavitary brachytherapy applications regardless of treatment planning technique. The ABS also recommends adoption of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology guidelines for contouring, image-based treatment planning and dose reporting. Interstitial brachytherapy may be considered for a small proportion of patients whose disease cannot be adequately encompassed by intracavitary application and should be performed by practitioners with special expertise in these procedures. Quality management measures must be performed, and follow-up information should also be obtained.

**CONCLUSIONS:** Updated ABS guidelines are provided for LDR and PDR brachytherapy for locally advanced cervical cancer. Practitioners and cooperative groups are encouraged to use these guidelines to formulate their clinical practices and to adopt dose-reporting policies that are critical for outcome analysis. © 2012 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

### Keywords:

Cervical cancer; Brachytherapy; Low-dose-rate; Pulsed-dose-rate; Guidelines

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In formulating guidelines, it should be noted that variations in approaches to cervical cancer brachytherapy, as with most medical procedures, are commonplace and may readily fall within accepted and appropriate management of such patients. The guidelines presented here are a means to aid practitioners in managing patients, but are not to be viewed as rigid practice requirements by which to establish a legal standard of care.

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### Introduction

Brachytherapy is an integral component of the definitive treatment of cervical cancer. By taking advantage of the inverse square law, brachytherapy has the ability to selectively deliver high doses to tumor while minimizing delivered dose to critical pelvic organs. Low-dose-rate (LDR) brachytherapy has been a mainstay in the treatment of cervical cancer for more than a century. Inferior survival and increased complication rates have been reported in

patients who receive higher doses of external-beam radiotherapy (EBRT) and concomitantly lower intracavitary doses (1–6). Validated by long-standing clinical experience, the source loading patterns, treatment time, and total delivered dose for LDR brachytherapy have been well described to maximize tumor control and minimize the risk of complication.

With the advent of remote afterloaders and availability of new radionuclides, pulsed-dose-rate (PDR) brachytherapy was introduced to replicate the radiobiologic advantages of LDR while allowing for dose optimization with a stepping source and variable dwell times (7–9). PDR brachytherapy delivers a radiation dose every hour that approximates the average LDR dose rate of 0.4–0.6 Gy/h using an  $^{192}\text{Ir}$  source with source strength  $\leq 4.2$  kU (1 Ci). Possible physical advantages of dose optimization with PDR brachytherapy include both improved target coverage and normal tissue sparing (10–13). From a radiobiologic standpoint, the low radiation dose rates of LDR and PDR brachytherapy allow for enhanced sublethal damage repair and reduced normal tissue toxicity (7). The major practical advantages of PDR include reduced exposure of personnel, facilitated nursing, and visitation for patients between pulses. The major disadvantage of PDR brachytherapy compared with high-dose-rate (HDR) brachytherapy is the movement of the applicator during treatment.

Previous guidelines of the American Brachytherapy Society (ABS) provided a framework that has since been modified in the context of image-based treatment planning recommendations from North American and European working groups (14–17). Because of changes in clinical practice and the availability of imaging devices, the ABS has developed updated guidelines for quality practice of LDR and PDR brachytherapy for locally advanced cervical cancer. This report reflects these changes in technology, including 3D-based treatment planning and for PDR, remote afterloading systems. To assess the normal tissue doses per fraction accurately, computed tomography (CT) or magnetic resonance (MR) imaging with the brachytherapy apparatus in place is recommended. The formulation of a quality management program pertinent to LDR and PDR brachytherapy is also addressed.

## Methods

The ABS guidelines for LDR and PDR cervical cancer brachytherapy were revised by members of the ABS with expertise in gynecologic brachytherapy. The literature was reviewed to identify relevant peer-reviewed articles, organizational guidelines, and regulatory reports. The guidelines also address image-guided treatment planning and delivery and recommended reporting parameters for quality assurance. Specific commercial equipment, instruments, and materials are referenced in this report to fully describe the necessary procedures. Such identification does

not imply recommendation or endorsement by the presenter nor imply that the identified material or equipment is necessarily the best available for these purposes. The specific recommendations were established by consensus opinion of the authors, with the support of the published literature when available. Where major controversy or lack of evidence persists, the ABS declines to make specific recommendations. This report was reviewed and approved by the Board of Directors of the ABS.

## Results

### *LDR and PDR cervical brachytherapy applicators*

LDR brachytherapy applicators are manual afterloading devices using  $^{137}\text{Cs}$ . PDR brachytherapy requires a remote afterloader using  $^{192}\text{Ir}$ , similar to that used in HDR brachytherapy. However, PDR uses a source strength of approximately 4 kU (1 Ci) instead of 42 kU (10 Ci) as in HDR.

The most commonly used applicator system for LDR brachytherapy is the tandem and shielded Fletcher-Suit-Delclos colpostats (18, 19). The Fletcher mini-colpostats, Henschke-type applicator, or tandem and ring applicator for PDR applications may be used in a narrow vagina that cannot accommodate regular Fletcher colpostats. The dosimetry and dose delivery of most of these systems are very similar (20). However, mini-colpostats may increase the risk of major complications because of increased bladder and rectal doses (21). Shielded colpostats may help reduce the bladder and rectal doses if the colpostats are positioned correctly with adequate vaginal packing. Modified Fletcher and Henschke applicators are now available in CT- and MR-compatible versions (22–25). The radiation oncologist should be familiar with the applicators used as described in detail in “The American Brachytherapy Society treatment recommendations for locally advanced carcinoma of the cervix. Part I. General principles” and select the appropriate applicator based on optimal coverage of the tumor.

### *Timing of brachytherapy application*

The ABS recommends the use of two LDR or PDR applications to allow for reduction in tumor volume and improved tumor coverage with the second application. The first intracavitary application should be performed within 4–6 weeks of the initiation of EBRT. The second application should be performed 1–2 weeks later to complete all therapy within 8 weeks. Select cases with excellent applicator geometry and a small tumor volume may allow for a single brachytherapy application.

### *Treatment planning and optimization*

Optimization cannot be used to compensate for substandard applicator positioning. Optimal tandem and colpostat

selection and application are essential for an appropriate dose distribution.

#### *LDR intracavitary brachytherapy*

With LDR intracavitary therapy using 18–22 mm  $^{137}\text{Cs}$  tube sources, a tandem of 5–7.5 cm length is usually loaded with approximately 36–43 U (5–6 mg radium equivalent) of cesium per cm of tandem length. The tip of the tandem is often loaded with slightly higher activity than the distal tandem to provide adequate coverage of tumor in the lower uterine segment. Although most facilities maintain an inventory of only 3 or 4 different activity tube sources, refinements in dose distribution can be achieved by using differential source strengths, spacers, or selective changes of the source strengths during the implant, recognizing the biologic effects of time-varying source strengths. A typical tandem loading in a patient without bulky residual disease is, cephalad to caudad, 108–72–72 U (15–10–10 mgRaeq). The loading of vaginal colpostats is determined by the diameter of the colpostats and the dose to tumor and critical structures. Small (2-cm) colpostats are usually loaded with 70–108 U (10–15 mgRaeq); mini-ovoids, which lack internal shielding, are not usually loaded with more than 36–54 U (5–7.5 mgRaeq). Vaginal cylinders are loaded with an activity calculated to deliver a prescribed dose to the vagina at different proximal-to-distal levels.

#### *PDR intracavitary brachytherapy*

PDR brachytherapy allows an even greater ability to optimize the dose distribution through the use of an afterloader that steps the source in increments of 0.25 cm and permits dwell times in 0.1-s increments to shape isodose volumes. The ABS recommends a standard loading pattern prescribed to point A as a valid starting point for computer-aided optimization available for PDR brachytherapy application. CT- or MR-based treatment planning enables optimization for improved target coverage and sparing of normal tissue structures by adjusting the dwell times within the tandem and vaginal applicators. The isodose curves should be reviewed to appreciate any changes in the spatial dose distribution because of modification of the standard loading pattern. Further discussion of dose optimization using a stepping source may be found in “The American Brachytherapy Society treatment recommendations for locally advanced carcinoma of the cervix. Part II: High-dose-rate brachytherapy.”

#### *Interstitial brachytherapy*

To achieve an optimal dose distribution, an intrauterine tandem should be placed for all interstitial cervical cancer applications to escalate the dose to the central region of the tumor, parametrial tissues, and nodal regions (26). For LDR, differential loading of sources with the higher activity at each end is recommended (27). With 1-cm needle spacing, the activity of  $^{192}\text{Ir}$  in the inner needles should be approximately

one-half to one-third the strength of the peripheral sources to avoid unnecessary high-dose regions within the implant. Image-based treatment planning should be performed to evaluate dosimetry, target coverage, and dose to critical structures. For PDR, dwell times and positions may be manually optimized to achieve target coverage while sparing the organs at risk. Interstitial implants may deliver considerable dose to the vagina, urethra, and adjacent soft tissues and bone, which should be evaluated by the practitioner by reviewing the dose distribution. Additional treatment planning considerations may be found in “The American Brachytherapy Society treatment recommendations for locally advanced carcinoma of the cervix. Part I: General principles” and “The American Brachytherapy Society recommendations for interstitial brachytherapy for vaginal cancer.”

#### *Dose recommendations for definitive radiation therapy*

The ABS recommends a target therapeutic dose of 80–90 Gy for locally advanced cervical cancer. After EBRT to the pelvis with a dose of 45 Gy, an additional 35–45 Gy should be prescribed with intracavitary or interstitial brachytherapy with a dose rate of 0.4–0.6 Gy/h. Prescriptions should include the dose rate in Gy/h to point A or to the 100% isodose line on the graphic plan with the  $D_{90}$  (minimum delivered dose to 90% of the target volume) and  $V_{100}$  (volume that receives 100% of the prescribed dose) of the high-risk clinical target volume greater than 90% of the prescribed dose rate (17, 28). The recommended normal tissue constraints for  $D_{2\text{cc}}$  (minimum delivered dose to a 2cc volume) for the sigmoid and rectum are less than 70–75 Gy and for bladder less than 90 Gy.

The 0.4–0.6 Gy/h dose rate applies to LDR intracavitary brachytherapy with conventional  $^{137}\text{Cs}$  sources and to the average dose rate with  $^{192}\text{Ir}$  PDR intracavitary brachytherapy. With PDR brachytherapy, the linear quadratic model predicts essentially identical relative effects on normal tissue and tumor for any  $\alpha/\beta$  ratio and for a repair half time  $>0.75$  h (29, 30). Mathematical models suggest that wider pulse intervals and larger doses per pulse may be equivalent or could even result in a more favorable relative effectiveness if the normal tissue half time for repair is significantly greater than the tumor tissue repair half time or if critical structures are receiving a much lower dose per pulse than the tumor. Of course, with sufficiently large pulses and pulse intervals, the relative effectiveness of PDR begins to approximate fractionated HDR. Higher dose rates of 0.8–1.2 Gy/h at point A edge into the medium-dose-rate range and may be associated with a greater risk of late complications (31). Because of the complexity of the required biologic modeling needed to prevent patient injury, medium-dose-rate brachytherapy will not be considered in this document.

#### *Quality management*

The published guidelines for treatment planning, dosimetry, and quality management for intracavitary brachytherapy

are applicable for the treatment of cervical cancer (32–34). The purpose of quality assurance is to identify major errors in treatment planning and delivery by performing tests of consistency. Quality control measures include visual inspection of applicators to ensure good working condition before sterilization and at the time of insertion. Additional recommendations specific to LDR and PDR intracavitary brachytherapy are detailed below.

The treatment plan should be independently reviewed by the physician and a physicist or medical dosimetrist not involved with the generation of the treatment plan to verify the following:

- Consistent and correct dosimetry input, including patient's information, applicator type, source configuration, and source strength. The measured source strength should be independently verified from the calibration by a decay calculation to the date of the implant;
- The dose and dose specification should match the treatment prescription following the institution's protocol for treatment of patients with locally advanced cervical cancer;
- With three-dimensional dosimetry, the dose distribution should achieve coverage of the target volume and meet dose-volume histogram (DVH) constraints; and
- The computer reconstruction of the implant should match the image used for treatment planning.

Preprocedure checks should be performed to ensure that the correct sources are loaded into the patient at the beginning of treatment and unloaded and accounted for at the end of the application. For PDR brachytherapy, checks of the catheter numbers and attachments and dwell times for each dwell position are performed.

## Conclusion

The ABS has established guidelines for quality practice of LDR and PDR brachytherapy for locally advanced cervical cancer that incorporates the use of image-based treatment planning.

Practitioners and cooperative groups are encouraged to use these recommendations to formulate treatment and dose-reporting policies.

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